Application of medical device regulatory science to life cycle for a wearable bladder monitoring system

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Application of medical device regulatory science to life cycle for a wearable bladder monitoring system

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Abstract

Application of medical device regulatory science to life cycle for a wearable bladder monitoring system

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Medical device regulatory science is a diverse scientific method for evaluating safety, effectiveness, quality, and performance of a medical device throughout its life cycle. As various regulatory requirements are supplemented to keep pace with technological development and the rising importance of post-market management, regulatory framework covering entire product life cycle has been introduced.

Conventional research has focused primarily on design and development rather than on the overall product life cycle, or on specific approaches such as risk management or specific requirements such as cybersecurity and usability. In addition, there is a lack of research that comprehensively covers the application of regulatory science throughout the life cycle of a medical device, from idea to launch, end of lifetime, disposal, and even discontinuation.

This paper proposed a life cycle management process applying medical device regulatory science and demonstrated in two ways. First, the process from conceptualization to launch is presented step by step through the development of wearable bladder monitoring system. Second, the requirements to be considered from post-market management after product launch to discontinuation are presented from the viewpoint of regulatory science through literature review on current regulations in Republic of Korea and case analysis of predicate devices. In addition, decision factors and implementation, including regulatory aspects, of discontinuation were presented.

In this research, the wearable bladder monitoring system selected as a major case to demonstrate design and development process complying with usability engineering approaches. It suggested possible design implications that can be used in the various software medical devices including mobile health applications. In addition, the process presented in this thesis is expected to be used for the first time in developing a medical device or by a medical device manufacturer in the early stages of a startup, where a process for the entire life cycle has not been established.

Keywords: medical device regulatory science, product life cycle, usability engineering, post-market management, bladder monitoring

Chapter 1

Introduction

1.1 Background

A medical device is defined as any instrument, apparatus, implement, machine, appliance, implant, *in vitro* reagent, software, material, or other similar or related article intended by the manufacturer to be used—alone or in combination—for a medical purpose. Here, a medical purpose can be diagnosing illness, monitoring treatments, assisting disabled people, or intervening in and treating both acute and chronic illness. Medical devices directly or indirectly impact health; therefore, they are subject to regulatory controls by regulatory authorities in most countries.

Historically, the legal basis for regulation has been established and improved for tightening control after adverse incidents. The Sulfanilamide Disaster of 1937 resulted in the final enactment of the Unites States Federal Food, Drug, and Cosmetic Act—the basis for the United States (US) Food and Drug Administration (FDA) regulation of medical products—in the following year (1). Further, the Dalkon Shield Scandal led to the Medical Device Amendments of 1976, which established risk-based classification with three classes and two regulatory pathways: pre-market approval and pre-market notification (2). Recently, a new regulatory framework—the European Union Medical Devices Regulation

(EU MDR) including regulations 2017/745 and 2017/746—has been published and come into force. It was the result of the PIP Breast Implant Scandal that triggered a review of the existing policy on medical devices in Europe (3).

Regulatory science has been evolving with reinforcement of regulations in the drug and medical device industry. The term “regulatory science” in this dissertation is used as a term describing research and regulatory activities of regulatory authorities in relation to medical products. The FDA defines regulatory science as the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products (4). In addition, regulatory science is defined as the range of scientific disciplines that are applied to the quality, safety, and efficacy assessment of medicinal products and that inform regulatory decision making throughout the life cycle of a medicine (5). Considering these definitions, application of regulatory science covers various activities to prove the safety, effectiveness, quality, and performance of medical products throughout their life cycle.

1.2 Objective

This dissertation aims to provide an approach to manage medical device life cycle from conceptualization to discontinuation from the perspective of regulatory science. A wearable ultrasound bladder monitoring device is presented as an example to illustrate how regulatory science is applied or works during its life cycle. Regulatory requirements considered in the research presented herein are mainly focused on the medical device regulation in Republic of Korea (hereinafter Korea) with globally harmonized standards. Some standards and requirements are applied to advance into foreign markets such as the Unites States and European countries.

Product life cycle is characterized by three phases: beginning of life (BOL), middle of life, and end of life (EOL) (6). The research presented in this dissertation follows the medical device life cycle management process reflecting regulatory science perspectives as shown in Figure 1.1.

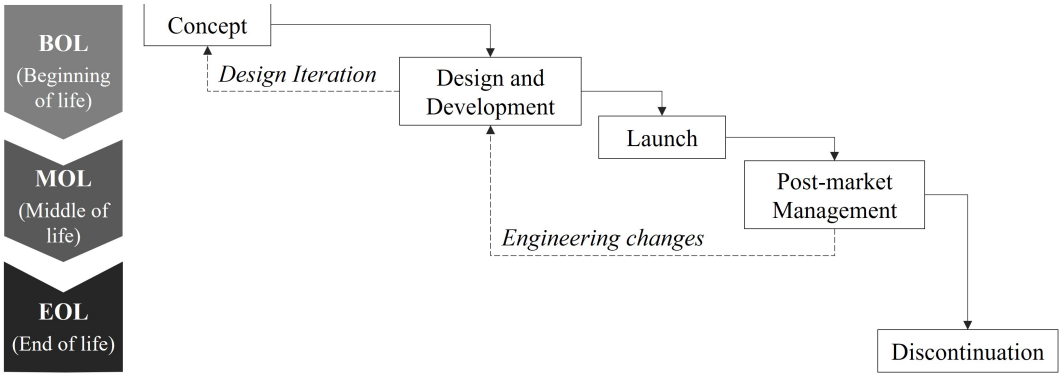


Figure 1.1 Medical device life cycle management process

1.3 Outline

This dissertation comprises seven chapters including this chapter. Chapters 3–5 constitute the main body describing the research results, whereas Chapter 6–7 discusses and recapitulates the results of this research.

Chapter 1 introduces motivations and the objective of the research. The outline of this dissertation is also presented in this chapter.

Chapter 2 explains the methodology of the research and the medical device life cycle management process. This chapter also describes the medical device design process by applying the usability engineering process.

Chapter 3 illustrates the proposed process with a case study on the development of a wearable bladder monitoring system. This chapter mainly describes the BOL phase representing several design iterations based on the usability engineering approach.

Chapter 4 demonstrates regulatory affairs to start a business in the medical device industry. This chapter prioritizes regulatory affairs for product launch of bladder scanners that are developed as an intermediate product before a wearable monitoring device.

Chapter 5 deals with post-market management, including post-market surveillance, design change management, and regulatory renewal. This chapter also explains discontinuation with four steps from the end of lifetime to the end of service life.

Chapter 2

Methodology

2.1 Medical device life cycle management process

Product life cycle is defined as the stages from the very first idea or a product all the way through until it is retired and disposed of. As presented in Table 2.1, each of phases in the product life cycle comprises several stages with following steps. In this section, medical device life cycle stages are described from the aspect of regulatory science.

Phase	Stage	Steps
BOL	Concept	• Idea development & User research • Market analysis • Definition • Strategy establishment
	Design and Development	• Design & Implementation • Verification & Validation • Design transfer & Pre-production
	Launch	• Regulatory approval • Production • Distribution & Installation
MOL	Post-market Management	• Post-market surveillance • Maintenance • Engineering change • Post-market inspection & Renewal
EOL	Discontinuation	• End of lifetime • End of sales and end of development • End of service life

Table 2.1 Medical device life cycles

2.1.1 Concept

The concept stage starts with an idea about a new medical device. The idea can be market driven with customer needs or technology driven with the application of new technology. Further, the idea should be implementable into a product with a company's capacity. Although the idea may not be unique or ground-breaking, it should not infringe existing patents. Intellectual property (IP) represents a key corporate asset, particularly for startups; therefore, IP strategy should be considered at the outset (4, 7). The initial idea is an abstract concept of an instrument with a function or purpose; it is defined as a medical device with a specific intention and functions at the end of this stage.

User research includes identifying user needs, use environment, and potential user's profile. This step is essential both in this and the next stage because additional user requirements can be identified in the design process. User research is not limited to an operator; it also includes study on patients to determine target indications or patient populations. In addition, clinical workflows related to interactions between a device and people, including an operator and a patient, should be analyzed to determine the intended use and features.

Financial feasibility is also a crucial business strategy. Through analysis of the target market, economic viability can be validated with potential profits evaluated on the basis of domestic and global market scale. Benchmarking or analyzing predicate or similar devices requires establishment of a market penetration strategy or identification of customers'

unmet needs. By comparing specifications or characteristics of benchmarks, minimum requirements or common features are also identified.

Results from the previous steps are merged into a definition of the medical device that a company wants to realize. The definition comprises intended use, user, use environment, and major principles. Establishment of regulatory strategy should be in parallel with device definition. A regulatory pathway is established depending on the product classification or class, which is determined according to intended use and operational principle.

2.1.2 Design and development

The design and development stage includes design, implementation, verification, validation, and design transfer. Design inputs from requirements initiate the design and development process, and translate specification design from the architecture level to detailed components. Then, verification and validation are conducted to confirm that the system or device is designed and developed according to the requirements or user needs.

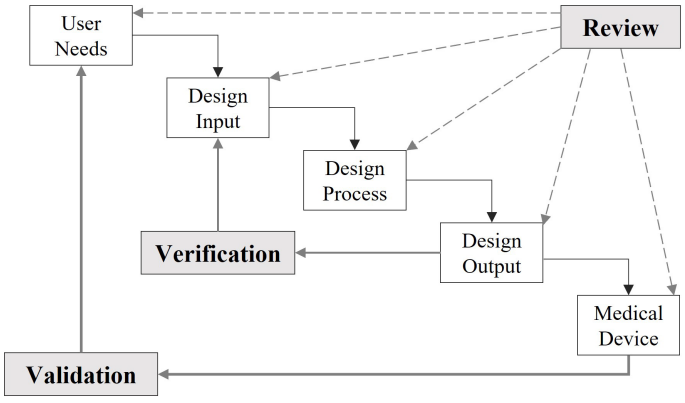


Figure 2.1 An example of design controls provided by the FDA

The FDA provides an example of design controls in a waterfall design process (8) as shown in Figure 2.1. The waterfall model is a sequential development process with each phase completely wrapping up before the beginning of the next phase. Typically, medical device software development organizations follow the V-Model as shown in Figure 2.2, which facilitates achieving traceability in verification and validation (9). The comparative method of this model is the agile method, which involves simultaneous, overlapping processes.

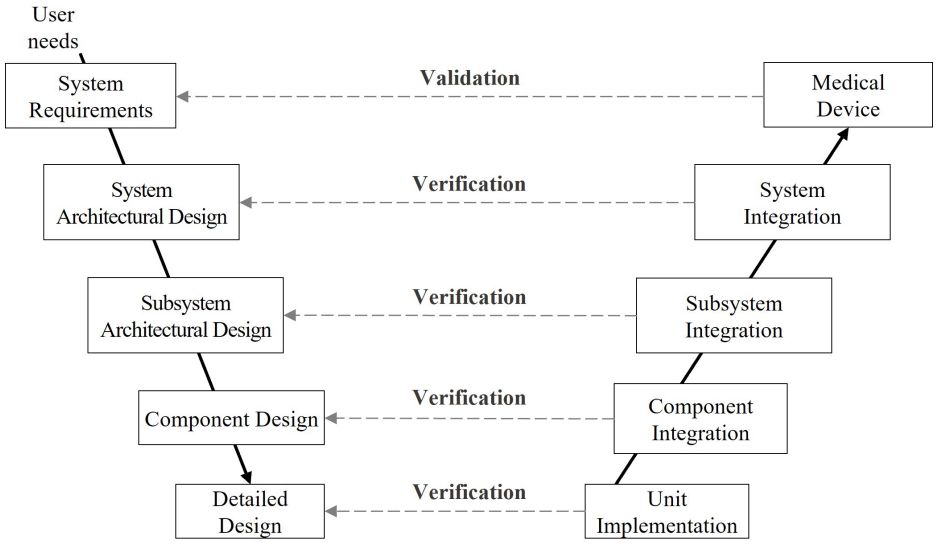


Figure 2.2 V-model based on IEC 62304

There are agile practices applicable to the development of medical device software. Figure 2.3 the result of a hybrid model from a previous study (9). Use cases, user stories, and user involvement are agile practices adopted when identifying requirement. This study implies that iteration and a full study on use can reduce the burden of design change after the commencement or completion of development.

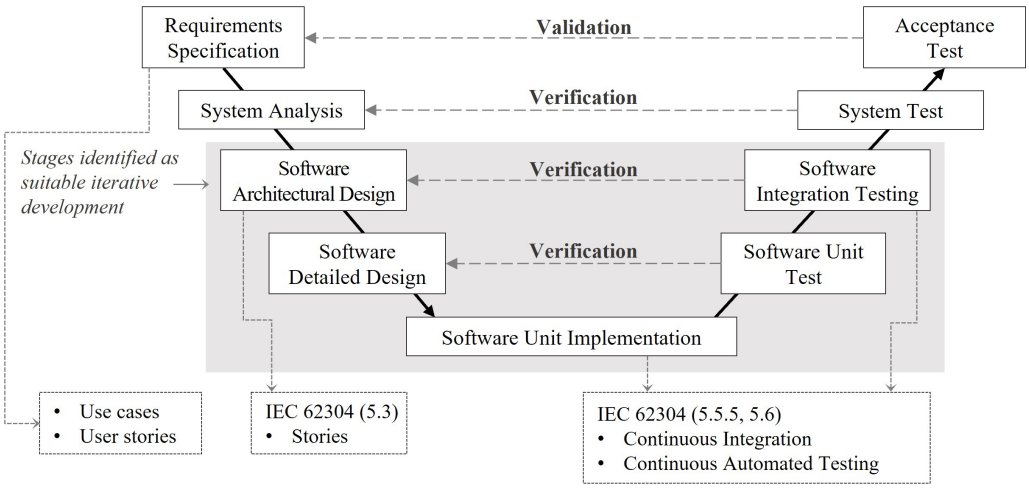


Figure 2.3 The Agile V-Model for medical device software development

Usability engineering emphasizes early involvement of users or evaluation in the design process. Many small-scale iterations in the earliest design stages may lead to a better design quality (10, 11). Furthermore, an increased proportion of formative evaluation is recommended considering summative evaluation—the final step of evaluation for certification—is likely to be a formality (12). Thus, this dissertation recommends a design process applying usability engineering, which requires design iteration with several times of small-scale evaluation.

If a medical device is validated as safe and effective, then the design and development is transferred for production. Design transfer should ensure that design and development outputs are verified as suitable for manufacturing before becoming final production specifications. This dissertation does not describe the details of production or manufacturing.

2.1.3 Launch

After a final product is released after validation, a medical device is ready to be subjected to regulatory pathways. Regulatory pathways vary according to regulatory authorities, classifications, and risk levels. As shown in Figure 2.4, medical devices are classified according to four levels, and regulatory pathways for manufacturers are distinguished depending on the risk levels. This dissertation only demonstrates the certification process given that a device similar to a wearable bladder monitoring system, namely, an ultrasonic bladder volume measurement system, is classified as a class II device in Korea.

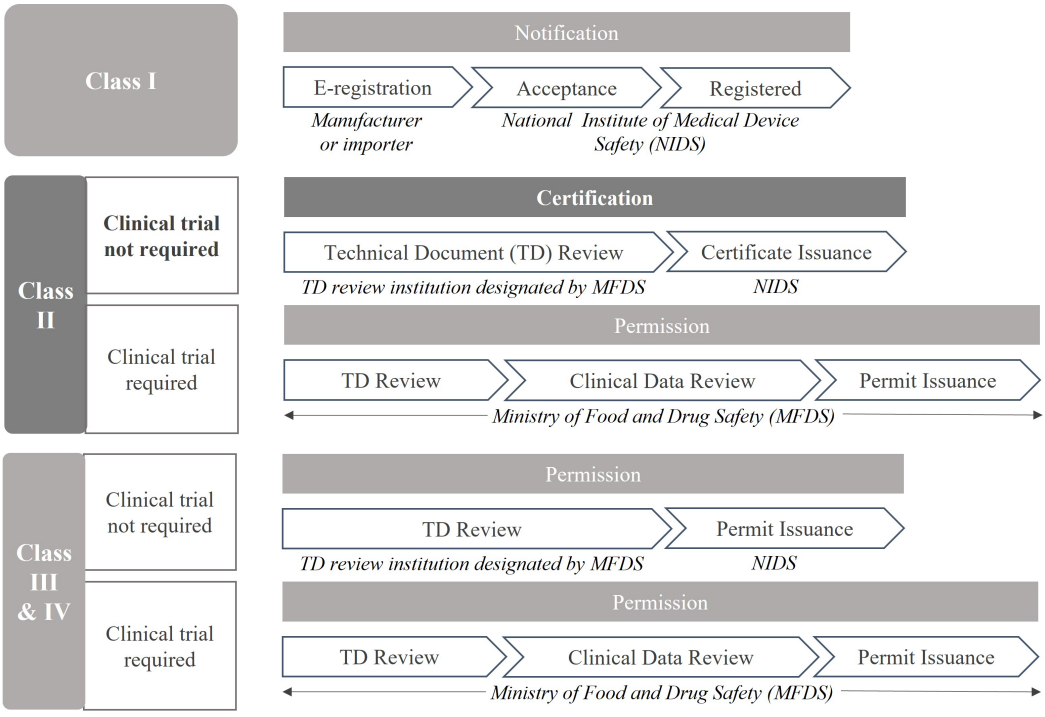


Figure 2.4 Regulatory pathways of medical devices in Korea

The Korean government operates a public health insurance system for all citizens, and all medical technologies must be registered in the list of medical care benefit items in accordance with the National Health Insurance Act to enable patients to claim the cost of treatment. Medical technology that is not listed in the medical care benefit list cannot be billed, except when a treatment is for research purpose and patient consent is received. Although the ratio of the bill that is charged to patients and the national health insurance varies, registration of medical technology in the list of care benefits is crucial.

The Health Insurance Review and Assessment Service evaluates a new technology according to economic feasibility and adequacy, and clinical data from clinical trials and literature review are grounds for evaluation. This dissertation only analyzes current benefit items related to bladder monitoring without addressing assessment of new medical technology.

2.1.4 Post-market management

In ISO 13485:2016, activities after the production are identified as installation, servicing, monitoring, and measurement, including customer feedback, complaint handling, and reporting to regulatory authorities. Moreover, improvements should be implemented to ensure and maintain the safety and performance of the medical device through post-market surveillance, analysis of data, corrective actions, and preventive actions. These activities lead to engineering changes. If the design changes, the product should undergo the design and development process again with a focus on risk management for determining whether

new risk-hazards have been identified or existing risk-hazards have been mitigated or must be reconsidered. Depending on the size or complexity of changes, additional regulatory approval would be required.

Post-market surveillance in Korea consists of re-examination, re-evaluation, renewal, tracking and control, and reporting of adverse events. Re-examination should be implemented if the device is a newly developed medical device or an orphan medical device designated by the Ministry of Food and Drug Safety (MFDS). Re-evaluation is also limited to a medical device that MFDS deems necessary to review for safety and effectiveness. The tracking and control system is applied to a medical device designated by MFDS among implantable medical devices and life-support devices. Only reporting of adverse events is a common activity for all medical devices if any adverse event occurs.

In Korea, a renewal system for medical devices was recently introduced with enforcement of regulations on renewal of medical device manufacturing permits in 2021. The renewal system has a five-year cycle; thus, renewal of existing permits is a significant regulatory consideration in post-market management. Renewal requires technical documents and safety tests; hence, harmonized or recognized conformance standards should be considered.

2.1.5 Discontinuation

There are two concepts in the EOL cycle: end of lifetime, which is related to the product's warranty or expiration date, and EOL, which implies discontinuation and end of development and service. Discontinuation originally indicates the latter; however, it is used as a broad term incorporating the end of an individual device and the discontinuation of the product. The discontinuation stage in this work is illustrated in Figure 2.5.

