

## **Lecture 19 - Contents**

An overview of the main sections in this lecture.

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FDA Regulatory Pathways

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Legal and Liability Issues

### **Hands-on**

Regulatory Strategy Planning

This outline is for guidance. Navigate the slides with the left/right arrow keys.



Lecture 19:

# **Navigating Medical AI Regulations: Global Frameworks**

**Ho-min Park**

[homin.park@ghent.ac.kr](mailto:homin.park@ghent.ac.kr)

[powersimmani@gmail.com](mailto:powersimmani@gmail.com)

## Global Regulatory Landscape

Medical AI systems are **directly linked to patient safety** and are subject to **strict regulatory frameworks**

**FDA**

United States

**EMA**

European Union

**MHRA**

United Kingdom

**Health Canada**

Canada

**PMDA**

Japan

**MFDS**

South Korea

### Risk-Based Classification

Application of differentiated regulatory levels based on device risk

### Clinical Evidence Requirements

Submission of data to demonstrate safety and effectiveness

### Post-Market Surveillance

Continuous performance monitoring and reporting obligations

### International Harmonization

Efforts to unify regulatory standards through IMDRF

**Part 1/3:**

# FDA Regulatory Pathways

1. FDA AI/ML Pathway - Adaptive Regulatory Framework
2. 510(k) Clearance - Substantial Equivalence Certification
3. PMA Approval - High-Risk Device Approval
4. De Novo Classification - New Device Classification
5. Software as Medical Device (SaMD)
6. Predetermined Change Control Plan (PCCP)
7. Clinical Validation Requirements

## FDA AI/ML Regulatory Pathway

The FDA is developing an **adaptive regulatory framework** for **continuously learning AI/ML-based medical devices**

### Continuous Learning

Model continuously updates with new data

### Pre-Specified Changes

Updates allowed within pre-approved change scope

### Performance Monitoring

Real-time performance tracking and reporting system

### Transparency Requirements

Transparent disclosure of algorithm changes



## 510(k) Clearance - Substantial Equivalence

510(k) is a pathway that enables **rapid market entry** by demonstrating **substantial equivalence to an existing approved device**

### **Substantial Equivalence**

Same intended use and technological characteristics as predicate device

### **Review Period**

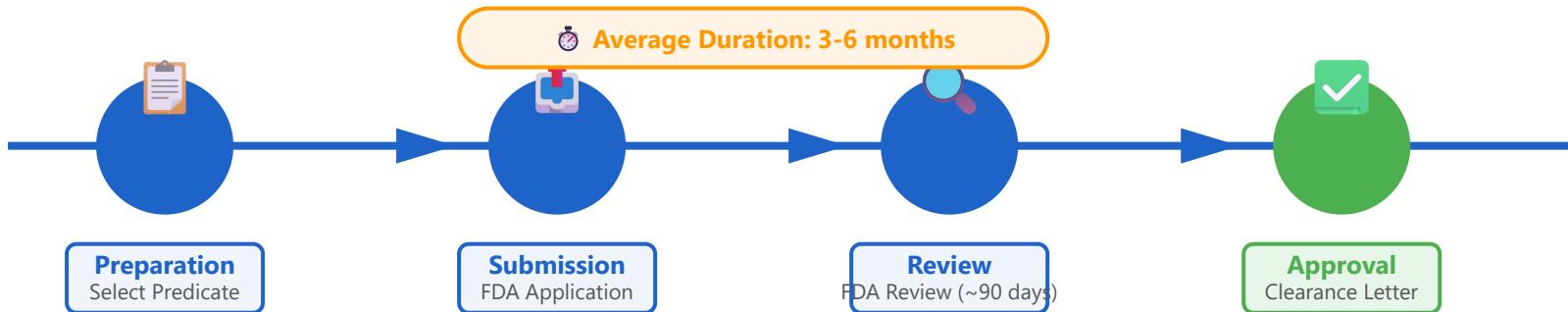
Generally decided within 90 days

### **Submission Documents**

Technical documentation, performance testing, comparative analysis

### **Approval Conditions**

Mainly applicable to Class II devices



## PMA (Premarket Approval) - High-Risk Devices

PMA is the **most stringent regulatory pathway** required for **Class III high-risk medical devices**

