

Adaptive Regulation for Digital Health:

Enhancing Australia's Regulation System

FEBRUARY 2021



Contents

Executive Summary	3
About this Research	4
About the Authors	4
About the Steering Committee	5
1. Introduction	6
2. Adaptive Regulation of Digital Health	10
3. Engaging with the Regulatory Framework	18
4. Enhancing Australia's Regulatory System	27
5. Discussion and Conclusion	36
Appendix A Project Methodology	40
Appendix B What is Digital Health?	42
Appendix C Regulatory Frameworks for Digital Health	51
Appendix D Adaptive Regulation	65
6. References	68

Executive Summary

Digital health technologies (DHTs) have the potential to disrupt both the medical technology, biotechnology and pharmaceutical sector and the broader delivery of healthcare, creating challenges for the effective and timely regulation of new therapeutic goods.

This report examines how digital health industry stakeholders are engaging with the Australian therapeutic goods regulatory framework.

Focusing on DHTs regulated as medical devices – including software as a medical device (SaMD) and physical medical devices with associated software – the research has sought to:

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|---|--|---|--|--|
| 1. Ascertain the current state of knowledge regarding regulatory pathways and regulation compliance for DHTs; | 2. Identify key challenges in digital health regulation within the current regulatory framework; | 3. Identify potential alignments and misalignments between current regulatory requirements and new product development processes; | 4. Clarify how current regulatory policies and frameworks could accommodate an adaptive approach to digital health regulation; and | 5. Identify areas where greater education and awareness are needed within industry. ⁱ |
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The emergence of DHTs has seen companies unfamiliar with the regulated health environment entering the sector. They bring different work and investment practices and may delay, or even avoid, regulatory engagement. At the same time, falling manufacturing and distribution barriers have substantially boosted the number of new digital health products.

Australia's regulatory framework for medical devices is currently risk-weighted, outcomes-based and moving towards international harmonisation. There are, however, different perspectives and understandings of DHTs within the industry that have implications for regulation.

New and some existing developers often have little understanding of regulatory requirements, including the level of clinical evidence required for market approval.

In contrast, experienced developers actively build regulatory processes into their product development cycles from the outset by enacting risk-based assessments during their commercialisation process, from proof of concept to prototyping.

Using case studies, this report highlights the rapid and diverse development pathways for digital medical devices in Australia. Each device progresses from initial needs assessment and idea generation (Stage 1); through screening, feasibility testing, proof of concept and evidence building (Stages 2–5); to market launch (Stage 6); and, finally, market uptake and post-market reporting (Stage 7). The development process is typically iterative rather than linear, with feedback loops between stages of development for improvement, rework, enhanced functionality, enhanced cybersecurity and useability.

A complex environment characterised by the speed and frequency at which new technologies emerge; the need for extensive iterative technology improvements; the quantity of data generated; and the number of new developers unfamiliar with medical industries all create regulatory challenges.

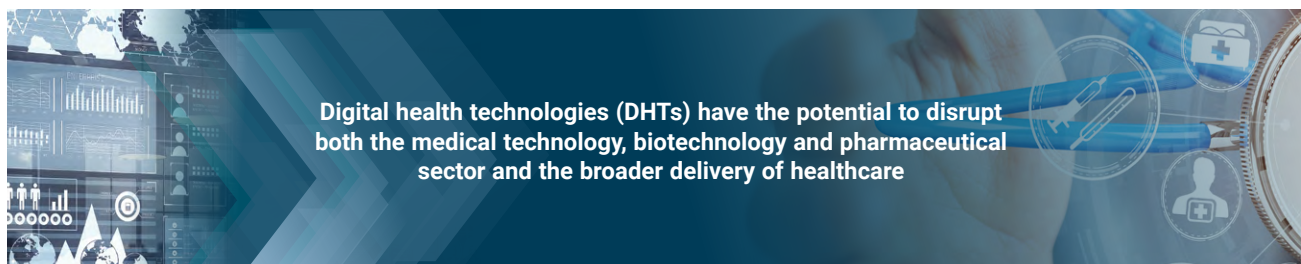
The need for flexible regulatory frameworks supported by education and awareness programs across the industry is clear. Policy cannot predict technological disruption – but it can be designed to deliver proactive and responsive regulation to capture and assess new data and support evidence-based decision-making. Regulation that is flexible and adaptive would better suit the rapid pace of technological change.

Australia can lead the way in the regulation of DHTs. This will require change to the existing regulatory framework. This is a challenge, not just for the Therapeutic Goods Administration (TGA) as the regulator, but for all stakeholders.

In doing so, Australia will have the opportunity to take the global lead in ensuring timely consumer access to cutting-edge medical technologies.

ⁱ The intent of this report is to assess and review the current Australian Therapeutic Goods Administration (TGA) regulatory pathway as applied to digital health. The report does not include cybersecurity or privacy issues even though they do clearly apply to digital health.

About this Research



The research presented in this report was conducted by researchers at The University of Queensland's (UQ) Australian Institute for Business and Economics (AIBE), under UQ Institutional Human Research Ethics Approval (2019000069). It was led and funded by MTPConnect, Australia's Growth Centre for the medical technology, biotechnology and pharmaceutical sector. Input into the design and additional assistance was provided by a national steering committee comprised of representatives from MTPConnect; CSIRO; the Australian Government Department of Industry, Science, Energy and Resources (DISER); the TGA; ANDHealth; the AIBE; and Allens. The authors thank members of the steering committee and their representatives for suggestions, comments and edits on this report.

The research was conducted between February and April 2019, and the findings reflect the digital health industry and case study companies at that time. Significant progress may have been made since then. For example, Cardihab began and completed the process of ensuring compliance with TGA regulation, and version 2 of their platform was released in July 2020 and registered on the ARTG as a Class I medical device. In addition, Section 41BD of the Therapeutic Goods Act was updated in September 2020 to expand the reference to software in the definition of a medical device, as well as expansion of the purpose to include prediction and prognosis (see Appendix B-6-1). Further guidance was released by the TGA in late 2020 including new exclusions and exemptions for software-based medical devices which came into effect 25 February 2021.

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The Australian Institute for Business and Economics

AIBE leverages world-class collaborative research capabilities across The University of Queensland's Business School, School of Economics and TC Beirne School of Law. The institute focuses on Australian and global innovations and new horizon research to address current needs and future challenges of businesses.

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Alex Smith is a Principal Research Officer at AIBE. His expertise is in the area of technology commercialisation and strategy, disruptive innovation and digital health.

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About the Steering Committee

MTPConnect

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MTPConnect is the growth centre for the medical technologies, biotechnologies and pharmaceuticals sector in Australia. It is a not-for-profit organisation that aims to accelerate the rate of growth of the sector through greater collaboration and commercialisation.

CSIRO

Dr Rob Grenfell (Director Health & Biosecurity) and Dr Peter Kambouris (Director BD&C, Health & Biosecurity)

CSIRO is the Australian national science research agency, and Australia's largest patent holder. The Health & Biosecurity team consists of strong multidisciplinary researchers aiming to tackle major national and international health and biosecurity challenges. In doing so, they protect the health of Australia's farming sector, environment, people, and way of life.

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DISER drives growth and job creation for a more prosperous Australia by facilitating economic transformation and boosting business competitiveness.

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The TGA is Australia's regulatory authority for therapeutic goods. It is part of the Australian Government Department of Health and is responsible for regulating therapeutic goods including prescription medicines, vaccines, sunscreens, vitamins and minerals, medical devices and blood products.

ANDHealth

Bronwyn LeGrice (Managing Director & CEO) and Grace Lethlean (COO)

ANDHealth is an industry-led, multisectoral, national digital health initiative established to facilitate and support the development and commercialisation of clinically validated DHTs across Australia.

The Australian Institute for Business and Economics

Professor Damian Hine, Dr Lisette Pregelj

AIBE focuses the renowned collaborative research capabilities of The University of Queensland's Faculty of Business, Economics and Law to address pressing social and structural issues.

