NARLabs
National Applied Research Laboratories

Biochip Translation

Taiwan Instrument Research Institute (TIRI)
National Applied Research Laboratories(NARLabs)

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Outline

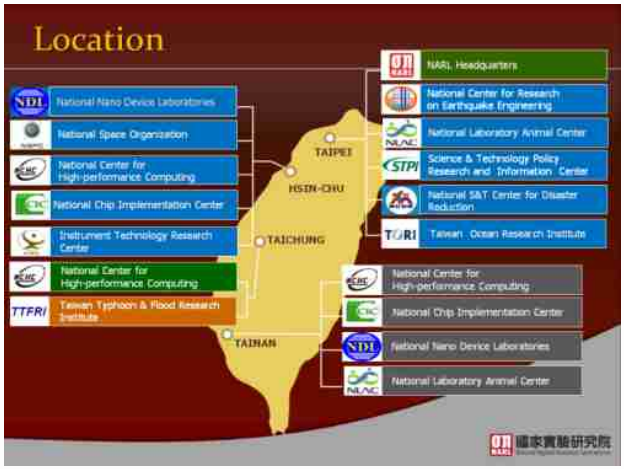
- **NARLabs Innovative Medical Devices Accelerator**
- **Biochip technology and medical device regulation**

NARLabs

National Applied Research Laboratories

Providing Scientific Solutions for Future Society

- *Core Technology & Facilities*
  NCHC/ NCREE/ NSPO/NLAC/
  TIRI/ TSRI/ STPI/ TORI
- *Earth sciences and environmental/ disaster mitigation technology*
- *Information, Electronics, and Communications*
- *Biomedical Technology*
- *Space Science & Technology*



Global Excellence, Local Impact

Hsinchu Biomedical Science Park (HBSP)

The Park covers an area of approximately 38.1 hectares, including the layout of medical complex area, incubation R&D area, industrial area and public service facilities.

(Aerial view)

HBSP Hospital

2020

Development Process of Medical Devices

R&D team Incubation

Project Manager

ISO13485/QSR

Prototyping Specification

Function/ in vitro/animal validation

Pilot run

Clinical Trial

GMP preparation

Market application

Product launch

Core Lab	V & V Lab	GMP Lab	Clinical Study	Start-ups	Product transfer
AM(3D print) MRI、CT Bio-chip IVD Bio-material	ASTM ISO10993 IEC60601-1	GMP Compliance		BP	TFDA, CFDA, CE, FDA

12 Research teams march into bio-medical sciencepark;

89 research teams served;

17 new start up companies founded;

Software Service platform （DHF/DHR/DMR/EP/STED）

- Patent
- Regulatory
- Bill Of Material (BOM)
- Design and Document Control System

NARLabs

Biochip and IVD Products Development Platform

Service/Application：

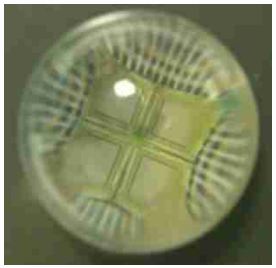
- Biomolecular analysis: biomolecule isolation, biomolecules interaction, cell counting,qPCR, digital imaging
- IVD: Immunochromatography, FET sensors, Surface plasmon resonance
- Biochip processing: vapor deposition, 3D imaging and metrology, dry film embossing, die bonding

Dry film embossing


Vapor Deposition


Die bonding

Implant & IVD products


Retinal prosthesis


Surface plasmon resonance


Automated extraction & purification


Capillary electrophoresis


Disposable biochip


FET sensors


Immunochromatography


Flow cytometer

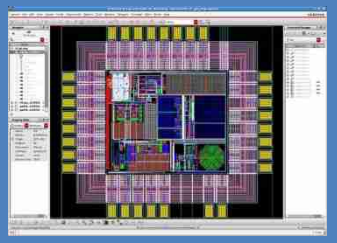

Biomolecules interaction analyzer

Biochip and IVD Products Development Platform

Biochip supply chain

Linking the wafer manufacturing industry and unmet medical needs

ICdeign



Supporting infrastructur

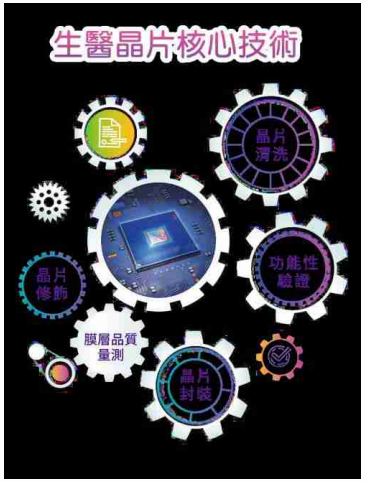
Wafer fab

World class foundry

Biocompatible packaging

診斷檢測晶片　植入式晶片

Need backend process



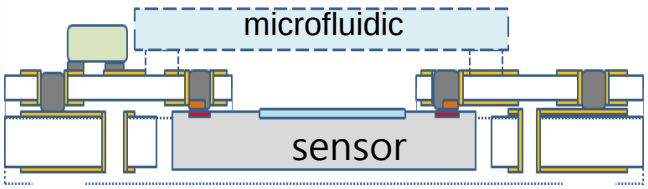
Animal test clinical test

Clinic trial 20 medical center

FDA

Biochip and IVD Products Development Platform

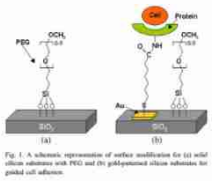
Bio-chip Lab provide bio-chip back end process, including Micro fluidics processing, Biosensor packaging



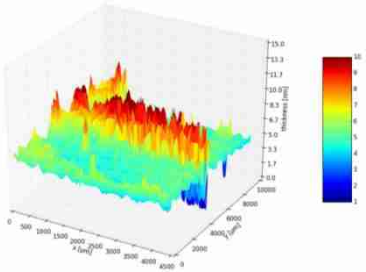
3 D Heterogeneous stacking Packaging process

Biochip and IVD Products Development Platform

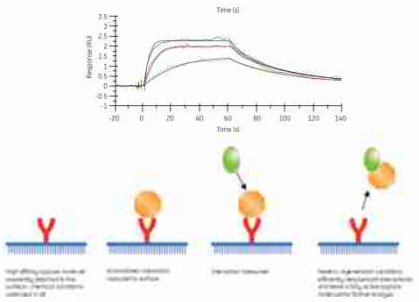
Vapor phase surface modification, nano film surface analysis



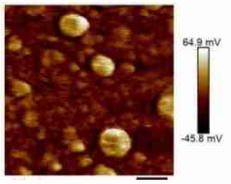
Vapor phase surface modification



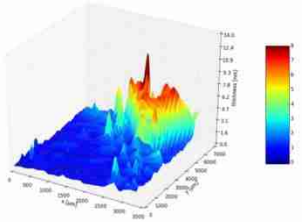
Nano film metrology



Biomolecular interaction(SPR)



以AFM量測SAM
200nmX200nm



以影像式奈米膜厚儀
3.5mm X7mm

Biochip and IVD Products Development Platform

IVD Lab provide facility for Bio-sample preparation, purification, Gene and protein expression metrology

QIAGEN Nucleic Acid Extraction System

ÄKTA pure Protein Purification system

FEMTO Pulse Capillary Electrophoresis System

Qubit 3.0 Fluorometer

Analytik Jena PCR

Real-time PCR instrument

SpectraMax microplate reader

Fluorescence/Chemiluminescence Imaging System

Flow Cytometry

Potentiostat/Galvanostat Instrument

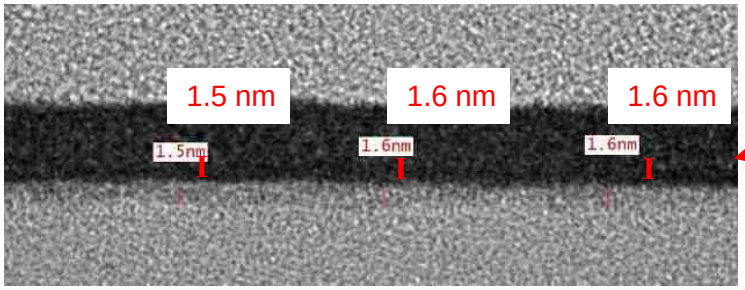
Nano film surface analysis

Large area linker layer、biomolecular layer mapping

FET Chip

(Chen, Hsiao-Chien et al.,2014. Analytical chemistry. 86. 10.1021/ac5001898.)

(1)By TEM **TEM image(x600K)**



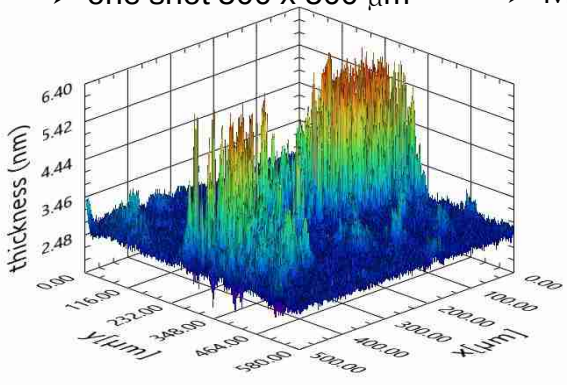
Quality Measurement System of Nano-Film

	best fit
A_n(Cauchy#0,GPTMS)	1.042
B_n(Cauchy#0,GPTMS)	426673
thickness(layer#1,sample)	1.6
RMSE	28.030
OK	

➢ Z Axis resolution 0.1 nm, XY 0.6 um.