### Required Submission Materials

- Pre-clinical research data
- Clinical trial results
- Manufacturing and quality control information
- Labeling and instructions for use
- Risk-benefit analysis

### Review Timeline

- Standard: 180 days (filing decision)
- Total process: 1-3 years
- Advisory panel review possible

### 510(k) PMA Comparison

Comparison Item	510(k) Clearance	PMA Approval
Evidence Level	Substantial Equivalence (Substantial Equivalence)	Safety & Effectiveness (Safety & Effectiveness)
Clinical Trials	Optional	Required
Review Timeline	~90 days (3 months)	~180 days (1-3 years)

## De Novo Classification - Novel Devices

De Novo is an **alternative pathway** for **new low-to-moderate risk devices without a predicate**



### Novel Device

Innovative devices that cannot be compared to existing devices



### Low-Moderate Risk

Risk level that can be classified as Class I or II



### Special Controls

Special management measures for risk mitigation



### Future Predicate

Can be used as a predicate for future 510(k)s



**Key Point:** After De Novo approval, the device can be used as a predicate for similar future devices, facilitating market entry for innovative technologies

## Software as Medical Device (SaMD)

SaMD refers to **medical purpose software** that **operates independently without hardware**

### **Definition**

Standalone software, not part of a medical device, used for medical purposes

### **IMDRF Framework**

Internationally harmonized SaMD classification and regulatory system

### **Risk Classification (IMDRF Framework)**

#### **Level I**

Informational purpose

#### **Level II**

Diagnostic support

#### **Level III**

Treatment decision

### **SaMD Examples**

- Image analysis software (lesion detection, measurement)
- Clinical Decision Support Systems (CDSS)
- Remote patient monitoring apps
- AI-based diagnostic algorithms



**Key Point:** SaMD is distinguished from general wellness apps and is regulated as a medical device when used for diagnosis, prevention, monitoring, treatment, or mitigation of disease

## Predetermined Change Control Plan (PCCP)

PCCP is a framework that enables **predefined changes** to be **implemented without separate approval**

### Purpose

Enable continuous learning and improvement of AI/ML models within a regulated environment

### Includes

Change types, evaluation methods, implementation protocols, monitoring plans

### Elements that should be included in PCCP

#### 1. Description of Modifications

- Scope and types of permitted changes

#### 2. Methodology

- Methods for implementing and validating changes

#### 3. Impact Assessment

- Analysis of effects on safety and effectiveness

#### 4. Monitoring Protocol

- Real-world performance tracking and reporting system

### Permitted Changes

Performance improvements, data updates, algorithm optimization

### Restricted Changes

Changes in intended use, addition of new indications

### Reporting Requirements

Regular change logs and performance reports

 **Key Point:** PCCP strikes a balance between innovation and regulation, enabling continuous improvement of AI technology while maintaining patient safety

## Clinical Validation Requirements

Clinical validation is the process of demonstrating the **safety and effectiveness of medical AI** in a **real clinical environment**

### Analytical Validation

Verify that the algorithm works accurately as intended

### Clinical Validation

Evaluate whether it provides meaningful results in actual clinical settings

### Validation Design Considerations

**Study Design:** Prospective vs. Retrospective

**Sample Size:** Sufficient data to ensure statistical power

**Control Group:** Compare with existing standard of care or clinical judgment

**Endpoints:** Sensitivity, Specificity, AUC, Clinical Outcomes

**Subgroup Analysis:** Evaluate demographic diversity

### Performance Metrics

Sensitivity, Specificity, PPV, NPV, AUC

### Clinical Impact

Diagnostic accuracy, treatment outcomes, patient safety

### Bias Assessment

Performance consistency across race, gender, and age

### Real-World Evidence

- Performance data in actual clinical settings
- Post-market surveillance data
- Registry studies

- Electronic Health Record (EHR) analysis

 **Key Point:** Clinical validation must go beyond simple algorithm accuracy to demonstrate improvement in patient outcomes within actual clinical workflows

## **Part 2/3:**

# **International Regulatory Frameworks**

- 1.** EU MDR/IVDR - European Medical Device Regulations
- 2.** CE Marking - Conformity Assessment
- 3.** UK MHRA Guidelines - Post-Brexit Regulations
- 4.** Health Canada Requirements
- 5.** APAC Regulations - Asia-Pacific Regulations
- 6.** Harmonization Efforts - International Harmonization