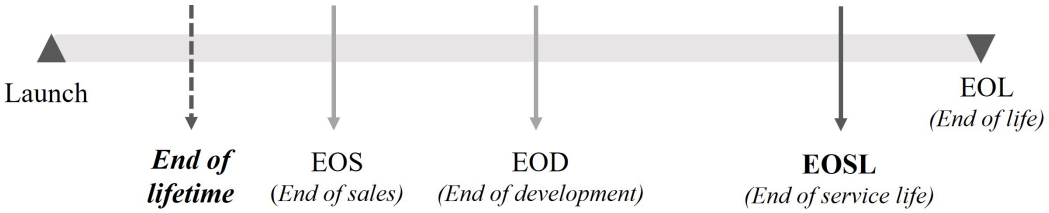


Figure 2.5 Product life cycle at discontinuation stage

Factors to determine the lifetime of the medical device include batter depletion, deterioration of materials and failure of components due to ageing, wear, fatigue or repeated use (13). Expected lifetime is defined as the time period specified by the manufacturer during which the medical device is expected to maintain safe and effective use (14). Maintenance, repairs, or upgrades may be necessary during the expected lifetime. Definition of lifetime is important not only for manufacturers but also for operators and purchasers. Operators decide decommissioning considering the expected lifetime indicated by the manufacturer, and hospital purchasers make decisions by comparing the lifetimes of similar devices.

Regulatory considerations related to EOL are risk management results from post-market

management, conformity with current regulations, regulatory activities to be implemented after product discontinuation decision, and so on. In addition, the manufacturer would analyze whether the device meets customer requirements that can evolve with the development of medical technology. When customer requirements for higher performance and new functions are discovered, the possibility of meeting them by improving the current product or the necessity of developing a new product must be decided through extensive considerations with marketing and technology insights.

2.2 Key considerations in regulatory science

There are three main questions to apply regulatory science into a medical device's life cycle as below:

a. What is the scope of the medical device life cycle that the company will cover?
b. Which countries are the target market?
c. What standards should be applied to prove the safety, effectiveness, and performance of the target medical device?

There are many businesses related to medical devices, including design, development, manufacturing, distribution, and customer management. The scope of the life cycle varies according to a company's business category. Considering a medical device manufacturer, the company decides which components to produce itself and which services to carry out. Even though the manufacturer outsources some of them, they have the ultimate responsibility for the medical device. This dissertation aims to deal with the overall life cycle; therefore, all stages in the life cycle are covered.

The second question identifies the regulatory authorities to deal with. There are differences in definitions, classifications, and regulatory frameworks depending on regulatory authorities. Regulatory authorities also define standards of a specific product or processes for compliance. International organizations, including the International Organization for Standardization and International Electrotechnical Commission, develop industrial standards. Regulatory authorities such as the European Union and the FDA have harmonized or recognized these international standards as their regulatory requirements.

This dissertation deals with regulatory science mainly focused on medical device regulations in Korea.

Two fundamental principles are adopted by most regulatory authorities as processes for compliance: quality management and risk management process. In this dissertation, establishment of quality management follows ISO 13485:2016 (15) and application of risk management follows EN ISO 14971:2012 (16). The latest version of the risk management standard is ISO 14971:2019 (17) , while the current safety compliance standard in Korea, IEC 60601-1:2012 (18), is referenced with ISO 14971:2007 (19). Application of EN ISO 14971:2012 was a strategic decision to transition to the latest standard.

Chapter 3

Beginning of life cycle: a case study of a wearable bladder monitoring system

3.1 Background

Lower urinary tract symptoms (LUTS) are prevalent and have a significant impact on quality of life. The terminology encompasses all urinary symptoms, including storage, voiding, and postmicturition symptoms (20). Aging and obesity are parts of underlying factors that affects to LUTS, so LUTS has become social problems in many countries where aging and obesity are regarded as serious public agenda. There are many other diseases and health problems accompanying LUTS.

Bladder volume measurement is widely used for diagnosing and evaluating patients with LUTS, because postvoid residual (PVR) is frequent consequence of lower urinary tract dysfunction (LUTD). Although transurethral catheterization is the golden standard to assess PVR, but this invasive method may cause discomfort for patients and increase risk of urinary tract infections and trauma (21). Thus, portable ultrasound bladder scanner, which is non-invasive tool to measure the volume, has replaced catheterization as its technology has improved with acceptable measurement accuracy (22).

Portable ultrasound bladder scanners have constraints that users and the use environment are limited to health experts and clinical settings, respectively. Thus, they cannot measure the bladder volume continuously. The needs of continuous monitoring on bladder volume have confirmed with several recent studies on bladder monitoring system (23). Continuous monitoring of bladder volume can be helpful to treat or manage symptoms in LUTS patients.

3.2 Methodology

This study deals with BOL, the first phase of medical device life cycle, including the concept stage and design and development stage. Usability was a key consideration when designing this system because it had to be usable in both inpatient and outpatient settings and for various users including the elders. Moreover, usability has become a regulatory requirement of medical devices as it turned out that poor medical device inter-faces and usability facilitates medical errors (24-26).

An iterative design process that included usability engineering was used in design and development phase in accordance with international standards of usability engineering for medical devices (27-29). In this study, the design process iterated four times and the design cycle consists of research, design, development, and evaluation as shown in Figure 3.1. The research in this dissertation deals with a mobile smartphone application, graphical user interface (GUI), industrial designs, and overall workflows.

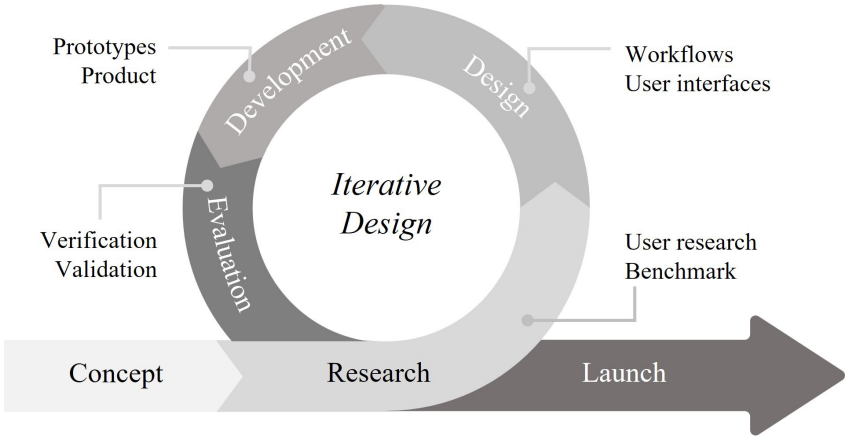


Figure 3.1 User interface design cycles applying usability engineering process

3.3 Concept

3.3.1 Idea development

The research in this dissertation illustrates with a wearable bladder monitoring system was proposed. The idea was a blending of technology and clinical needs. A research team at Sogang university has a system-on-chip solution which is optimized for point-of-care (30) and a technology of wearable ultrasound sensors (31). Feasibility of an ultrasound-based wearable device has validated through previous studies conducted by the research team.

As LUTS and disorders are prevalent and bothersome in the rapidly growing aging population (32), clinical needs were captured in voiding management. Patients who cannot sense bladder fullness or have problems with timeliness voiding their bladder, such as neurogenic bladder, urinary incontinence, were identified as our target indications. Continuous measurement of urine volume in the bladder can be helpful for those patients. Also, continuous bladder volume data can help patients keep bladder diaries, which is used as an evaluation tool of voiding dysfunctions.

Based on these ideas, an ultrasound-based wearable bladder monitoring system is proposed. As shown in Figure 3.2, an ultrasound sensor should be wearable to measure the bladder volume continuously and connected to a patient's or caregiver's smartphone to provide bladder volume data or recommend on voiding management.

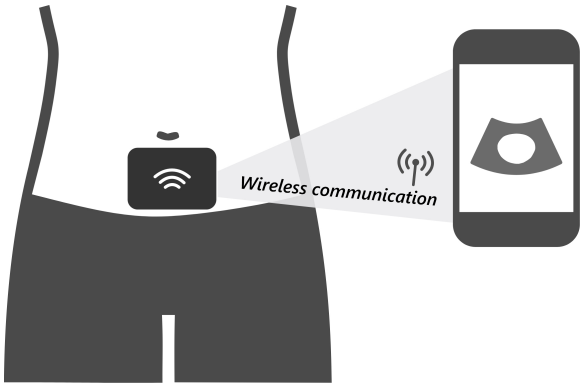


Figure 3.2 Idea sketch of a wearable bladder monitoring system

3.3.2 User research

There are many diseases that cause or accompany LUTS, however, initial target indications in this research are prostatism, neurogenic bladder, and pediatric non-neurogenic voiding dysfunction (PNVD). Prostatism is prevalent in men over 50 years (33, 34) and common diseases that cause neurogenic bladder, including dementia, cerebral infarction, are highly prevalent in the elderly (35, 36). Voiding dysfunction and urinary incontinence in children is also common (37). Urinary symptoms and treatment for these indications varies as shown in Table 3.1.

Indication	Prostatism	Neurogenic bladder	PNVD
Symptom	• Bladder outlet obstruction - Weak stream - Feeling of incompleteness - Hesitancy - Nocturia • Overactive bladder - Urgency - Frequency - Incontinence - Nocturia	• Detrusor hyperreflexia - Incontinence - Nocturia • Detrusor areflexia - Inability of emptying bladder	• Overactive bladder - Urgency - Frequency • Daytime urinary frequency • Nocturnal enuresis • Dysfunctional voiding - Fractionated voiding - Staccato voiding - Incontinence
Treatment	• Pharmacological treatments • Prostatectomy • Clinical procedure (e.g., HIFU) • Palliative treatment with follow-up	• Indwelling catheterization • Intermittent catheterization	• Pharmacological treatments • Biofeedback • Intravesical electrical stimulation • Behavioral therapy with bladder diaries

Table 3.1 Urinary symptoms and treatments of targeted indications

The wearable bladder monitoring system can be used in palliative treatment for prostatism, and it can help neurogenic bladder patients, their caregivers, and medical professionals notifying the adequate time of catheterization. For children with non-neurogenic voiding dysfunction, the wearable bladder monitoring system can assist behavioral therapy notifying their urine volume and recording the monitored volume in bladder diaries. As identified use cases of the wearable bladder monitoring system, user profiles and use environments are specified as shown in Table 3.2. The user groups are

divided into the general public and medical professionals represented by nurses, and the use environments are home and hospital.

Indication	Prostatism	Neurogenic bladder	PNVD
Use case	Palliative treatment	Catheterization • Indwelling • Intermittent	Behavioral therapy
User group	• Patient • Caregiver	• Patient • Caregiver • Nurse	• Patient • Caregiver
Use environment	Home	• Home • Hospital	Home
Demographic characteristic (e.g., age, gender, education)	• Patient - Middle-aged to old - Male • Caregiver - 20–50s - Female, male	• Nurse - 20–50s - Female, male - Educated in nursing • Patient - All ages - Female, male	• Patient - Child - Female, male • Caregiver - 20–50s - Female, male

Table 3.2 Use specification of the wearable bladder monitoring system

3.3.3 Market analysis

There are around 420 million adults with dysuria worldwide, and 8.7% of them suffer from urinary incontinence (38). The global bladder disorders market is expected to account for USD 22.3 trillion by 2029. Moreover, the global portable ultrasound bladder scanner market was valued at USD 126.3 million in 2021 and is expected to reach USD 191.7 million by 2028 with 6.1% CAGR (39).

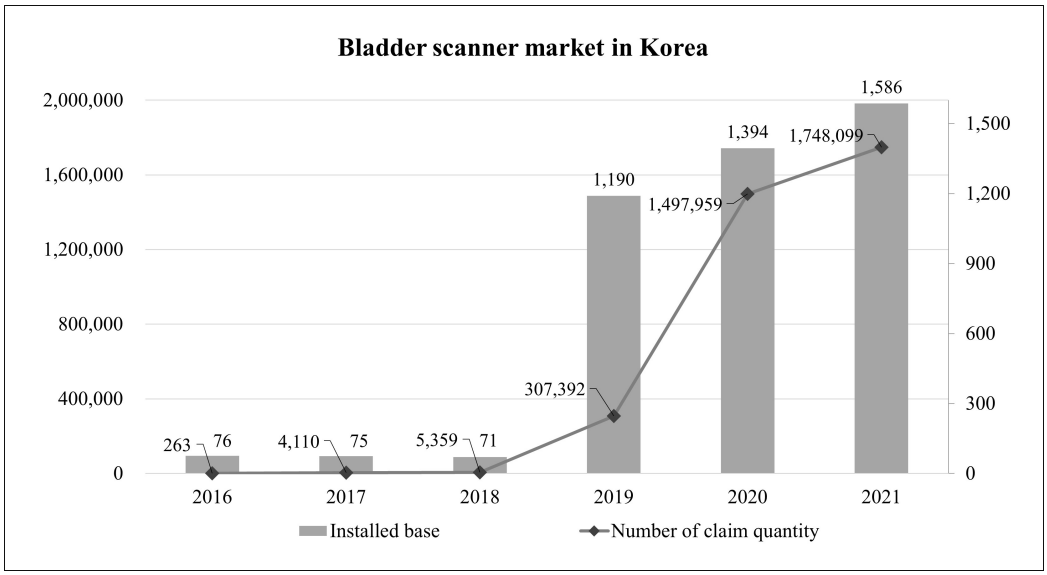


Figure 3.3 Bladder scanner market in Korea

In Korea, the prevalence of urinary disorders characterized by urinary incontinence is 6.4% for men and 7.2% for women (40). Recently, the ultrasound bladder scanner market in Korea has grown as post-void residual (PVR) measurement using bladder scan has been listed among the benefit items under national health insurance since 2019. As shown in Figure 3.3, the number of claims on PVR measurement using bladder scan has soared from 263 claims in 2016 to 1,748,099 in 2021. The domestic installation base of bladder scanners has also shown a similar increasing trend. The number of installed bladder scanners increased by 20 times in 2021 compared to 2016.

Product Name	BladderScan Prime Plus	BioCon-900S	MD-6000
Manufacturer	Verathon (Bothell, WA, USA)	Mcube Technology (Seoul, Korea)	MEDA (Tianjin, China)
Primary Component	• Console with touch screen • Probe	• Probe with touch screen	• Console with touch screen • Probe
Battery	User-replaceable (lithium-ion rechargeable battery)	Internal (lithium-ion rechargeable battery)	Internal (lithium-ion rechargeable battery)
Environment	Professional healthcare environments, such as hospitals, and clinics		
Measurement	Bladder volume • Range: 0–999ml • Accuracy: ± 7.5ml (<100ml) ±7.5% (>100ml)	Bladder volume • Range: 0–999ml • Accuracy: ± 15%, ±15ml	Bladder volume • Range: 0–999ml • Accuracy: ± 15%
Features	• Urine volume calculated with NeuralHarmonics® technology • Live imaging of the bladder	• Live imaging of the bladder • Wireless charging • Barcode scanning using an optional barcode reader	• Live imaging of the bladder in pre-scan • Image can be zoomed in

Table 3.3 Comparison of bladder scanners

There are two categories of benchmark products for the proposed system, which are bladder scanners and bladder monitoring devices. Benchmark comparison results include system configuration, battery operation, measurement performance, and features. Bladder scanners are intended as medical devices and mostly contain touchscreen provided in Table 3.3, whereas bladder monitoring devices are intended as medical devices and connected to a mobile application except Dfree as shown in Table 3.4.

Product Name	Dfree	SENS-U	Lilium a-200
Manufacturer	Triple W Japan Inc. (Tokyo, Japan)	Novioscan (Nijmegen, Netherlands)	Lilium Ostuka Co., Ltd (Kanagawa, Japan)
Primary Component	• Wearable ultrasonic sensor • Mobile application	• Wearable ultrasonic sensor • Mobile application	• Portable ultrasound bladder scanner • Continuous monitoring
Battery	Internal (lithium-ion rechargeable battery)		Internal (Two AA batteries)
Use environment	Home	Home	Professional healthcare environments
Measurement	Relative fullness of the bladder (level: 1 – 8)	Relative fullness of the bladder (range: almost full–full)	Bladder volume • Range: 1–999ml • Accuracy: ±15% ±20mL
Features	• Initially wired type (2018) • New product: wireless type (2022) • Urination notifications	• Wireless communication via Bluetooth • Position checking using the smartphone application • Urination notifications	• A-mode • PVR Mode • Urination timing mode • Periodic measurement mode • Urination diary functions

Table 3.4 Comparison of bladder monitoring devices

3.3.4 Definition

By combining overall activities in the concept stage, the wearable bladder monitoring system was defined as shown in Table 3.5.

Product name	Ultrasonic bladder monitoring system
Intended use	The device is intended for monitoring bladder volume by measuring bladder volume periodically. By projecting ultrasound energy through the lower abdomen of the patent, the device obtains bladder images and uses them to calculate the bladder volume. The device includes a mobile application, which is a software to control the ultrasonic sensor, display volume data, and notify or make recommendations to the user on the basis of monitoring results.
Anatomical site	• Contacted to lower abdomen skin • Clinical application using ultrasound energy: bladder
Components	• An ultrasonic sensor that can be wearable • Smartphone mobile application connected to the sensor • Ultrasound gel pad that can be attached to patient's skin
Patient / User	• Target population: male, female, and pediatric (> 6 years of age) • User: general public including patients and caregivers, medical professionals
Ultrasonic characteristics	• Modes of operation: B-mode • Center frequency: 2–4 MHz
Essential performance	• Acoustic output • Bladder measurement accuracy

Table 3.5 Product definition of proposed system

3.3.5 Strategy establishment

Regulatory strategy should be established in the early stages of the life cycle. The wearable bladder system shares similarity with an ultrasound imaging system and an ultrasonic bladder measurement system, which is also known as a bladder scanner, in terms of operational principles. The applicable international standards, which are regulatory requirements considered in this research, are listed in Table 3.6.

Standard	Title
ISO 13485:2016	Medical Devices Quality Management System – Requirements for Regulatory Purposes
ISO 14971:2007 EN ISO 14971:2012	Medical Devices - Applications of Risk Management to Medical Devices
IEC 60601-1:2005+AMD1:2012	Medical electrical equipment – Part 1: General requirements for basic safety and essential performance
IEC 60601-1-2:2014+AMD1:2020	Medical electrical equipment – Part 1-2: General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances – Requirements and tests
IEC 60601-1-6:2010+AMD1:2013	Medical electrical equipment – Part 1-6: General requirements for safety – Collateral standard: Usability
IEC 62366:2007+AMD1:2014 IEC 62366-1:2015	Medical device – Application of usability engineering to medical devices Medical devices – Part 1: Application of usability engineering to medical devices
IEC TR 62366-2:2016	Medical devices – Part 2: Guidance on the application of usability engineering to medical devices

Standard	Title
IEC 60601-2-37:2007+AMD1:2015	Medical electrical equipment – Part 2-37: Particular requirements for the basic safety and essential performance of ultrasonic medical diagnostic and monitoring equipment
IEC 62304:2006+AMD1:2015	Medical device software – Software life-cycle processes
ISO 15223-1:2021	Medical devices – Symbols to be used with medical device labels, labelling and information to be supplied – Part 1: General requirements
ISO 7010:2019	Graphical symbols – Safety colors and safety signs – Registered safety signs
ISO 10993-1:2018	Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process
ISO 10993-10:2021	Biological evaluation of medical devices — Part 10: Tests for skin sensitization
ISO 10993-12:2021	Biological evaluation of medical devices — Part 12: Sample preparation and reference materials

Table 3.6 Conformance standards

In Korea, ISO 10993 series are not regulatory requirements because an ultrasonic probe is not considered a surface-contacting device, given that the probe should be used with an adequate amount of ultrasound gel and contact only undamaged skins. However, in the Unites States, the ultrasonic probe is categorized as a surface-contacting device that has limited exposure to undamaged skin. If the exposure time is longer than 24 hours, the exposure is classified as prolonged exposure requiring additional tests. Considering skin sensitization issues, the exposure time was assumed as under 24 hours in this research.