Allens

Dr Ric Morgan (Special Counsel)

Allens is a leading Australian law firm with a strong interest in the healthcare sector and digital and e-health. As part of its support of industry in this sector, Allens works with ANDHealth.



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CREATE CHANGE

Introduction

1. Introduction

DHTs fit neatly with the megatrends of a rapidly changing society. From the diagnosis of disease; delivery and dosing of pharmaceuticals; disease and patient health data management; through to behavioural intervention via apps, online advice and collaborative programs, healthcare is undergoing a digital transformation.

*"The digital health sector is new.
The digital health sector
is different in Australia."
Regulator/Policy Maker (P02)*

Sector megatrends overview

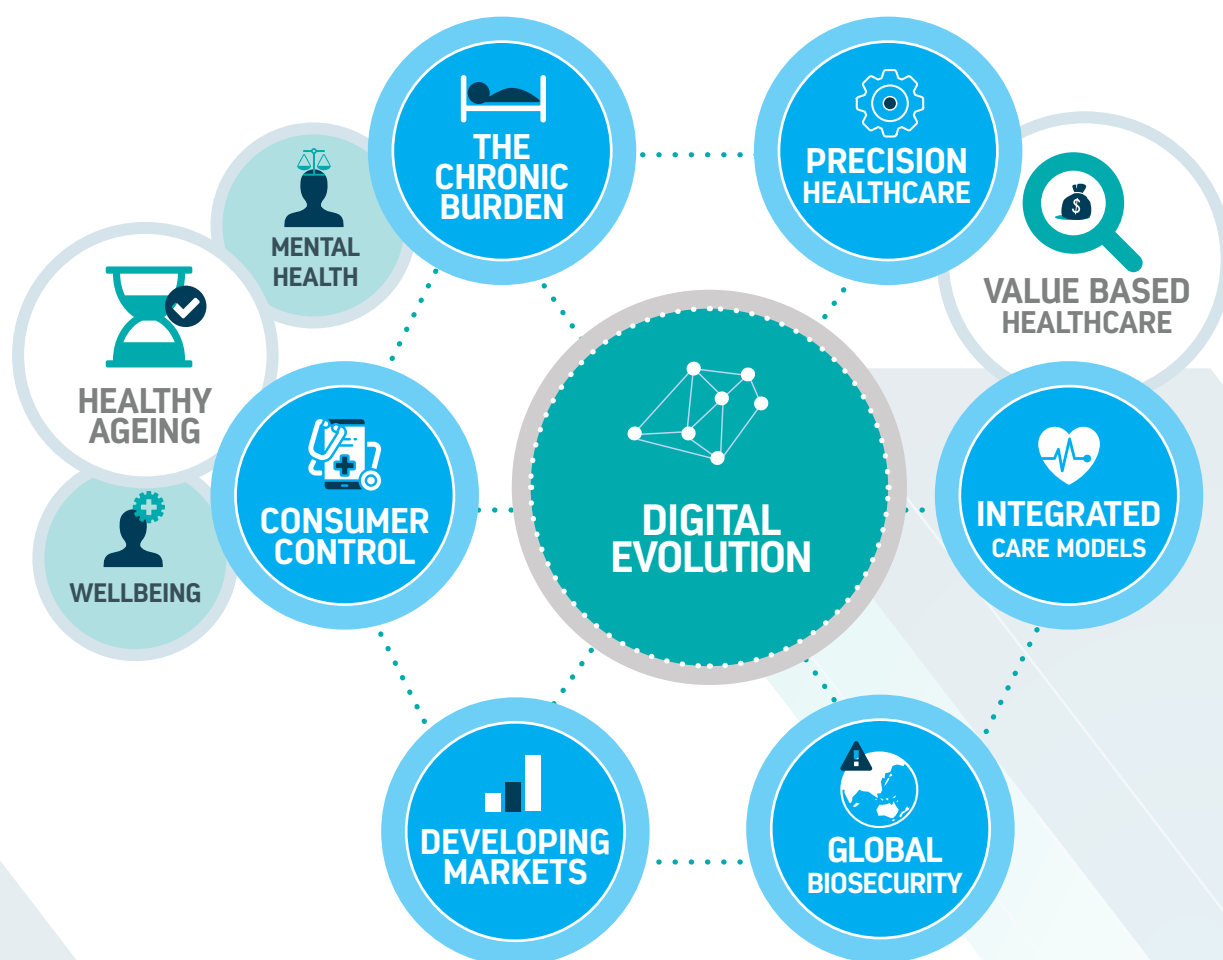


Figure 1. Emerging megatrends identified by MTPConnect¹

Influencing this transformation are policy incentives towards value-based healthcare, rising healthcare costs, advancements in digital technologies such as artificial intelligence (AI) and machine learning and increased availability of health information from connected smartphones and other devices.²

While early behavioural and lifestyle interventions are being increasingly deployed, claims of both preventative and curative health benefits to individuals requires a system of quality control and assurance. At the core of this is a robust and efficient regulatory system.

Consumers and clinicians require assurances that health interventions – be they pharmacological, medical, surgical or service-based – will be of a high quality, safe and efficacious and with clinical and/or therapeutic benefits outweighing possible risks and side effects. These assurances are traditionally provided through non-clinical, pre-clinical and/or clinical testing, and are assessed according to the nature of the intervention and the risks it poses by a national therapeutic goods regulator before being approved for market launch.

In Australia, this regulator is the TGA; in the United States (US) the US Food and Drug Administration (FDA). In the European Union (EU) the regulation of drugs and devices is handled separately, with the European Medicines Agency (EMA) regulating drugs, and a number of appointed commercial entities called Notified Bodies providing oversight of medical devices on behalf of therapeutic goods regulators. These and other equivalent national agencies regulate the manufacture, distribution and sale of therapeutic goods, which ultimately protects the health and safety of consumers.

Regulation and regulators can also actively shape how and which health technologies develop, as well as when and where they are deployed. Product developers respond to pathways that are more easily navigated, have faster approval timeframes, or represent lower costs.^{3,4} However, when industries evolve and innovate at a rapid pace, legislation, policy and regulation can often lag behind. This can lead to tensions among industry stakeholders, which may threaten organisational and industry competitiveness.

As such, keeping abreast of ongoing technological, social and economic developments is a major challenge for policy makers and regulators. Legislation, policy and regulation may need to be reviewed and revised to address the 'pacing problem' of technology developing faster than corresponding regulation.⁵ The challenges and dangers of regulation failing to be fit-for-purpose due to accelerated contextual changes has led to the concept of 'adaptive regulation'.

'Adaptive regulation' describes two distinct but related concepts. Firstly, the process of assessing the effectiveness of current regulation and making recommendations for legislative or policy amendments.⁶ Rather than 'set and forget', legislation, policy, and/or regulatory frameworks are periodically reviewed and changed to ensure they remain fit-for-purpose. Secondly, it describes regulations that are sufficiently broad to be flexible to change, with additional adaptive features and mechanisms. For example, regulatory sandboxes or principles-based regulations that can be applied flexibly and accommodate disruptive innovations.^{7,8}

1.1 Project background and aims

In response to the potential disruption to the MedTech and Pharma (MTP) and broader healthcare sector from digital health innovations and the ensuing regulatory challenges, MTPConnect is leading a project investigating adaptive regulation of DHTs. As part of that project, this report examines how digital health industry stakeholders are engaging with the Australian therapeutic regulatory framework, particularly as novel products incorporating patient-centric DHTs emerge onto the market. The goals of this research are to:

1. ascertain the current state of knowledge regarding regulatory pathways and regulation compliance for DHTs;
2. identify key challenges in digital health regulation within the current regulatory framework;
3. identify potential alignments and misalignments between current regulatory requirements and new product development processes;
4. clarify how current regulatory policies and frameworks could be enhanced towards an adaptive approach to digital health regulation; and
5. identify areas where greater education and awareness are needed within industry.