## EU MDR/IVDR - European Medical Device Regulations

The EU has strengthened medical device regulations with **MDR (Medical Device Regulation)** and **IVDR (In Vitro Diagnostic Regulation)**

### MDR (EU 2017/745)

Fully implemented May 2021, general medical device regulation

### IVDR (EU 2017/746)

Fully implemented May 2022, in vitro diagnostic medical device regulation

### Key Changes

- **Enhanced risk classification:** Increase in Class IIb/III devices
- **Increased clinical evidence requirements:** More stringent clinical evaluations
- **Expanded Notified Body role:** Strengthened independent body reviews
- **UDI (Unique Device Identification):** Improved device traceability
- **EUDAMED database:** Centralized information system
- **Enhanced post-market surveillance:** Mandatory PSUR, PMS

### Class I

Low risk, self-declaration

### Class IIa/IIb

Medium risk, NB review

### Class III

High risk, NB review



**Key Point:** MDR/IVDR prioritizes patient safety, and AI/ML devices must also be appropriately classified and evaluated within this framework

## CE Marking - Conformity Assessment

CE Marking is a **mandatory conformity marking** required to **sell medical devices in the EU market**

### CE Mark Meaning

Declares that the product complies with EU medical device directives and regulations

### Legal Requirements

Legal requirement for sale within the EU

### Conformity Assessment Routes

**Class I:** Manufacturer self-declaration

**Class IIa:** Technical documentation review by Notified Body

**Class IIb:** Quality system + design review by Notified Body

**Class III:** Full quality assurance audit by Notified Body

### Steps to Obtain CE Marking

1. Device classification and applicable regulations identification
2. Technical documentation preparation
3. Clinical evaluation conduct
4. Quality management system establishment (ISO 13485)
5. Notified Body audit (if applicable)
6. Declaration of Conformity (DoC) preparation
7. CE mark affixing and EUDAMED registration



**Key Point:** CE Marking is not a one-time event but requires ongoing compliance maintenance, with regular technical documentation updates and post-market surveillance required

## UK MHRA Guidelines - Post-Brexit Regulations

After Brexit, the UK established an **independent MHRA regulatory system** and introduced **UKCA marking**

### GB UKCA Marking

Conformity marking exclusively for UK (GB) market

### Transition Period

CE marking recognized with limitations (deadline may be extended)

### MHRA Regulatory Requirements

- **Registration:** Manufacturer and device registration with MHRA required
- **UK Responsible Person:** Designation of legal representative in the UK
- **Approved Body:** Review organization equivalent to EU's Notified Body
- **Northern Ireland:** CE marking can continue to be used

### GB (England, Wales, Scotland)

UKCA marking required

### Northern Ireland

Uses CE marking

### Dual Marking

Required for simultaneous entry into EU+UK markets



**Key Point:** If planning to enter both EU and UK markets, you must comply with both regulatory systems and undergo separate conformity assessments

## Health Canada Requirements

Canada operates a **risk-based classification system** according to **Medical Devices Regulations**



Canadian Department of Health, Medical Device Regulatory Authority



Medical Device Establishment Licence

### Canadian Device Classification (Class I-IV)

**Class I:** Low risk, manufacturer's own declaration

**Class II:** Low-medium risk, license required

**Class III:** Medium-high risk, license + detailed review

**Class IV:** High risk, most stringent review

### Approval Pathways

- **Standard Pathway:** Standard review process
- **Expedited Pathway:** Expedited review (when specific conditions are met)
- **Agile Licensing:** Flexible pathway for innovative devices such as AI/ML



Class II: 60 days, Class III/IV: 75 days (target)



MDEL requires annual renewal



**Key Point:** Health Canada has introduced Agile Licensing for AI/ML devices, providing adaptive regulation for continuously learning algorithms

## APAC Regulations - Asia-Pacific Region

The Asia-Pacific region has **diverse regulatory systems by country**, and **harmonization efforts** are underway

