工業技術研究院
Industrial Technology Research Institute

How to Market Your In Vitro Diagnostic Medical Device in Taiwan

Albert T.W. Li
Center for Measurement Standards
Industrial Technology Research Institute

Copenhagen Denmark
May 30 2007

工業技術研究院
Industrial Technology Research Institute

Outlines

1. Medical device distributor/ manufacturer license
2. IVD classification
3. Medical device Good Manufacturing Practice
4. Premarket submission

工業技術研究院
Industrial Technology Research Institute

Medical Device Distributor/Manufacture License

- Medical device distributor shall apply license before importing or distributing medical device
- Domestic medical device manufacturer shall have manufacturer license and pharmaceutical manufacturer license before applying for GMP inspection
- Health and industrial departments of prefectural government inspect Domestic medical device manufacturer in accordance with Chapter 2 of Pharmaceuticals Factory Establishment Standard

Make sure that your local distributor are knowledgeable about regulations

工業技術研究院
Industrial Technology Research Institute

Outlines

1. Medical device distributor/ manufacturer license
2. IVD classification
3. Medical device Good Manufacturing Practice
4. Premarket submission

工業技術研究院
Industrial Technology Research Institute

Medical Device Classification

	Type	Number of Items		
		Class I	Class II	Class III
IVD	CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES	137	86	1
IVD	HEMATOLOGY AND PATHOLOGY DEVICES	41	61	4
IVD	IMMUNOLOGY AND MICROBIOLOGY DEVICES	113	52	4
	ANESTHESIOLOGY DEVICES	51	76	4
	CARDIOVASCULAR DEVICES	12	109	22
	DENTAL DEVICES	63	50	12
	EAR, NOSE, AND THROAT DEVICES	25	27	2
	GASTROENTROLOGY-UROLOGY DEVICES	27	40	7

- *Source: Medical Device Regulation*

工業技術研究院
Industrial Technology Research Institute

Medical Device Classification

Type	Number of Items		
	Class I	Class II	Class III
GENERAL AND PLASTIC SURGERY DEVICES	36	37	6
GENERAL HOSPITAL AND PERSONAL USE DEVICES	49	36	1
NEUROLOGICAL DEVICES	23	66	11
OBSTETRICAL AND GYNECOLOGICAL DEVICES	15	62	16
OPHTHALMIC DEVICES	60	38	7
ORTHOPEDIC DEVICES	19	50	21
PHYSICAL MEDICINE DEVICES	37	29	7
RADIOLOGY DEVICES	25	42	2

- *Source: Medical Device Regulation*

工業技術研究院
Industrial Technology Research Institute

Medical Device Classification Search Database

http://medical.cms.itri.org.tw/classification/

工業技術研究院
Industrial Technology Research Institute

IVD GMP/Pre-market Registration

Class	I	II	III
Number of Items	291	199	7
GMP	Not Required (except for sterile)	All Required	All Required
Premarket Registration	•All Required	•All Required	All Required + Clinical data