3.4 Design and development

3.4.1 First design iteration

The GUI is displayed on the mobile application providing measurement control, displays of measurement results. At the early stages in design process mainly focuses on designing graphical user interfaces where most interactions with users occur. The first design iteration initiated with identifying functional requirements based on benchmark and clinical workflow analysis as given in Table 3.7. Patient management, device positioning, data management, and review are common features, whereas bladder volume measurement and notification varied by disease, and symptom.

Use scenarios are distinguished depending on the patient type, so the home screen was designed to make the user select a patient type for entering main screens for each scenario. Patient icons on the home screen respectively indicates a patient with prostatism, a patient with neurogenic bladder, and a patient with non-neurogenic pediatric voiding dysfunction. As shown in Figure 3.4, which were developed using Microsoft PowerPoint (Microsoft Corporation, Redmond, WA, USA), each patient type has own main screen with different functions. For example, the main screen for pediatrics contains urgency recording function to merge urine volume, which can be calculated with bladder volume difference, and urgency to record in a bladder diary.

Function	Requirements
Patient management	• Patient type which affects to use scenarios or ultrasound imaging parameter should be selected at initial setup • An operator can start scanning without patient registration • Patient information: ID, name, gender, birthdate
Device status	• Users can easily confirm the device connection status • Users can easily confirm the battery level and power status of the device
Device positioning	• Positioning is required prior to measurement • Instruction about how to position the device on the patient's abdomen should be provided
Bladder volume measurement	• Measurement results should be displayed • Volume should be measured automatically with a period set by the user • Users can measure the volume manually • Users can record urination urgency
Review	• Volume data can be reviewed as trends over various time periods
Data management	• Volume data should be integrated with patient data • Users can view, export and delete data
Notification	• Urination can be recommended by continuous volume monitoring • Patients who need intermittent catheterization should be notified voiding in regular basis. • Patients with nocturia need limitation on fluid intake at night.

Table 3.7 Functional requirements identified at first design iteration

(A) Common GUI

(B) Patient type – Prostatism

(C) Patient type – Neurogenic bladder

(D) Patient type – Pediatric non-neurogenic voiding dysfunction

Figure 3.4 User interface designed at the first iteration

Use scenarios by patient type or major symptoms are defined as described in Figure 3.5. Prostatism patients with bladder outlet obstruction have difficulty in completing urination, so they need to confirm PVR volume after urination triggered by feeling urge to void. Confirming the measured bladder volume, they can decide whether to go a toilet for completion of voiding. The use scenario for neurogenic bladder is intended to help the efficient bladder management of inflow due to water intake and discharge through catheterization. Overactive bladder is a symptom that occurs in both patients with prostatism and pediatric non-neurogenic voiding dysfunction, so they share the same workflows. Patients can decide urination based on volume measurement results and they may wait until the urine is accumulated sufficiently.

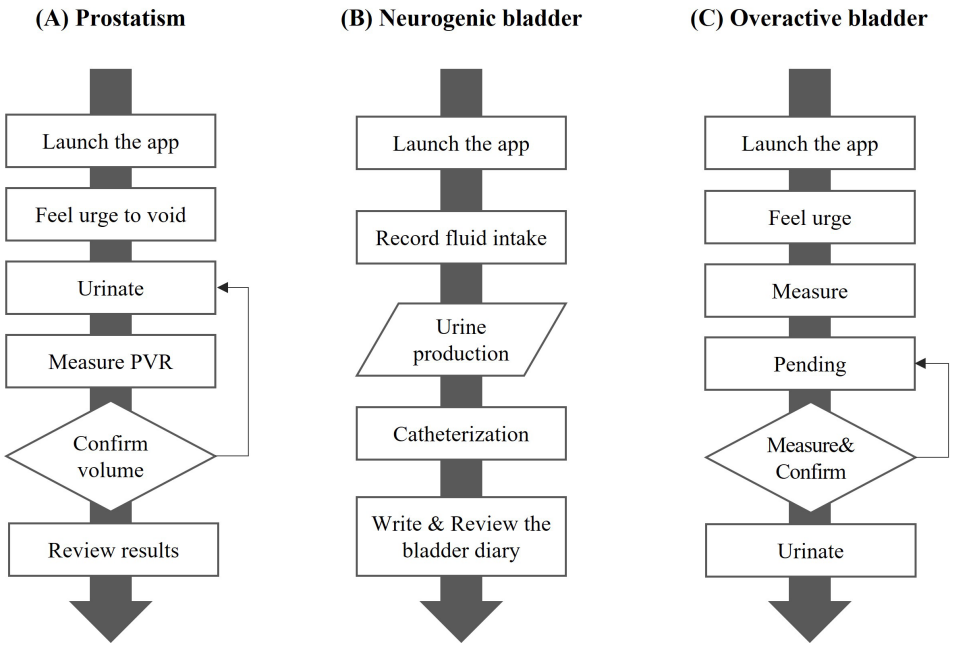


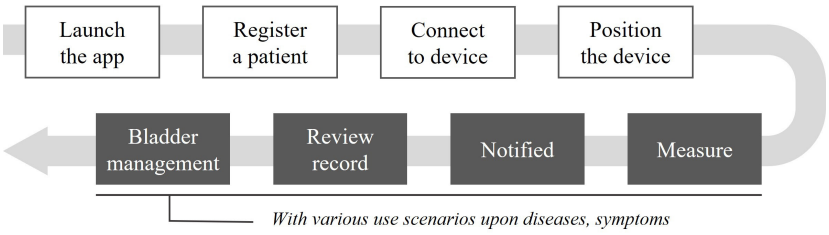
Figure 3.5 Use scenarios of the mobile application

An advisory panel review was conducted to evaluate design concepts, and the user interface. The panel consisted of various experts including urologists, biomedical engineers, a nurse, and a sonographer. The panel suggested that it is inefficient to select the disease type on the launch screen, because healthcare practitioners sometimes need to measure urine volume without registering a patient. It also noted that the diseases that clinical workflows were designed for were relatively limited given the variety of LUTS. From a usability viewpoint, the icons and language should be changed to better accommodate wide range of users including the elderly and children.

3.4.2 Second design iteration

The second design cycle was initiated to improve the user interface based on the advisory panel review. Prostatism patients with bladder outlet obstruction often overactive bladder (41), so the clinical workflow for overactive bladders was integrated with the one for prostatism. As fluid intake volume is a common component of bladder diaries, so it was made a common part of the user interface. As a result, the workflow was integrated providing same GUI that users can setup measurement configuration according to their needs. Figure 3.6 shows the integrated workflow and the mobile application prototype developed using Adobe XD (Adobe Inc., SanJose, CA, USA). Design components, like a navigation menu, graphical icons, and tabs, were adopted to enhance usability.

(A) Integrated workflow



(B) Mobile application prototype

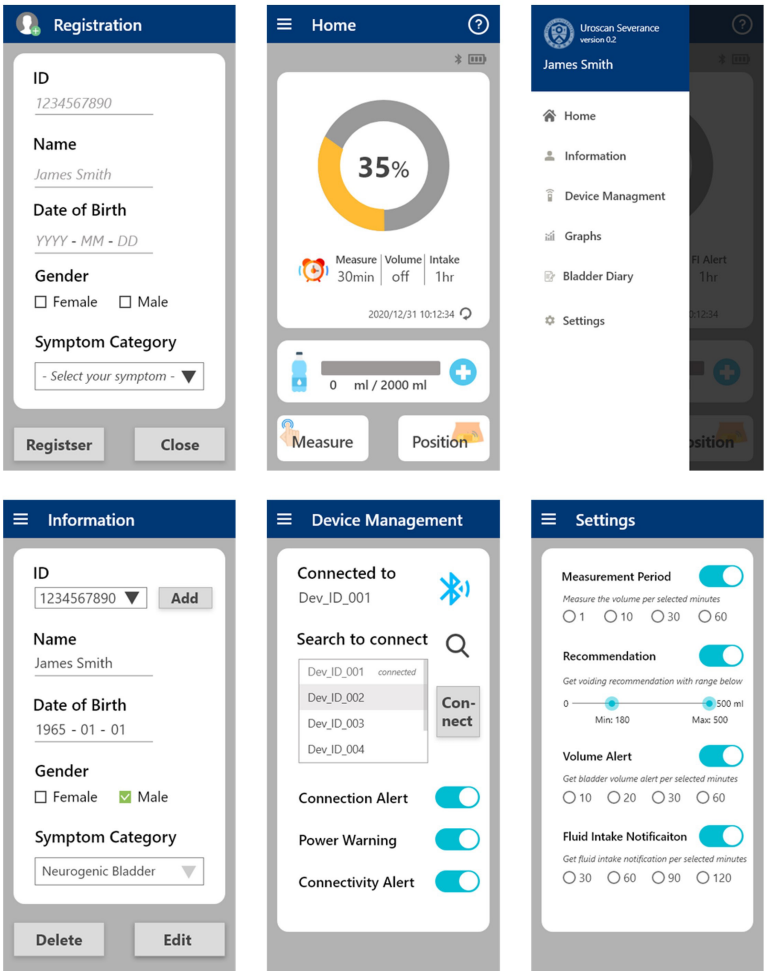


Figure 3.6 Second design iteration of the user interface

At second design cycle, ultrasonic sensor module was designed providing a dimension a weight of the ultrasonic sensor estimated with components data including a system board, a power board, a battery, and a transducer. With this information and the prototype of the mobile application, a second advisory panel review was conducted. Feedback from the review was categorized as relating to either the physical user interface such as the ultrasonic sensor and the ultrasound gel pad, and the application's GUI in Table 3.8.

Above all, the thickness of the ultrasonic sensor should be considered as appropriate to be wearable. There were concerns about remaining attachment with various factors including skin characteristics, shapes of abdomen and patient's movement. Considering its wearable characteristics, the device should be resistant to water invasion and the ultrasound gel pad should be biological compatible not causing skin irritation. The panel also emphasized that the application's procedure for positioning the device should be more efficient and provide more detailed descriptions. One of important feedback related to technological requirement was measurement results format that should be displayed in milliliters rather than percentages.

Category		Feedback
Ultrasonic sensor	Dimension	The thickness of the device should be considered when hardware components are selected and arranged.
	Battery capacity	Fully charged devices should last about a day or users should be able to replace discharged batteries with charged ones.
	Measurement accuracy	• Factors that influence on the attachment of the device to the patient, such as abdominal circumference and skin characteristics, should be confirmed. • Impact of patient posture should be verified.
	Durability	• The device should be waterproof to be able to be used in everyday situations.
Ultrasound gel pad		Long time attachment of the gel pad shall not cause skin irritation.
Application	Device positioning	Detailed descriptions should be provided in the application to help the user understand positioning procedures.
	Measurement	• Automatic measurements should take place every 30 minutes to 4 hours. • Measurement results should be displayed in milliliters rather than percentages.
	Notification	Voiding recommendation notifications should be customizable by disease and symptoms.
	Input of fluid intake	It is uncommon to use a scroll bar to input fluid intake volume. An easier method should be used considering the wide age range of potential users.
	Record management	• Bladder diaries and graphs of measurement results would be useful for clinicians. • It would be better to have bladder diaries synchronize with the electronic medical record (EMR) system or hospitals' network servers.

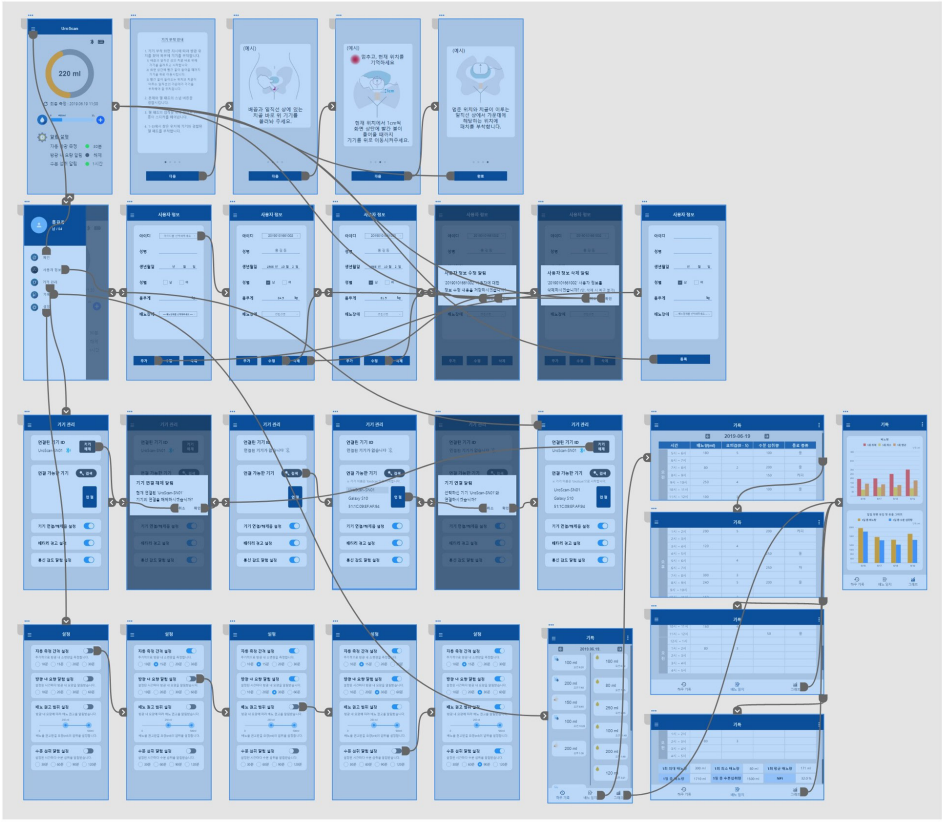
Table 3.8 Summary of the secondary advisory panel's user interface feedback

3.4.3 Third design iteration

The third design cycle was initiated based on requirements derived from the second advisory panel. The bladder diary and related graphs were modified to help urologists evaluate patients' symptoms. A daily record function was added to allow patients to better understand and manage their bladder activities. To help users understand certain procedures, like how to connect the device to the application via Bluetooth and how to position the device, instructions in pop-up windows were added with sample pictures. Figure 3.7 includes results of designing the application using Adobe XD that allows users to design both graphical components in screens and interaction among screens.

In this cycle, the industrial design of the system was also addressed. To design components including buttons and light-emitting diode (LED)s, design requirements were identified. Two buttons are required for the power and wireless communication, and the LED color should be three to indicating battery status, communication status, and the device status. IEC 60601-1-8 and AAMI HE 75 presents recommended color coding. For instance, green indicates that the device is ready to use and red means warning requiring immediate response of an operator. An ultrasound adhesion gel pad was also designed to maintain the position of the device on the patient's abdomen.

(A) Mobile application prototype including interactions among screens



(B) Design sketch of the wearable bladder monitoring system

Figure 3.7 Third design iteration of the user interface

A usability test was conducted using a simulated version of the mobile application and a mockup of the proposed device. Formative usability evaluation is a useful tool to evaluate overall designs before the components are integrated or the device is completed to be developed. Three nurses and two urologists participated the evaluation. Participants were instructed to use the mobile application and score its usability and leave relevant comments if they were able to. They were also asked to rate their satisfaction using the After-scenario Questionnaire (ASQ). As shown in Table 3.9, the results indicate that participants were satisfied with the proposed system overall, though some tasks had large standard deviation (SD)s. Those who were less satisfied with certain tasks indicated that the application's usability should be enhanced because elderly patients would likely have difficulty using their smartphones.

Task	**Questionnaire**	**Satisfaction**	
		Mean	**SD**
Patient registration	Ease of task completion	5.40	1.95
	Time to complete a task	6.20	0.84
	Adequacy of supporting information	6.20	0.45
	Average score	**5.93**	**0.98**
Device connection	Ease of task completion	5.20	2.39
	Time to complete a task	5.40	2.51
	Adequacy of supporting information	6.40	0.55
	Average score	**5.67**	**1.73**
Measurement	Ease of task completion	5.60	2.07
	Time to complete a task	5.60	2.07
	Adequacy of supporting information	6.40	0.55
	Average score	**5.87**	**1.50**
Review	Ease of task completion	5.80	1.64
	Time to complete a task	5.80	1.64
	Adequacy of supporting information	6.40	0.55
	Average score	**6.00**	**1.22**

Table 3.9 Usability test result: user satisfaction by ASQ score

Participants were asked to attach the gel pad to themselves when rating their satisfaction with the device along a 5-point Likert scale. Table 5 shows the results of subjective evaluation of the device and the ultrasound gel pad. Participants suggested that the device should be smaller and lighter to be more convenient to wear and that other methods of wearing the device, such as a belt or medical dressing, should be developed.

Category	Questionnaire	Mean	SD
Device	I was satisfied with the size and weight of the device	2.20	0.84
	I was satisfied with the position of the control buttons	3.20	1.10
	I was satisfied with the aesthetics of the device	3.20	1.10
Ultrasound gel pad	I found the gel pad easy to attach to the device	3.20	1.10
	I found the instructions about how to attach the gel pad to the device and the patient's body easy to understand	3.60	0.89
	I was satisfied with the adhesion of the gel pad	3.20	0.45
	I found the gel pad be wearable	2.80	0.45

Table 3.10 Usability test result: subjective evaluation

3.4.4 Fourth design iteration

After analyzed evaluation results, improvements to the overall user interface were derived given in Table 3.11. A major improvement was made in the product form similar to the initial version of Dfree—one of benchmark devices—which comprises a small wearable sensor and main body with a LED, power button, and USB connecting port. The change in the small sensor wired to the main body is intended to satisfy the requirements of miniaturization and attachment persistence.

Feedback from usability test	Improvement
Better to become smaller and lighter	Miniaturization and weight reduction
Rectangular shape is more stable than circular shape	Make the shape of the device enclosure rectangular
Button position adjustment is required, as the device is attached to the belt line	Move the buttons to the side of the device and consider other types of buttons (e.g., push, sliding)
Additional apparatus for fixing should be considered, e.g., belt, dressing	• Separate the ultrasonic sensor from the power module to minimize the device attachment surface • Manufactured in the form of a clip on the rear of the unit containing the power and communication modules

Table 3.11 Design improvement reflecting feedback from usability test

Figure 3.8 Design sketch of the wearable bladder monitoring system

Some improvement methods were suggested for the mobile application as presented in Table 3.12, and these were translated into software requirements which were documented in the software requirements specification.

Feedback	Improvement method
Difficulty entering ID when entering user information	• Generate patient ID automatically • Read patient's barcode • Load from EMR database
Adequate measurement period is 15–30 minutes	Set 15 minutes as the default measurement period
Duplicate alarms—visible and audible—are needed	Display a notification window with a vibration or sound
Difficulty faced by the elderly in using the mobile application	Make the patient use only simple basic functions (e.g., measurement and input fluid intake) and let the medical staff set up the configuration, register the patient, or connect the device
The font size is too small for the elderly	Enlarge font size

Table 3.12 Suggestible design improvement for the mobile application

Minor revisions to the GUI were made to improve its usability, and the revised GUI was evaluated through heuristic analysis. Zhang's heuristics (presented in Table 3.13), which were developed for usability evaluation of medical devices (42), were used in this study. During heuristic evaluation, evaluators examine an interface for usability problems by perusing the interface and identifying elements that violate the heuristics.