These insights are intended to help ensure policy, regulatory and strategic objectives are aligned with the emerging digital health sector, and that the regulator is supported in its oversight of a robust and safe industry that meets community needs and expectations for the next generation of healthcare.

These insights are intended to help ensure policy, regulatory and strategic objectives are aligned with the emerging digital health sector...

1.2 Research design and approach

Developing a comprehensive picture of how Australia's digital health industry is engaging with regulatory frameworks requires a multi-perspective approach. Four key stakeholder perspectives have been investigated:

1. **product developers** who develop, manufacture and/or commercialise novel DHTs;
2. **regulators and policy makers** who provide the frameworks and oversight to ensure the quality, safety, efficacy (if medicine related), performance (if medical device related), and timely access of therapeutic goods;
3. **the wider industry** including industry bodies, accelerators, regulatory affairs consultants and research organisations such as CSIRO and universities; and
4. **users/consumers** of DHTs (see Figure 2 below).

Appendix A-1 outlines the full research methodology, including the phased research design beginning with desktop research into existing regulatory frameworks followed by an in-depth qualitative study of stakeholder perspectives and experiences. Included in the qualitative research phase were case studies of four exemplar companies: Atmo Biosciences Pty Ltd (www.atmobiosciences.com), Vitalic Medical Pty Ltd (www.vitalicmedical.com), Cardihab Pty Ltd (www.cardihab.com) and ResMed Inc. (www.resmed.com). Integrating different stakeholder perspectives provides a holistic and multi-level account of current understandings of the regulation of novel DHTs, including potential points of alignment and misalignment between regulatory, technical and commercial considerations during pre- and post-market activities.

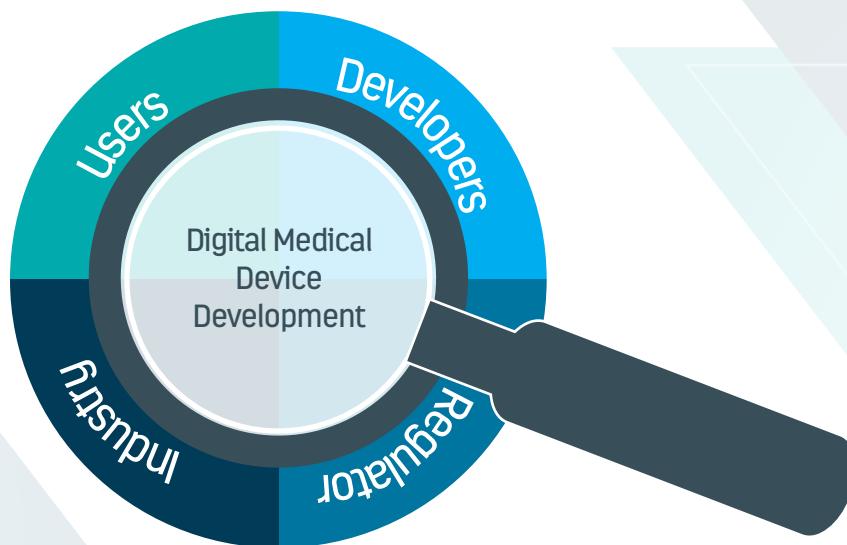


Figure 2. Digital health industry stakeholder perspectives captured in this study

Adaptive Regulation of Digital Health

2. Adaptive Regulation of Digital Health

The term digital health has been used to describe a range of different technologies, only some of which are regulated by national therapeutic goods regulators. This section of the report reviews and synthesises current knowledge and understanding of digital health based on definitions and discussions in the extant literature, government and not-for-profit organisations, national therapeutic goods regulators such as the TGA and FDA, and Australian digital health industry stakeholder interviews. This enables clear identification of which DHTs are regulated by national therapeutic goods regulators, as well as how they are currently regulated. Adaptive regulatory features inherent in the existing frameworks can then be identified. These findings can provide background and context in ascertaining the current state of knowledge of regulatory pathways for DHTs in Australia and other leading jurisdictions and identify the current challenges in digital health regulation within the current framework.

2.1 Digital health

The term 'digital health' has increasingly been incorporated into the scientific and medical lexicon (see Appendix B-1). Across scientific literature and reports from industry, governments and other organisations such as the World Health Organization, the definitions and descriptions of digital health and DHTs are varied and nuanced. Lee and Kesselheim provide a partial definition, that digital health software is considered to be innovative medical software meeting the definition of a medical device, which they define as: an article intended to diagnose or treat a disease [or other condition] or to affect the structure or function of the body, provided the article does not achieve its purpose through chemical action or by being metabolised.⁹

More broadly, digital health products include the use of the internet for health-related activities such as telehealth, electronic health and medical records (EMRs), treatment interventions implemented by mobile technologies and mobile applications, personal health and fitness applications and the use of advanced electronic communication technologies to exchange health information (see Appendix B-2 through B-4). Within this broad range of products lies DHTs, which we define in the following two sections.

2.1.1 Stakeholder perspectives of DHTs

Stakeholder views of DHTs – their definition, potential impact and future evolution – were diverse.

"The firm definition of what a digital technology is and what it isn't has been one that has actually challenged the biomedical and biotechnology industry, and certainly even healthcare providers, to actually understand what is a digital therapeutic." Industry – research organisation (P06)

"It means different things to different stakeholders and for a long time, digital health was centred on digitalisation of medical records, health IT, health informatics and things. We think that there is actually an evolution of the definition of digital health and we're moving past that primarily patient-focused record system solution ... I would actually look at the definition that FDA uses for digital health ... it talks about mobile health, health information technology, wearable devices, telehealth, telemedicine and also the importance of personalised or precision medicine." Industry – industry body (P01)

Two key themes emerged in stakeholder interpretations of digital health:

- 1) the nature and defining features of the DHTs themselves; and
- 2) the boundaries around digital health as a sector.

2.1.2 Defining features of DHTs

A prominent point of difference among industry stakeholders was which inherent features within the products and services marked them as DHTs. For some, it was the inclusion of software into a medical device:

"Digital health technologies are any health-related technologies that have a software component to them." Industry – research organisation (P09)

For others, software componentry has long been a part of health and medicine. Instead, the novel aspect of digital health is its 'data layer', including the incorporation of patient or device-collected data, cloud storage and the leveraging of this data into future product iterations:

"I think the whole move towards digital health is really adding another element to medical. There was still, obviously, a very large software component to those products. It just wasn't that you were pumping up the data to the cloud or capturing it in the ways that we can now, and the ways we are looking it." Product developer (P13)

2.1.3 Boundaries around digital health as a sector

Other prominent points of difference include the idea of digital health being a sub-sector of the broader health and medical industry, as opposed to its own emerging industry, versus digital technologies as merely enablers of health.



Stand-alone sector

"Everyone keeps telling me digital health is part of medtech. It is just not. There is no evidence to substantiate that beyond the fact that the existing medtech service providers want to tap into a gigantically growing market, which is a new industry. None of them are upskilling. They are just saying, 'We do digital health, because we do medtech,' and lots of medtech has software ... It is not a medical device. It is a new class of product."
Industry – industry body (P10)



Sub-sector

"If someone wants to call their product 'digital health,' that's okay. What matters to us, is it a medical device or not?" **Regulator/Policy Maker (P04)**



Enabler

"I'm not convinced that it needs to be different. My thinking on that is because it's an enabler more than it is the outcome." **Regulator/Policy Maker (P02)**

2.2 Regulation of digital health

The focus of this report is on the regulation of DHTs by national therapeutic goods regulators, in particular the TGA. Cybersecurity and privacy issues as applied to digital health are beyond the scope of this report.

Leading national therapeutic regulators regulate DHTs if those technologies meet the legislated definition of a medical device (see Appendix B-5). The definitions of medical devices in Australia, the US and the EU are included in Appendices B-6-1, B-6-2 and B-6-3, respectively.