- *Source: Medical Device Regulation*

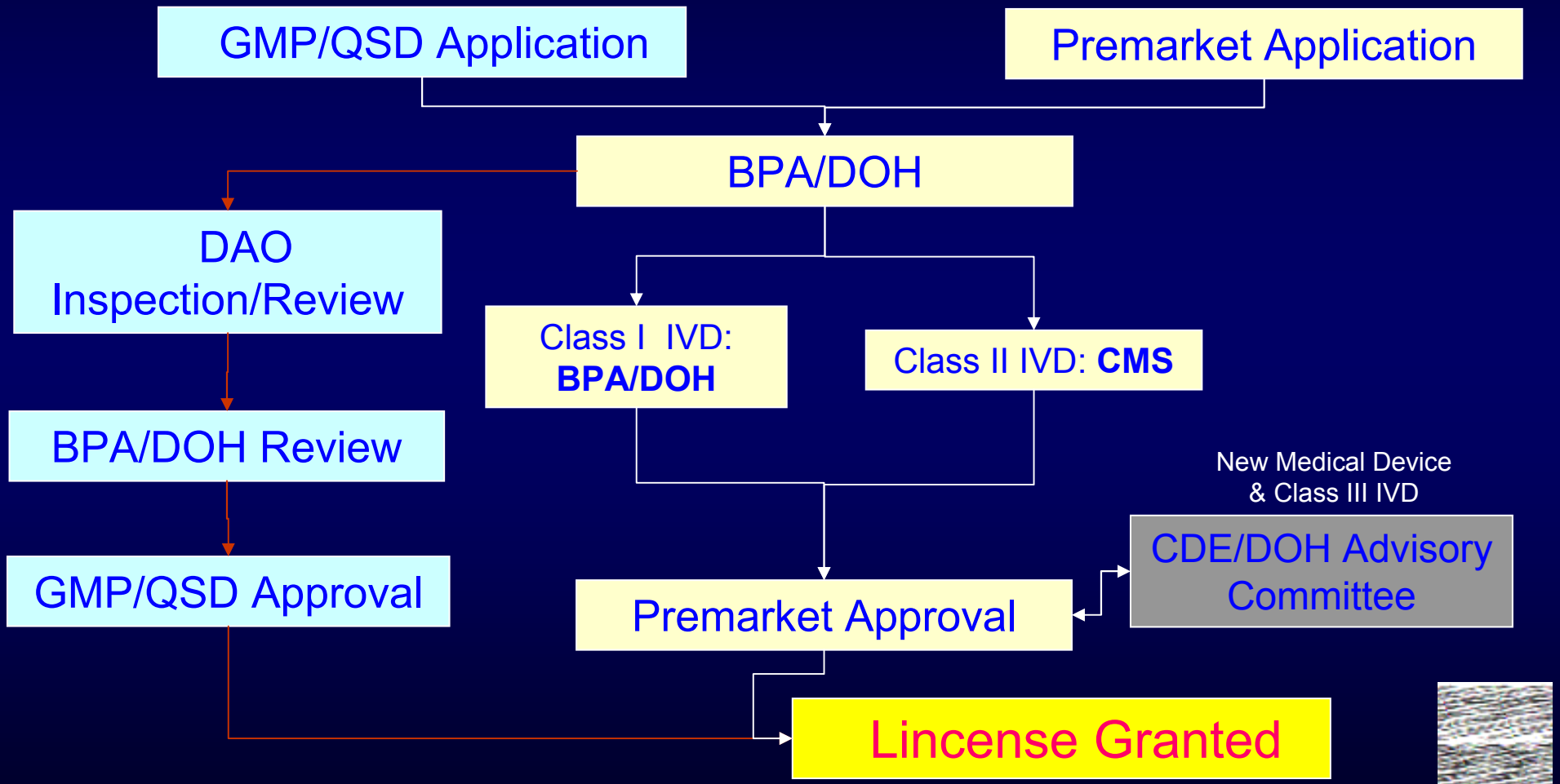
工業技術研究院
Industrial Technology Research Institute

Outlines

1. Medical device distributor/ manufacturer license
2. IVD classification
3. Medical device Good Manufacturing Practice
4. Premarket submission

工業技術研究院
Industrial Technology Research Institute

IVD GMP/Pre-market Registration Process



工業技術研究院
Industrial Technology Research Institute

Pharmaceuticals Factory Establishment Standard

- Part 1 General principles
  - Article 1~3
- Part 2 Basic requirements for pharmaceutical factories
  - Article 4~33
- Part 3 Pharmaceutical GMP
  - 13 chapters, Article 34~96
- Part 4 Medical device GMP
  - 21 chapters, Article 97~156
- Part 5 Supplementary provisions

工業技術研究院
Industrial Technology Research Institute

Part 4 Medical Device GMP

- Chapter 1 General provisions
  - Article 97~99
- Chapter 2 Management responsibility
  - Article 100~104
- Chapter 3 Quality system
  - Article 105~107
- Chapter 4 Contract review
  - Article 108~109
- Chapter 5 Design control
  - Article 110~117