### JP Japan (PMDA)

Pharmaceuticals and Medical Devices Agency

### KR Korea (MFDS)

Ministry of Food and Drug Safety

### CN China (NMPA)

National Medical Products Administration

### AU Australia (TGA)

Therapeutic Goods Administration

### SG Singapore (HSA)

Health Sciences Authority

### TW Taiwan (TFDA)

Taiwan FDA

### Key Features

- **Japan:** Class I-IV classification, SAKIGAKE system (priority review for innovative devices)
- **Korea:** Class I-IV classification, fast-track review for innovative medical devices
- **China:** Class I-III classification, strict clinical trial requirements
- **Australia:** TGA recognizes EU CE marking (under certain conditions)
- **Singapore:** Fast approval, references ASEAN medical device guidelines

### AHWP (Asian Harmonization Working Party)

- A collaborative body for harmonizing medical device regulations in the Asian region
- Member countries: Japan, Korea, China, Australia, Singapore, Taiwan, etc.
- Promotes harmonization based on IMDRF principles

**💡 Key Point:** When entering the APAC market, it is important to understand regulatory differences by country and collaborate with local partners or regulatory consultants

## International Harmonization Efforts

**International harmonization** reduces duplicate regulations and facilitates **global market access**



International Medical Device Regulators Forum - Global regulatory harmonization forum



Global Harmonization Task Force - Predecessor to IMDRF

### IMDRF Member Countries

- United States (FDA), Europe (EC), Japan (MHLW), Canada (Health Canada)
- Australia (TGA), Brazil (ANVISA), China (NMPA), Russia (Roszdravnadzor)
- South Korea (MFDS), Singapore (HSA)

### Key Harmonization Documents

- **SaMD Framework:** Software as Medical Device classification and regulation
- **UDI Guidance:** Unique Device Identification system
- **Clinical Evidence:** Clinical evaluation principles
- **Risk Classification:** Risk-based classification principles
- **AI/ML Framework:** AI medical device regulatory guidelines

### Benefits of Harmonization

Reduced duplicate testing, shortened approval time, cost savings

### Future Direction

AI/ML specialized regulations, expanded use of real-world evidence

**Key Point:** Following IMDRF guidelines allows you to simultaneously meet regulatory requirements of multiple countries, making global market entry efficient