There are similarities across all three jurisdictional definitions of medical devices (see Appendix B-6-4). They all include a broad description of a medical device as an instrument, apparatus or other article; intended for the diagnosis, prevention or treatment of disease; statements to the effect that the intended action is not achieved through pharmacological or metabolic means; and all include mention of software. Both the Food, Drug and Cosmetic Act (FD&CA) in the US and Regulation 2017/745/EU in the EU identify software functions that are not considered medical devices – usually software for general purposes in healthcare settings or for lifestyle or wellbeing purposes. The TGA similarly "does not regulate health and lifestyle apps and software that do not meet the definition of a medical device".¹⁰

2.2.1 A spectrum of DHTs

Published literature, industry reports, stakeholder interviews and national therapeutic goods regulators all suggest that there is a spectrum of DHTs that have their own requirements for regulation (see Figure 3). This ranges from medical devices incorporating or comprising software (digital medical devices), medical information and communication technologies, and products incorporating or comprising software that do not meet the definition of a medical device and are not regulated by national therapeutic goods regulators (wellness technologies). Whilst this spectrum of DHTs partially overlaps with medical devices, not all medical devices are considered DHTs and not all DHTs are regulated as medical devices. Those DHTs not regulated as medical devices include medical information and communication technologies and apps and digital devices that are for lifestyle or wellbeing purposes. At the far end of the spectrum are non-digital devices for lifestyle and wellbeing purposes.

This spectrum may also assist developers and other industry stakeholders to understand and identify which DHTs are regulated as therapeutic goods and which therapeutic medical devices are considered to be digital health.

This report focuses on DHTs regulated as medical devices.

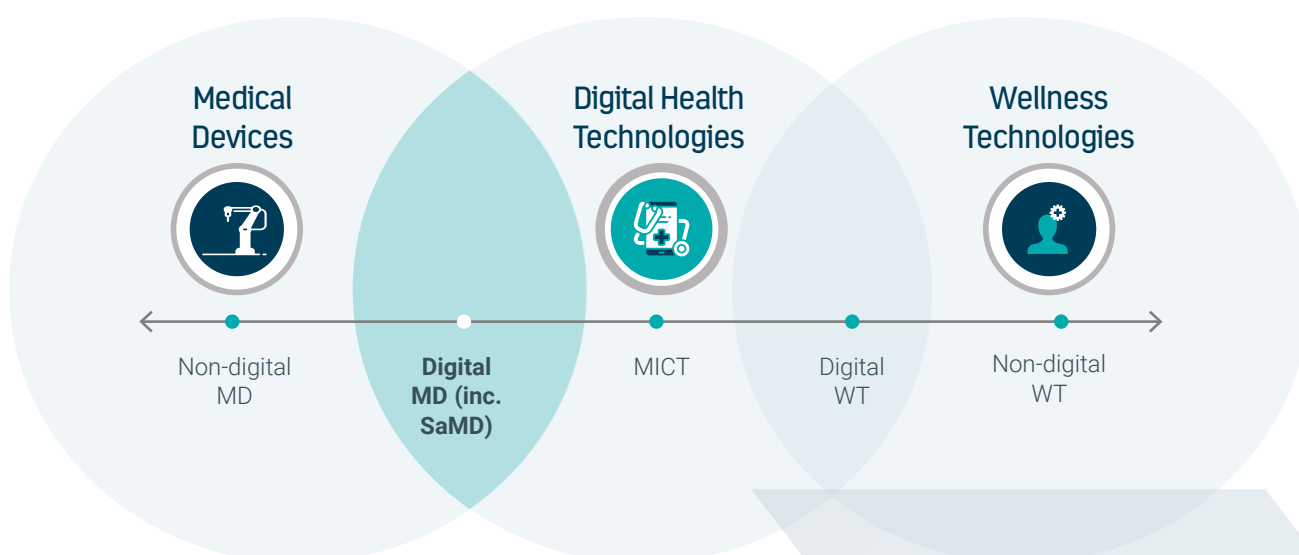


Figure 3. Spectrum of DHTs

Non-digital Medical Devices (Non-digital MD): Medical devices that are non-digital in nature, not connected to any inter- or intra-net, and are either non-powered (not active) or are powered and non-digital. These devices and technologies fall outside the scope of digital technologies, but inside the scope of regulated medical devices. Examples include hip joints and tongue depressors.

Digital Medical Devices (Digital MD): Medical devices incorporating as a component part, or fully comprising, software or programmed or programmable hardware. This includes medical devices that are software (such as smartphone apps), also known as software as a medical device (SaMD). Digital medical devices fall within the definition of a medical device as well as within the scope of digital health. Examples include MRI machines, CPAP machines, pacemakers, and smartphone apps for diabetics that calculate patients' insulin doses based on their blood glucose levels.

Medical Information and Communication Technologies (MICT): Software, databases, and communication technologies that are used in a healthcare setting, and so fall within the scope of DHTs, but do not fall within the scope of a medical device. Examples include electronic medical records and telehealth/telecare software and communications.

Digital Wellness Technologies (Digital WT): Health-focused technologies and products incorporating as a component part, or fully comprising, software and intended to be used for lifestyle or wellbeing purposes but do not meet the definition of a medical device. Examples include wearable running and exercise trackers, exercise, fitness or dietary tracking websites and mobile apps.

Non-digital Wellness Technologies (Non-digital WT): Traditional wellness products that are non-digital, do not fall within the scope of a medical device, and are intended for lifestyle and wellbeing purposes. Examples include non-electrical exercise equipment.

2.2.2 Adaptive regulation of digital medical devices

A broad review of existing regulatory frameworks for medical devices in Australia, the US, and the EU are included in Appendices C-1, C-2, and C-3 respectively. Variation exists among jurisdictions in the design of legislation and regulation for digital medical devices. The scope ranges from broad to precise and the frequency of required updates in response to innovation can vary from static through to continuously or automatically updated (see Figure 4). The different concepts of adaptive regulation (see Appendix D-1) reflect a trade-off between the scope and frequency of regulation review. With broad regulation, adaptation to new and ongoing technological innovation can occur less frequently and be more easily achieved through revision of guidance documents and post-market monitoring. Regulation of precise scope requires more frequent review and change at the legislation, policy and regulation level in order to accommodate emergent and disruptive innovations.

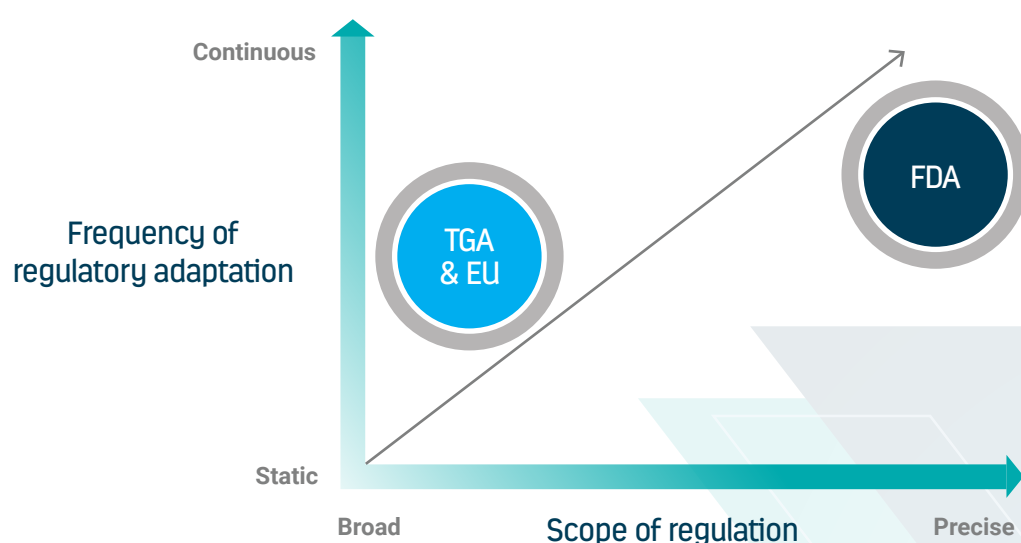


Figure 4. Scope and frequency of regulatory adaptation

The FDA classification of medical devices and subsequent inclusion in the Code of Federal Regulations (CFR) is an example of a system with a more precise regulatory framework. Each device classified through a 'De Novo' pathway is published to the register with a general description including its intended use and the class to which it belongs. All new devices seeking approval that are substantially equivalent to this device must be classified in the same regulatory category. The precise nature of the rules also necessitates the updating of legislation and regulation at frequent intervals as seen in the initial provision and amendments to the 21st Century Cures Act (2016).¹¹