Harmonized with ISO 13485:1996

工業技術研究院
Industrial Technology Research Institute

Part 4 Medical Device GMP

- Chapter 6 Document and data control
  - Article 118~119
- Chapter 7 Purchasing
  - Article 120~121
- Chapter 8 Control of customer-supplied product
  - Article 122
- Chapter 9 Product identification and traceability
  - Article 123~124
- Chapter 10 Process control
  - Article 125~132

Harmonized with ISO 13485:1996

工業技術研究院
Industrial Technology Research Institute

Part 4 Medical Device GMP

- Chapter 11 Inspection and testing
  - Article 118~119
- Chapter 12 Control of inspection, measurement and test equipment
  - Article 120~121
- Chapter 13 Inspection and test status
  - Article 122
- Chapter 14 Control of non-conforming product
  - Article 123~124
- Chapter 15 Corrective and preventive action
  - Article 125~132

Harmonized with ISO 13485:1996

工業技術研究院
Industrial Technology Research Institute

Part 4 Medical Device GMP

- Chapter 16 Handling, Storage, Packaging, preservation and delivery
  - Article 148~149
- Chapter 17 Control of quality records
  - Article 150~151
- Chapter 18 Internal quality audits
  - Article 152~153
- Chapter 19 Training
  - Article 154
- Chapter 20 Servicing
  - Article 155
- Chapter 21 Statistical techniques
  - Article 156

Harmonized with ISO 13485:1996

工業技術研究院
Industrial Technology Research Institute

Medical Device Manufacturer Inspection

- Inspection Types
  1. Initial inspection: establishment, move, expansion, re-opening or new product scope of the factory
  2. Follow-up inspection: every three years
  3. Special inspection: ex. accusation, adverse event
  4. Other

---Pharmaceuticals Manufacturer Inspection Regulation Article 3

工業技術研究院
Industrial Technology Research Institute

Follow-Up Inspection

- Routine inspection shall be conducted once every three years
- The manufacturer/distributor shall apply three months before GMP expiry
- Unannounced inspection may be initiated by Department of Health

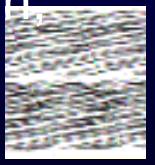
For foreign manufacturer, inspection is carried out through document review. See the following pages.

---Pharmaceuticals Manufacturer Inspection Regulation Article 8

工業技術研究院
Industrial Technology Research Institute

DOH Designated Auditing Organizations

- Comply with law/regulation applicable to government agencies
- Monitored and accredited by DOH Medical Device GMP Committee
- Routine Inspection by DOH and DOH Medical Device GMP Committee
- Shall establish a quality system according to applicable requirements of ISO Guide 62
  - Staff with medical device and quality system auditing expertise
  - Not-for-profit organizations established by the government
  - Prevention of conflict of interest
  - Confidentiality
- Designation are only granted to Center for Measurement Standards/Industrial Technology Research Institute, Metal Industry Research and Development Center, Electronic Testing Center Taiwan and Plastic Industry Development Center



工業技術研究院
Industrial Technology Research Institute

Medical Device GMP Compliance Letter

- DOH issues Medical Device GMP compliance letter to the manufacturer/distributor (for foreign manufacturer)
- Medical Device GMP compliance letter is valid for 3 years
- Medical Device GMP compliance letter may be withdrawn by Department of Health if the manufacturer fails to comply with GMP regulations

Product scope of GMP registration is based on classification/product names

---Pharmaceuticals Manufacturer Inspection Regulation Article 10

工業技術研究院
Industrial Technology Research Institute

Inspection Enforcement

- Investigator shall identify himself/herself upon inspection
- Investigator may copy, photograph, record or sample to collect objective evidence
- Refuse or fail to be inspected will lead to GMP non-compliance

---Pharmaceuticals Manufacturer Inspection Regulation Article 14

工業技術研究院
Industrial Technology Research Institute

Non-compliance

- Non-compliance shall be corrected and reported to the health authority or auditing organization
- Fail to correct non-compliance in a timely manner may lead to penalty in accordance with the regulations

---Pharmaceuticals Manufacturer Inspection Regulation Article 15

工業技術研究院
Industrial Technology Research Institute

Subcontractor

- A medical device manufacturer with product license may apply to DOH for subcontracting the following activities to another manufacturer :
  - Full process
  - Part of continuous process
  - Or any part of critical process
- Subcontracting shall be approved by DOH in advance
- Subcontractor shall comply with Medical Device GMP