Heuristic	Definition
Consistency (standards)	Users should not have to wonder whether different words, situations, or actions mean the same thing. Standards and conventions in product design should be followed
Visibility	Users should be informed about what is going on with the system through appropriate feedback and display of information
Match – between system and world	The image of the system perceived by users should match the model the users have about the system
Minimalist	Any extraneous information is a distraction and a slow-down
Memory – minimize memory load	Users should not be required to memorize a lot of information to carry out tasks. Memory load reduces users' capacity to carry out the main tasks
Feedback	Users should be given prompt and informative feedback about their actions
Flexibility (efficiency)	Users always learn and users are always different Give users the flexibility of creating customization and shortcuts to accelerate their performance
Message – good error messages	The messages should be informative enough such that users can understand the nature of errors, learn from errors, and recover from errors
Error – prevent errors	It is always better to design interfaces that prevent errors from happening in the first place
Clear closure	Every task has a beginning and an end. Users should be clearly notified about the completion of a task
Undo – reversible actions	Users should be allowed to recover from errors Reversible actions also encourage exploratory learning
Language – Use user's language	The language should be always presented in a form understandable by the intended users
Control – users in control	Do not give users that impression that they are controlled by the systems
Help and documentation	Always provide help when needed

Table 3.13 Zhang's 14 heuristics for usability evaluation of medical devices

In this study, five usability experts independently evaluated the GUI of the mobile application developed in the fourth design cycle. At the beginning of the heuristic evaluation session, evaluators were trained on the Zhang's 14 heuristics and the evaluation subject. Once they finished to identify the violated heuristics, the separate lists were compiled into a single master list as given in Table 3.14.

Task	Usability problem
Register a patient	• List icon (▼) of symptom classification, and bladder measurement interval is too small • Difficult to view application guide (suggestion: change colors or bold only for important content) • When inputting information, the input field does not go up on the keypad, so it is inconvenient. • Requires uniform font size for bladder model input • The maximum number of input characters needs to be fixed for entering date of birth.
Edit the information	• Lack of haptic feedback when selecting the bladder model (suggestion: button color change)
Connect a device and setup	• Match the text color of "Find" to improve visibility • Text color changes when connecting with a connectable device, or a status message is required • The text color of the attachment guide should be darker • Inconsistent color, size, and spacing between buttons
Measure manually	• Refreshing the volume is confusing because there is no refresh icon next to the recent measured time. • Measurement instructions with photos or animations are needed.
Confirm the notification	• There should be an indication for unacknowledged notifications • Notification content is not easy to view or read (suggestion: highlight with text color) • Notification windows should be matched with the overall design • The alarm/alert is expected to ring for notification.

Task	Usability problem
Input urination	• There should be a displayed numeric value for selected urine urge • The urge level should be displayed with a numeric value, same as it is displayed in bladder diaries.
Input fluid intake	• The button, which is located at the center, has low visibility • The "-" icon on the fluid intake input screen is gray, so it is difficult to view (suggestion: change the color to red).
Bladder diary	• Unit (ml) of water intake should be written in a bladder diary • The landscape screen of the bladder diary is inconsistent with others.
Setup	• Difficult to check the setup value when setting the urination advisory notification range (suggestion: display with numbers, input max/min, provided as a list) • Notification settings need grouping of notification setup.

Table 3.14 Identified usability problems from the heuristic evaluation

With the master list, the evaluators assess the severity of each violation following the severity rating scale (43) as presented in Table 3.15. When rating the severity, the evaluators consider that the problem will persistently bother or cause harm to the patient or operator. The severity rating was used as a reference or criterion for prioritizing design changes to address the usability problems identified from the mobile application.

Scale	Description
0	Not a usability problem at all
1	Cosmetic problem only. Need not be fixed unless extra time is available
2	Minor usability problem. Fixing this should be given low priority
3	Major usability problem. Important to fix. Should be given high priority
4	Usability catastrophe. Imperative to fix this before product can be released

Table 3.15 Severity rating scale

The ratings from the individual evaluators were averaged as Table 3.16. The most frequently violated heuristic was visibility, but the severity was rated low. The overall design should be improved to increase visibility, and some screens related to device connection, notification confirmation, and urination input should be improved.

Task	Heuristics violated	Severity (Mean)
Register a patient	Visibility	1.33
	Errors	1.00
	Consistency	1.00
Edit the info	Feedback	1.00
Connect a device	Visibility	1.00
	Consistency	3.00
	Feedback	1.00
Setup the device (Device management)	Visibility	1.00
	Consistency	1.00
Measure manually	Visibility	1.00
	Help and documentation	1.00
Confirm the notification	Visibility	1.00
	Match	3.00
	Consistency	1.00
	Feedback	3.00
Input urination	Visibility	1.50
	Consistency	3.00
	Undo	1.50
Input fluid intake	Visibility	1.00
Bladder diary	Flexibility	1.00
	Consistency	1.50
Setup	Minimalist	1.00

Table 3.16 Heuristic violations for the mobile application

3.5 Launch

This research, development of a wearable bladder monitoring system, was carried out by cooperation between Medical Device Design and Usability laboratory at Yonsei University and Medical Imaging Computing Systems laboratory at Sogang University. The research was supported by the Bio & Medical Technology Development Program of the National Research Foundation funded by the Korean government. As a result of the research project, the researchers at Sogang university started a business.

Most of the core technology development and patent securing for the wearable bladder monitoring system were carried out through tasks; however, launching new equipment that does not exist in the market is difficult. There are two problems in obtaining medical device approval in Korea for the proposed system. Primarily, a wearable bladder monitoring system should be newly classified for regulatory approval. In Korea, a regulatory pathway of a class II medical device determines whether the device is essentially equivalent to those already permitted, or the country of manufacture, company, and product name are the same. The equivalence is dependent on the intended use, operational principle, performance, raw materials, test specifications, and instructions for use. There are significant differences between the bladder measurement system and the monitoring system in terms of intended use, exposure time considering continuous usage, and instructions for use, and characteristics, e.g., it contains a mobile application with alert functions.

Moreover, continuous bladder volume measurement is not covered by the South Korean National Health Insurance Program. Korea has a unique health expenditure payment

system. Because of the nature of the public health insurance system, the launch of medical devices without their listing as benefit items under the national health insurance is difficult to lead to actual sales. For an ultrasonic bladder measurement system, PVR measurement using a bladder scanner is listed as a benefit item. However, there are limits on the equipment used and the number of times per day. Thus, there should be clinical evidence that continuous bladder monitoring has clinical benefits for its eligibility to be covered by the health insurance.

Mcube Technology dominates the domestic bladder scanner market with an 81% share, followed by Verathon with 16% and MEDA with 2%. Moreover, the demand for bladder scanners has surged owing to their listing as benefit items. For a new manufacturer breaking into this market, launching a device fast is important. Considering these factors, the company made a strategic decision on the launch of a bladder measurement device (hereafter bladder scanner) as an intermediate step to launch a wearable bladder monitoring device.

There are two objectives in the launch of the bladder scanner. First, clinical trials should be conducted using the bladder scanner with the company's technology to validate and improved ultrasound imaging and volume measurement technology. Internal validation in the design and development stage is conducted using a tissue-equivalent bladder phantom. Testing with the phantom has limitations because various factors that affect performance in actual clinical practice, such as physical characteristics (e.g., the patient's skin, abdominal circumference), are not reflected. Therefore, improving ultrasound imaging and

bladder volumetric techniques through in vivo experiments is possible.

Moreover, a wearable-type ultrasonic sensor should be validated for transforming into a monitoring device. Thus, two types of bladder scanners were designed and developed: one with a handheld ultrasonic probe and the other with a flat-type ultrasonic probe that could be placed on the lower abdomen. The two scanners have the same platform except for the shape of the probe. The flat-type model, which corresponds to the prototype of the wearable bladder monitoring device, is defined as a derivative model of the predicated handheld type and the existing bladder volume measurement device. Therefore, we intend to proceed with the licensing process efficiently by proceeding with the licensing of the two models in parallel.

Chapter 4

Regulatory affairs to start a business and launch a medical device

In this chapter, regulatory affairs to obtain manufacturing and product certifications are mainly discussed. As described in section 3.5, a decision was taken to launch a bladder measurement system in advance of the launch of a bladder monitoring system. The regulatory pathways and affairs described in this chapter are intended for a bladder scanner.

4.1 Risk management

Risk management is defined as a systematic application of management policies, procedures, and practices to the tasks of analyzing, evaluating, controlling, and monitoring risks. Guidance on the development and inclusion of aspects of safety in international standards for medical devices specifies that risk management concepts and methodology are the basis of safety consideration. The basic concept of risk management is that risks must be balanced against other demands, including benefit, suitability, and availability. Moreover, as zero risk is unattainable, safety is defined as freedom from unacceptable risk (44). Practically, risk can be managed considering its safety level.

Severity level		Possible description
1	Negligible	Results in inconvenience or temporary discomfort
2	Minor	Results in temporary injury or impairment not requiring medical or surgical intervention
3	Serious / Major	Results in injury or impairment requiring medical or surgical intervention
4	Critical	Result in permanent impairment or irreversible injury
5	Catastrophic / Fatal	Result in patient death

Table 4.1 Five qualitative severity levels

Probability level		Probability range
1	Improbable	$< 10^{-6}$
2	Remote	$< 10^{-5}$ and $\geq 10^{-6}$
3	Occasional	$< 10^{-4}$ and $\geq 10^{-5}$
4	Probable	$< 10^{-3}$ and $\geq 10^{-4}$
5	Frequent	$\geq 10^{-3}$

Table 4.2 Five semi-quantitative probability levels

The risk management system for the bladder scanner adopts five level of probability and severity (13) as described in Table 4.1 and Table 4.2. The criteria for risk acceptability in design and development of the bladder scanner system utilize an example of a semiquantitative risk evaluation matrix as given in Table 4.3. Once the criteria have established, all risks should be analyzed and evaluated according to the criteria. All risks have to be reduced as far as possible rather than as low as reasonably practicable (16).

: acceptable, : unacceptable

Probability \ Severity		Negligible	Minor	Serious	Critical	Fatal
		1	2	3	4	5
Frequent	5	5	10	15	20	25
Probable	4	4	8	12	16	20
Occasional	3	3	6	9	12	15
Remote	2	2	4	6	8	10
Improbable	1	1	2	3	4	5

Table 4.3 Risk acceptability criteria for the system

4.1.1 Risk analysis

Risk is a combination of the probability of occurrence of harm; therefore, risk analysis is preceded by identification of hazards related to the target device. To find the potential sources of harm, manufacturers should first identify safety-related characteristics. ISO/TR 24971:2020 Annex A.2 provides questions to identify characteristics of the medical device that could affect safety (13). Table 4.4 presents the identification of the bladder scanner's characteristics that could affect safety. Identified characteristics that vary include intended use, energy, environment, data security, and usability.

Questions	Characteristics
What is the intended use and how is the medical device to be used?	
• The role of the medical device	Measurement of bladder volume
• Indications for use	Intended to measure bladder volume or residual urine volume
• Contraindication	Not intended for fetal use or for use on fetal or pregnant patients, patients with open skin or ascites, or wounds in the suprapubic region
• Device to sustain or support life	N/A
• Special intervention necessary in the case of failure of the medical device	N/A (Special intervention is not needed)
Is the medical device intended to be implanted?	N/A
Is the medical device intended to be in contact with the patient or other persons?	Surface contact: contacted with skin Contact duration: limited (≤ 24 h)
What materials or components are utilized in the medical device or are used with, or are in contact with, the medical device?	N/A (Not compatible with relevant substances, tissues or body fluids and not utilize materials of animal origin)
Is energy delivered to or extracted from the patient?	Ultrasonic energy • Gain control: level 1 ~ 5 • Depth control: 10, 15, 20, 25 cm • Mode: fundamental, harmonic
Are substances delivered to or extracted from the patient?	N/A
Are biological materials processed by the medical device for subsequent reuse, transfusion or transplantation?	N/A
Is the medical device supplied sterile or intended to be sterilized by the user, or are other microbiological controls applicable?	N/A
Is the medical device intended to be routinely cleaned/disinfected by the user?	Clean the probe after using with disinfectant and disinfectant wipes

Questions	Characteristics
Does the medical device modify the patient environment?	N/A
Are measurements taken?	The device measures the patient's bladder volume or residual urine volume
Is the medical device interpretative?	N/A
Is the medical device intended for use in conjunction with other medical devices, medicines or other medical technologies?	N/A
Are there unwanted outputs of energy or substances?	• Temperature • Leakage current • Electromagnetic wave
Is the medical device susceptible to environmental influences?	N/A
Does the medical device influence the environment?	N/A
Does the medical device require consumables or accessories?	Ultrasound transmission gel
Is maintenance or calibration necessary?	N/A
Does the medical device contain software?	Built-in software to provide graphical user interface which can be
Does the medical device allow access to information?	Review data can be accessed by connecting the USB cable or Wi-Fi
Does the medical device store data critical to patient care?	N/A (Stored data including patient information, volume measurement result is not critical to patient care)
Does the medical device have a restricted shelf life?	N/A
Are there any delayed or long-term use effects?	N/A
To what mechanical forces will the medical device be subjected?	N/A

Questions	Characteristics
What determines the lifetime of the medical device?	Expected lifetime is calculated by considering the lifespan of the battery
Is the medical device intended for single use?	N/A
Is safe decommissioning or disposal of the medical device necessary?	Disposal should be complied with the WEEE directive
Does installation or use of the medical device require special training or special skills?	N/A
How will information for safety be provided?	Information is provided through its user manual for end users, who is health care professionals, and no training is required for special skills or installation works
Are new manufacturing processes established or introduced?	N/A
Is successful application of the medical device dependent on the usability of the user interface?	
• Can the user interface design features contribute to use error?	Design features, including icons, fonts, and terms, on the screen can contribute to use error
• Is the medical device used in an environment where distractions can cause use error?	N/A (It is a device usually used in ICU where distractions or repetitive stress occurred by alarms from monitoring devices)
• Does the medical device have connecting parts or accessories?	It is connected to a power adapter for charging and a cradle station for charging and printing
• Does the medical device have a control interface?	It has a user interface to control the gain and depth when scanning, and imaging mode selection at setup
• Does the medical device display information?	The ultrasound images and measured volume values are displayed on the screen

Questions	Characteristics
• Is the medical device controlled by a menu?	It is controlled by menus and there are four main menus on the home screen
• Is the successful use of the medical device dependent on a user's knowledge, skills, and abilities?	The intended users are healthcare professionals with at least a basic level of general ultrasound training and training for measuring the bladder/urine volume
• Will the medical device be used by persons with specific needs?	N/A
• Can the user interface be used to initiate unauthorized actions?	Users can enter ADMIN mode only with the password
Does the medical device include an alarm system?	N/A
In what ways might the medical device be misused (deliberately or not)?	Users can use the device for not intended clinical application, however, the ultrasonic energy related to safety is assured
Is the medical device intended to be mobile or portable?	Console (main body with probe) is hand-held and the cradle station is portable
Does the use of the medical device depend on essential performance?	Essential performance – bladder volume measurement with accuracy: • 0-100 ml: ± 7.5 ml • 100-999 ml: ± 7.5 %
Does the medical device have a degree of autonomy?	N/A (It is not a robotic device that has autonomy level)
Does the medical device produce an output that is used as an input in determining clinical action?	The measurement result is used to evaluate symptoms of urinary dysfunction

Table 4.4 Identification of safety related characteristics of the bladder scanner

Known and foreseeable hazards and hazardous situations can be derived from identified characteristics related to safety. There are external resources to identify known and foreseeable hazards and hazardous situations, such as post-market databases, publications, and scientific literature. FDA's manufacturers and user facility device experience (MAUDE) database is a useful resource that manufacturers without previous devices can use to identify or predict harms, hazards, and hazardous situations. Figure 4.1 shows device problems using bladder scanners reported in the US. Ninety-nine case reports were collected from FDA's MAUDE database.

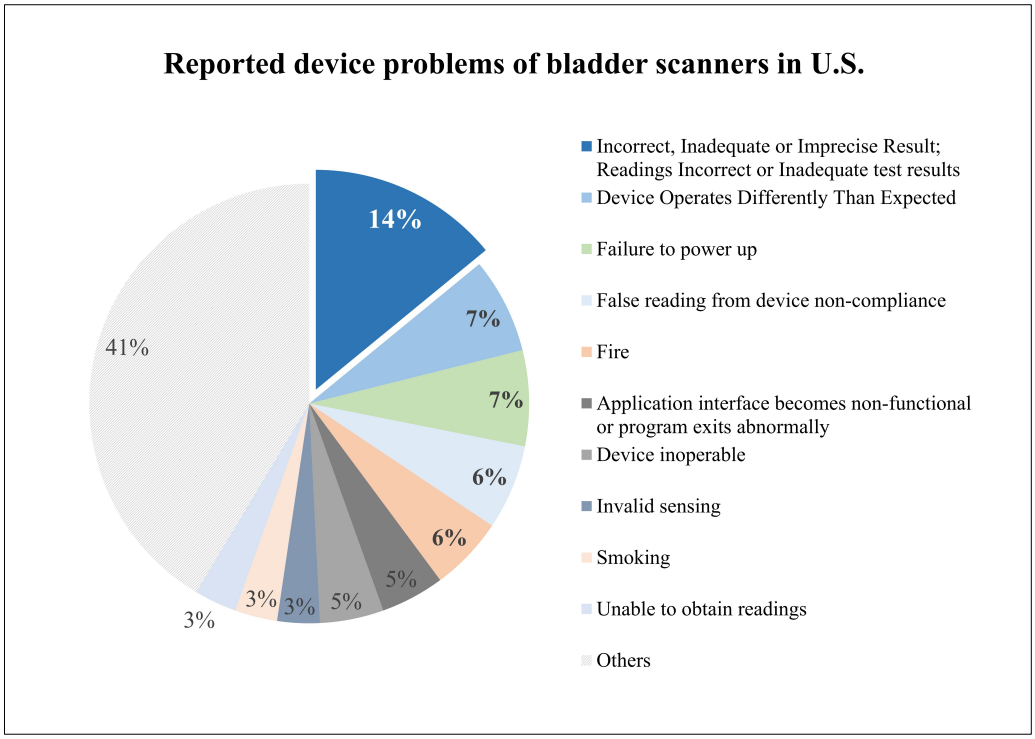


Figure 4.1 Device problems from known adverse events of bladder scanners

The most frequent problem is incorrect results, and there are similar problems such as false reading, invalid sensing, and unable to obtain readings. In addition, the problem that the device operates differently than expected is also mainly about false measurements. Analysis of reported data revealed that hazards or hazardous situations were similar even though the adverse event codes were different. Therefore, the events were regrouped into hazards from device problems as presented in Table 4.5. There are multiple device problems reported for one adverse event; therefore, events can be counted in duplicate.

Hazard	Representative hazardous situations	Count
Measurement	The bladder scanner measures inaccurately	65
Electrical energy	Fire occurs with smoking or sparking	16
Functionality (Malfunction)	The device is inoperable	14
Functionality (Power supply)	The device is not turned on	12
Functionality (Battery)	The battery is not charging, so the device cannot be operated	6
Mechanical energy (Moving parts)	The probe is broken and oil leaks from the crack on the probe	6
Mechanical energy (Falling)	The device is falling to the floor	4
Functionality (Boot up)	The device is failed to boot up	3
Usability (Lack of feedback)	Users cannot take adequate actions to operate the device	1
Usability (Instructions/training)	The user cannot replace batteries, so the device cannot be operated	1

Table 4.5 Known device problems regrouped into hazards

There are techniques that support risk analysis, including preliminary hazard analysis, fault tree analysis, and failure mode and effects analysis (FMEA). In this study, risks of bladder scanners were analyzed using FMEA. FMEA is a bottom-up method for identifying and evaluating consequences of an individual fault mode. FMEA can be extended to incorporate an investigation of faults, including their probability of occurrence and the degree of severity of the consequences (13); thus, it is widely used for risk analysis and evaluation.

4.1.2 Risk evaluation and risk control

Newly designed and developed bladder scanners, which are the subject of risk evaluation in this study, have no direct resource, such as post-market surveillance or customer feedbacks, related to the devices' risks. Thus, hazards identified in this study were only limited to data from predicate device's adverse event reports and requirements of conformance standards including IEC 60601-1 and IEC 60601-2-37. Table 4.6 presents risk analysis results based on data from the predicate device's adverse event reports. Severity assessment uses five levels according to Table 4.1, and the probability level is estimated from the occurrence values calculated from the reported adverse events in Table 4.5. Risk is a combination of severity and probability; thus, it is calculated as the multiplication of these two scores. Risks are evaluated with acceptance criteria based on Table 4.3. Unacceptable risks should be controlled with applicable measures, and they are re-evaluated after risk control measures are implemented.