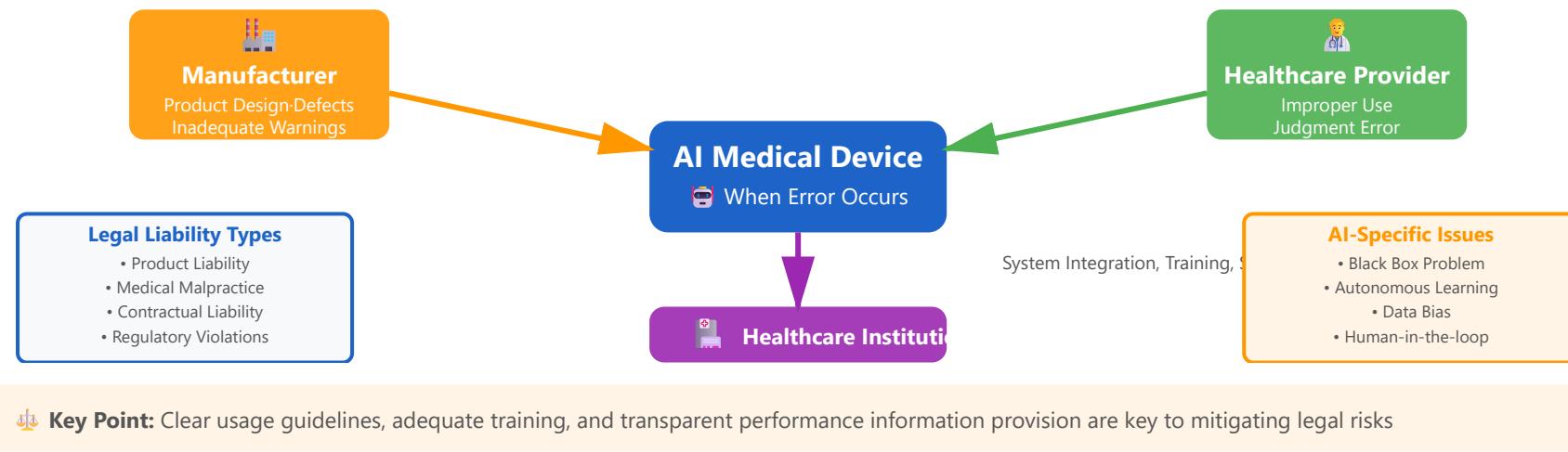
## **Part 3/3:**

# **Legal and Liability Issues**

- 1.** Liability Framework - AI Responsibility Structure
- 2.** Malpractice Insurance - Medical Malpractice Insurance
- 3.** Intellectual Property - Intellectual Property Rights
- 4.** Data Rights and Ownership - Data Rights
- 5.** Clinical Trial Regulations - Clinical Trial Regulations
- 6.** Post-Market Surveillance - Post-Market Surveillance
- 7.** Compliance Auditing - Compliance Auditing

## Liability Framework - AI Responsibility

The **liability** of AI medical devices involves **complex legal issues**



## Malpractice Insurance - AI Coverage

The introduction of AI medical devices adds **new considerations to malpractice insurance**

### Institutional Insurance

Coverage for AI systems used by healthcare institutions

### Individual Insurance

Coverage for AI-assisted diagnostic/treatment decisions by healthcare professionals

### Insurance Coverage Considerations

- **AI System Type:** Decision support vs. autonomous diagnosis
- **Scope of Use:** Whether used within approved indications
- **Training Completion:** Proof of adequate user training
- **Documentation:** Record of AI recommendations and final decisions
- **Update Management:** Software version control and validation

### Premium Impact

Risk level may change with AI use, potentially affecting premium adjustments

### Claims Process

Need for evidence preservation and reporting protocols in AI-related incidents

**Key Point:** It is important to consult with insurance providers before implementing AI to clarify coverage and secure additional protection if necessary

## Intellectual Property - AI Patents

**Intellectual property protection** for AI medical devices is the core of **securing competitiveness**

### Patents

Exclusive rights to algorithms, systems, and methods

### Copyright

Software code, UI/UX design

### Trademark

Product names, brand identity

### AI Patent Strategy

- **Patentability:** Requires novelty, inventive step, and industrial applicability
- **Disclosure vs. Trade Secret:** Public patent vs. non-disclosure strategy
- **Defensive Patents:** Building a portfolio to defend against competitor litigation
- **Licensing:** Technology transfer or cross-licensing strategy

### Data-Related IP

- **Training Data:** Securing rights to datasets
- **Model Weights:** Protection of trained model parameters
- **Database Rights:** Special database protection recognized in the EU and elsewhere



**Key Point:** Since AI technology evolves rapidly, it is important to establish an IP strategy early and continuously update your portfolio

## Data Rights and Ownership

**Data ownership and usage rights are the legal foundation of AI development**

### Patient Rights

Personal information protection, consent, access rights, deletion rights

### Institutional Rights

Management authority over collected and stored data

### Key Legal Frameworks

- **GDPR (EU):** Personal data protection regulation, strict consent requirements
- **HIPAA (US):** Health information protection and privacy law
- **PIPEDA (Canada):** Personal Information Protection and Electronic Documents Act
- **PIPA (Korea):** Personal Information Protection Act

### Data Contract Terms

- **Data Ownership:** Who owns the data?
- **Purpose of Use:** Scope of research, development, and commercial use
- **Re-identification Prohibition:** Provisions to prevent re-identification of anonymized data
- **Third-party Sharing:** Conditions and limitations for data sharing
- **Retention Period:** Data storage and deletion policies



**Key Point:** Clear Data Use Agreements (DUA), appropriate consent procedures, and robust security measures are essential to minimizing legal risks

## Clinical Trial Regulations - AI Studies

Clinical trials for AI medical devices require **different considerations than traditional devices**

### Trial Design

Selection of appropriate methodology including prospective, RCT, observational studies

### Ethics Approval

IRB/IEC approval, obtaining patient consent

### Special Considerations for AI Clinical Trials

- **Locked Algorithm:** Algorithm must be locked during trial period
- **Version Control:** Clear documentation of software version
- **Integration Validation:** Performance evaluation within actual clinical workflow
- **User Training:** Providing appropriate training for clinicians
- **Subgroup Analysis:** Performance evaluation across diverse populations