工業技術研究院
Industrial Technology Research Institute

Process Validation

- Process validation guidance
- cleaning process validation guidance
- sterilization validation guidance
- water system validation guidance
- air-conditioning guidance
- analytical method validation guidance
- computer system validation guidance

工業技術研究院
Industrial Technology Research Institute

Class III IVD GMP Inspection

- Inspection team comprises of auditors from Designated Auditing Organizations and Bureau of Food and Drug Analysis
- More emphasis on process validation, testing validation and environmental monitoring

工業技術研究院
Industrial Technology Research Institute

IVD Reagent GMP Guidance

Part 1 General
Part 2 Quality system requirement

- Quality system
- Reagent specification
- Process validation
- Process control
- Production environment control
- Clothing of personnel
- Cleanliness and hygiene
- Component
- Finished product inspection and testing
- Stability test and expiration date
- Investigation of complaint and product failure
- Quality trend analysis

工業技術研究院
Industrial Technology Research Institute

IVD Reagent GMP Guidance

Part 3 Class III IVD Reagent

- Water supply system
- Heating, ventilation and air conditioner
- Infection and cross-contamination
- Computer system

工業技術研究院
Industrial Technology Research Institute

Medical Device GMP for Foreign Manufacturer

- Application shall be made by domestic distributor
- Foreign manufacturer shall offer through its domestic distributor:
  - ISO 13485 equivalent certificate
  - factory layout
  - production process diagram
  - Master list of quality document
  - quality system documentation (QSD) including quality manual and general procedures
- DOH may perform overseas inspections when necessary or requested by domestic distributor/manufacturer

工業技術研究院
Industrial Technology Research Institute

Overseas Inspection

- Application shall be made by domestic distributor/manufacturer
- Foreign manufacturer shall authorize its domestic distributor/manufacturer to apply for overseas inspection and agree to be inspected by DOH DAO
  - Overseas inspection fee
  - Quality manual
  - Agreement for inspection
  - Legality for business operation and production
- Audit language: English
- Fee: € 12,500

工業技術研究院
Industrial Technology Research Institute

GMP Inspection Guidelines

- GHTF SG4(99) 28 Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 1: General Requirements
- GHTF SG4 (00) 3
  Training Requirements for Auditors (Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 1: General Requirements - Supplement 2)
- GHTF SG4 N(99) 24R3
  Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers: General Requirements - Supplement No. 4 - Compilation of Audit Documentation (Clause 5.7)

工業技術研究院
Industrial Technology Research Institute

GMP Inspection Strategy

- Initial inspection
  - Top-down approach
  - Product scope is based on classification names defined in Medical Device Regulation
- Follow-up inspection
  - Top-down approach
  - Review production records by sampling
- Increase product scope
  - Review quality system and pilot production records of new device
  - Sample quality system

工業技術研究院
Industrial Technology Research Institute

GMP Inspection Guidelines

- GHTF SG4/N30R20: 2006 Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers - Part 2: Regulatory Auditing Strategy will apply
- SG4(PD)N33R13:2006 Guidelines for Regulatory Auditing of Quality
  Management Systems of Medical Device Manufacturers – Part 3: Regulatory Audit Reports will apply when it is final document