Hazard	Hazardous situation	Harm	Severi -ty	Proba- bility	Risk (evaluation)	Control measures
Measurement	The bladder scanner measures inaccurately	Delay in providing care, pain caused by unnecessary catheterization	2	4	8 (unacceptable)	Enhancement of measurement accuracy, Probe design that calibration not needed
Electrical energy	Fire occurs with smoking or sparking	Damage to property, possible damage to operators (e.g., burn)	3	3	9 (unacceptable)	Usage power adapter with current or voltage cutoff circuits, Cutoff circuit in the charging part of device
Functionality (Malfunction)	The device is inoperable	Delay in providing care	2	3	6 (acceptable)	Exception handling, Reset/restore function
Functionality (Power supply)	The device is not turned on	Delay in providing care	2	2	4 (acceptable)	Battery low handling, use of stable adapters
Functionality (Battery)	The battery is not charging, so the device cannot be operated	Delay in providing care	2	2	4 (acceptable)	Usage of stable batteries, periodic battery inspection
Mechanical energy (Moving parts)	The probe is broken and oil leaks from the crack on the probe	Delay in providing care, pain caused by unnecessary catheterization, damage	3	2	6 (acceptable)	All electronic probe design without motors, oils
Mechanical energy (Falling)	The device is falling to the floor	Damage to property	2	2	4 (acceptable)	Provide with rolling stand or hand-strap
Functionality (Boot up)	The device is failed to boot up	Delay in providing care	2	2	4 (acceptable)	Error handling, reset function for re-booting
Usability (Lack of feedback)	Users cannot take adequate actions to operate the device	Delay in providing care	2	2	4 (acceptable)	Provide messages or feedbacks on the UI
Usability (Instructions)	The user cannot replace batteries, so the device cannot be operated	Delay in providing care	2	2	4 (acceptable)	Provide a quick guide for battery replacement

Table 4.6 Risk analysis on adverse events of predicate bladder scanners

4.2 Design controls

4.2.1 User-centered design

To identify user requirements regarding product design and workflows, a survey was conducted using Google Forms (Google Inc., Mountain View, CA, USA). Participants were recruited from the Department of Urology at Severance Hospital. Seventeen medical staff members, including four urologists and 13 nurses working in the urology department, participated the survey.

Demographic	Numbers (%)
Gender	Female: 7 (41.2) Male: 10 (58.8)
Occupation	Urologist: 4 (23.5) Nurse: 13 (76.5)
Age	From 30 to 39 years old: 13 (76.5) From 40 to 40 years old: 4 (23.5)
Experience in bladder scanners	Less than 1 year: 3 (17.6) From 1 years to 2 years: 2 (11.8) From 3 years to 4 years: 2 (11.8) More than 5 years: 10 (58.8)

Table 4.7 Profile of survey participants

The survey results related to the bladder scanner exterior design include scores for evaluating preference for six design drafts (coded as 2G, 2H, 2I, 2J, 2K, 2L) presented as examples and subjective opinions for each draft. As shown in Figure 4.2, the most preferrable design across the console, probe, and cradle station was 2G followed by 2L. Analysis of subjective opinions was conducted to identify factors affecting preference.

Portability and a display free from viewing angle or holding position were found to be decisive factors for the console. Most participants mentioned that it would be easy to use if the scan button were also placed on the probe. For the cradle station, participants preferred a shape that would fit on the probe, which would make the probe being stored stably. Further, the need for an ultrasound gel holder was identified. Approximately 65% of the participants responded that the appropriate length of the probe cable connected to the console should be between 60 and 100 centimeters.

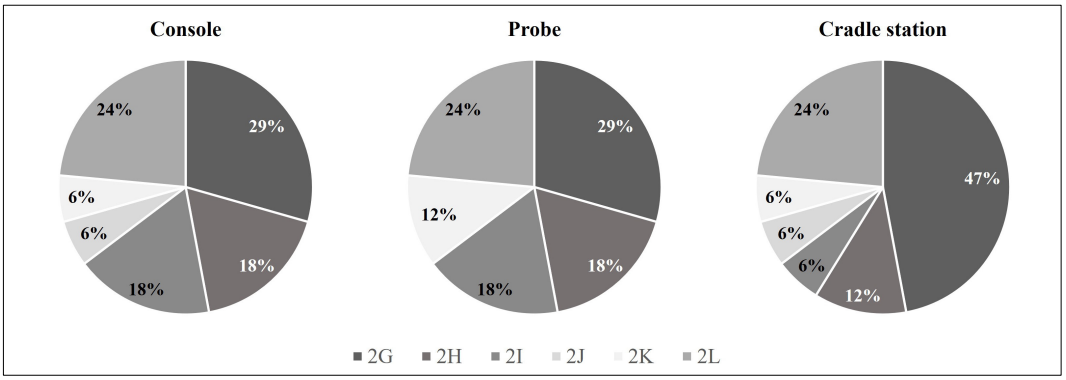


Figure 4.2 Survey results on design preference

Requirements for software and GUI were also identified through the survey. Participants responded that they wanted to review the optimized imaging result even though there were multiple scanned images in an exam. Thus, an optimized result selection function was implemented in scan results and the exam review screen. Many participants mentioned that they wanted to proceed with scanning without patient registration; accordingly, automatic ID generation was implemented. Moreover, a camera was included in the hardware to read a patient's barcode, thereby helping the user input the patient's ID easily.

4.2.2 Regulatory considerations in development

Once design specifications and functions are determined at the design stage, components should be selected to develop the actual product. Electronic medical devices are essentially electronic products, and when selecting major parts, including batteries and power adapters, they should be certified for medical use or international certifications related to the parts must be selected for parts with a certificate. The component selection flowchart is illustrated in Figure 4.3 (18).

The term “critical component” is widely used in the field of electronic medical devices when selecting components. IEC 60601-1 does not use this term; however, critical components are integral parts of a test report in the IECEE CB test certification scheme. IECEE OD 2020 provides an example of a critical component table comprising an AC inlet, a fuse, an enclosure, insulation wire, and so on. Critical components in electronic medical devices are commonly identified as power-supplying units, including power adapters and batteries, enclosures, printed circuit board, and objects used for insulation. There would be various standards from different standardization organizations or certification for proving a component’s safety. Because an electronic medical device is a combination of various electrical components that function according to medical objectives, identifying and understanding safety standards that are outside the scope of medical devices is crucial for medical device regulatory affairs.

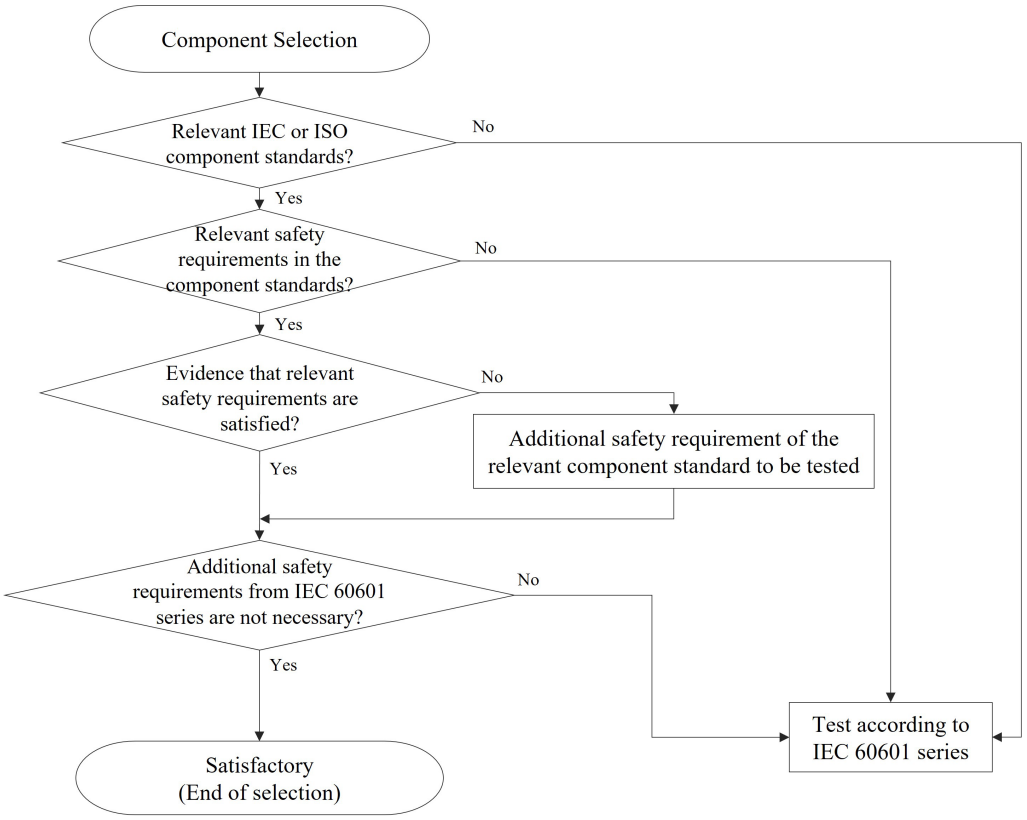


Figure 4.3 Schematic flow chart for component qualification

Table 4.8 provides an example of critical components with applicable safety standards for the portable bladder scanner. To be specific, manufacturers can select a medical-grade AC/DC power adapter or nonmedical grade which usually regarded as commercial one. Medical grade indicates that the adapter is certified with IEC 60601-1, whereas a nonmedical-grade adapter is certified with other standards such as IEC 609501-1 and IEC 62368-1. For small-business manufacturers, depending on the order quantity, manufacturing scale, and material costs, the second option is chosen as the power adapter for the manufactured medical devices.

Component	Safety standards
AC/DC adapter	IEC 60950-1:2005+AMD1: Information technology equipment – Safety – Part 1: General requirements
	IEC 62368-1:2018 Audio/video, information and communication technology equipment – Part 1: Safety requirements
Rechargeable Li-ion battery	IEC 62133-2:2017+AMD1:2021 Secondary cells and batteries containing alkaline or other non-acid electrolytes – Safety requirements for portable sealed secondary cells, and for batteries made from them, for use in portable applications – Part 2: Lithium systems
Plastic enclosures	UL 94 Tests for Flammability of Plastic Materials for Parts in Devices and Appliances IEC 60695-11-10:2013 Fire hazard testing – Part 11-10: Test flames – 50 W horizontal and vertical flame test methods
PCB (Printed circuit board)	UL 94 Tests for Flammability of Plastic Materials for Parts in Devices and Appliances UL 796 Printed Wiring Boards CSA-C22.2 No. 0.17

Table 4.8 An example of critical components with applicable safety standards

When considering relevant safety standards, introduction and replacement plans in targeted countries are important. For example, IEC 62368-1:2018 has replaced existing safety standards of AC/DC adapters for commercial purpose. The new standard covers all products, components, and subassemblies that were previously covered by IEC 60950-1 and IEC 60065-1. The transition date from IEC 60950-1 to IEC 62368-1 varies with the country. In Korea, IEC 60950-1 will be withdrawn on December 31, 2022, with transition to IEC 62368-1:2018 on January 1, 2023. Products certified with K 60950-1, which is a Korean standard harmonized with IEC 60950-1, can maintain their KC certification even after December 31, 2022, only if there is no change.

Components without applicable component-specific standards should be tested in medical equipment in accordance with IEC 60601-1 to demonstrate their conformity. The IEC 60601-1 series are primary standards that are widely harmonized international standards for medical devices. IEC 60601-1 provides common requirements for medical electrical (ME) equipment, whereas the IEC 60601-2-xx series identify requirements for particular devices. Further, the IEC 60601-1-xx series specify collateral requirements. Bladder scanners considered in this dissertation should conform to IEC 60601-1, IEC 60601-1-2, IEC 60601-1-6, and IEC 60601-2-37. This chapter mainly focuses on basic requirements in accordance with IEC 60601-1.

Clause	Applicable classification
6.2 Protection against electric shock	Internally powered ME equipment Class II ME equipment (when charging and printing)
6.3 Protection against harmful ingress of water or particular matter	IPX4 for ultrasonic probe
6.6 Mode of operation	Continuous operation

Table 4.9 Classification of the bladder scanners according to IEC 60601-1

The 60601-1 standard specifies the normative requirements regarding hazards and classifies a medical electronical equipment to satisfy its purpose. The classifications specified in clause 6 of the standard for the bladder scanners developed in this research are given in Table 4.9. The bladder scanners considered in this work are powered by rechargeable batteries, so they can be classified as internally powered equipment. However, they are also categorized as class II equipment when charging and printing because they

are powered through the power adapter. The 60601-1 standard stipulates that foot-operated control devices should be at least IPX1, and the enclosures of such devices used in emergency rooms or operating rooms should be classified as at least IPX6. Except for this case, there is no specified IPX grade required for the ME equipment in IEC 60601-1. IEC 60601-2-37, a particular standard for ultrasonic medical diagnostic and monitoring equipment, specifies the minimum requirement of ultrasonic transducer assembly with IPX1 (45). In addition, the standard states that the assembly should meet the requirements of watertight equipment (IPX7) if the manufacturer has specified the transducer assemblies as intended to be immersed during normal use. As the developed devices are not intended to be immersed, they are classified as IPX4 as well with specifications of benchmark devices.

Some ME equipment is intended for noncontinuous operation owing to energy- and temperature-related issues. Ultrasonic surgical equipment is one example of non-continuously operating equipment. For instance, it operates with a duty cycle of 60 seconds on and 30 seconds off. Furthermore, some wireless ultrasound systems have noncontinuous operations conditions: scanning up to 10 minutes, with 10 minutes resting time. This is presumably due to the temperature, and this is a problem that can occur in designing small-sized wireless ultrasound transducers. Several measures were taken to solve this problem in developing the bladder scanners in this research.

The devices are also classified as handheld because of the console and portable for the cradle station considering its installation and use. The ultrasonic probe head is classified as

type BF applied part. Requirements specified in the 60601-1 standard have different levels depending on the classification as given in Table 4.10. These requirements should be considered when designing and developing the devices for passing certification testing.

Clause	Requirement	Testing conditions
4.10.2	Maximum rated voltage for ME equipment intended to be connected to supply mains	< 250 V (for hand-held)
		AC/DC 250 V or single-phase AC or 500 V poly-phase AC (Rated input < 4kVA)
8.10.4.1	Operating voltage for cord-connected hand-held parts	AC 42.4 V peak or DC 60 V (Maximum)
15.3.2	Push test – no damage resulting in an unacceptable risk sustained	Force = 250 N ± 10 N for 5 s (for hand-held and portable)
15.3.4.1	Drop test with safe working load tested – no unacceptable risk resulted	Free fall height (m) = 1 m (for hand-held ME equipment or its parts)
15.3.4.2	Drop test with safe working load withstood stress as demonstrated by test – no unacceptable risk resulted	Drop height (cm) = 5 cm (for portable ME equipment or its parts weigh ≤ 10 kg)
15.3.6	Mold stress relief – no damage resulting in an unacceptable risk	7 h in oven at temperature (℃) = 70 ℃
8.7	Maximum allowed patient leakage current	10 μA in normal condition, 50 μA in single fault condition (for type BF applied part with DC current)
		100 μA in normal condition 500 μA in single fault condition (for type BF applied part with AC current)

Table 4.10 Applicable IEC 60601-1 requirements of subject devices

4.2.3 Validation

The final product should be validated, while verification can be conducted with a prototype during the design and development process. Electronic medical devices should be validated both on the software and on the entire system that integrates hardware and software. Design validation ensures that devices conform to defined user needs and intended uses. User needs are interpreted as system requirements in the early phase of design controls; therefore, validation is implemented to confirm whether the product meets the requirements. Table 4.11 illustrates the validation results of design requirements for bladder scanners.

Requirement	Validation	
Bladder volume measurement	Confirm that the bladder scanner shows ultrasound images and the bladder volume is calculated	Pass
Battery operation	After inserting a battery to the bladder scanner, verify whether it is turned on and scanning and measurement function is working	Pass
LED as a power status indicator	Check that the LED color (green, blue, orange, magenta) changes upon power status	Pass
Charging using the cradle station and the power adapter	Confirm that the console is charging by directly connecting with the power adapter via the USB cable and by connecting to the cradle station	Pass
Data Export	Connect the device to a PC via the USB cable and check the folder is accessible in the file browser	Pass
Wi-Fi connection	Check Wi-Fi function by connecting to a router	Pass
Safety information	Warnings, cautions, how to use, operation and storage condition are written in the instructions for use (IFU)	Pass

Table 4.11 Example of design validation – a case of the bladder scanner

As software has become an integral part of medical devices, IEC 62304 has been established to provide a framework of life cycle processes and risk management requirements contributed by software factors. The standard does not cover validation and final release of the medical device; it covers the overall requirements of medical device software. Manufacturers should assign a software safety class to the software system in the medical device in accordance with IEC 62304. IEC 62304 provides a flowchart to explain the selection of safety class as shown in Figure 4.4 (46).

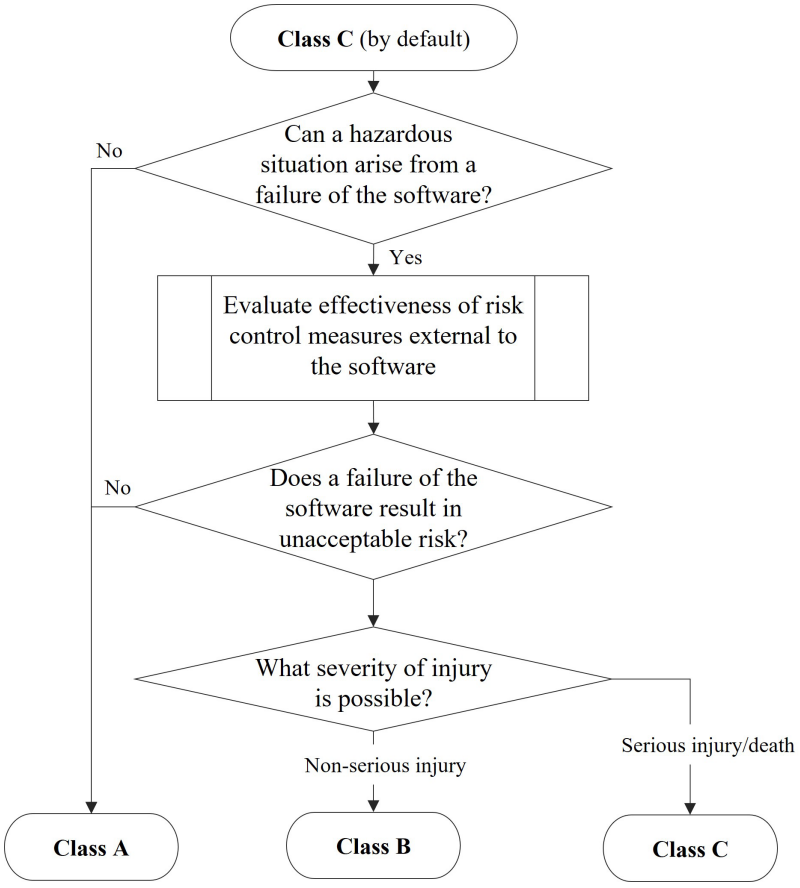


Figure 4.4 Flowchart of software safety class

The software of the bladder scanner can contribute to a hazardous situation, which may result in unacceptable risk after consideration of risk control measures external to the software system, and the resulting possible harm is a nonserious injury. In particular, the bladder scanner generates ultrasonic energy, which is applied to a patient; thus, a hazardous situation induced by excessive temperatures may arise if the system does not limit the ultrasound transmission. Inclusion of thermoregulation hardware elements can be a risk control measure external to the software system. However, there are still risks such as delay in delivery of appropriate clinical practice caused by low imaging quality or inaccurate bladder volume measurement. The resulting possible harm is a nonserious injury; hence, the bladder scanner can be categorized under software safety class B.