Both the TGA and the EU conformity assessment procedures are based on meeting essential principles of safety and performance that provide flexibility for product manufacturers and developers to meet compliance requirements in line with the classification of their device. A benefit of broad regulatory parameters is the ability to accommodate both newly emerging and established technologies, which require less frequent adaptation.

The adaptive regulatory design features and mechanisms (see Table 1 on the following page and as outlined in Table 15 in Appendix D-1) have direct applications to DHTs. Some, such as outcomes-based and risk-weighted features, are inherent in the current broad regulatory scope of the TGA and those applicable in the EU, whereas others, such as adaptive authorisation and experimental co-design, are being trialled by other jurisdictions including the US.

Table 1. Adaptive regulatory design features and mechanisms in digital health

Features and Mechanisms	Examples in Digital Health Regulation
Outcomes-based	Both the TGA and the EU operate with a principles-based regulatory framework based on certification of the manufacturer (developer) – a form of flexibility in demonstrating regulatory compliance that gives the regulated entity freedom to determine how they meet requirements. ¹² <i>“Because we have a principles-based system, we can capture novel technologies. You must demonstrate your device meets the principles of safety and performance. You get the freedom to do your risk assessment and you get freedom to determine how you’re going to prove you meet those principles.” Regulator/Policy Maker (P03)</i>
Risk-weighted	The TGA, FDA, and EU currently operate with risk-weighted regulation, where the risk is assessed according to the potential of the device to cause harm. ¹³ The FDA is undertaking a Software Pre-Cert pilot program where the precertified developer “could then qualify to be able to market their lower-risk devices without additional FDA review or with a more streamlined premarket review.” ¹⁴ The United Kingdom’s National Institute for Health and Care Excellence (NICE) introduced an evidence standards framework for DHTs with different evidence tiers based on functional classification and potential risk to users. ¹⁵
Harmonisation through collaboration	The International Medical Device Regulators Forum (IMDRF) attempts to address issues of harmonisation of regulatory frameworks across international jurisdictions. Its guidance documents on SaMD and international medical device standards can be used to align international pathways for technology developers. ¹⁶ Additional guides are currently in development around cybersecurity, personalised medical devices and improving the quality of international medical device standards. ¹⁷
Adaptive authorisation	Most examples emerge from drug approval processes such as the EMA (referred to as ‘adaptive licensing’), which defines a ‘staggered approval’ process initially focusing on restricted populations, which is modified as real-world evidence (RWE) becomes available. ¹⁸
Experimentation and co-design	The Singapore Ministry of Health is conducting the Licensing Experimentation and Adaptation Programme (LEAP) for telemedicine, a controlled market trial of selected telemedicine and mobile medicine providers prior to the introduction of the new Healthcare Services Act (HSCA) in December 2020. The program allows the regulator and companies to work in closer alignment to assess the requirements of meeting regulatory approval and post-market monitoring. ¹⁹ The FDA’s novel Breakthrough Devices Program provides opportunities for manufacturers and the regulator to work together during the development process, through interaction and timely feedback, to efficiently address issues as they arise during premarket review. ²⁰

2.3 Emerging regulatory challenges in digital health

Interviews with Australian digital health stakeholders identified a number of emerging regulatory challenges in digital health. These include:

- 1) new entrants to the health space;
- 2) uncertainty about the regulatory process;
- 3) the speed and volume of new product emergence; and
- 4) potential misalignments between regulatory and development processes.

2.3.1 New entrants to the health space

The rise of digital health has seen new kinds of companies and professionals moving into the health space. These new entrants are not always familiar with the regulated health environment, bring with them different work and investment practices and may delay or even avoid regulatory engagement:

“Look, the ones that come from the consumer space or telecom space, it’s a bit of a shock to the system to see how highly regulated medtech is ... Software developers, they are not the regulated environment type, so they are just ‘oh, I’m just writing some code and I want to sell it, like, tomorrow’. They are not used to the constraints, you know, the strict rules, the documentation. You have to write it down... So culturally, I think that is a bit of a struggle sometimes.” Industry – industry body (P07)

"[There is] an active avoidance of regulation in companies arising from the tech sector and mentored by tech investors and tech accelerators. Being told literally to get revenue to drive their valuation and worry about regulation later." Industry – industry body (P10)

2.3.2 Uncertainty about the regulatory process

The need to gain and maintain knowledge of regulatory processes is not confined to new entrants. There were mixed levels of understanding about the regulatory process amongst some stakeholders, specifically around: a) identifying which DHTs are subject to medical device regulation; and b) the appropriate regulatory path if products are captured by regulations. Three potential 'gaps' drive this ambiguity.

First, new entrants, especially those with a tech industry background, are not always aware of regulatory obligations for novel DHTs (awareness gap). Second, even if product developers are aware of regulatory requirements, the information on how to navigate these, while available from regulators, can be complex and difficult to comprehend (comprehension gap). Third, some participants suggest existing frameworks and pathways do not always easily accommodate the new kinds of products and services made possible by DHTs, such as products based on machine learning and AI (framework gap).



Awareness Gap

"... people who are working to develop in that kind of start-up mindset, are not even necessarily aware of the regime that they need to worry about and so they can come to the 'Oh my Lord we need to worry about the regulatory side of things' late in the process."

Industry – regulatory affairs (P11)



Comprehension Gap

"... it's almost impenetrable, the information that's available is very hard to understand, very difficult to know whether you're going to fall within it or outside of it, and one of the other things I think that happens, because it's complex, people say, 'We'll just try to stay outside of it.'"

Industry – regulatory affairs (P12)



Framework Gap

"I think we're trying to retrofit some regulation to a relatively new industry that requires a slightly different approach to development and access to data. I think we need more expertise in the ecosystem more broadly but also within our regulators to understand ... those developments that could be coming down the pipe. And some that are going to be completely disruptive and may well try and move 'round the regulatory frameworks'."

Industry – industry body (P01)

Further, developers and manufacturers are not always clear about what changes to existing products requires notification or resubmission, and how long that might take:

"Probably the biggest one [misalignments] that I see is where a company has actually released and marketed a regulated piece of medical device software. But they've set themselves up with a flexible development environment – either Agile or DevOps or something like that, where they can easily push changes. And there's always a tension. Like can we just ... write this new feature so can't we just push it out? You know? We're kind of ready to go. Trying to push it out. Hit the button, bang, it'll be there in five seconds, you know? Versus 'oh, if there's 10 changes, changes three, five and seven we've done the analysis; they can go out, that's fine, we can do a note to file. The rest of them we're going to have put into a notified body consultation or something like that.'"