工業技術研究院
Industrial Technology Research Institute

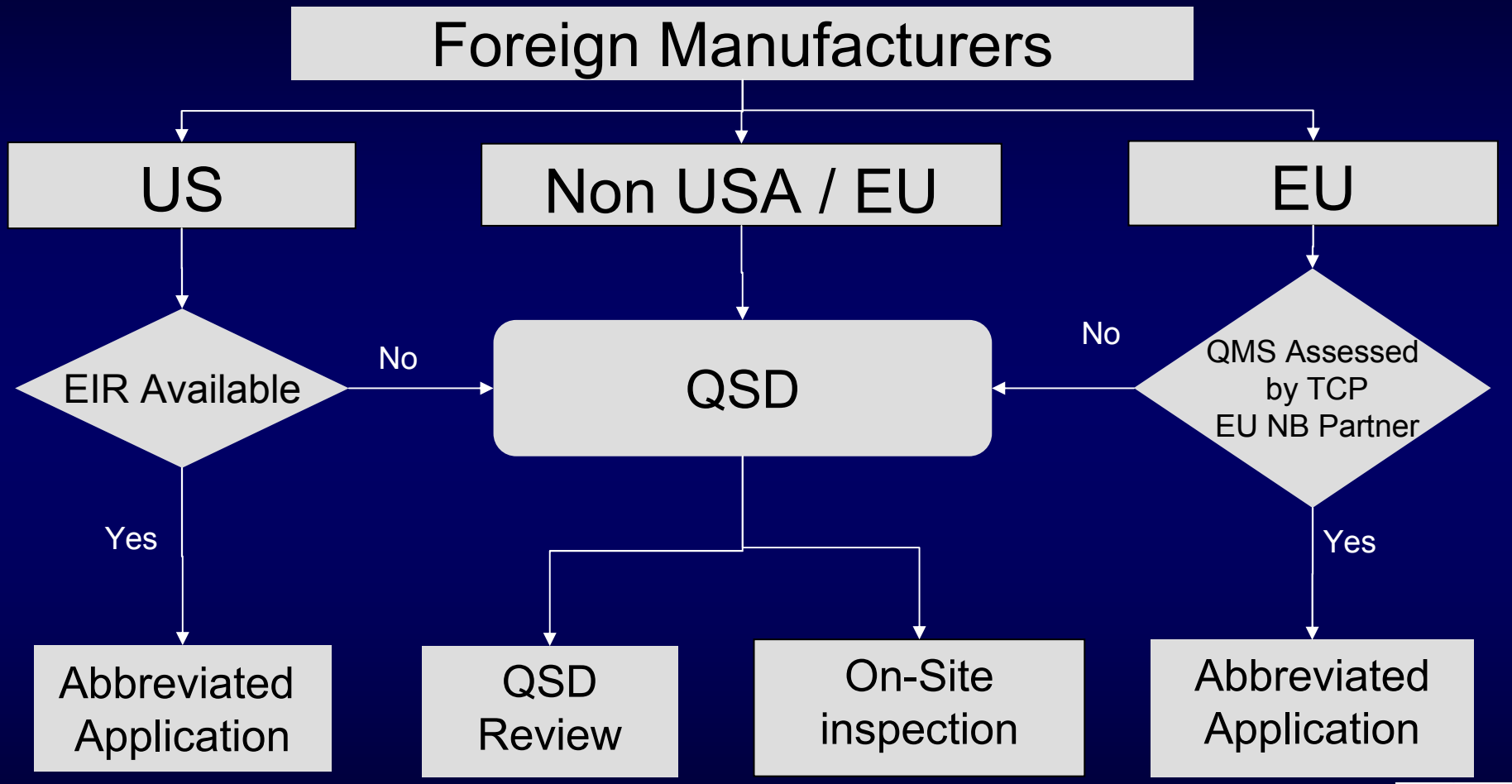
GMP Registration for Foreign Manufacturer

- Quality System Documentation (QSD) Review
- Abbreviated application for U.S. manufacturers
- Abbreviated application for EU manufacturers

Applications shall be made by pharmaceutical distributor and license is granted to the distributor