The FDA provides detailed assessment questions for the software safety level, which is called the level of concern in the FDA's guidance (47). The FDA classifies the level of concern for the software device under three levels: major, moderate, and minor. The level of concern of the bladder scanner is assessed to be major as presented in Table 4.12. If the answers to any one of the questions under the major category is Yes, the level of concern is likely to be major. Further, if the answers to all the questions in the major category for the bladder scanner are No but some answers to questions under the moderate category are Yes, the level of concern for the bladder scanner is likely to be moderate.

Category	Question	Answer
Major	Does the software device quality as blood establishment computer software?	No
	Is the software device intended to be used in combination with a drug or biologic?	No
	Is the software device an accessory to a medical device that has a major level of concern?	No
	Prior to mitigation of hazards, could a failure of the software device result in death or serious injury, either to a patient or to a user of the device? Examples of this include the following:	No
	a. Does the software device control a life supporting or life sustaining function?	No
	b. Does the software device control the delivery of potentially harmful energy that could result in death or serious injury, such as radiation treatment systems, defibrillators, and ablation generators?	No
	c. Does the software device control the delivery of treatment or therapy such that an error or malfunction could result in death or serious injury?	No
	d. Does the software device provide diagnostic information that directly drives a decision regarding treatment or therapy, such that if misapplied it could result in serious injury or death?	No
	e. Does the software device provide vital signs monitoring and alarms for potentially life-threatening situations in which medical intervention is necessary?	No

Category	Question	Answer
Moderate	Is the software device an accessory to a medical device that has a moderate level of concern?	No (It is a part of the medical device with moderate level of concern)
	Prior to mitigation of hazards, could a failure of the software device result in minor injury, either to a patient or to a user of the device?	Yes (A SW failure can result in minor burns)
	Could a malfunction of, or a latent design flaw in, the software device lead to an erroneous diagnosis or delay in delivery of appropriate medical care that would likely lead to minor injury?	Yes (If there is an error in measurement, it can lead delay)

Table 4.12 Questions to decide level of concern for the bladder scanner

Each software safety class has different requirements. The requirements for software class B in IEC 62304 are listed in Table 4.13. The software validation files, including software requirements specification, software detailed design file, software test (verification) plan and report, and software validation plan and report, have been established to demonstrate these requirements. Risk controls for hazards related to software are a part of risk management of the final product, i.e., the bladder scanner; details of risk management regarding software are specified in the risk management report.

Validation is a requirement of the quality management system. Validation files of the entire system and software system are reviewed in the audit of quality management system. For the software system, compliance with IEC 62304 is inspected in safety compliance testing, as it is a requirement of programmable electrical medical systems in IEC 60601-1.

Clause			Requirement
4 General requirements		4.1	Quality management system
		4.2	Risk management
		4.3	Software safety classification
5 Soft- ware develop- ment process	5.1 Software development planning	5.1.1	Software development plan
		5.1.2	Keep software development plan updated
		5.1.3	Software development plan reference to system design and development
		5.1.5	Software integration and integration testing planning
		5.1.6	Software verification planning
		5.1.7	Software risk management planning
		5.1.8	Documentation planning
		5.1.9	Software configuration management planning
		5.1.10	Supporting items to be controlled
		5.1.11	Software configuration item control before verification
	5.2 Software requirements analysis	5.2.1	Identification and avoidance of common software defects
		5.2.2	Software requirements content (e.g., function)
		5.2.3	Include risk control measures in requirements
		5.2.4	Re-evaluate medical device risk analysis
		5.2.5	Update system requirements
		5.2.6	Verify software requirements
5 Soft- ware develop- ment process	5.3 Software architectural design	5.3.1	Transform requirements into an architecture
		5.3.2	Develop an architecture for the interfaces of software items
		5.3.3	Specify functional and performance requirements of SOUP item
		5.3.4	Specify system hardware and software required by SOUP item
		5.3.6	Verify software architecture

Clause			Requirement
5 Software development process	5.4 Software detailed design	5.4.1	Refine software architecture into software units
	5.5 Software unit implementation and verification	5.5.1	Implement each software unit
		5.5.2	Establish software unit verification process
		5.5.3	Software unit acceptance criteria
		5.5.5	Software unit verification
	5.6		Software integration and integration testing
	5.7		Software system testing
	5.8 Software release	5.8.1	Ensure software verification is complete
		5.8.2	Document known residual anomalies
		5.8.3	Evaluate known residual anomalies
		5.8.4	Document released versions
		5.8.5	Document how released software was created
		5.8.6	Ensure activities and tasks are complete
		5.8.7	Archive software
		5.8.8	Assure repeatability of software release
6 Software maintenance plan	6.1		Establish software maintenance plan
	6.2 Problem and modification analysis	6.2.1	Document and evaluate feedback
		6.2.2	Use software problem resolution process
		6.2.3	Analyze change requests
		6.2.4	Change request approval
		6.2.5	Communicate to users and regulators
7 Software risk management process	7.1 Analysis of software contributing to hazardous situations	7.1.1	Identify software items that could contribute to a hazardous situation
		7.1.2	Identify potential causes of contribution to a hazardous situation
		7.1.3	Evaluate published SOUP anomaly lists
		7.1.4	Document potential causes
		7.1.5	Document sequences of events

Clause			Requirement
7 Software risk management process	7.2 Risk control measures	7.2.1	Define risk control measures
		7.2.2	Risk control measures implemented in software
	7.3 Verification of risk control measures	7.3.1	Verify risk control measures
		7.3.2	Document any new sequences of events
		7.3.3	Document traceability
	7.4 Risk management of SW changes	7.4.1	Analyze changes to medical device software with respect to safety
		7.4.2	Analyze impact of software changes on existing risk control measures
		7.4.3	Perform risk management activities based on analyses
8 Software configuration management process	8.1 Configuration identification	8.1.1	Establish means to identify configuration items
		8.1.2	Identify SOUP
		8.1.3	Identify system configuration documentation
	8.2 Change control	8.2.1	Approve change requests
		8.2.2	Implement changes
		8.2.3	Verify changes
		8.2.4	Provide means for traceability of change
	8.3		Configuration status accounting
9 Software problem resolution process	9.1		Prepare problem reports
	9.2		Investigate the problem
	9.3		Advise relevant parties
	9.4		Use change control process
	9.5		Maintain records
	9.6		Analyze problems for trends
	9.7		Verify software problem resolution
	9.8		Test documentation contents

Table 4.13 Requirements of safety class B software

4.3 A regulatory pathway to market in Korea

A regulatory pathway includes safety tests, good manufacturing practice (GMP) certification, technical document review, and product/manufacturing certification as described in Table 4.14. The pathway is targeted for this study is that all certifications are initial cases for the product and the corporate entity. For the initial case, the application of manufacturing business permission should be accompanied with the application of manufacturing certification for one product at least.

Step		Pre-requisite	Authority
1	Testing & Certification (Safety, Performance)	• Pre-production product • Risk management file, usability engineering file, SW validation file, user manual, labels	Accredited body
2	GMP certification (Document review, On-site audit)	• Quality document • Medical device file • 1 set of the finished product • Test certificates as evidence of validation	Institution designated by MFDS
3	Technical document review	• Comparison table with predicate devices • Technical document • Test certificates and reports • Cybersecurity report with SW validation files	Institution designated by MFDS
4	Manufacturing certification on product	• GMP certificate • Technical document • Test certificates and reports	NIDS
5	Manufacturing business permission	• Qualification of the quality manger	Regional office of MFDS

Table 4.14 Overall regulatory pathway applied in this research

4.3.1 Establishment of quality management system

In Korea, medical device manufactures must undergo a conformity review for medical device manufacturing and quality control, which is also known as Korean Good Manufacturing Practices (KGMP), by item group. Class II medical devices must undergo a regular review once every three years after the initial review. The bladder measurement system belongs to an item group of biological phenomenon measurement systems.

Exclusion	Justification
6.4.2 Contamination control	The manufactured products are not sterile medical devices and do not require contamination control.
7.5.2 Cleanliness of product	The products are not sterilized when manufacturing, and do not require sterilization after use.
7.5.3 Installation activities	The products do not require installation.
7.5.5 Particular requirements for sterile medical devices	The products are not sterilized when manufacturing, and do not require sterilization after use.
7.5.7 Particular requirements for validation of processes for sterilization and sterile barrier systems	The products are not sterilized when manufacturing, and do not require sterilization after use.
7.5.9.2 Particular requirements for implantable medical devices	The products are not under the category of implantable medical devices which subject to tracking management.
7.5.10 Customer property	Customer property is not provided to the manufacturer, and it is not used for commercialization.

Table 4.15 Exclusions with justifications from ISO 13485:2016 requirements

Among the KGMP requirements based on ISO 13485:2016, there are exclusions from the scope of ISO 13485:2016 requirements owing to the characteristics of the product being

developed. Exclusions should be stated in the company's quality manual. Excluded requirements including sterilization, implantation, and installation are attributed to device-specific characteristics. The details of justifications for exclusions are listed in Table 4.15; however, this table only presents an example in this case. Thus, there could be variations of exclusions depending on the device characteristics and range of the organization's activities.

ISO 13485:2016 includes eight clauses specifying requirements for the management system that can be used by an organization involved in one or more stages of the life cycle of a medical device (15). Each clause represents the organization's responsibility or activity from Clause 4 to Clause 8. As quality management requirements can be excluded depending on the organization's activity, quality procedures also vary. If the company in this case decides to manufacture disposable ultrasound gel pads such as single-use electrocardiograph electrode, then procedures related to sterilization should be established.

Once the scope of the quality management system and procedures are determined in the organization's quality manual, each procedure is documented, and the documented information related to the procedure, including quality documents and records, are established as given in Table 4.16. An organization has an overall quality management system sharing common procedures and documentation forms; the organization shall establish and maintain medical device files for each medical device type or family to conform to applicable requirements.

Clause	Procedure	Quality documents
4.1 General requirements	Process monitoring and change management	Process flow chart
		Process monitoring checklist
		Request for change process
		Process changes impact assessment table
4.2 Documentation requirements	Documentation and Records management	Quality document format
		Document and form management register
		Medical device file management register
		Document distribution and withdraw management register
		Exclusive execution document management register
		Internal draft form
		Internal drafts ledger
		Template of an official letter for external use
		Official letter management register
		Confidentiality agreement
5.1 Management commitment	Quality policy and objectives management	Quality management system plan
		Quality policy and objectives
5.5 Responsibility, authority, and communication	Responsibility, authority, and communication	Organization chart
		Responsibility and authority relationship table
		Job description
5.6 Management review	Management review	Meeting minutes
		Management review report
6.2 Human resources	Human resources management	Education and training plan
		Education and training report
		Education and training history card
		Qualification evaluation table
		Qualification certificate
6.3 Infrastructure 7.6 Control of monitoring and measuring equipment	Workspace, Utilities, and equipment management	Workspace, utilities, and equipment management register
		Workspace, utilities, and equipment history card
		Workspace, utilities, and equipment management checklist
		Calibration plan

Clause	Procedure	Quality documents
6.4 Work environment and contamination control	Work environment management	Environmental and hygiene management checklist
		Hum and humidity management checklist
		Insect prevalence management plan and checklist
		Armistice prevention management checklist
7.1 Planning of product realization	Risk management	Risk management plan
		Risk management report
		Process risk management plan
		Process risk management report
7.2.1 Customer-related processes	Contract review	Quote form
		Quote management register
		Contract document management register
		Transaction receipt
7.3 Design and development	Design and development management	Design and development input requirements specification
		Design and development plan
		Design and development review report
		Design and development verification report
		Design and development validation report
		Design and development completion report
		Design change request
		Drawing management register
		Design and development file list
4.1.5 Conformity of outsource 7.4 Purchasing	Purchasing and supplier management	Order management register
		Purchase order
		Supplier evaluation table
		Supplier management register
7.5.1 Control of production and service provision	Control of production management	Production plan
		Production log

Clause	Procedure	Quality documents
4.1.6 Validation of the application of computer software 7.5.6 Validation of processes for production and service provision 7.6 Control of monitoring and measuring equipment	Software validation management	SW deployment and configuration management register
		SW design and development plan
		SW detailed design file
		SW input requirements specification
		SW verification plan
		SW review report
		SW verification report
		SW validation report
		Process SW validation report / UDI validation report
7.5.8 Identification 7.5.9 Traceability	Identification and traceability management	Raw material identification symbol management register
		Product identification symbol management ledger
		Product production history card
7.5.11 Preservation of product	Preservation of product and parts	Incoming and outcoming management register
		Handling and storage checklist
		Shipment management register
5.2 Customer focus 7.2.3 Communication 8.2.1 Feedback 8.2.2 Complaint handling	Customer management	Customer complaints
		Customer satisfaction survey
		Customer complaints report
8.2.4 Internal audit	Internal audit	Audit plan
		Audit checklist
		Audit report

Clause	Procedure	Quality documents
8.2.6 Monitoring and measurement of product	Testing and inspection management	Incoming inspection report
		Process inspection report
		Outgoing (Final) inspection report
8.2.1 Feedback 8.3 Control of nonconforming product	Nonconforming product management	Nonconforming product management ledger
		Nonconforming product report
8.4 Analysis of data	Data analysis	Quality objective statistics and analysis table
8.5.2 Corrective action 8.5.3 Preventive action	Corrective and preventive action	Correction and prevention measures register
		Correction and preventive measure processing document
7.2.3 Communication 8.2.1 Feedback 8.2.3 Reporting to regulatory authorities	Safety information	Advisory notice format
		Adverse case report of medical devices
7.3.3 Design and development inputs 7.3.9 Control of design and development changes	Usability engineering process	Usability engineering plan
		Use specification
		Usability evaluation plan
		Usability evaluation report

Table 4.16 Established quality procedures and documents

The retention period of documents and records should be at least the lifetime of the medical device, or as specified by applicable regulatory requirements, but not less than two years from the release of the medical device by the organization. Korea requires retaining manufacturing and quality management records for at least five years from the manufacturing date (48). Meanwhile, EU MDR stipulates a period of at least 10 years after the last device covered by the EU declaration of conformity has been placed on the market (49). Thus, the retention periods of documents and records illustrated in Table 4.16 vary, with a minimum period of five years.

4.3.2 Testing and certification

Critical safety standards, such as electrical, mechanical, and electromagnetic compliance (EMC), and essential performance should be validated by accredited bodies. For electronic medical devices, safety (IEC 60601-1) and EMC (IEC 60601-1-2) tests are common tests to be conducted as regulatory requirements. IEC 60601-1 and IEC 60601-1-2 are widely harmonized or recognized standards related to medical devices safety. If a manufacturer is planning to enter the European overseas market by obtaining CE MDR and the US market by getting approval from the FDA, obtaining CB certification adding national differences including Korea and the US is recommended.

Furthermore, several accredited bodies have direct certification authorization; therefore, manufacturers can consider adding countries for marketing. In particular, the accredited body selected in this research has direct marking authorization including USA/Canada

(NRTL), Taiwan (BSMI), Singapore (PSB), and Brazil (INMETRO). In North America, many states additionally require NRTL certification for the sale of electronic products in the US, similar to KC certification in Korea. Therefore, NRTL certification was also applied when safety and EMC testing was initiated.

As an ultrasound device, the bladder scanner should conform to the standard for ultrasound medical diagnostic and monitoring equipment, IEC 60601-2-37. This is a particular standard replacing or supplementing electrical and mechanical safety requirements with the requirements in IEC 60601-1. Table 4.17 illustrates examples of requirements for the bladder scanner in accordance with IEC 60601-2-37.

Clause	Condition / Requirement	Application
201.4.3 Essential performance	The potential sources of unacceptable risk identified to characterize the essential performance of ultrasonic diagnostic equipment should be also considered	Address essential performance in the risk management
201.7.2.9 IP classification	Marking of the IPX code on the transducer assembly is not required, for partial IPX classification of the transducer assembly	N/A (Not required, but IPX is marked on the main label)
201.7.2.101 Acoustic output	Action to directly adjust output levels is clear to the operator displaying relating information including indices	N/A (The output level is fixed when scanning)
201.7.9.2.2 Warning and safety notices	Information on how to interpret the displayed ultrasonic exposure parameters, thermal index (TI) and mechanical index (MI)	Describe in the IFU
	Procedure necessary for safe operation, pointing out possible safety hazards due to inadequate electrical installation when applied part is type B	N/A (Applied part: type BF)

Clause	Condition / Requirement	Application
201.7.9.2.2 Warning and safety notices	Information on safe use of transducer assemblies indicating the device is of the correct type for its intended application	Describe in the IFU
	Identification of interference with other equipment and mitigation techniques included in the IFU when a reduction in test levels is claimed by the manufacturer	Describe in safety information section of the IFU
201.7.9.2.2 Warning and safety notices	A description of transducer assembly parts which may be immersed in water or other liquids normal use or performance assessment purposes	N/A (It is not intended to be immersed in water or other liquids)
	A recommendation calling the operator's attention to the need for regular testing and periodic maintenance including inspection of the transducer assembly for cracks which allow the ingress of conductive fluid	Describe in safety information and maintenance section of the IFU
	Instructions regarding the avoidance of unintended control settings and acoustic output levels	Describe imaging mode change which affects the acoustic output in the IFU
	Output limits for each application should be declared for multi-purpose ultrasonic equipment	N/A (It is not a multi-purpose equipment)
	For ultrasonic diagnostic equipment intended for the home care use, information provided to address this type of user	N/A* * Applicable for bladder monitoring devices in the future
201.7.9.2.10 Messages	List all system messages, error messages and fault messages unless these messages are self-explanatory	Describe notification messages in the IFU

Clause	Condition / Requirement	Application
201.7.9.2.12 Cleaning, disinfection, and sterilization	List of the pertinent parts, components and/or functions that should be checked after each cleaning, disinfection or sterilization cycle, and method(s) of inspection	Describe cleaning and disinfection procedure in the IFU
201.7.9.3 Technical description	Operator's manual includes technical data on acoustic output levels providing the maximum value of each index for each mode and declaration that the TI and MI are 1.0 or less for all device settings	Describe in the IFU
201.8 Protection against electrical hazard	The transducer assembly tested with the applied part immersed in a 0.9% saline solution for patient leakage current and auxiliary current test, dielectric strength test	Applied part should be tolerant with the test condition
201.10 Protection against unwanted & excessive radiation hazards	Risks associated with ultrasonic energy in the risk management process is addressed by manufacturer	Demonstrate in the risk management file
201.11 Protective against excessive temperatures & other hazards	Contact surface temperature ≤ 43 ℃ in simulated use condition operating continuously for 30 min	Verify by measuring surface temperature with given conditions
	Contact surface temperature ≤ 50 ℃ in still air condition operating continuously for 30 min	

Clause	Condition / Requirement	Application
201.11 Protective against excessive temperatures & other hazards	Compliance with the requirements of maximum temperature during normal use and temperature of applied parts should be documented in the risk management file.	Demonstrate in the risk management file
	Parts of transducer assembly likely to come into contact with operator or patient meet the requirements of drip-proof equipment (IPX1) *This requirement not applied to connectors of transducer assembly	Ultrasonic transduce is designed as IPX4
	Parts of transducer assembly intended to be immersed in normal use meet the necessary requirements of watertight equipment (IPX7)	N/A (Not intended to be immersed in normal use)

Table 4.17 Requirements for bladder scanners based on IEC 60601-2-37

4.3.3 Technical document review

In Korea, the technical document for regulatory approval is reviewed by an institution designated by MFDS. A bladder scanner is a class II device that requires a regulatory certificate; therefore, the authority reviewing technical document is one of the designated institutions. In addition to an application document, the manufacturer shall submit a comparison table with predicate devices selected by the manufacturer, technical documents, test certificates and reports, a software validation report, and a cybersecurity report. Technical documents represent a list of documents on the quality of a medical device, such as performance and safety, as listed in Table 4.18.