(2)Large area metrology

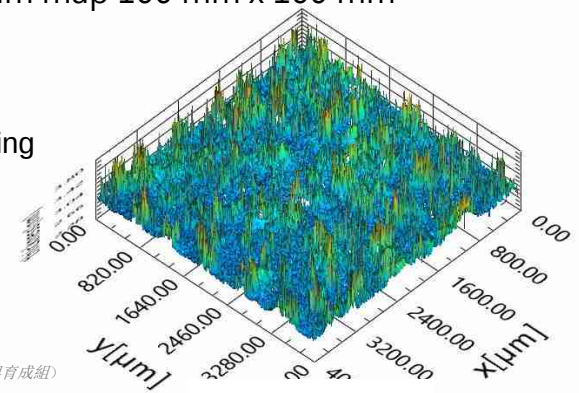
➢ one shot 500 x 500 μm



500 x 500 μm

➢ Maximum map 100 mm x 100 mm

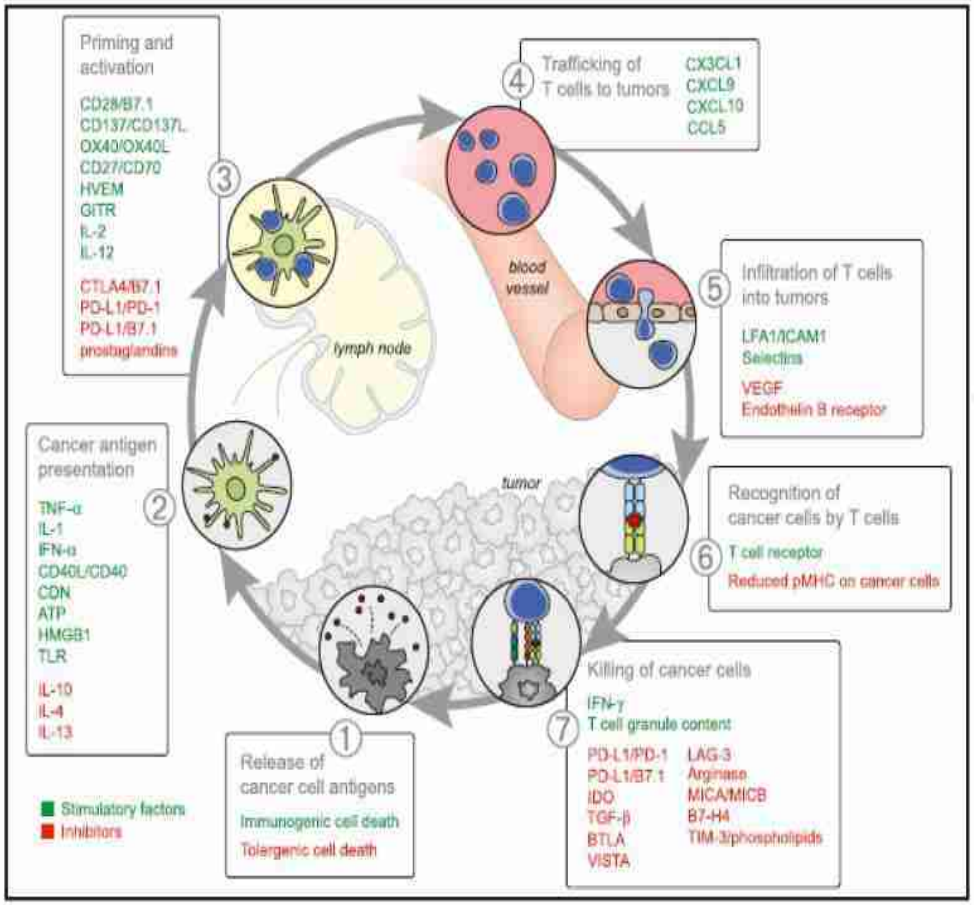
Mapping

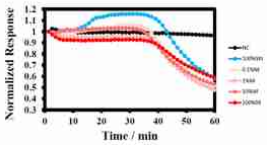


4000 x 4000 μm

Biochip in Precision Medicine

tumor microenvironment monitoring

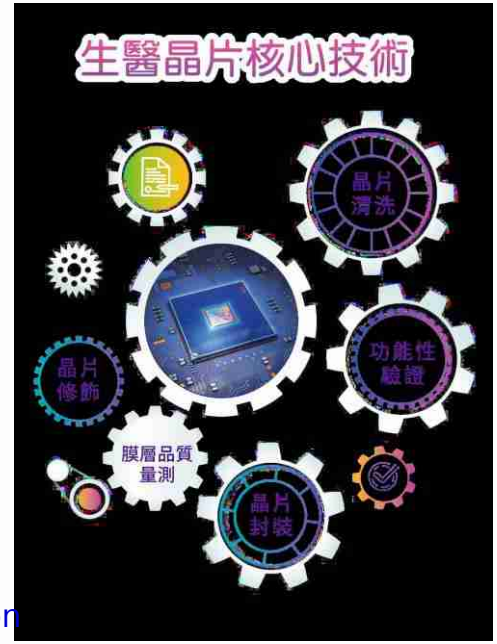




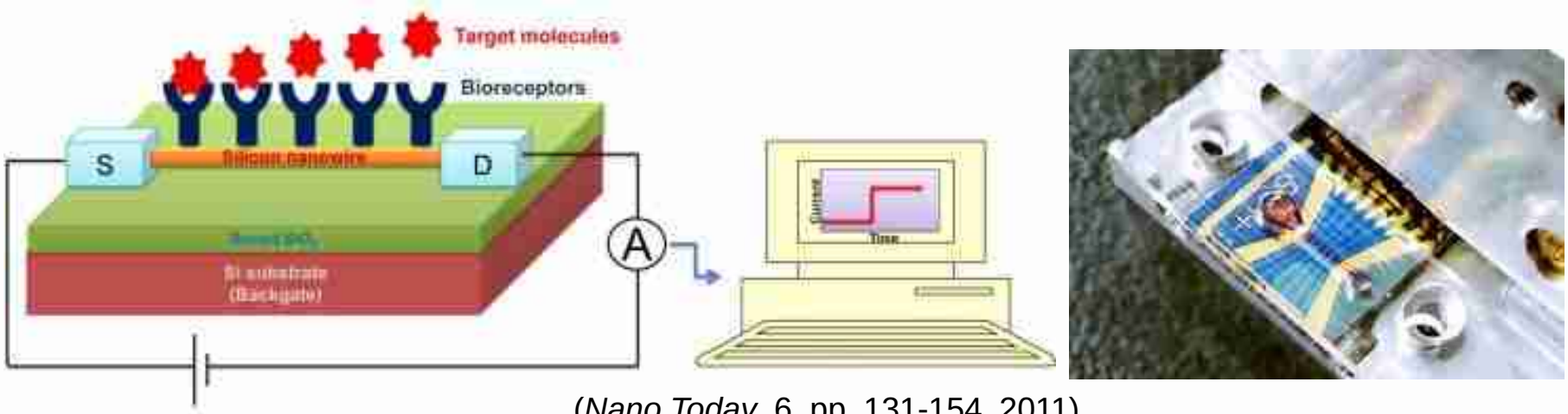
Gene Mutation test

isFET biosensor

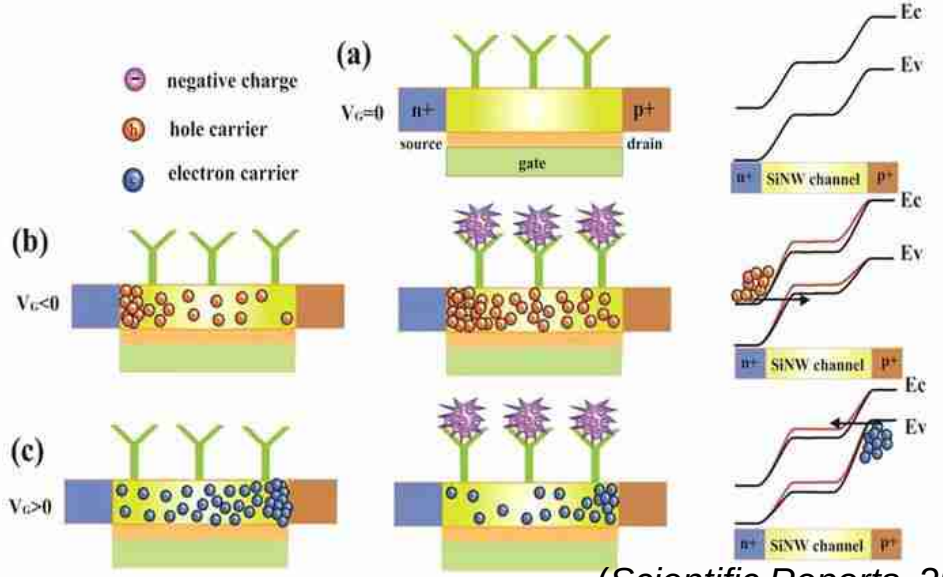
Liquid-biopsy CTC detection



isFET bio-sensor



(*Nano Today*, 6, pp. 131-154, 2011)



- Ultra-sensitive
- Label-free
- Real-time detection
- Multiple detection
- Low cost

(*Scientific Reports*, 2016)

IVD

- **Definition:** In vitro diagnostic products are those reagents, instruments, and systems intended for use in diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. [21 CFR 809.3]

STED Summary Technical Documentation

Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of IVD Medical Devices

- Device Description including Variants (Configurations) and Accessories
- Essential Principles (EP) Checklist
- Risk Analysis and Control Summary
- Design and Manufacturing Information
- Product Verification and Validation

Ref : GHTF/SG1/N63:2011《Summary Technical Documentation (STED) for Demonstrating Conformity to the Essential Principles of Safety and Performance of IVD Medical Devices》
IMDRF website：http://www.imdrf.org/

LDTS -Lab. Developed Tests and Service

- for new technology- ex. Precision Medicine

  in certificated Lab. only
- QMS ISO 15189 Medical laboratories — Requirements for quality and competence
- ISO17025 General requirements for the competence of testing and calibration laboratories

STED-Device Description

Device Description including Variants (Configurations) and Accessories

- a) the intended use of the IVD medical

  b) the intended user (lay person or professional);

  c)……

STED-Device Description

- 6.2 Reference to the Manufacturer's Previous Device Generation(s) and/or Similar Devices or Device History

  6.2.1 For an IVD medical device not yet available on any market

  provide a summary of:

  a) the manufacturer's previous generation(s) of the IVD medical device

  b) the manufacturer's similar IVD medical devices available on the market.