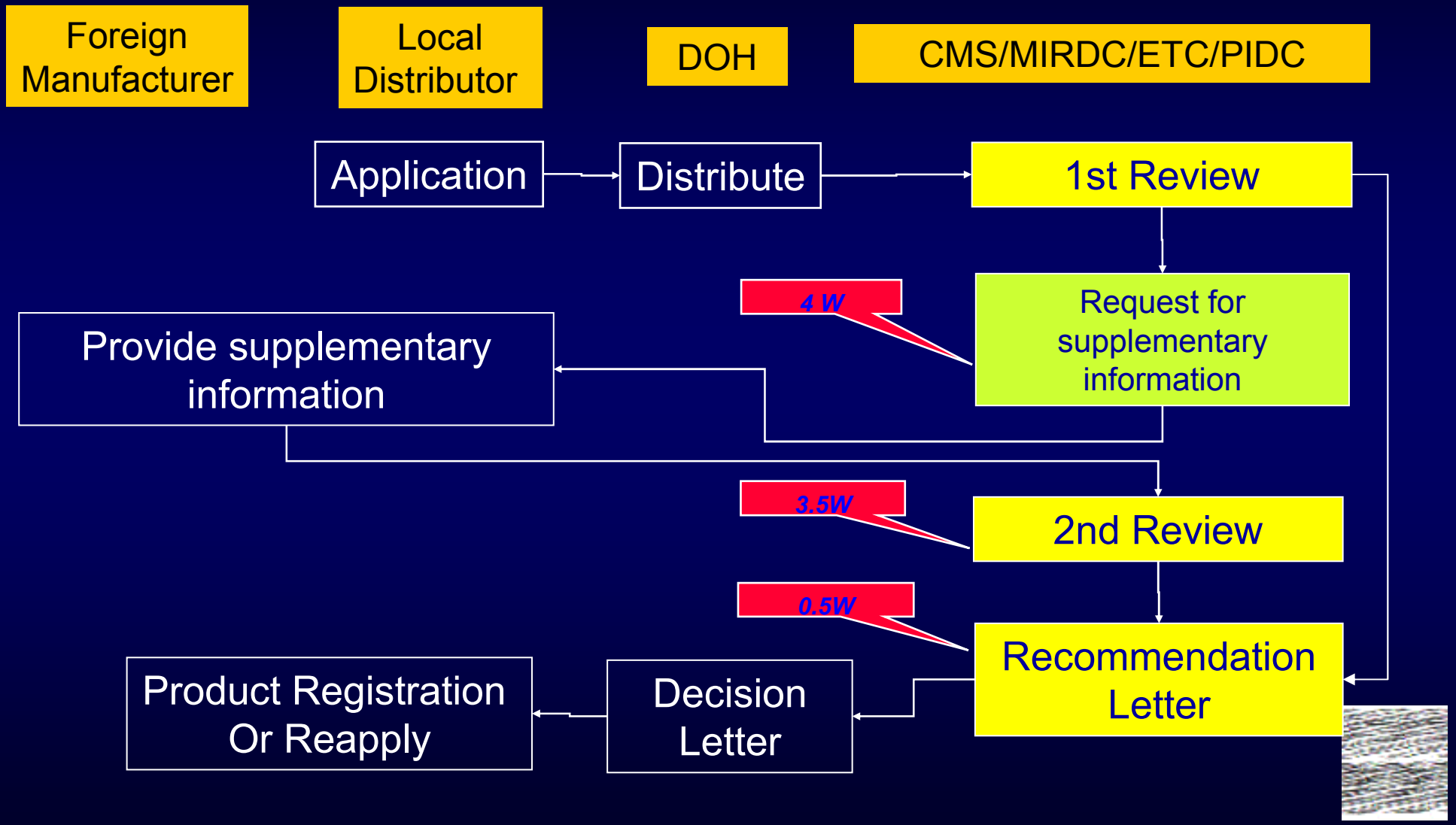
工業技術研究院
Industrial Technology Research Institute

Registration Process



工業技術研究院
Industrial Technology Research Institute

QSD Review Process



工業技術研究院
Industrial Technology Research Institute

QSD Application

- Application form
- Quality manual
- General procedures referring GMP requirements
- List of quality system documents
- Factory and production area layout
- Production flow chart for the product (s)
- List of major equipment
- Copy of ISO 13485 certificate or FDA CFG (which indicating the firm complies with GMP)

工業技術研究院
Industrial Technology Research Institute

TIPS

- Pharmaceutical manufacturer is the organization which produces the finished product
  - Manufacturer's information shall be indicated on the product labeling
  - Please do not mix up with the "Legal Manufacturer" as defined in EU
- ISO 13485 certificate or CFG is necessary even if the product is not regulated as medical device in some jurisdictions
- Document shall be provided in English or Traditional Chinese
  - Simplified Chinese is not applicable
- Provide general procedures of QMS, purge proprietary information when necessary
- Avoid any inconsistency in factory name, address, and product scope information in the submission
- Check if the manufacturer name and address are indicated on the ISO 13485 Certificate or Certificate to Foreign Government

工業技術研究院
Industrial Technology Research Institute

US Manufacturer Abbreviated Application

- Application form
- FDA Certificate to Foreign Government (valid for 2 years from issued date to the date when DOH receives application)
- Establishment Inspection Report (the latest one), FDA response to the firm's CAPA plan to 483 observations (if applicable)
- ISO 13485 certificate

* The factories located in Porto Rico & Guam are eligible for abbreviated application.