### Regulatory Submission Requirements

- **Protocol:** Detailed trial protocol and statistical analysis plan
- **Case Report Forms (CRF):** Standardized data collection forms
- **Safety Monitoring:** DSMB composition and interim safety analysis
- **GCP Compliance:** Good Clinical Practice compliance

 **Key Point:** The key to AI clinical trials is demonstrating algorithm transparency, reproducibility, and generalizability, with appropriate control group setup being crucial

## Post-Market Surveillance (PMS)

Post-market surveillance is a system that **continuously monitors safety and performance** in **real-world environments**

### Performance Monitoring

Track accuracy, sensitivity, and specificity in real-world environments

### Safety Surveillance

Report and analyze adverse events, malfunctions, and user errors

### PMS Activities

- **Active Surveillance:** Regular performance data collection and analysis
- **Passive Surveillance:** Receive reports from users and patients
- **Complaint Management:** Investigate complaints and implement corrective actions
- **Field Safety Corrective Action (FSCA):** Recall or update when necessary

### Periodic Reporting

- **PSUR (Periodic Safety Update Report):** EU MDR requirement
- **MDR (Medical Device Report):** FDA adverse event reporting
- **PMCF (Post-Market Clinical Follow-up):** Ongoing clinical data collection

### Data Collection

Usage patterns, performance metrics

### Trend Analysis

Performance changes over time

### Early Warning

Early detection of problem indicators



**Key Point:** Since AI systems are sensitive to deployment environments and data distribution changes, proactive and continuous PMS is particularly important

## Adverse Event Reporting

Adverse event reporting is an essential element to **ensure patient safety** and maintain **regulatory compliance**

### Adverse Event Definition

Death, serious injury, or malfunction related to device use

### Reporting Obligation

All manufacturers, healthcare facilities, and importers have reporting responsibilities

### Reporting Deadlines (FDA MDR)

- **Death events:** 30 calendar days (manufacturer to FDA and user)
- **Serious injury:** 30 calendar days (manufacturer to FDA)
- **Malfunction:** 30 calendar days (manufacturer to FDA)
- **5-day report:** In case of immediate public health risk

### Reporting Channels

- **USA:** FDA MedWatch, MAUDE database
- **EU:** EUDAMED, Competent Authority
- **Canada:** Health Canada MedEffect
- **Korea:** MFDS medical device adverse event reporting

### Report Content

Event details, device information, patient information (anonymized), investigation results

### Follow-up

Submit supplementary report when additional information is found

**⚠ Key Point:** Failure to make timely and accurate reports may result in regulatory sanctions and threaten patient safety. Establishing clear internal processes is



## Compliance Auditing

**Compliance auditing** is the process of **systematically verifying** compliance with regulatory requirements

### Internal Audit

Self-compliance inspection

### External Audit

Third-party certification body review

### Regulatory Audit

FDA, EMA and other authority inspections

### Audit Checklist Items

- **QMS (ISO 13485):** Quality Management System conformity
- **Design Control:** Design input, verification, and validation documents
- **Risk Management (ISO 14971):** Risk analysis and mitigation measures
- **Software Verification:** IEC 62304 compliance
- **Clinical Evaluation:** Securing sufficient clinical evidence
- **Labeling:** Appropriateness of instructions for use and warning labels
- **CAPA:** Corrective and Preventive Action System
- **Complaint Handling:** Complaint management process

### Document Preparation

Complete DHF, DMR, Design History File, etc.

### Continuous Improvement

Process improvement based on audit findings

**💡 Key Point:** It is important to maintain regulatory readiness through regular internal audits and to identify and resolve issues in advance before external audits

## Case Law Analysis - AI Medical Device Cases

Case law related to AI medical devices serves as the foundation for future regulations and liability interpretation

### Key Dispute Cases

- **Misdiagnosis Liability:** Physician's diagnostic error following AI recommendations - Who is responsible?
- **Black Box Transparency:** Legal liability for unexplainable AI decisions
- **Data Bias:** Harm caused by poor performance in specific populations
- **Software Updates:** Accidents due to performance degradation after updates