STED-Device Description

- 6.2.2 For an IVD medical device already available on the market in any jurisdiction

  include a summary of the number of adverse event reports related to the safety and performance of this IVD medical device in relation to the number of IVD medical devices placed on the market.

External certificates and documents which give written evidence of conformity with the Essential Principles may be annexed to the STED.

STED-Essential Principles (EP) Checklist

- a) the Essential Principles;
- b) for each Essential Principle whether it applies to the IVD medical device and if not, why not;
- c) the method used to demonstrate conformity with each Essential Principle that applies;
- and d) the reference to the actual technical documentation that offers evidence of conformity with each method used.

STED-Essential Principles (EP) Checklist

Summary Technical Documentation for Demonstrating Conformity to the Essential Principles of Safety and Performance of IVD Medical Devices (STED)
Study Group 1 Final Document GHTF/SG1/SG1/N063:2011

Essential Principles Checklist	GHTF
Identity of IVD medical device:	

Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
General Requirements				
5.1 Medical devices should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training of intended users, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.				

STED-Essential Principles (EP) Checklist EXAMPLE

A. 一般要求

醫療器材安全性與功效性基本原則(EP)	是否適用於該器材？	適用法規或標準	佐證資料
5.1 醫療器材對病患所產生之效益應大於可能產生之風險，且應保障對病患與使用者的健康與安全。醫療器材之設計與製造應確保在預期條件(如使用者的醫療與健康狀態)與用途下使用時不得危害病患或安全，亦不得危及使用者或其他人員之安全與健康。某些醫療器材之預期使用者須具備相當專業知識、經驗、教育或訓練。	適用	《體外診斷醫療器材查驗登記須知》 ISO14971:2007	仿單目錄、使用說明書、包裝標籤所載之警告與注意事項 五、風險分析與控制
5.2 製造業者對醫療器材設計與製造方案應考量工業界普遍認定的技術水平，符合安全性原則。必要時，製造業者應管制風險，使醫療器材相關危害之殘餘風險降至可接受之範圍。製造業者應依序採用以下原則： (1) 鑑別已知之危害，估計預期的使用、可能的誤用所帶來的風險； (2) 藉由安全的設計與製造，盡量消除風險； (3) 採取適當的保護措施（包括警報器）以盡量降低殘餘風險； (4) 告知使用者殘餘風險。	適用	ISO14971:2007	仿單目錄、使用說明書、包裝標籤所載之警告與注意事項 五、風險分析與控制

STED-Essential Principles (EP) Checklist

Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Reference to Supporting Controlled Documents
5.1 Medical devices should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training of intended users, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.	YES	Guidelines for Registration of IVD Medical Device ISO14971:2007	• Instruction leaflet catalog packaging, and labeling, instructions for use • Risk analysis and control
5.2 The solutions adopted by the manufacturer for the design and manufacture of the devices should conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, the manufacturer should control the risk(s) so that the residual risk(s) associated with each hazard is judged acceptable. The manufacturer should apply the following principles in the priority order listed: • identify known or foreseeable hazards and estimate the associated risks arising from the intended use and foreseeable misuse, • eliminate risks as far as reasonably practicable through inherently safe design and manufacture, • reduce as far as is reasonably practicable the remaining risks by taking adequate protection measures, including alarms, • inform users of any residual risks.	YES	ISO14971:2007	• Instruction leaflet catalog packaging, and labeling, instructions for use • Risk analysis and control

STED-Essential Principles (EP) Checklist Reference

- ISO14971:2007 risk management to medical devices
- IEC/EN 62366-1:2015 usability engineering
- IEC/EN 13640:2002 Stability Testing of IVD
- CLSI EP25-A Evaluation of Stability of IVD Reagents
- ISO 17511: 2003 traceability of IVD
- ISO 14155 Clinical investigation of medical devices for human subjects
- ……

STED-Risk Analysis and Control Summary

Reference: ISO 14971:2007 Annex H
ISO/DTR 24971(2019)
Medical devices -- Guidance on the application of ISO 14971

Ex1: The risk from false positive or false negative results.

Ex2: Instability, which could lead to erroneous results

Ex3: Reagents containing infectious agents.

Typically for a Class D IVD medical device a detailed report would be provided.

STED-Risk Analysis and Control Summary
example

以下為體外診斷醫療器材風險分析與管制之舉例：

風險分析（舉例）	風險管制措施（舉例）	風險管制措施之有效性研究（舉例）
使用錯誤導致人員感染、測試結果錯誤、環境汙染。	• 仿單標籤包裝記載使用與記載之注意事項、限制、使用環境、使用方法、運送與儲存條件。	• 可用性測試 • 臨床證據
器材失效以致於無法正確判讀結果	• 器材設計搭配陽性及陰性品管液，與預設品管液試驗結果不符時，需搭配其他試驗步驟	• 分析性能 • 臨床證據
偽陰性、偽陽性結果可能導致病患接受錯誤醫療處置。	• 器材設計搭配陽性及陰性品管液，與預設品管液試驗結果不符時，需搭配其他試驗步驟 • 臨床試驗設計接受與排除受試者基準，建立臨床結果判讀參考方法 • 仿單記載判讀結果之參考方法，配合臨床試驗結果搭配額外臨床徵狀由專業人員判讀。	• 分析性能 • 臨床證據
實驗室人員使用校正液、試劑、儀器或檢體錯誤、未依仿單規定步驟執行檢測、儀器未定期維護	• 器材設計搭配陽性及陰性品管液，與預設品管液試驗結果不符時，需搭配其他試驗步驟 • 臨床試驗設計接受與排除受試者基準，建立臨床結果判讀參考方法	• 可用性測試 • 分析性能 • 臨床證據

STED-Risk Analysis and Control Summary example

Risk analysis (Example)	Risk management procedures (Example)	Validity study of risk management procedures (Example)
Incorrect use causes operator infection, erroneous results and environmental pollution	Instruction leaflet of package should label the notices, limitations, environment and method of usage, shipping and storage conditions	• Usability testing • Clinical evidence
The equipment failed to correctly read the results	Test with positive and negative control. If the results do not match with the control, it is necessary to do other tests.	• Analytical performance • Clinical evidence
False negative or false positive results may lead to patients receiving wrong treatment	• Test with positive and negative control. If the results do not match with the control, it is necessary to do other tests. • The design of clinical test should include and exclude subject benchmarks, establish the reference of clinical outcome • Instruction leaflet should label the the reference method of interpretation, and combine the clinical results and symptoms for professionals interpreting.	• Analytical performance • Clinical evidence
Improper use of calibration fluids, reagents, instruments or samples；the test is not performed according to the instruction leaflet；the instrument is not regularly maintained.	• Test with positive and negative control. If the results do not match with the control, it is necessary to do other tests. • The design of clinical test should include and exclude subject benchmarks, establish the reference of clinical outcome	• Usability testing • Analytical performance • Clinical evidence

STED-Design and Manufacturing Information

- 9.1 Device Design

  For instruments this would include a description of major subsystems, analytical technology (e.g. operating principles, control mechanisms), dedicated computer hardware and software.