Industry – regulatory affairs (P12)

2.3.3 Speed and volume of new product emergence

Finally, recent years have seen a lowering of barriers to the manufacture and distribution of DHTs, leading to a dramatic rise in the volume and pace at which new products emerge onto, and scale within the market:

"Previously, medical software was produced by software companies. The big ones, like the scale of Microsoft. Now anybody can produce an app, publish it very easily. How easy it is to do that and put that up without realising it's regulated, versus a conventional device, a joint replacement. Nobody makes a joint replacement overnight. The challenge is the ease of producing medical devices has changed, and that just makes the volume continue to increase." Regulator/Policy Maker (P04)

This leads to concerns about the level of clinical validation and safety for DHTs sidestepping regulatory oversight:

"One of the biggest challenges we have is that there's a lot of non-clinically validated digital health." Industry – research organisation (P09)

Regulators are thus under pressure to rise to the challenge of increased product volume and speed, and to continue to provide clear 'signals' of product quality to the community:

"... because [there is] such a huge volume of things, but also a fast-paced iterative development cycle, there needs to be clear signals from established bodies of authority for which ones are good. Because there's so many out there that it's really unreasonable for consumers to have to try and make that assessment without any assistance." Consumer advocacy group (P19)

2.3.4 Tensions between development and regulatory processes

Development processes do not always align with current regulatory approval pathways for DHTs and services. Developers may place less emphasis on plans and documentation and more emphasis on the speed of development and iterative improvement:

"Regulatory focuses on plans and documents and rigid – more rigid processes where everybody has to find processes for everything. More agile development methodologies focus on change, adapting to change, doing it quickly. Having a conversation is more valuable than writing it down in a document." Product developer (P16)

"The mindset of a start-up type business that's thinking about developing their product in that kind of typical iterated way, is an uncomfortable fit for a regulator that is used to seeing things in their finished form, validated, finalised, substantiated with evidence, and it's just a difficult fit." Industry – regulatory affairs (P11)

Additionally, there are tensions between the rapidity of software development and the need for product validation in human settings, the latter of which is limited by the length of time it takes to observe health outcomes (e.g. disease progression and measuring efficacy of treatments):

"In normal drug discovery, the timelines of discovery align with the timelines of health. Here, we're outside that circle now. The timelines of discovery are in orders of magnitude faster than the health outcome. This is what I meant, you've got the guys [software developers] ... wanting to do these iteration sprints every four weeks [you have to say] 'guys, chill!'. We need to get an outcome and we need to do X, Y and Z." Industry – research organisation (P09)

2.4 Conclusion

Australia's therapeutic regulatory framework for DHTs is currently risk-weighted, outcomes-based and moving towards harmonisation with other jurisdictions through the IMDRF. However, there are different perspectives and understandings of these technologies within the industry that have implications for regulation. New and existing entrants with a lack of experience in the healthcare sector are confused about whether their DHTs are regulated as therapeutic goods and the level of clinical evidence required to support market approval.

Engaging with the Regulatory Framework

3. Engaging with the Regulatory Framework

To better understand the industry and regulatory landscape, we employ a multiple case study method to compare the experience of four Australian companies developing DHTs: Atmo Biosciences, Vitalic Medical, Cardihab and ResMed. Each is at varying stages of technology maturity, company size and experience. The case studies detail how these exemplar companies are currently navigating the DHT product development process.

3.1 Atmo Biosciences

Atmo Biosciences is an early-stage venture focused on the development and commercialisation of an innovative gas-sensing capsule. The ingestible capsule is designed to offer a safe and highly specific method for measuring the concentration of various gases in the gastrointestinal tract in real time. As the capsule moves through the gut, data is wirelessly transmitted to a receiver and subsequently through a mobile phone app to cloud-based servers accessed by consulting physicians. The intention is for the capsule to be cheaper and more accurate than conventional methods and for the aggregation of patient data to yield a normative dataset of gas profiles that can facilitate the development of clinical analysis and predictive algorithms. Potential indications for the technology span gut disorders from malabsorption through to inflammatory bowel disease (IBD).

Atmo was formed in 2017; however, the technology underpinning the capsule design had a long gestation within the Royal Melbourne Institute of Technology (RMIT) where it was originally directed at animal health applications, including methane mitigation. In 2010, following conversations with gastroenterologists, the possibility of adapting the technology for human applications led to a device for sensing intestinal gases in humans. In 2016/17, a Phase I human clinical trial provided initial validation of the capsule's safety and accuracy. During this time, the relationship between RMIT and Planet Innovation (PI), a leading health technology innovation and commercialisation company, formed, with PI first engaged to provide advice on commercialisation and later selected via a competitive process to bring the capsule to market. Atmo Biosciences was established as a vehicle for commercialisation and a licensing deal secured from RMIT. Atmo's development was further supported by its acceptance into the ANDHealth+ market and investment readiness program in 2017 and a successful seed funding round in 2019.

While still within the early stages of development, regulatory requirements have been a focus for the Atmo team.

"We spent a lot of time, at PI and at RMIT, trying to determine what our initial indications should be. Because it would then inform the regulatory strategy and vice versa the development and commercial strategy. One of the reasons we needed to do the regulatory aspect first, or early, was because it would then have knock-on implications for pretty much everything else that we did."

Atmo sought advice from separate regulatory consultants, one Australian and one US-based, in the development of its regulatory strategy. The reports presented were largely in alignment and confirmed Atmo's initial assumptions of a pathway that best combined speed to market with probable payers. The decision to focus on a US launch was prompted by the combination of indication, regulatory classification (Class II) and the existence of predicate devices allowing for an FDA 510(k) market clearance application. This was supported by the existence of established reimbursement pathways forged by predicates that would aid in technology adoption.

"The idea is that once we get motility and transit time as an initial indication ... It's a means to an end, so it gives us a foothold from which we can leverage additional indications, possibly using our own product as the predicate for subsequent 510(k)s, where we apply for additional indications. ... But the objective of getting a product into market is just so that we have some validation for the technology, and for the business model, and it's more easily included in additional clinical trials, which will provide us with insight into new indications and additional indications."

A focus on the indication and intended regulatory pathway allowed Atmo to begin transitioning the manufacturing processes and documentation to become aligned with necessary quality management systems. The experience within PI and their manufacturing capabilities under ISO 13485 has helped with this process of bridging and, where necessary, reworking the hardware and software designs from a research setting to one that will meet regulatory standards. This step is also part of a staged approach to development that sits in tandem with the approach to regulatory compliance.

"The idea was that with the first generation capsule we simply take what is a mature design, from the university, and we change very little. We change as little as possible, in order to get it into the right framework under 13485, with Planet Innovation. And then from there we can upgrade the capsule ... So it's a first step in what will be several iterations of development, in order to produce a system that could be marketed commercially."

Atmo has received interest from other companies in using the capsules to validate their own treatments under development. This could be useful for Atmo, not only to build further prototypes and have devices in use, but also to inform the strategy around seeking additional indications. Using their own studies and those of others to build a large normative set of gas profiles will form another valuable asset for further refinement and development of the technology.

Atmo will next progress and 'de-risk' their regulatory strategy by confirming their regulatory path with the FDA and completing their next clinical trial:

"We need to expand our regulatory strategy and get into more depth, such that we take these next steps around pre-submission meeting, and confirming with the relevant regulatory authorities, in this case the FDA, that the path that we're taking is going to be acceptable. ... The first trial that we're going to do [is] to demonstrate substantial equivalence. ... Once we have those data, we'll have a lot more confidence that the path we're taking is relevant. It is essentially de-risking the regulatory pathway."

3.2 Vitalic Medical

Vitalic Medical was formed in 2016 to develop and commercialise a digital patient monitoring platform "helping nurses spend more time with the patients who need them most".²¹ Its origins lie in a working group formed by PI; PI formed a partnership with Ramsay Health Care, Australia's largest private hospital operator, to collaboratively develop the platform. Vitalic is currently incubated at PI.