工業技術研究院
Industrial Technology Research Institute

TIPS

- Check the product scope carefully!!
  - Scope shall be referred to certificate, provide explanation if necessary
  - product classification name or
  - Brand name
  - Be aware that QSD and product registration are reviewed by different organizations
- Check the information (e.g. name, address) of the manufacturer!!
  - Provide clarification when necessary
- If there is FDA 483 observation indicated in the EIR, FDA's affirmative response to the CAPA plan is necessary
- EIR could be provided by the US manufacturer or FDA through TECRO-AIT process

工業技術研究院
Industrial Technology Research Institute

EU Manufacturer Abbreviated Application

- Application form
- Free Sale Certificate issued by Competent Authority
- The most current audit report issued by TCP EU NB Partner (TUVPS, G-MED, NSAI, MDC, TUVR PS, BSI PS, KEMA, DGM, MEDCERT, AMTACT, SGS UK, UL UK)
- ISO 13485 certificate issued by the same TCP EU NB Partner

工業技術研究院
Industrial Technology Research Institute

Free Sale Certificate

- Issued by EU Competent Authority or its designated organization
- Manufacturer's information including name and address
- Product scope
- Certify the device compliance to AIMD/MDD/IVDD and national regulation (if applicable) and is eligible for sale in the country

工業技術研究院
Industrial Technology Research Institute

TIPS

- Free Sale Certificate shall indicate the product is eligible for manufacture and sale in the country, or
- When EU legal manufacturer locates in country A and finished device is produced by factory located in country B
  - certificate/letter of sale legally in A country + certificate/letter of produced legally in B country

工業技術研究院
Industrial Technology Research Institute

Outlines

1. Medical device distributor/ manufacturer license
2. IVD classification
3. Medical device Good Manufacturing Practice
4. Premarket submission

工業技術研究院
Industrial Technology Research Institute

Labeling and Commercials

- Advertisement of pharmaceuticals: PAA Chapter 7 Article 66~70
  - Advertisement and commercials shall be approved by DOH or prefectural government
- Labeling: PAA Chapter 8 Article 75
  - Chinese (and English for imported device)
  - Labeling, instruction for use and label shall be included in premarket submission
  - Requirements for labeling is specified in 31 December 2004 Medical Device License Review Regulation and IVD Premarket review guidance

PAA: Pharmaceutical Affairs Act

工業技術研究院
Industrial Technology Research Institute

Premarket Registration

- Class I IVDs are reviewed by BPA/DOH
- Class II IVDs are reviewed by CMS/ITRI
- Class III IVDs are reviewed by Center for Drug Evaluation and DOH Medical Device Committee
- License is valid for 5 years

工業技術研究院
Industrial Technology Research Institute

Class I Device Submission

1. Application form
2. Copy of pharmaceutical distributor/manufacturer license
3. Truth and accuracy statement (made by applicant)
4. Registration fee ($ 300)
5. Certificate for foreign government issued by national health authority of export country
6. Letter of Authorization to register issued by the foreign manufacturer

License of Class I device could be granted in a day.