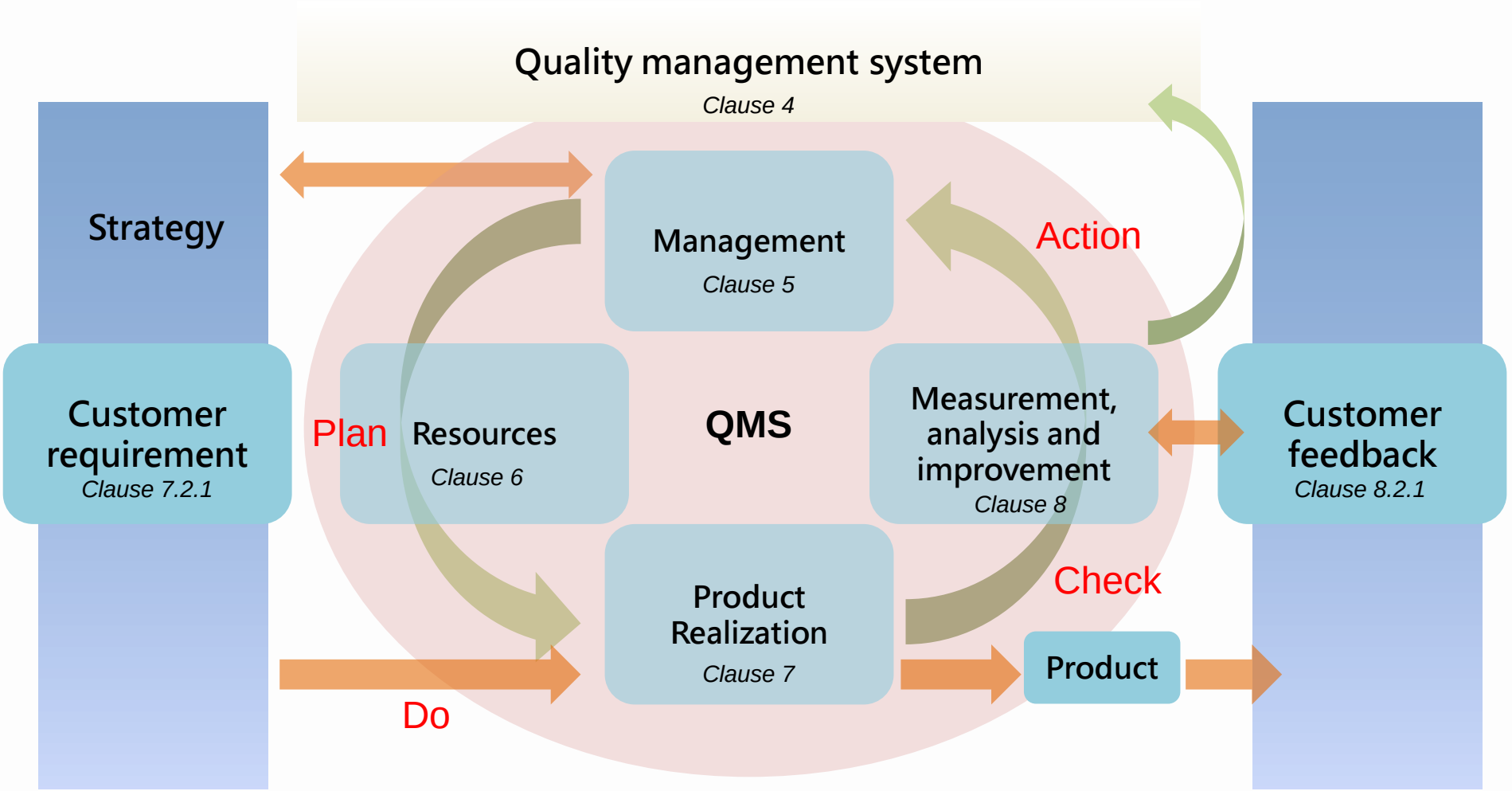
- 9.2 Manufacturing Processes

  This information may take the form of a process flow chart showing This section should include details of any in-process and final product testing (e.g. the manufacturer's QC release program).

- 9.3 Manufacturing Sites

  If QMS certificates, or the equivalent, exist for these sites, they may be annexed to the STED.

QMS:ISO 13485 Process Model



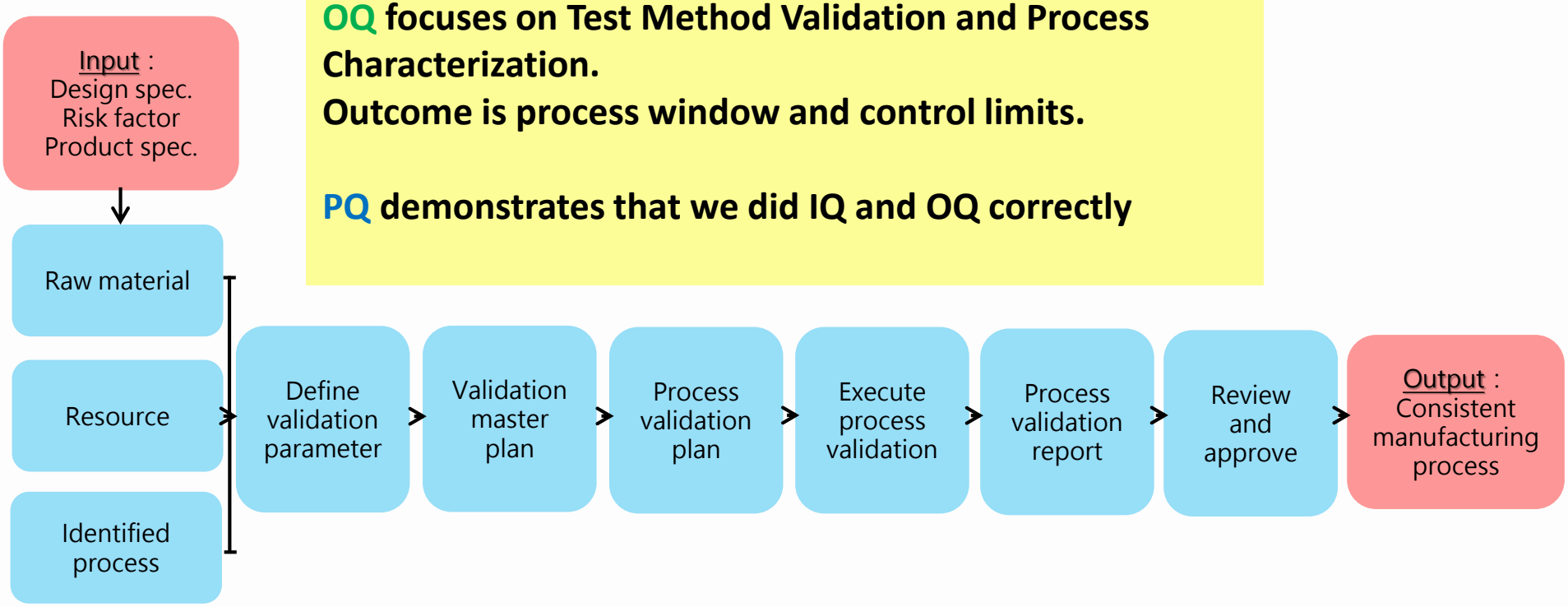
Process Validation

In semiconductor process, need to focus on process validation according to medical device regulatory requirement.

IQ focuses on Mistake Proofing Equipment
Outcome is Equipment Qualification.

OQ focuses on Test Method Validation and Process Characterization.
Outcome is process window and control limits.

PQ demonstrates that we did IQ and OQ correctly



STED-Product Verification and Validation

- ISO 9000:2000
- **Verification**: Confirmation, through the provision of objective evidence (3.8.1), that **specified requirements (3.1.2) have been fulfilled**.
- **Validation**: Confirmation, through the provision of objective evidence (3.8.1), that the requirements (3.1.2) for a **specific intended use or application have been fulfilled**

STED-Product Verification and Validation

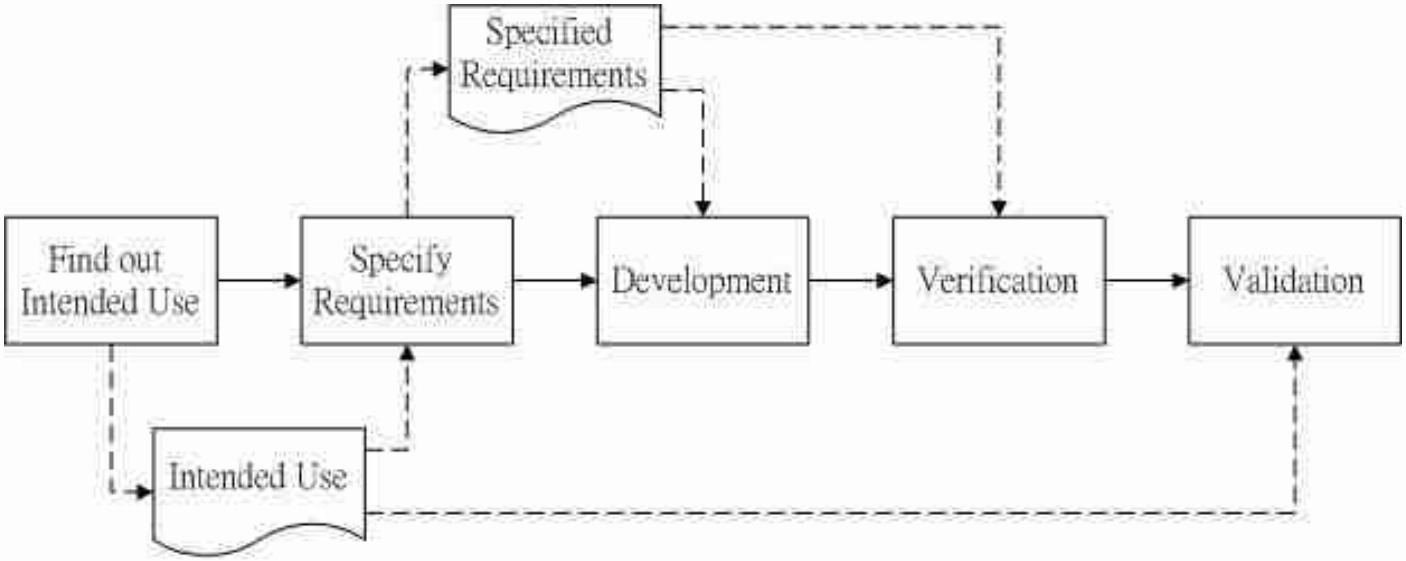


圖 Verification(驗證) 與 Validation(驗收)