No	Technical document		Remark
1	Essential equivalence comparison table (Compared with products already get regulatory approval)		Mandatory
2	Technical document	Operating principles	Mandatory
3		Structure of the item	Mandatory
4		Dimensions	Mandatory
5		Characteristics (e.g., electrical rating, protection from electrical shock, safety measures, system block diagram, insulation diagram including insulation distance, software architecture)	Mandatory
6		Raw materials	Mandatory
7		Manufacturing method	Mandatory* *No need to provide detail information
8		Intended use	Mandatory
9		Performance	Mandatory
10		Instructions for use	Mandatory
11		Precautions for use	Mandatory
12		Storage method	Mandatory
13		Expiration date (available period)	N/A
14	Performance and safety	Electrical and mechanical safety	Mandatory
15		Biological safety	N/A** **Test reports not strictly required for ultrasonic probes in Korea
16		Radiation safety	N/A
17		Electromagnetic compliance	Mandatory
18		Performance data	Mandatory

No	Technical document		Remark
19	Performance and safety	Physical and chemical properties	Required for invasive or direct contact devices
20		Stability data	Required for a device with expiration date
21	Data regarding origins, discovery, and reasons for development		Not required for devices that are essentially equivalent to those already got regulatory approval
22	Data regarding clinical trials		
23	Data regarding the current status (e.g., use in other counties)		

Table 4.18 List of documents to submit for technical document review in accordance with Korean regulation

As software has played important roles in electrical medical devices, a software validation report and cybersecurity report are additional documents for submission. ISO 14971:2019 specifies security as an item that can cause hazardous situations. In particular, unsecured data ports that are externally accessible, data without encryption, and software vulnerabilities are illustrated as examples of events and circumstances related to security (17). Further, ISO/TR 24971:2020 mentions cybersecurity as risks related to security (13). Table 4.19 presents a checklist for cybersecurity stipulated in a regulation on notification, certification, and approval for medical devices. These requirements should be considered when designing and implementing the software according to the risk level of functions. If a requirement is not applied, then there should be a rationale or alternatives.

No	Requirement		Example
1	Secured commu-nication	Manufacturers should consider how the medical device should connect (wired/wireless communication, etc.) with other devices or network	Wi-Fi, ethernet, USB, Bluetooth
2		Manufacturers should consider design characteristics that verify the validity of all inputs, both internal and external, and also consider communication in devices and environments that support only communication with weak security (e.g., home network or existing devices).	Validation in weak security environments, if applicable, and consider additional measures for security
3		Manufacturers should consider secure data transmission/reception methods of medical devices to prevent unauthorized access/change/repetition.	Mutual authentication method between devices and systems, password for data communication
4	Data protec-tion	Manufacturers should consider whether a certain level of protection, such as encryption, is required when safety-related data is stored or transmitted/received from the device.	Passwords must be stored as encrypted secure hashes
5		Manufacturers should consider protecting messages in the control/sequencing fields of communication protocols or preventing cryptographic key material from being compromised when confidentiality risk control measures are required.	Separately store cryptographic key preventing data loss
6	Device integrity	Manufacturers should evaluate the architecture at the system level to determine if design features are needed to ensure data non-repudiation.	Provides audit log recording function

No	Requirement		Example
7	Device integrity	Manufacturers should consider risks to the integrity of the device, such as unauthorized changes to the device software.	Setting a password to access system configuration menu
8		Manufacturers should consider control measures such as anti-malware programs to prevent malicious code that may run on devices, such as viruses, spyware, and ransomware.	Provide security warnings of the PC connected to the device in the IFU
9	User authenti-cation	Manufacturers should consider user access controls that allow users who have been proven to use the device, grant permission to users in other roles, or allow access in emergency situations. Additionally, the same credential should not be shared between devices and customers.	Login function, Separate user account with passwords for administrative functions
10	SW main-tenance	The manufacturer shall establish and notify the implementation procedures for the implementation and distribution of periodic updates.	Establish SW updates plans and provides annual inspection on software updates
11		Manufacturers should consider when operating system (OS) software, third-party software, and open-source software will be updated or controlled. In addition, the manufacturer shall establish a response plan for software update or expiration of the operating environment by external control.	Plans for medical device software running on an unsecure operating system version
12		Manufacturers should consider how to update medical devices to respond to new cybersecurity vulnerabilities.	Validation of updates, Make user intervention when updating

No	Requirement		Example
13	SW main-tenance	Manufacturers should consider what kind of linking is required to perform the update and the authenticity of the linking or update through code signing or other similar means.	Authentication procedure when updating with the authentication key in the update file
14	Physical access	Manufacturers should consider controls to prevent access by unauthorized persons to the medical device.	Physical lock or physical restriction of port access, physical cable access restriction that does not require authentication
15	Reliabi-lity and availabi-lity	Manufacturers should consider design features that allow medical devices to detect, resist, respond to, and recover from cybersecurity attacks in order to maintain requisite performance.	Provides emergency contact information through the user manual in case of cybersecurity incidents while using medical devices

Table 4.19 Cybersecurity requirements and examples of applicable measures

4.3.4 Regulatory approval of Class II medical device

Manufacturers who initially obtain approval of medical devices in Korea should simultaneously apply for manufacturing certification of their product and manufacturing business permission. The MFDS grants manufacturing business permission within 25 working days from the date of receiving the application for permission. Thus, a conjoined application of manufacturing certification for the product and manufacturing business permission requires 25 working days following the longest processing date, even though

the manufacturing certification on product takes five working days.

A manufacturing business permission for medical devices is issued by a local office of MFDS. The reviewer confirms information about manufacturing facilities where the manufacturer gets GMP certification. The manufacturer submits a manufacturing facility floor plan to guarantee that there is at least a storage area, testing area, and workplace at the facility. In addition, the qualification of the quality manager should be proved with evidence such as a degree certificate in a medical device-related major and career certificate of relevant jobs.

Manufacturing certification of products requires detailed information on the medical device, including product classification name, code, a name of the device, and category of equivalence. Technical documents are attached to be revealed to the public. Additionally, the GMP certification, notification of the technical document review, and safety and performance testing reports should be submitted. In the present case of bladder scanners, two models—one with a handheld type probe and the other with a patch-type probe were submitted for certification simultaneously. As the difference was only in the appearance, the patch-type probe was considered the variant of the model with a handheld probe in safety tests and technical document review.

4.3.5 Reimbursement

As identified in market analysis at the concept phase, PVR measurement using a bladder scanner is covered by the national health insurance system in Korea. Before the specific benefit item was established, there were some items related to PVR measurement as described in Table 4.20. A hospital can claim payment for EZ754 only if the hospital owns an ultrasonic bladder measurement system, which is the so-called bladder scanner.

Item (EDI Code)	Standard Ultrasonography (I) One Point Ultrasonography	EB450 Urology Ultrasonography – Bladder	EB450001	EZ754 PVR measurement using bladder scan (1 day)
Category	Standard Ultrasonography	Diagnostic Ultrasonography	Limited Ultrasonography	Kidney & Urinary Examination
Equipment Inspection	N/A (It is not required inspection to check whether the hospital has the medical device to perform the designated medical practice.)			Ultrasonic Bladder Measurement System (A24700)
Medical Practice	PVR	Confirm all anatomical parts of bladders, PVR	Focus on problematic areas of bladder, PVR	PVR
Remark	Standard ultrasonography used as an auxiliary role	Recommended to implement ultrasonography items for standard ultrasonography	Only accepted for follow-up exam after diagnostic ultrasonography	Benefited once a day (Maximum twice a day if prescribed)

Table 4.20 Benefit items related to postvoid residual urine measurement

Chapter 5

Post-market management and considerations on discontinuation

5.1 Post-market surveillance process

In pre-market phases, regulatory science focuses on safety and effectiveness of medical devices. As medical devices are designed, developed, manufactured, and distributed in markets, a residual risk regarding safety and performance remains throughout the product's life cycle owing to a combination of various factors, such as different end-user interactions, unforeseen failure, or misuse (50). Thus, post-market surveillance (PMS) is crucial for ensuring that medical devices that have been placed in the market remain safe and effective and to consider necessary actions if the risk under continual usage of the device outweighs the benefit (51). ISO 13485 and ISO/TR 20416 define PMS as the process of performing monitoring by collecting and analyzing information from post-production activities and markets. This chapter illustrates the method of establishing the PMS process for the bladder scanners considering their users, use environments, and targeted markets.

5.1.1 Establishment of post-market surveillance process

The PMS process aims to eliminate identified uncertainty by collecting and analyzing new relevant information. The objectives of the PMS activities address various aspects of the medical devices from the input processes as shown in Figure 5.1 (50). The input processes provide collection and analysis criteria, and the result of the PMS process facilitates decisions or actions related to these processes.

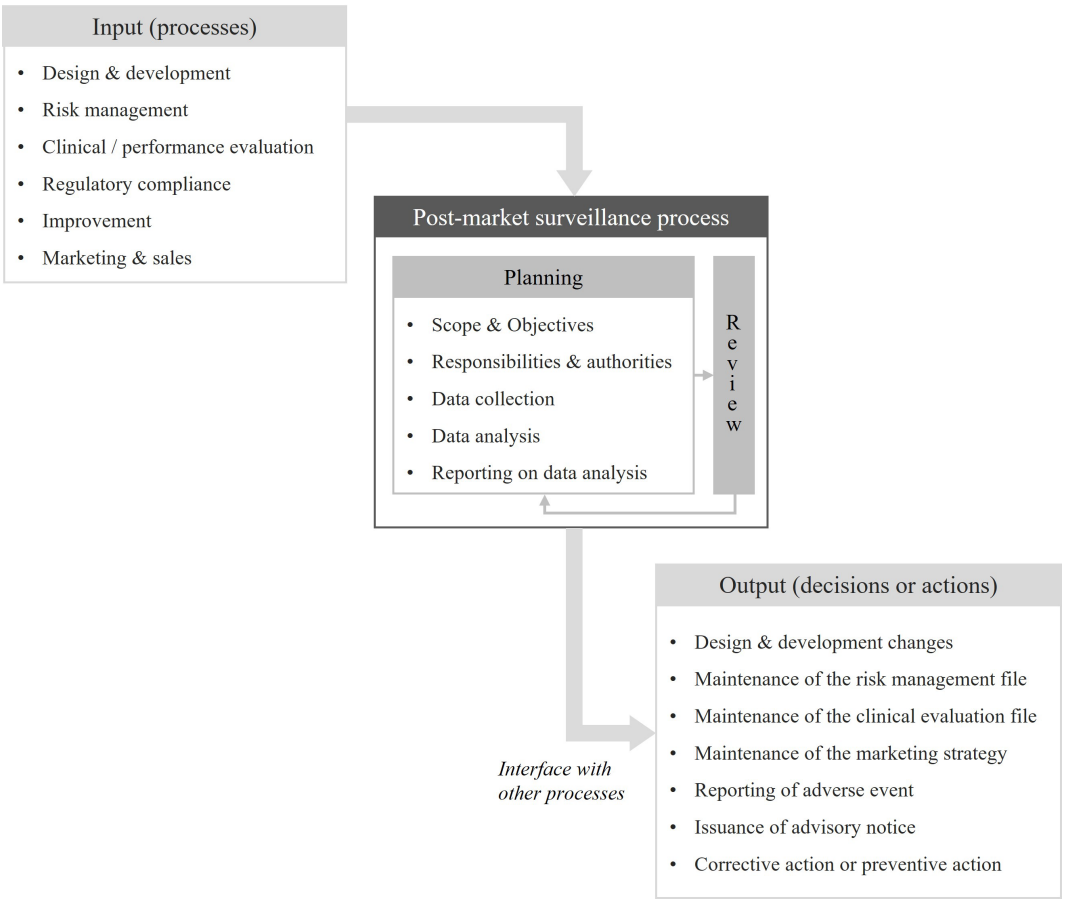


Figure 5.1 Example schematic representation of post-market surveillance

5.1.2 Planning of post-market surveillance

The scope of the PMS plan depends on the type of the medical device, and it may include a brief description of the medical device and types of users. The scope of the PMS plan for bladder scanners can be described as follows:

a. Brief description of the medical device: Bladder volume measurement, which can be represented as a PVR urinary volume test, is a well-established and common examination in the diagnosis and evaluation of patients with lower-urinary-tract symptoms. Domestically, around 60,000 patients are examined with bladder scanners every day according to the claim numbers of PVR using bladder scans provided by the healthcare bigdata hub in Korea. PVR measurement using bladder scan is noninvasive, and this examination can be executed in both outpatient and inpatient environments.

b. Types of users: Bladder scanners are used by professional users, urologists, and nurses. All of these users are expected have received relevant education and training.

The objective of the PMS plan for a bladder scanner is to maintain product compliance, improve the bladder volume measurement system, and collect actual (clinical) evidence. In particular, the PMS activities can be implemented to maintain the currency of the design and development and manufacturing information, IFU, labeling, training, and servicing activities or to update the risk management documentation considering newly identified risks.

The responsibilities of the person who maintains the PMS process include coordinating the PMS activities with the relevant process owners on a yearly basis, performing collection and analysis of the data and interlink with other processes, and organizing a review meeting on the PMS activities. In the meeting, the participants are various departments or persons responsible for quality assurance, regulatory affairs, clinical management, and safety engineering.

5.1.3 Data collection and analysis

The sources of PMS data should be sufficiently reliable to provide information regarding the specified goals of the PMS plan. The collection of data is a combination of both proactive and reactive activities because it allows manufacturers to identify safety and performance issues early. Data collection methods should be specified in relevant quality procedures such as customer management procedures and safety information management procedures. Furthermore, there should be protocols for data collection considering responsible persons for data integrity and quality, data collection, monitoring, and evaluation methods. Examples of data collection for bladder scanners as given in Table 5.1.

When collecting or analyzing data, subjective metrics or parameters should be determined. The method of analysis should also be specified in relevant quality procedures along with data collection methods. The data analysis methods for the data sources listed in Table 5.1 are given in Table 5.2. In particular, the analysis method should be selected

considering the objective specified in the PMS plan.

Data source	Data collection activities	Owner
Complaints	• Document customer feedbacks gotten directly or via local distributors • Report customer complaints to a quality manager	Marketing/ Sales manager
Feedbacks	• Document external (e.g., feedback from conferences or exhibitions, and user feedback during training) and internal suggestions for product improvements or enhancements • Conduct customer surveys on a yearly basis	Product manager, Marketing/ Sales manager
Adverse events and non-serious incident cases	• Receipt incidents, including adverse events and non-serious incidents, from users and report to a quality manager	Sales manager
	• Analyze and distinguish adverse events and report to regulatory authorities according to regulations	Quality manager
	• Analyze adverse event reports for similar devices (e.g., using FDA's MAUDE)	Risk manager
Clinical research	• Document clinical evaluation and literature search results and report inputs to product manger	Clinical manager
Service/repairs reports	Analyze service/repairs trends based on spare part or work order analysis	Service manager

Table 5.1 Examples of data collection methods for bladder scanners

Objective	Data source	Data analysis method
What are the most common complaints?	Complaints	Plotting data using Pareto diagram or bar charts
How many complaints relate to specific issues?	Complaints	Plotting data using a bar chart
What are findings from customer surveys?	Feedbacks	Qualitative
Reliability issue	Service/repair reports	Trend analysis of plotted data

Table 5.2 Examples of data analysis methods for bladder scanners

5.2 Post-market requirements in Korea

PMS has been a key agenda of medical devices regulatory policies in Korea. Specifically, advertising, re-evaluation, safety information including adverse effects, and tracking controls have been major policies since the enforcement of the Medical Device Act. Even after decades have passed since the enactment of the law, social issues regarding the safe use of medical devices have arisen, such as mass infection incidents due to reuse of disposable syringes. The absence of a comprehensive medical device information and distribution information management system was indicated as a limitation of follow-up management such as recall and disposal.

Considering the limitations of post-market management of domestic medical devices, the need to establish a safety management system throughout the life cycle from medical device approval to production, distribution, and use has emerged in Korea (52). The Medical Device Act was amended in 2016 to establish and operate an integrated medical device information system to track and manage the entire process from approval to distribution and use by attaching internationally standardized codes to all medical devices. The integrated medical device information system, which is also called the UDI system, has been operational since 2019.

5.2.1 Identification and traceability of distribution

Medical device standard code denotes numbers and bar codes (including RFID tags) in accordance with a standardized system, which are marked on containers to identify and manage medical devices in a systematic and efficient manner (53). It is widely known as UDI code, which is a combination of device identifiers (UDI-DI) and production identifiers (UDI-PI). UDI-DI comprises manufacturer number, country, and classification, whereas UDI-PI consists of lot or batch number, expiration date, manufacture date, and serial number. Individual devices have different UDI-PI, enabling traceability of distribution.

In Korea, medical device manufacturers, importers, distributors, and lessors supply medical devices to medical institutions, and medical device distributors and lessors shall report details of such provision to the Minister of Food and Drug Safety (53). The relevant regulation, article 31-2 of the Medical Device Act, in Korea entered into force and class II medical devices began to be reported after being supplied from July 1, 2022. However, the regulation has been postponed until 2023 reflecting demands from the medical device industry. Table 5.3 items of the supply report including product classification information, UDI-DI, manufacturing identifier, and price of supply. The report shall be submitted at the site of the integrated medical device information system by the end of the month following the month when the medical devices are supplied.

No	Category	Required information	
1	Supplier information	Business type: manufacturer, importer, distributor, lessor	
2		Supply type: delivery, return, disposal, lease, withdraw	
3		Supply target • to manufacturers, importers, distributors, lessors • to medical institutions • to a person who has established a pharmacy or a pharmaceutical wholesaler • as samples, donations, military supplies	
4	Information of a person who is supplied medical devices	Name of company	
5		Business registration number	
6		Health care institution identifier	
7	Product information including UDI codes	Permission (certification or notification) number	
8		Classification number	
9		Product name	
10		Model name	
11		Medical device standard code (UDI-DI)	
12		Manufacturing number	Lot number
13			Serial number
14		Manufacturing date	Manufacturing date
15			Use-by date
16		Packaging unit	
17		Quantity per pack	
18	Supply information	Supply quantities (total amounts of supplied devices)	
19		Supply date	
20		Supply of price	
21		Supply of unit price	

Table 5.3 Details of a medical devices supply report

The process of preservation of products and the contract review process are relevant quality procedures for managing supply. Records of these processes, including shipment register, invoice, and contract, should be documented and stored; however, records of manufacturers that establish the sales network through supplying or distributing agencies may address transactions with agencies. In this case, the agencies have the responsibility to report the final supply to medical institutions.

5.2.2 Reporting adverse events

A medical device handler shall immediately report to the MFDS if they discover any cases or risk of death or occurrence of a serious adverse effect on human health while in use (53). A quality manager is responsible for inspecting the incidents reported by the medical device handler. Examples of actions to be taken after analysis of the incidents include additional post-market management, provision of information to users using advisory notices, corrective actions for future production or products in use, and recall.

In Korea, the criteria for reporting adverse events stipulated in the Enforcement Rule of the Medical Devices Act are as follows:

a. Death or life-threatening side effects
b. Adverse events or side effects specified in each of the following items:
    - In case hospitalization or extension of hospitalization is required
    - If recovery is not possible or serious disability or deterioration of functions is caused

- In case of congenital deformity or abnormality

Although around 100 adverse events of bladder scanners were reported on the FDA's MAUDE, only one event was available in the MFDS's safety information sites (54) as presented in Table 5.4.