#### Precedent Analysis

Study of judgment patterns in similar cases

#### Legal Doctrine Formation

Development of AI medical device-specific legal principles

### Risk Mitigation Strategies (Based on Case Law)

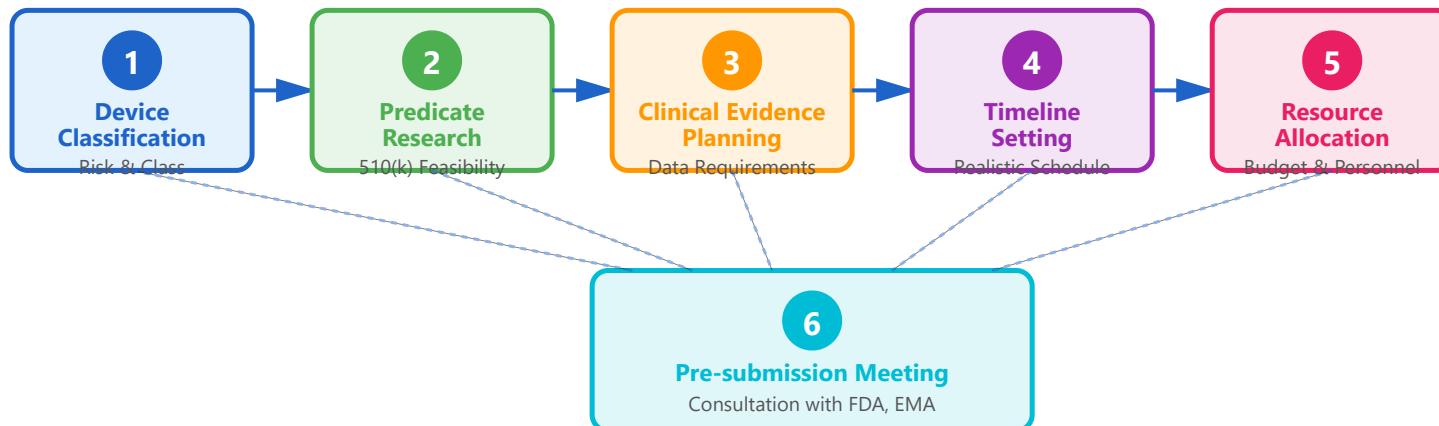
- **Clear Usage Guidelines:** Specify indications, limitations, and contraindications
- **Comprehensive Validation Documentation:** Performance evidence in diverse environments
- **User Training:** Appropriate training programs and completion certificates
- **Quality System:** Robust QMS and PMS operations

 **Key Point:** While case law is still in its early stages, transparency, verifiability, and proper oversight are emerging as core elements of legal defense

## Regulatory Strategy - Pathway Selection

An effective **regulatory strategy accelerates market entry** and reduces costs

### 6-Step Strategy Development Roadmap



#### Fast Track

510(k), Expedited review

#### Balanced Pathway

De Novo, Class IIa

#### Comprehensive Pathway

PMA, Class III

**Key Point:** Collaborating with regulatory experts in the early stages to establish a strategy reduces the risk of development direction changes and increases approval success rates

## Future Policy Directions

**Future regulatory policies are evolving in line with AI technology development**

### **AI Act (EU)**

Comprehensive regulatory framework for high-risk AI systems

### **Adaptive Regulation**

Flexible regulatory model for continuously learning AI

### **Expected Policy Changes**

- **Real-World Evidence Expansion:** Increase in RWE-based approvals
- **Digital Health Integration:** Integrated regulation of SaMD, wearables, and telemedicine
- **Enhanced Algorithm Transparency:** Growing requirements for Explainable AI
- **Fairness Assessment:** Mandatory bias testing and fairness metrics
- **Strengthened Cybersecurity:** Expanded software security requirements
- **Accelerated International Harmonization:** Global standardization centered on IMDRF

### **Performance Standards**

Standardized benchmarks and metrics

### **Audit Automation**

AI-based regulatory compliance tools

### **Digital Twin**

Simulation-based validation

 **Key Point:** Regulations are evolving to ensure patient safety without hindering innovation, and companies must proactively prepare for these trends

# Thank you

## 핵심 포인트

- FDA, EU, 국제 규제 프레임워크 이해
- 적절한 규제 경로 선택 및 전략 수립
- 법적 책임과 리스크 관리
- 시판 후 감시 및 컴플라이언스 유지

Ho-min Park

[homin.park@ghent.ac.kr](mailto:homin.park@ghent.ac.kr)

[powersimmani@gmail.com](mailto:powersimmani@gmail.com)