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STED-Product Verification and Validation

- Specimen type
- Accuracy of measurement
- Metrological traceability of calibrator and control material values
- Analytical sensitivity
- Analytical specificity
- Measuring range of the assay
- Definition of assay cut-off
- Stability (excluding specimen stability)
- Clinical Performance
- Electrical safety, electromagnetic compatibility
- Software Verification and Validation

TFDA Human papillomavirus serological reagents guidance

項目	規格、需求及/或應進行測試	參考指引或採認標準
1. 偵測極限 (Limit of Detection)	建議使用連序列稀釋之HPV基因體DNA或RNA轉錄物（transcript）定出產品之偵測極限，如適用，以樣	US FDA guidance (2011)[2] 第V.A節
	本收集緩衝液進行序列稀釋。基因體DNA及/或RNA轉錄物可來自轉殖或合成物質。應包含每一種宣稱的HPV基因型別、細胞株及檢體類型之序列稀釋，可使用概率單位（Probit）做為統計分析方法。 若產品宣稱適用液相細胞學（Liquid-Based Cytology，以下簡稱LBC）檢體，並且操作步驟包括離心及丟棄LBC收集液，則應使用與回溶（re-suspend）細胞沉澱物（pellet）相同的液體來評估偵測極限。 若使用LBC泡製的仿檢體（內含HPV感染的細胞株進行分析研究（如『2. 實驗室內部精密度/重複性』所述），則也需要以此樣本評估偵測極限。 建議參考CLSI EP17-A，或是藉由檢出率（hit rate），即能被偵測到的病毒百分比，來推估偵測極限。以檢出率進行檢測之檢體濃度，應涵蓋	CLSI EP17-A(2004)[3]

Item	Specifications, requirements and / or should be tested	Reference guideline or adoption standard
Limit of Detection	It is recommended to use serial dilutions of HPV genomic DNA or RNA transcript to determine the detection limit of the product. If necessary, serially dilute with sample collection buffer. The genomic DNA and/or RNA transcript can be taken from a transgenic or synthetic material. Sequence dilutions of each of HPV genotypes, cell lines, and specimen types should be included, and can use probit model as a statistical analysis method. If the product claims to be a liquid-based cytology (LBC) specimen and the procedure includes centrifugation and disposal of the LBC collection, the same fluid as the re-suspend pellet should be used to assess the limit of detection.	US FDA guidance(2011) V.A CLSI EP17-A(2004)

- provides guidance for evaluation and documentation of the detection capability of clinical laboratory measurement procedures (ie, limits of blank, detection, and quantitation), for verification of manufacturers' detection capability claims, and for the proper use and interpretation of different detection capability estimates.
- CLSI EP 5、7、12、15…..

STED-Product Verification and Validation Traceability required

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- ISO 17511: 2003 traceability of IVD
- High ordered Reference Measurement Procedure
  - ISO 15193
- Qualified Reference Materials
  - ISO 15194
- Suitable Reference Laboratories
  - ISO 15195

STED-Product Verification and Validation

Cut off value

- Clinical expertee
- Retrospective study
- Perspective study
- Systemic review

STED-Product Verification and Validation

Clinical Performance

- Where relevant, the STED should contain data on the clinical performance of the IVD medical device.
- This clinical performance data is one of the elements of clinical evidence that demonstrates the conformity of the IVD medical device to the Essential Principles that apply to it.
- Note : Analytical performance and clinical performance are elements of clinical evidence. More detailed recommendations regarding these elements of the STED will be provided in guidance developed in cooperation with SG5.

STED-Product Verification and Validation

Clinical Performance

To conduct a clinical evaluation, a manufacturer needs to:

- identify the Essential Principles that require support from relevant clinical data;
- Clinical Evaluation identify available clinical data relevant to the device and its intended use;
- evaluate data in terms of its suitability for establishing the safety and performance of the device;
- generate any clinical data needed to address outstanding issues;
- bring all the clinical data together to reach conclusions about the clinical safety and performance of the device.

STED-Product Verification and Validation

Clinical Performance Reference

- IVDs are subject to a performance evaluation in accordance with Annex III of Directive 98/79/EC (IVDD).
- Clinical Evaluation SG5/N2R8
- ISO 14155
- **Guidelines** for Registration of In Vitro Diagnostic Medical Device (TFDA)

STED-Product Verification and Validation

Electrical safety, electromagnetic compatibility

- **IEC /EN61010-1**
- **IEC/EN 61326-2-6**
- **IEC/EN 61010-2-101 Particular requirements for in vitro diagnostic (IVD) medical equipment**

STED-Product Verification and Validation

Software Verification and Validation

- The STED should contain evidence of the validation of the software, as used in the finished device. This information should typically include the summary results of all verification, validation and testing performed in-house and as applicable in an actual user environment prior to final release. It should also address all of the different hardware configurations and, where applicable, operating systems identified in the labelling.
- IEC/EN 62304

STED-Product Verification and Validation

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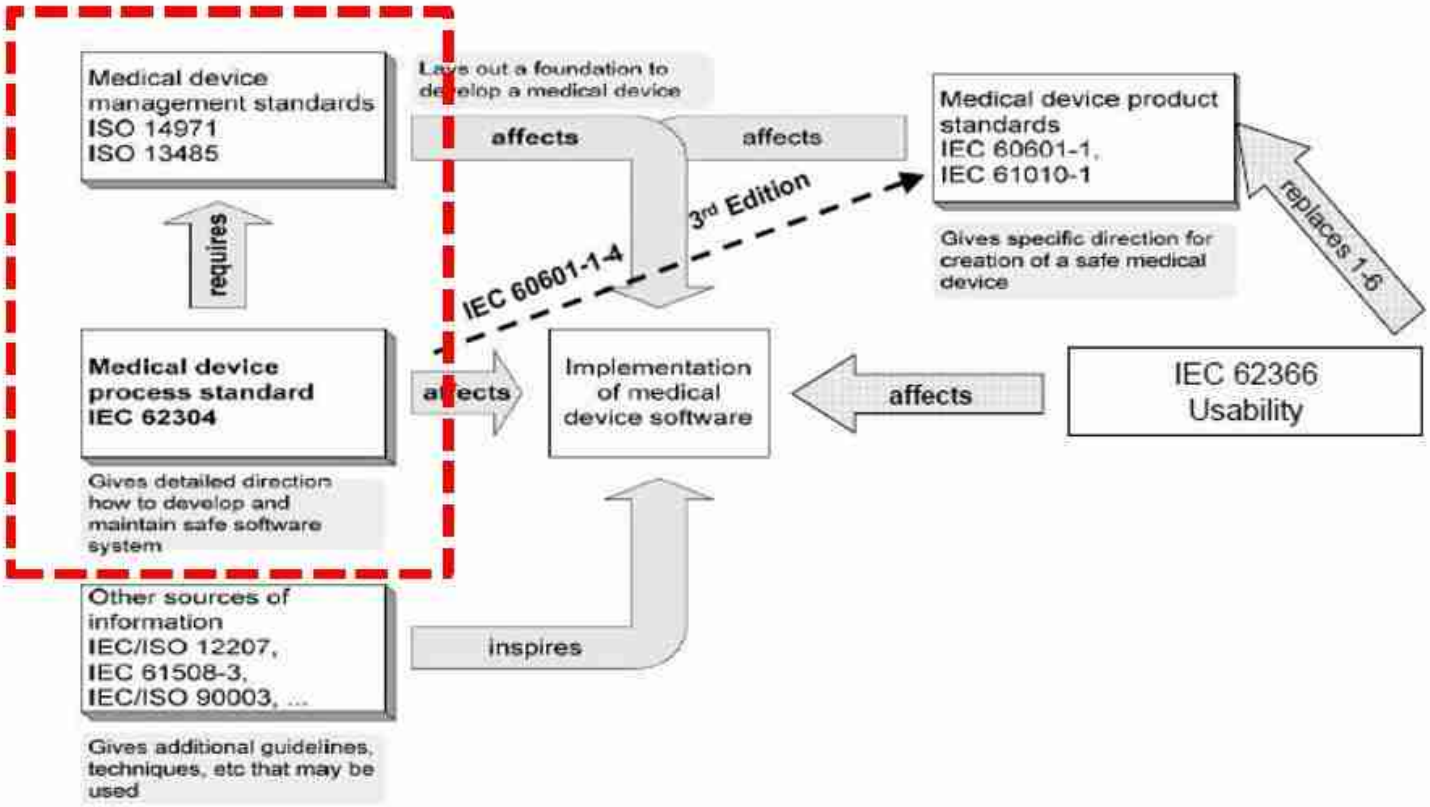
Software Verification and Validation



Source : Introduction into IEC 62304 Software life cycle for medical devices, Christoph Gerber, STRYKER