The partnership allowed Vitalic to develop its platform within a clinical environment from a very early stage. This led to the first hospital trial of the minimum viable product (MVP) in February 2017 focusing on usability and clinical outcomes:

"We developed that initial MVP prototype ...[to] test the usability to start with and confirm fit with the hospital. A very short trial where we could run it in-market over a 48-hour period. We were able to make the observations as well as capture the data, and then nurse feedback on how they found the system. ... We were also able to make updates that were going to help improve the system. For example, we purposefully over-alerted for the very first iteration, because we wanted to overcompensate. Very quickly, the nurses [provided feedback] like: 'I am getting alerts all the time. This is not relevant', so the alerting was adjusted to fit needs with changes positively received. This was incredibly valuable for us, and really helped us to give the initial tick to say: yes, we are on the right track."

A second in-hospital trial on a more developed platform was completed in November 2018.

Testing early and repeatedly allowed Vitalic to refine its product strategy according to risk and regulatory pathway. Due to its relationship with PI, Vitalic was also able to access PI's in-house regulatory expertise and ISO 13485 certification:

"Internally we have [regulatory] awareness yet it is only in the last six months or so that we have really started to define exactly what our regulatory pathway should be, and how we should classify and define all of that. ... Otherwise, if we went too early on regulatory, the system may not be bedded down enough e.g. system format and or sensors not finalised, and risk needing to redo regulatory assessment ... We needed to know where the true value was being delivered for the customer, and then aligning that with the claims being made – that has such a big impact on the regulatory classification."

Once the platform reached a certain level of clarity, Vitalic engaged an external consultant to more clearly define its regulatory path. This led to the decision to split the monitoring of falls from the monitoring of deterioration to create their first- and second-generation products:

"We consciously decided to focus on the falls-only model first, and then to add in the deterioration. It helps us streamline the MVP and also the resources around developing the system. We also know there is a longer regulatory path when we build in deterioration, and will require further development testing. Then, following the same philosophy we have throughout development, we will further build our insights by having the system in and launched, and then build the modules in from there."

In its current form, the falls-only platform incorporates third-party movement sensors that detect when falls-risk patients are stirring or sitting up. Sensor data is wirelessly transmitted to hubs that utilise algorithms of risk determination and prioritisation to alert nurses to potential falls via desktop and mobile apps. The platform is designed to enable Vitalic to seek registration as a non-measuring Class I device under TGA classification. This required consideration of the platform's features (e.g. information displayed to nurses, how the algorithms are built) and the leveraging of PI's established Quality Management System (QMS):

"[Next] by following our standard QMS, we will get our technical record in order and make sure we have got all the evidence that it meets the Essential Principles and then perform self-regulation."

Developing a system to fit the needs of a hospital environment and defining a regulatory pathway to enable Ramsay Health adoption were two central requirements for Vitalic. The next steps include plotting market expansion, including necessary regulatory approvals, and the development of the second-generation patient deterioration module.

3.3 Cardihab

Cardihab is an early-stage venture developing and commercialising a digital cardiac rehabilitation (CR) service designed to enhance patient engagement and adherence. It does this by enabling a flexible mobile health model of CR based on the scientifically validated MoTER platform, which uses a smartphone and the internet to deliver CR.

Heart attack, or myocardial infarction (MI), was the main cause of over 57,000 hospitalisations in Australia in 2016–17.²² CR programs are designed to support lifestyle changes and comprehensive health behaviour interventions to reduce the likelihood of recurring MI, thus reducing mortality and morbidity rates in post-MI patients.

Traditionally, CR programs have been based in dedicated centres, and despite studies consistently showing the benefits to patients of being part of CR programs, attendance and adherence have been low, particularly in women, older patients and ethnic minorities.²³

Based on collaborative research at the Australian e-Health Research Centre (AEHRC), the MoTER platform was developed to provide patients and clinicians with an alternative means of engagement. It involved developing a digital phone app to deliver a home-based Phase II CR program. By engaging patients in their own care regimes, the requirement for patients to travel to outpatient clinics for rehabilitation treatment is reduced. The patient-facing digital interface of the app engages patients in collecting relevant health data such as blood pressure, physical activity, smoking and symptoms. These measures are reviewed by a clinician who has access to the collected data via a web portal to monitor progress. Patients can access educational materials and motivational notifications through the app to help with program adherence. The system is flexible, allowing it to be used in conjunction with traditional CR programs with direct clinician meeting, or entirely remotely with clinical counselling delivered via telephone. A randomised-controlled trial in 2014 demonstrated that the digital CR program improved patient uptake, adherence, and completion, reduced the number of centre visits, and delivered equivalent outcomes compared to centre-based programs. The program also demonstrated significant reductions in depression and anxiety, and significant improvements in health-related quality of life.²³

This trial sparked significant interest in the technology, prompting investigation of its commercial potential. A team was formed to progress the commercial applications of the platform through participation in the ON and HCF accelerator programs, which led to the formation of Cardihab in 2016. Seed funding was secured in late 2017 to fund ongoing commercial and technical development. Part of the attraction for investors was that the platform could be further developed to manage other chronic conditions (e.g. pulmonary disease and diabetes). Around this time Cardihab formally considered its regulatory requirements and a consultant advised that the platform at that time would not need to be regulated as a medical device (due to its intended use and form).

Cardihab continued to develop a market-ready product. In May 2018, in response to user testing and feedback, it was decided to redevelop the platform (V2.0). This included enhancements to the user and clinician interface, modes of data acquisition and the addition of a medication adherence module. Planned new features, functions and enhancements to the platform were deemed to shift Cardihab's regulatory requirements towards Class I medical device classification.

3.4 ResMed

ResMed is an innovative connected health company that develops, manufactures and markets medical devices and cloud-based software applications for the diagnosis, treatment and management of respiratory disorders. It was founded in 1989 by Peter Farrell to commercialise a novel treatment for sleep apnoea – Continuous Positive Airway Pressure (CPAP). A combination of in-house development and acquisition has seen ResMed expand its product portfolio to include devices, diagnostic products, mask systems, headgear and other accessories, dental devices, portable oxygen concentrators and cloud-based software informatics solutions. ResMed currently employs approximately 6,000 people and sells its products in 120 countries. Its main manufacturing facilities are in Sydney, Australia; Loyang, Singapore; Chatsworth and Atlanta, US; Johor Bahru, Malaysia; and Suzhou, China.²⁴

For ResMed, DHTs are a key part of its vision for achieving a fully connected model of healthcare delivery:

“Our model moving into the future will involve connected everything. Everything we make, we want it to be part of the connected care ecosystem, because the way that the healthcare model is evolving, it’s too expensive to deliver healthcare in that brick and mortar environment. So, we have to find ways to bring it efficiently into the home but it has still got to be effective ... and by connecting devices, making this information available throughout the stream of care, we can unlock different opportunities where the clinician can get more involved, they can have better information when they are involved, [and] make it more convenient for the patient.”

ResMed’s connected healthcare ecosystem encompasses over 8 million cloud-connectable devices, more than 9 million patients in its ‘AirView’ monitoring network and nearly 80 million patient accounts in its out-of-hospital care network. ResMed’s capabilities in data analytics and online health monitoring enable it to provide real-world evidence of patient compliance and therapeutic outcomes, demonstrate the value of its products and services and aid its customers in obtaining reimbursement from private and public healthcare payers.

3.4.1 How does ResMed approach its regulatory obligations?

Not all of ResMed’s products are regulated as medical devices, but where they are, the predominant regulatory pathways have been as Class I or Class II devices via 510(k) pre-marketing clearances in the US, as CE marked Class I or Class II devices in the EU and as Class I and Class II devices in Australia. ResMed has developed organisational structures and processes to meet its regulatory obligations (see Table 2) and employs approximately 150 people in its quality assurance and regulatory affairs teams (QARA), with the majority working in product quality, followed by QMS and regulatory affairs.