工業技術研究院
Industrial Technology Research Institute

Class II/III IVD Premarket Submission

1. Application form
2. Insert, packaging, labeling and instruction for use (import device: original and Chinese translation)
3. Copy of pharmaceutical importer/manufacturer license
4. Truth and accuracy statement
5. Sample or photo
6. Registration fee (€ 500 or € 250)
7. Pre-clinical evaluation and QC records safety and effectiveness evaluation report Incoming and final inspection protocols and testing reports of three batches/lots

工業技術研究院
Industrial Technology Research Institute

Class II/III IVD Premarket Submission

8. Technical specification including construction, material, specification, intended use and drawing
9. For device with no similar product been registered in Taiwan scientific theory, research report safety evaluation and clinical trial report
10. Radiological safety information (when applicable)
11. Import devices: Certificate for foreign government issued by national

工業技術研究院
Industrial Technology Research Institute

Class II Abbreviated Submission

- US IVD Manufacturer: FDA CFG + EU Free Sale Certificate (EC Certificate)
- EU IVD Manufacturer: EU Free Sale Certificate + FDA CFG (510(k) Clearance Letter)
  - Pre-clinical evaluation, QC records, and stability study are exempt
- Additional information (e.g. product, manufacturer, product, 510(k), EU Free Sale Certificate) may be provided

工業技術研究院
Industrial Technology Research Institute

Safety and Effectiveness

- Class II device shall demonstrate its substantial equivalence to registered device
  - Physical, chemical, sterilization, electric safety, radiology, performance, stability, biological, etc.
- Class III device shall provide scientific and clinical trial evidence
- DOH recognized standards

工業技術研究院
Industrial Technology Research Institute

IVD Reagent Premarket Submission Guidance

- Chapter 1 Safety and Effectiveness Requirements
  - Technical information including product structure, composition, materials, performance, and the intended uses.
  - Method of manufacturing and packaging
  - Original quality control records from the manufacturer, including test specification, test methods and test report.
  - Method Validation
  - Stability

工業技術研究院
Industrial Technology Research Institute

IVD Reagent Premarket Submission Guidance

- Chapter 2 Special Requirements for Class III In Vitro Diagnostic Reagents
  - Specification and analytical method of material and in-process products
  - Manufacturing and purification process
  - Product specification and technical information
  - Process control or batch records
  - Stability study
  - Clinical evaluation

工業技術研究院
Industrial Technology Research Institute

TIPS

- BPA/DOH may revise Chinese labeling of the product reviewed
- Reviewer will determine the product safety and effectiveness by pre-clinical evaluation and QC records
  - Substantial Equivalence evaluation, or Essential Requirements assessment
  - QC records include receiving and finished inspection
  - Evaluation could be made according to DOH recognized standards and/or globally used standards

工業技術研究院
Industrial Technology Research Institute

DOH 75 Recognized Standards for IVD

衛生署科技計畫
醫療器材認可標準資料庫查詢系統

使用說明

查詢條件:未選擇標準組織/體外診斷醫療器材/未選擇產品代碼/未選擇標準編號/未選擇關鍵字
查詢結果: 共 75 筆　共 15 頁 目前位於第 1 頁 (一頁爲 5筆資料)

編號	類別	標準名稱	標準編號	標準制定組織
1	ABC.體外診斷醫療器材	In vitro diagnostic test systems -Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus	15197	ISO / BSI
2	ABC.體外診斷醫療器材	Definitions of Quantities and Conventions Related to Blood pH and Gas Analysis; Approved Standard (1994)	C12-A	NCCLS
3	ABC.體外診斷醫療器材	Performance Characteristics for Devices Measuring PO2 and PCO2 in Blood Samples; Approved Standard (1992)	C21-A	NCCLS
4	ABC.體外診斷醫療器材	Statistical Quality Control for Quantitative Measurements: Principles and Definitions: Approved Guideline - Second Edition (1999)	C24-A2	NCCLS
5	ABC.體外診斷醫療器材	Fractional Oxyhemoglobin, Oxygen Content and Saturation, and Related Quantities in Blood: Terminology, Measurement, and Reporting; Approved Guideline (1997)	C25-A	NCCLS

下一查詢畫面　最後查詢畫面
回資料庫首頁　上一網頁

工業技術研究院
Industrial Technology Research Institute

TIPS

- Class III device shall provide scientific and clinical trial evidence
  - Local clinical trial is necessary for HIV, HBV, HTLV, Blood Typing Reagents
- If you subcontract a manufacturer to package or label according to approved Chinese labeling, make sure that the subcontractor is a registered GMP manufacturer

工業技術研究院
Industrial Technology
Research Institute

Thank You and Good Luck!!