STED-Product Verification and Validation

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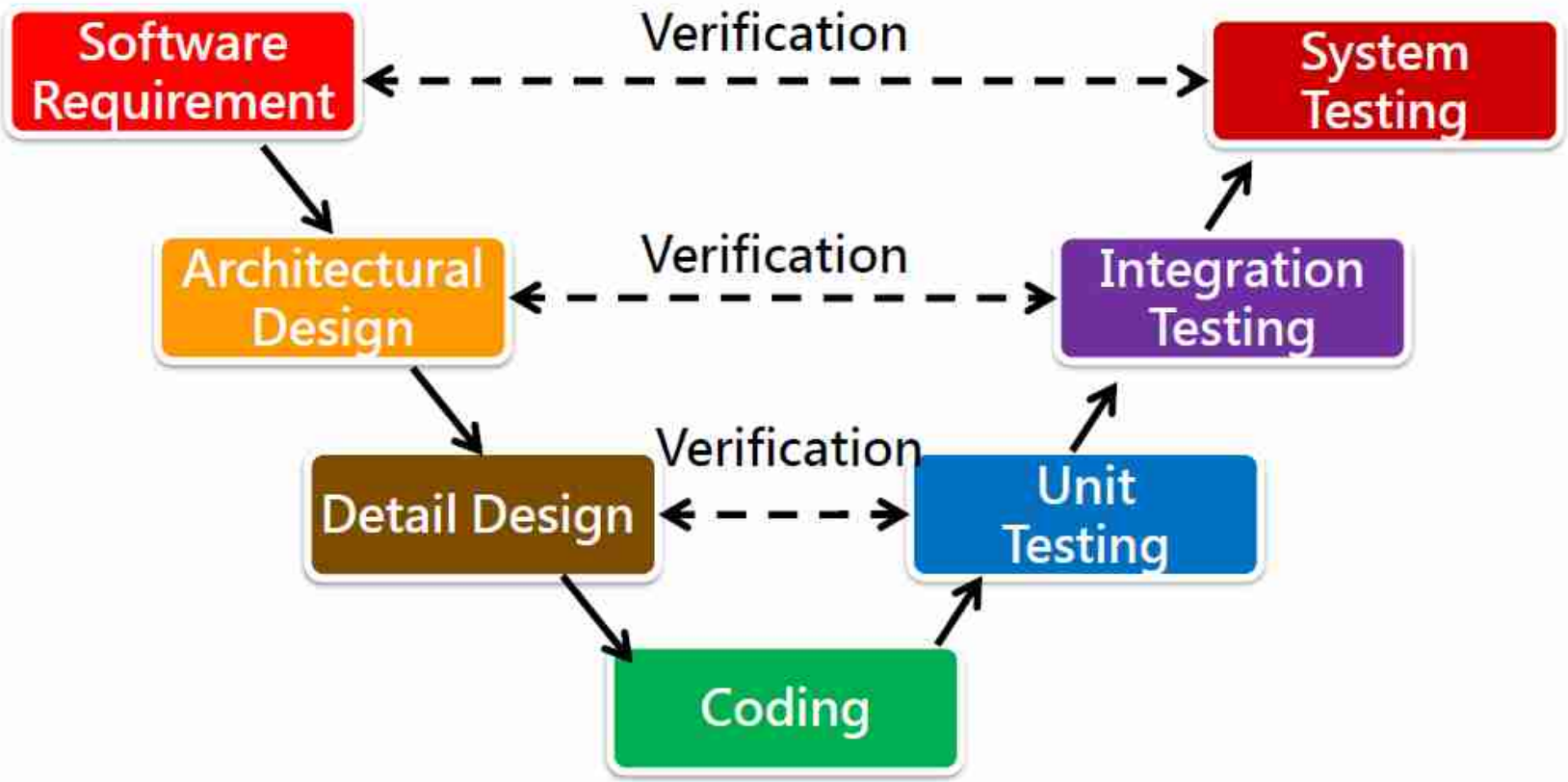
Software Verification and Validation



IEC-62304 REQUIRMENT

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- Risk Management File (clause 4.2, 7)
- Software Safety Classification (clause 4.3.c)
- Software Development Plan (clause 5.1.1)
- Software System requirements (5.2)
- Software Architectural Design (clauses 5.3, 5.4)
- Software Test Plan (clauses 5.5, 5.6, 5.7, especially 5.7.1 NOTE 1 and 2)
- Traceability Overview (clause 5.7.4)
- Software Test Report (clause 5.7.5)
- Residual Anomalies (clause 5.8)
- Configuration Management (clauses 5.8.4, 5.8.5, 8)

The SOFTWARE SYSTEM is software safety class A if:

- the SOFTWARE SYSTEM cannot contribute to a HAZARDOUS SITUATION; or
- the SOFTWARE SYSTEM can contribute to a HAZARDOUS SITUATION which does not result in unacceptable RISK after consideration of RISK CONTROL measures external to the SOFTWARE SYSTEM.

The SOFTWARE SYSTEM is software safety class B if:

- the SOFTWARE SYSTEM can contribute to a HAZARDOUS SITUATION which results in unacceptable RISK after consideration of RISK CONTROL measures external to the SOFTWARE SYSTEM and the resulting possible HARM is non-SERIOUS INJURY.

The SOFTWARE SYSTEM is software safety class C if:

- the SOFTWARE SYSTEM can contribute to a HAZARDOUS SITUATION which results in unacceptable RISK after consideration of RISK CONTROL measures external to the SOFTWARE SYSTEM and the resulting possible HARM is death or SERIOUS INJURY.

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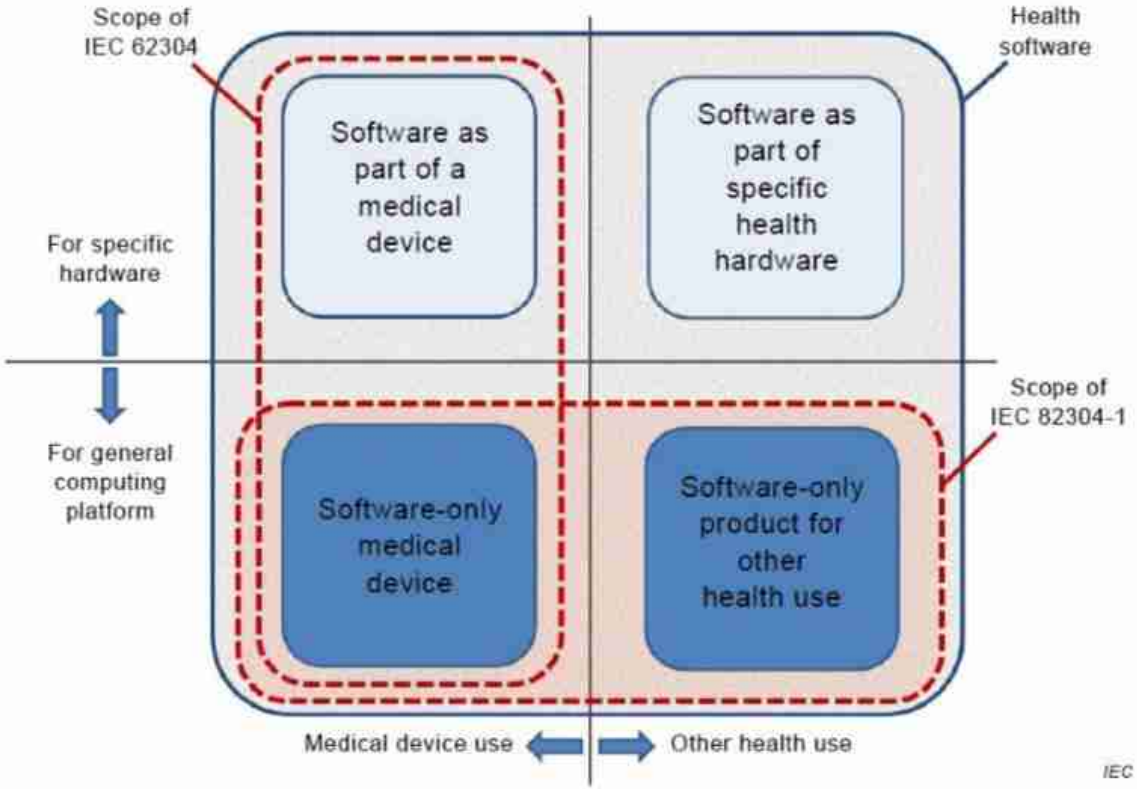
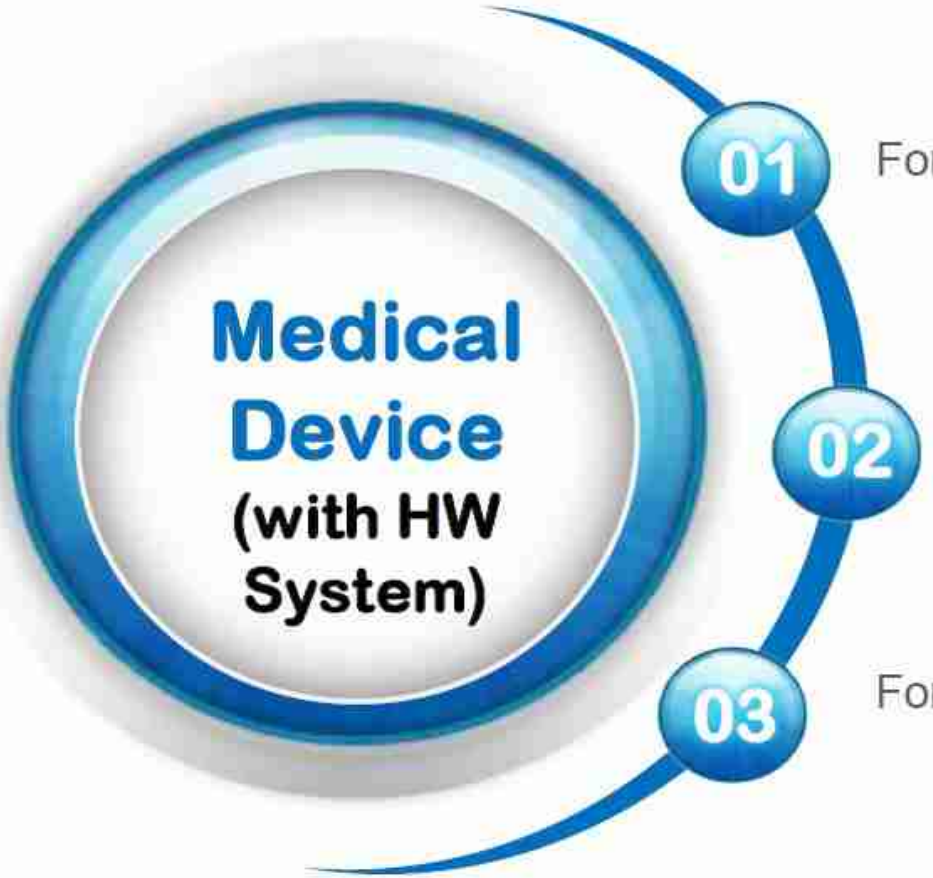
IEC 82304-1 IEC 62304