<table>
<tr><th colspan="2" rowspan="2">Adverse event</th><th colspan="3">Standard code</th></tr>
<tr><th>Device</th><th>Patient</th><th>Component</th></tr>
<tr><td>Adverse effect</td><td>N/A</td><td>N/A</td><td>N/A</td><td>N/A</td></tr>
<tr><td rowspan="2">Product defect</td><td rowspan="2">Due to a short circuit in the charging cable of the device, charging does not work and there is a burning smell.</td><td>Burn of device or device component (1071)</td><td rowspan="2">No patient involvement</td><td rowspan="2">Cord</td></tr>
<tr><td>Failure to charge (1085)</td></tr>
</table>

Table 5.4 Adverse events of bladder scanners in Korea

MFDS revised and announced the "Regulations on Safety Information Management Such as Adverse Effects on Medical Device" (55) in May 2022. In addition to the three existing categories of medical device adverse events standard codes—medical device problem, patient problem, medical device component—a cause investigation code has been newly established. Moreover, existing patient problem codes have been changed to health effect codes separating patients' symptoms with results.

5.2.3 Corrective and preventive actions

Recall is a serious measure against adverse events. As illustrated in Table 5.5, uncertainty of essential performance that may lead to temporary or medically reversible adverse health consequences should be considered as the subject of recalls. Bladder volume measurement might not cause health consequences directly; however, health impacts should be scrutinized.

Example #1 – Mobile ultrasound diagnostic imaging system	
Reason for recall	Overestimation bias in automatically calculated ejection fraction (EF) values while using an app on the product. Overestimated values can result in a normal indication of minor and moderate dysfunction.
Actions to recall	The manufacturer notified customers via a letter to notify urgent correction and sent an email notification to inform that the app update is available through the manufacturer's website.
Actions by customer	Contact the customer center indicated on the product or return it to the place of purchase.
Date / Status	2019-05-27 (initiated) ~ Open
Quantity	119 (worldwide)
Example #2 – Ultrasonic pulsed echo imaging system (bladder scanner)	
Reason for recall	• Calibration sensitivity • Calculation and use of an incorrect year in dates after 12/31/2009 • Double scans, continuous scans, and double printing
Actions to recall	The manufacturer sent a recall letter and called about the upgrade.
Actions by customer	Customers are guided to upgrade units using an online tool. Customers may elect to return their units to the firm for upgrading.
Date / Status	2009-05-18 (initiated) ~ 2010-10-07 (terminated)
Quantity	1,978 (worldwide)

Table 5.5 Examples of recall as a corrective action reported to the FDA

Recall can be triggered by post-market risk assessment and it can also lead to discontinue of the product as illustrated in Table 5.6. This table presents an example of a bronchoscope that is recalled both in Korea and the US; however, the decisions followed by the recall would vary upon countries.

Country	Republic of Korea	United States
Reason for recall	The manufacturer confirmed through post-market risk assessment that patient infection problems may occur if the product is used without proper reprocessing. The possibility is estimated to be significantly low, but the manufacturer decided to discontinue the product and recall the existing sales product to use the product more safely.	The product is being recalled because it does not have a 510(K) clearance, and the device is associated with a higher rate of patient infections than other comparable bronchoscopes.
Actions to recall	Recall of the product and provision of a replacement product	The manufacturer notified direct customer accounts via a recall notification letter.
Actions by customer	Contact the customer center indicated on the product or return it to the place of purchase	Contact service representatives and return or replace. The product may be continued to be used clinically until suitable alternatives are sufficiently available only if there is continued adherence to the IFU related to reprocessing.
Date	2020-08-31 (initiated) ~ 2020-11-12 (terminated)	2020-08-31 (initiated) ~ Open
Quantity	5,813 (worldwide)	
	5 (distributed in Korea)	2,648 (distributed in the US)

Table 5.6 Recall cases of the same product in two countries

5.2.4 Change management

Engineering changes are often requested after a medical device is marketed. Data collected and analyzed in PMS are common inputs of changes. From the regulatory perspective, a regulatory pathway of the change depends on whether the change affects safety or effectiveness. There are three pathways in Korea regarding change management: minor change requiring immediate reporting or yearly reporting and modification approval (permission, certification, and notification) with/without technical document review.

Modifications of operational principle and raw materials that are used in the domestic scenario for the first time require a new regulatory approval. Aside from these cases, primary criteria determining pathways of change management are as follows:

a. Is the device intended for export only?
b. Does the medical device itself not change by the modification?
c. Is it a change of a technological characteristic?
d. Is a change of a raw material?

The case of export-only devices requires modification approval without technical document review if the intended use is changed or the manufacturing site's location is changed, added, transferred, or taken over. Otherwise, it is classified as a minor change requiring annual reporting. The "Regulations on Medical Device Approval, Notification, Review, etc." (56) specifies nine types of minor changes at the Appendix 3 as given in Table 5.7, and it presents examples of applicable minor changes for bladder scanners.

Type	Minor change	Example
1	Not changing the device	Change of manufacturer name, addition to cautions
2	Name	Change of the classification name, product name, or model name
3	Raw material	• Change the name or identifier of parts in electrical devices • SW version change due to elimination of defects without any feature addition or modification of GUI color and menu position
4	Component	• Change quantity of thermal paper provided as components • Modification in exterior color of cradle station that is not a medical device solely
5	Appearance	• Change of scan button's shape or position only if the modification does not affect to electrical or mechanical safety • Modifications in product name or trade name on product exterior
6	Packaging & container	Change of packaging design, company trademark
7	Device only for export	N/A
8*	ME equipment	• Change the printer with the same performance for embedded printer • Addition of small mounting fixtures (e.g., mounting hooks or screws) • Change of internal memory with different capacity • Change of a battery that satisfies the same performance and standards (limited to cases where it is proven that the battery meets the safety requirements of the relevant IEC or ISO standards)
9	Medical supplies	N/A

* Safety should be confirmed in accordance with the common standards of the MFDS

Table 5.7 Examples of minor changes for bladder scanners

5.2.5 Renewal of regulatory approval

Since 2020, the medical device renewal system has enforced efficient management of medical device quality by reviewing safety and effectiveness of products periodically and arranging items that have not been manufactured or imported. Products licensed after the implementation of the medical device renewal system have a validity period of 5 years from the date of approval, and those who intend to continue manufacturing or importing after the expiration date must apply for renewal 180 days before the expiration date.

No	Submission material
1	Submission checklist for renewal
2	Original certificate or permit
3	Review data whether the device is conformed with the latest standards
4	Data that safety and effectiveness of the device are maintained
5	Data on production and import must be submitted
6	Data on safety information and measures collected during validity period

Table 5.8 Submission materials for renewal of certification/permit

Table 5.8 provides submission materials for renewal of certification or approval. For an example of bladder scanners, data on electrical, mechanical, and electromagnetic safety and performance should conformed to the latest version of standards specifications determined by the MFDS or a more recent version of the equivalent international standards. Current deviation between standards specifications and international standards are listed in Table 5.9.

Category	Current standards of the MFDS	Latest version of international standards
Basic safety & essential performance – Electrical ·mechanical safety	IEC 60601-1:2012	IEC 60601-1:2005+AMD1: 2012+AMD2:2020
Basic safety & essential performance – Usability	IEC 60601-1-6:2010	IEC 60601-1-6:2010+AMD1: 2013+AMD2:2020
	IEC 62366:2007	IEC 62366-1:2015+AMD1: 2020
		IEC TR 62366-2:2016
Basic safety & essential performance – Electromagnetic disturbances	KN 60601-1-2:2008 * converted to KS C IEC 60601-1-2 (57)	IEC 60601-1-2:2014+AMD1:2020
Ultrasonic medical diagnostic and monitoring equipment	KS C IEC 60601-2-37:2015	IEC 60601-2-37:2007+AMD1: 2015
Risk management	ISO 14971:2007	ISO 14971:2019
		ISO TR 24971:2020
Software life cycle	IEC 62304:2006	IEC 62304:2006+AMD 1:2015

Table 5.9 Comparison between current standards specifications of the MFDS and the latest version of international standards

If submission material No. 3 is a checklist confirming conformances, No. 4 is a test report or a certification corresponding to the No. 3 material. Finally, material No. 6 includes documents or records produced under the manufacturer's quality management system as primary and customer complaint handling records or preventive and corrective action procedures as substitutes.

5.3 Discontinuation

In this dissertation, life cycle covers all phases from the cradle to the grave, and the final stage—EOL—can be addressed in two ways. First, an individual device has its own lifetime related to its useful life; there are several procedures to handle the device after the end of its lifetime. Next, there is an end to the product's life cycle, i.e., discontinuation.

5.3.1 End of lifetime

Medical devices reach a state in which the cost–benefit ratio is negative, with declined performance, unreliability, and regular failure. When a medical device becomes obsolete or unusable or is no longer required by a health care facility, it enters the final phase of its life cycle, i.e., decommissioning.

Decommissioning is removal of a medical device from clinical practices in a healthcare institution. According to the World Health Organization's guideline, the two main pathways for decommissioning a medical device and determining its final disposition after decontamination are permanent elimination and reuse, as shown in Figure 5.2 (58).

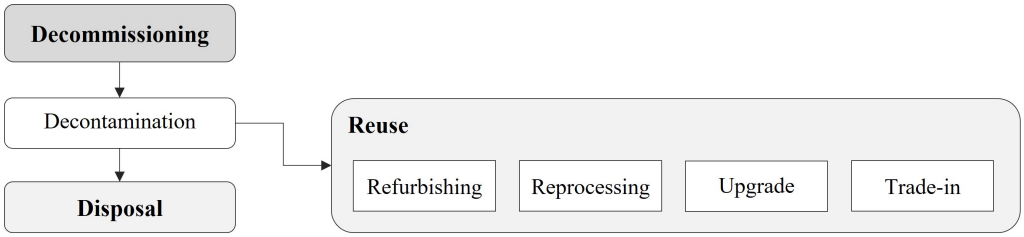


Figure 5.2 Decommissioning procedures of medical devices

5.3.2 Decision factors of discontinuation

The lifecycle of medical devices is normally shorter than that of pharmaceutical products, as devices can be replaced by newer, improved ones more frequently or easily (59). There are several factors that can prompt manufacturers to decide on discontinuation of products. The greatest motivation of discontinuation is an advent of innovative technology that can replace the existing technology or products. However, this process takes time to be widely used in clinical settings because adequate clinical evidence is required. Thus, there could be a period in which existing and new products coexist (60).

Electrical medical devices including various parts may encounter to the possibility of changing electronic components. If the change requires engineering change, which entails design change such as circuit modifications, it requires costs and time to repeat the design and development cycle including validation and safety test certification. Then, the decision should be made on the basis of benefit–risk analysis from the cost effectiveness viewpoint. Furthermore, operational software could be the reason to decide on discontinuation. In particular, if a medical device's operating system (OS) cannot be updated owing to compatibility issues and the OS does not support security updates, then discontinuation of the existing product is inevitable.

Above all, discontinuation should be preceded by consideration of safety and efficacy from the perspective of regulatory science. To be specific, post-market risk assessment also determine discontinuation.

5.3.3 Implementation of discontinuation

There are two types of discontinuation: discontinuation with voluntary recall and discontinuation without recall. Some devices that could lead to serious harm or death of patients could be recalled with discontinuation as presented in Table 5.10. Manufacturers need to consider whether there are no newly identified risks when deciding discontinuation, or they should assess cost effectiveness of discontinuation when they recall the device.

Product	Automated external defibrillators (non-wearable) (Product code: MKJ)
Reason for recall	The rotary therapy selector switch may fail, resulting in unexpected device behavior – the device may not turn on, the device may not perform the selected function, and the device may deliver a shock with an energy level different than the setting selected by the user. In any of these scenarios, appropriate therapy delivery may be delayed.
Description	The manufacturer distributed the "URGENT MEDICAL DEVICE RECALL" letter to affected customers informing of the device defect and possible unexpected behaviors. There have been three reported patient deaths potentially associated with the failure of the device's rotary therapy selector switch. Customers were advised that the device has been discontinued and has reached its end of life. Therefore, customers should replace and retire their units as soon as practically possible. Customers should continue to perform Shift Checks and Operational checks as recommended in the IFU as this reduces the risk of a failure until your units are safely retired.
Date	2020-04-13 (initiated) ~ 2021-04-07 (terminated)
Quantity	94,034 (worldwide distribution)

Table 5.10 A case that a product recalled and discontinued simultaneously

There are intermediate steps before the EOL: end of sales (EOS), end of development, EOL, and end of service life (EOSL). Manufacturers shall inform users via advisory notice providing information on the schedule from EOS to EOSL. After EOS, warranty extension may be possible if there are few years left until EOSL. Figure 5.3 shows an example of a letter notifying customers of a manufacturer's discontinuation plan.

[Company Logo]

Date of announcement

Dear customer,

[Company name] introduced **[Product Name]** in **[Launch year]**. As **[Company name]** continues to introduce new products into the marketplace, we decide to implement a phased discontinuation of the **[Product Name]**.

We are committed to providing the highest level of customer service and support while you determine the best plan for your products. Please see below for schedules regarding your **[Product Name].**

Discontinuation of **[Product Name]** announced : **20xx.xx.xx**
End of new product sales & End of extended warranty sales: **20xx.xx.xx**
End of service including support, non-/warranty replacements: **20xx.xx.xx**

For question about this phased discontinuation communication, your specific comprehensive warranty plan, or for information about available upgrade options, please contact your local **[Company]** representative at **[Contact information of local rep]**

New products for technology is available for your needs – please visit **[Company website]** to learn more.

We appreciate your business and look forward to serving you in the future.

[Signature & Information of announcer]

Figure 5.3 A template of discontinuation letter

Chapter 6

Discussion

Total product life cycle has become utilized as a regulatory framework integrating regulatory perspectives from pre-market review to post-market surveillance. There are three different life cycles covering total life cycle: marketing development life cycle from concept to obsolescence; regulatory life cycle from request for designation to recalls; and the scientific life cycle from design to end of life (61). These life cycles are interconnected because a safe and effective device only can be possible with comprehensive understanding of them. This dissertation proposed medical device life cycle management process, which is an integrated form with these life cycles, demonstrating that various activities such as product planning, design and development, and licensing are performed organically to form the life cycle of medical devices.

Safety, effectiveness, quality, and performance are regarded as primary objectives in regulatory science. Every activity of the life cycle was implemented to pursue and maintain these goals throughout the life cycle. Medical device manufacturers are responsible to make medical devices satisfying regulatory requirements by establishing appropriate quality management system. Also, risk-based approach is the most fundamental principle in regulatory science to maintain safety of a medical device. Existing studies addressing risk management process mostly focuses on development life cycle or illustrating of specific

analysis methods. On the other hand, this research included establishment of quality management and application of risk management process throughout the life cycle.

Designed and development phases are the most crucial phase of its life cycle because a poorly designed device will not make its way through regulatory compliance into the market (62). Usability engineering, also called as human factors engineering, is the evolving discipline that should be considered into the life cycle to ensure safety, effectiveness. To prevent poor interface design facilitating user errors, iterative design approach was conducted based on usability engineering process in this research. Conducting many small-scale iterations in the early phases of the design process is a good way to enhance system usability (10, 11, 63). This research also demonstrated design iterations with validation.

Initially proposed bladder monitoring system was designed to continuously measure bladder volume for use by lay patients of various demographics. However, only healthcare specialists evaluated the proposed system. Moreover, the usability test was conducted using a mock-up of the device and a simulated version of the mobile application, so some tasks were simulated rather than being performed with an actual device. Thus, the usability test's results may not reflect real-world conditions.

This dissertation aims to provide a life cycle management process for a wearable monitoring system; therefore, BOL deals with the design and development process conducted for a wearable monitoring system. However, devices developed and marketed

for real business are fabricated in different ways, which are more similar to that of the existing bladder scanner, after marketing and regulatory strategies are established for the business. Thus, the actual steps of product launch and regulatory affairs of a wearable bladder monitoring system remains a matter to demonstrate. With lessons learned from bladder scanner cases, life cycle management for a wearable bladder monitoring system would be continued in a future study.

Chapter 7

Conclusion

The research presented in this dissertation started with a motivation to propose a medical device life cycle management process applying regulatory science. In this research, the focus was on a case of design and development of a wearable bladder monitoring system for two reasons. One is because urinary problems represent one of the most common ailments in an aging society. The other is because a wearable bladder monitoring system is a combination of mobile health – a type of digital healthcare, which is a new paradigm in medical industry – and ultrasound technology with the advantage of non-invasiveness. In this research, a life cycle management process was suggested, and the process was demonstrated in different phases.

In chapter 3, a case study on a wearable bladder monitoring system demonstrated the early phase of medical device life cycle. At the concept stage, the need for bladder monitoring and applicable indications were identified. Then, design cycles aligning with the usability engineering process were implemented, and it was proved that the usability engineering process is an effective way to understand user needs and improve usability.

Chapter 4 presented two types of bladder scanners that were designed and launched as a strategic intermediate step for the launch of the wearable bladder monitoring system. This chapter described the applicability of regulatory sciences such as application of risk

management, design controls, establishment of quality management system, and regulatory affairs from technical document review to product and manufacturing certification.

In chapter 5, the final phase of the lifecycle, i.e., EOL, is addressed from post-market management and discontinuation viewpoints. A PMS process for bladder scanners based on ISO/TR 20416:2020 was established, and PMS activities were introduced to satisfy post-market requirements in Korea. There are various factors when deciding discontinuation of a product; however, it is determined on the basis of risk benefit or cost effectiveness analysis. The background and steps of discontinuation are illustrated with cases of other devices.

The research in this dissertation contributes toward understanding life cycle management with emphasis on application of regulatory science. Understanding and applying regulatory science is not only for a prerequisite of market entry, but also a key to ensuring safety, effectiveness, quality, and performance throughout the life cycle of a medical device. To make devices safe and effective, this research suggests design iterations based on usability engineering approaches at the concept, design and development stages in the BOL phase. The proposed life cycle management process is demonstrated with a case of a wearable bladder monitoring system which also includes mobile health; thus, the process is also applicable to medical device software.

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국문요약

웨어러블 방광모니터링 시스템의 생명주기에 대한 의료기기 규제과학의 적용

의료기기 규제과학은 생명주기 전반에 걸쳐 안전성, 효능, 품질 및 성능을 평가하기 위한 다양한 과학적 방법으로, 의료기기 설계 및 개발에 있어 필수적인 요소이다. 특히 기술 발전에 발맞추어 다양한 규제 요구사항이 추가되고 사후관리의 중요성이 대두됨에 따라, 제품의 생명주기 전체를 아우르는 규제 프레임워크가 도입되었다.

종래의 연구는 제품 생명주기 전반보다는 설계에 초점을 맞추거나 위험관리와 같은 특정 접근법이나 사이버보안, 사용적합성과 같은 특정 요구사항에 주로 초점을 맞추고 있다. 또한, 의료기기에 대한 아이디어에서부터 시작하여 출시, 수명 종료로 인한, 폐기, 더 나아가 단종에 이르기까지 생명주기 전반에서 규제과학이 적용되는 양상을 포괄적으로 다룬 연구가 부재하다.

본 논문은 의료기기 규제과학을 고려한 생명주기 관리 프로세스를 제안하고 두가지 방식으로 프로세스의 적용을 입증한다. 첫째, 웨어러블 방광모니터링 장비의 개발 사례를 통해 개념정립부터 인허가에 이르기까지의 과정을 단계별로 제시한다. 둘째, 국내 현행 규제에 대한 조사와 사례 분석을 통해 제품이 출시된 이후의 시판 후 관리에서부터 판매 종료에 이르기까지 고려되어야 하는 요구사항을 규제과학의 관점에서 보여준다.

본 연구에서는 웨어러블 방광모니터링 시스템을 통해 사용적합성 엔지니어링 접근법을 반영한 설계 및 개발 프로세스를 적용한다. 연구 결과는 모바일 헬스 애플리케이션을 비롯한 다양한 소프트웨어 의료기기 개발에 활용 가능한 디자인 함의를 포함한다. 또한, 본 논문에서 제시하는 프로세스가 의료기기를 처음 개발하거나 생명주기 전반에 대한 프로세스가 구축되지 않은 창업 초기의 의료기기 제조사에서 활용될 수 있을 것으로 기대한다.

핵심어: 의료기기 규제과학, 제품 생명주기, 사용적합성 엔지니어링, 사후관리, 방광모니터링