HEALTH SOFTWARE application domains and scope of related standards



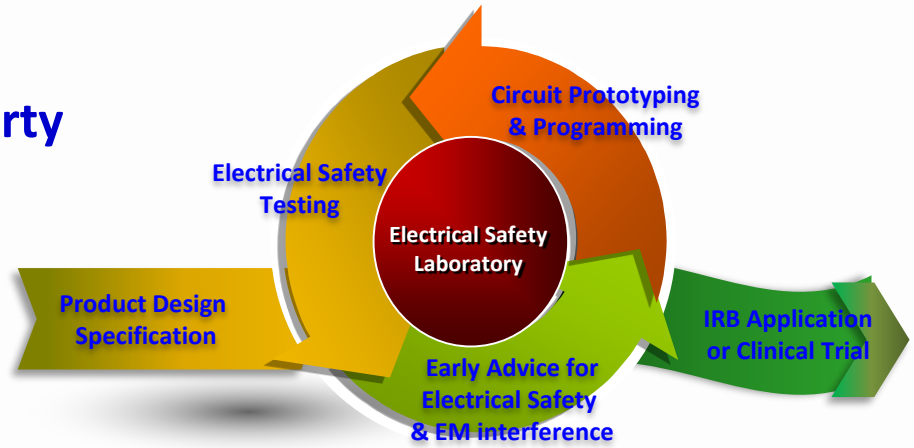
For Company:
- ISO 13485 (QMS)

For Product System:
- IEC 60601-1 Or IVD related
- ISO 14971 (Risk)
- IEC 62366-1 (Usability)

For Product Software System:
- IEC 62304 (SW Development)

V&V Laboratories for Medical Devices

- **Product specifications**
  - verification procedures and results
- **Build up joint venture with a third-party V&V labs**



- **Physical Characterization Lab.**
- **Biological & Chemical Lab.**
- **Electrical Testing Lab.**

Core Labs. ⇨ Testing Labs. ⇔ Third-Party

Regulatory advice	Biocompatibility	Electrical safety verification
Product spec. plan	ISO10993 GLP/GTP	Electrical safety IEC60601

IEC60601

TAF 3291

ISO13485

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Applications and Integration of Biomedical Imaging

Clinical Application	Surgical Guidance Platform	MRI Image Platform	Image Application

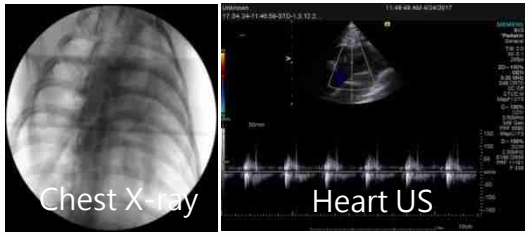
Spinal surgery
Knee surgery

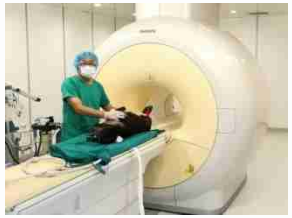
Animal testing,
Implantable
Medical Devices

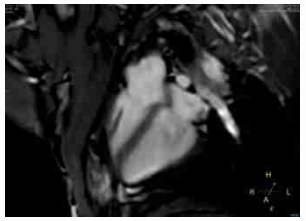
Surgical guidance
(minimally invasive)

Ultrasound,
MRI, X-ray
DICOM Image

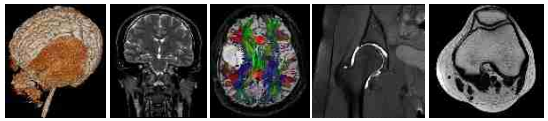
Medical Device Usability Lab.
(IEC62366 : 2007)

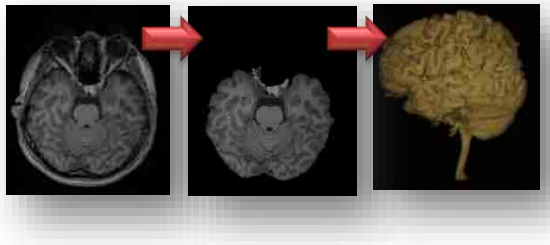


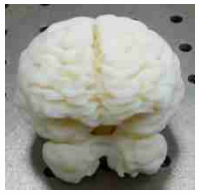




Cardiac MRI







Animal Testing images
- Implantable Medical Devices
- Contrast Media

Special Image Process
- MRI scan
- Brain research
- fMRI image

Medical Device Development
- MRI Compatible testing
- Surgical Guid system

Hardware
One stop service

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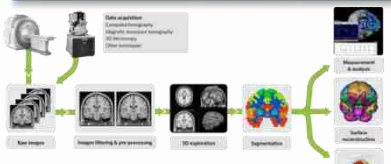
Biomedical Imaging



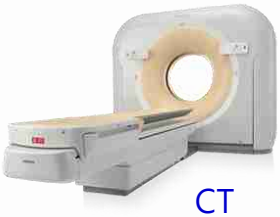
http://www.fei.com/

3D Scanner

Micro-CT

3T MRI

US



CT

C-ARM

Additive Manufacturing

Connex 500(Poly jet)
Material：Bio-compatible

Fortus 380
(Fused Deposition Modeling)
Material：Bio-compatible

Renishaw / AM250
Material：
- Titanium Ti6Al4V
- Cobalt-chrome (ASTM75)

Tongtai / AM250

Arcam / A2X (MIRDC)

Product V&V

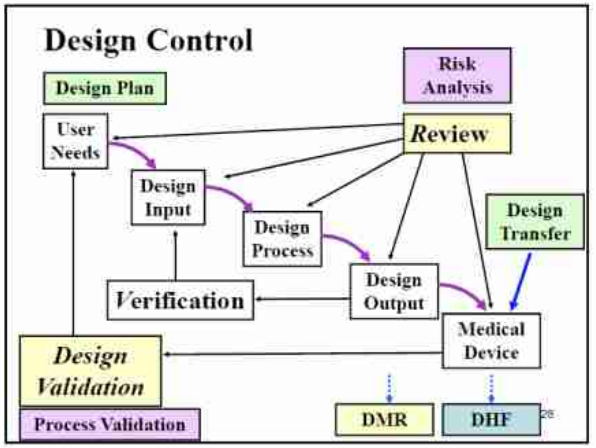
Universal testing machine

Coordinate Measuring Machine

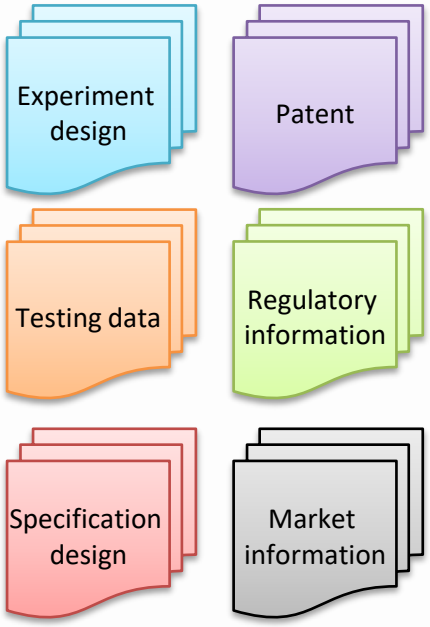
Optical Microimage Measurer

Software Service Platform

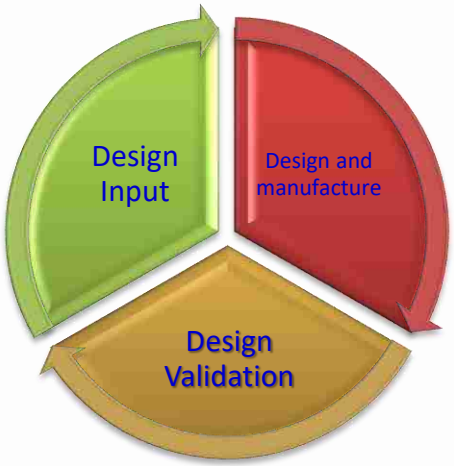
- Provide "Electronic Document System" Platform to R&D teams:
  - Documentation is required for FDA application
  - Design document control process (ISO 13485)
  - Risk analysis (ISO 14971)
  - Design Master Records (DMR)
  - Design History Files (DHF)



Design control guidance for MD, FDA, 1997



Electronic file system for medical device design



- Product
- Start-ups
- Market Application

Animal Center Service Locations

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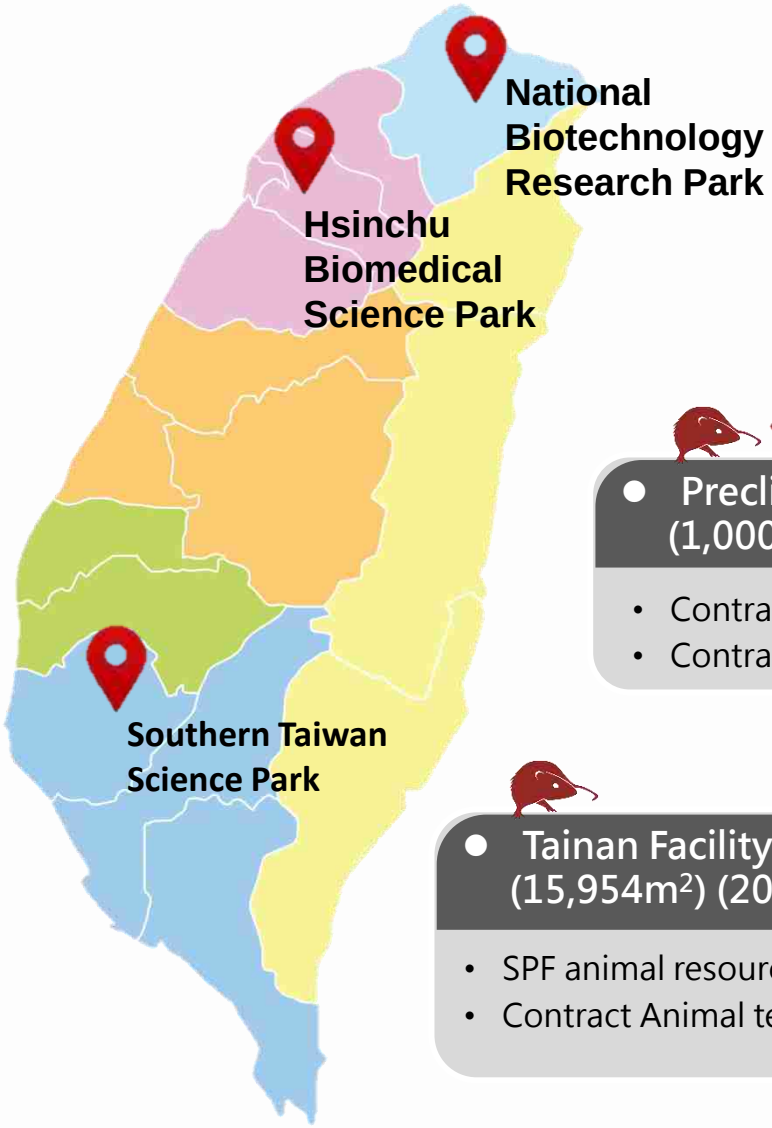

- **Taipei Facility (Headquarter)** (8517m²) (25,200m²)
  - SPF animal resource/ Repository
  - Contract animal testing (pharma)
  - Diagnostic laboratory
  - Education and Training

- **Preclinical Animal Testing Laboratory** (1,000m²) (2016)
  - Contract animal testing (medical devices)
  - Contract animal testing (pharma)

- **Tainan Facility** (15,954m²) (2008)
  - SPF animal resource/ Repository
  - Contract Animal testing (Pharma)

- **Animal Care and Surgery Facility** (1,000m²) (2015)
  - Contract animal testing (medical devices)
  - Contract animal testing (pharma)

Preclinical Testing Lab (PTL)

(operated by National Lab. Animal Center)

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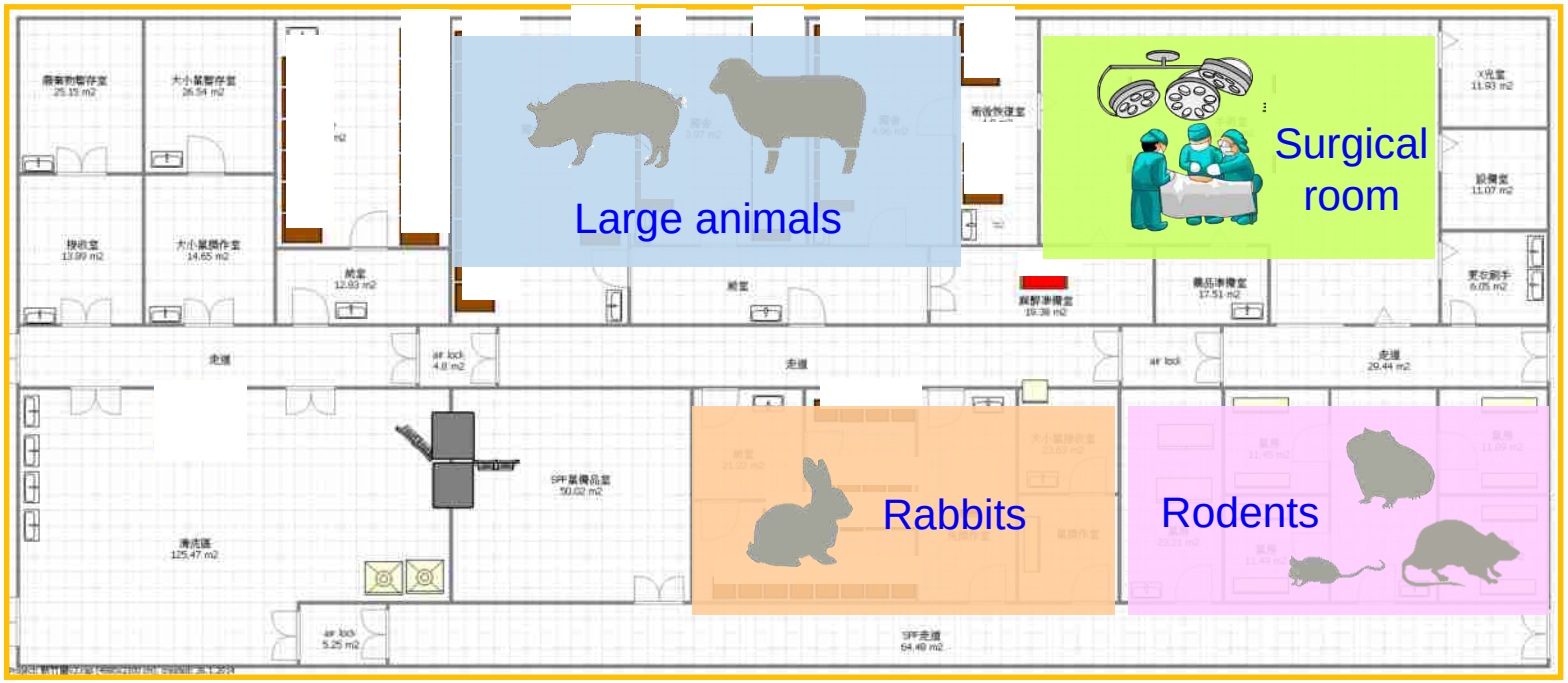
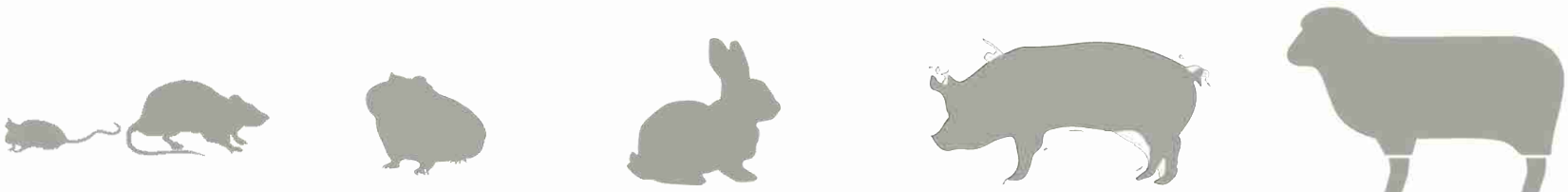
Multiple species: rats, mice, guinea pigs, rabbits, pigs and goats





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One-Stop Services (Accelerator)

- Biomedical imaging lab (mri/ct/us/c-arm)
- Additive manufacturing lab (3D printing / metal / polymer)
- Biomedical chip lab (surface decoration, chip encapsulation)
- In vitro diagnostics lab (bio reagent, system validation)

- Electrical security validation (IEC60601/IEC61010)
- Bio-compatibility validation (ISO10993)
- Physical properties validation (ASTM/TAF3291)
- Preclinical trials (IACUC/AAALAC)

- Quality system (ISO13485/QSR/DMR/DHF)
- Software assurance (ISO62304)
- Risk assurance (ISO14971)
- Patents, regulations, drawings

- Consulting R&D teams from academic, industry…..
- Start-up coaching
- Fund matchmaking
- Stationed spaces (office and labs.)
- Workshop and training

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國家實驗研究院

~Thanks for Your Attention~