Table 2. ResMed organisational structures to meet regulatory obligations

Teams	Examples of Roles and Functions
Product quality	New product development, supplier quality engineers, quality control inspectors
Quality management systems	Support procedure development, internal audits, supplier audits
Regulatory affairs	Regulatory strategy development for new and existing products, regulatory intelligence, regulatory submissions, engaging with regulatory bodies in different jurisdictions
Post-market	Collect and monitor data on post-market product performance
Quality data analytics	Develop actionable insights from quality data
New product servicing	Work with the product development team and downstream regional service teams to develop instructions, test software, protocols, etc.
Project management team	Focus on new regulation introduction (e.g. rolling out ISO 2016 13485, tackling the new European MDR)
CAPA	Corrective and preventive action for marketed products

ResMed's QARA structures and processes are driven by the complexity in managing a diverse portfolio of DHTs across multiple jurisdictions with varied regulatory requirements.

"We have things like fleet management software, which wouldn't necessarily fall into a regulated environment, versus things like medical device data systems which may be regulated, depending on the regulatory authority, and things that are clearly regulated like software features that allow the clinician to change the settings on the device remotely. There's always going to be different buckets, and as we start engaging in new regions those buckets are slightly different, which is creating a whole new layer of complexity for us."

ResMed manages all products – whether regulated as medical devices or not – under a compliant QMS. However, it has sought to configure its QMS to accommodate variation in regulatory classification and regulatory obligations across regions. This is intended to ensure market access is preserved while optimising allocation of organisational time and resources:

"Now we look[ed] at the quality management system and said, okay, can we flex this? Can we make it flexible enough that where we have a lower risk device, we were doing less activities, and where we had a higher risk device, we were doing more activities, so we wanted to make that scalable across risk. ... What that allowed us to do was at least maintain some level of flexibility from market to market. So, where the introductory market might have seen it as a non-medical device ... it allowed us to start in those markets but if we ended up in a market that was a little more strict, we were still okay, because we had built the product within the confines of a compliant quality system, and so would have market access regardless."

During new product development and commercialisation, ResMed follows design control processes and utilises cross-functional teams designed to bring together ***"people from regulatory, people from quality, your PD [product development] teams, there might be material people, there might be mechanical engineers, there might be software developers"***. Embedding regulatory and quality expertise across the entire product development process enables ResMed's developers and engineers to understand the regulatory implications of adding new features and functions to its connected devices and software applications (e.g. whether or not a new product would be a medical device, the likely regulatory classification and requirements for testing and validation). The product development team can then make informed choices about the consumer and commercial value of going down a regulated path.

"So, by connecting these devices we have to make a conscious decision every time we create a new function or feature, is it going to be regulated, and do we care? Part of that is, there is a lot of work around managing a regulated device, and so we want to make sure that we're getting that value out of it. If we're going to put the effort in, we want to make sure that it's worth it."

The recent development and commercialisation of ResMed's AirView platform illustrates this approach.

3.4.2 The development of 'AirView'

"AirView is a seamless, cloud-based system. It enables you to monitor and change your patients' device settings remotely without having to leave your desk. And it makes it easier to simplify workflows and collaborate more efficiently across the patient's care network."²⁵

The initial motivation for AirView's development was to solve a reimbursement challenge for ResMed's customers. In the US, the main customers for ResMed's CPAP devices are home healthcare dealers, hospitals and sleep clinics. These organisations provide CPAP devices to patients and are reimbursed by insurance companies or the government. However, there are strict rules determining reimbursement. Simply put, ResMed's customers must provide evidence of patient compliance in order to get paid. AirView's development was also driven by clinical need: being able to monitor patients' usage remotely can improve the efficiency and effectiveness of their therapeutic management in order to intervene earlier, more easily, with lower costs and better results.

MTPConnect Adaptive Regulation for Digital Health

ResMed saw a digital solution for these dual clinical and commercial imperatives. Since the late 2000s, it had marketed a wireless compliance technology – ResTraxx – that provided wireless transfer of sleep apnoea data to an internet system. However, advancements in cloud computing and the increasing connectedness of ResMed devices opened possibilities to advance this concept via new features and functionality.

Development of AirView began in 2013 and the first version of the cloud-based system took roughly 15 months to develop. AirView was first launched in 2015 in the US and later in the European and Asia-Pacific regions. While initially an accessory for ResMed's sleep apnoea machines (AirSense 10; AirCurve 10), it has since been integrated into the Lumis range of non-invasive ventilator solutions.

Regulation was considered alongside the commercial and technical development of AirView from the outset. ResMed recognised that in most jurisdictions the software would be regulated as a medical device as it is an accessory to its existing CPAP devices. As the US was the initial target market, ResMed plotted a regulatory path to market via a 510(k) submission to the FDA as a Class II device, asserting substantial equivalence to the existing ResTraxx product.

This regulatory strategy was reflected in design and development decisions, influencing what features and functions would be included and when they would be introduced.

"When developing a new product, we're thinking about that submission that we have to do. The submission itself takes a long time, particularly in the US. ... So you really have to take that into account in your development. You don't want to develop a thing and then do a submission at the end of it. ... We identify what we need to do for that submission. All of the key features, we then would develop in that process to do a submission based on that. Then we can keep developing other things that we think aren't essential for that submission."

This approach – ***"identify what the most important things are, do those first"*** – saw Version 1.0 of AirView deployed with a streamlined feature set. Following initial 510(k) clearance and market release, there was a gradual expansion of features in later versions (e.g. being able to remotely change therapy settings on the device). Additional features were added to meet new user and regulatory requirements as AirView was subsequently released in Europe and Asia Pacific. For the majority of software updates, adding new features has not triggered the need for regulatory resubmission, although all changes are documented as part of ResMed's QMS processes and are assessed during annual audits (ResMed participates in the Medical Device Single Audit Program [MDSAP] and it is also audited by its European Notified Body). However, the expansion of AirView to Lumis ventilator devices did require resubmission, as this included a change to its indications. Additionally, for Lumis, specific features were removed to avoid triggering a higher risk class and potentially longer regulatory path:

"For our ventilators at the moment, we don't have writable sets. So we've decided that we're not going to support changing the prescription on the device over the air remotely – that would potentially tip AirView from a Class II device into a Class III device. We developed it as a Class II device, so we didn't want to do that, so we limited that."

Currently, AirView is at its fourth major release. The patient base has grown from approximately 40,000 patients to more than 9,000,000. A major focus area for ResMed is to develop actionable insights from this data, developing capabilities in data analytics and machine learning:

"I mean, there's a huge amount of information there in terms of – this patient has kept using it for three years. This one stopped after 40 days. Let's have a look and see – let's use machine learning to try and see what's different, what's hidden in that data that ordinary people can't see ... When you unleash machine learning on it, there will probably be things you discover out of that that you didn't expect to find. So we're just starting on the journey."

It is anticipated this will increase opportunities to more effectively manage and target therapy, to intervene earlier, and to deliver value throughout its connected ecosystem of devices.

The reality that different aspects of technologies move at different rates through the TRLs, IRLs and CRLs presents a challenge with DHTs as software development can progress faster than the hardware components of a device

3.5 Mapping the case study companies

Medical device development should progress along parallel paths of product and regulatory development; however, progress can occur at different speeds. This can affect the time to market and the form the device takes to meet both developmental and regulatory needs (such as physical design, quality control and manufacturing). There are many ways to map the development pathway of novel technologies, including NASA's often used Technology Readiness Levels (TRLs),^{26, 27} Investment Readiness Levels (IRLs),²⁸ and Community Readiness Levels (CRLs).^{29, 30} The reality that different aspects of technologies move at different rates through the TRLs, IRLs and CRLs presents a challenge with DHTs as software development can progress faster than the hardware components of a device. One representation put forward by the Oxford Academic Health Science Network (AHSN) in collaboration with Oxford University Innovation is the Digital Health Roadmap. This is designed to "help innovators overcome the complexities and challenges related to developing digital products to improve health".³¹ The roadmap comprises seven stages, starting with needs assessment and idea generation, progressing through readiness screening, feasibility studies, development and proof of concept, evidence building, market launch, and finally market uptake and exit (see Figure 5).³¹

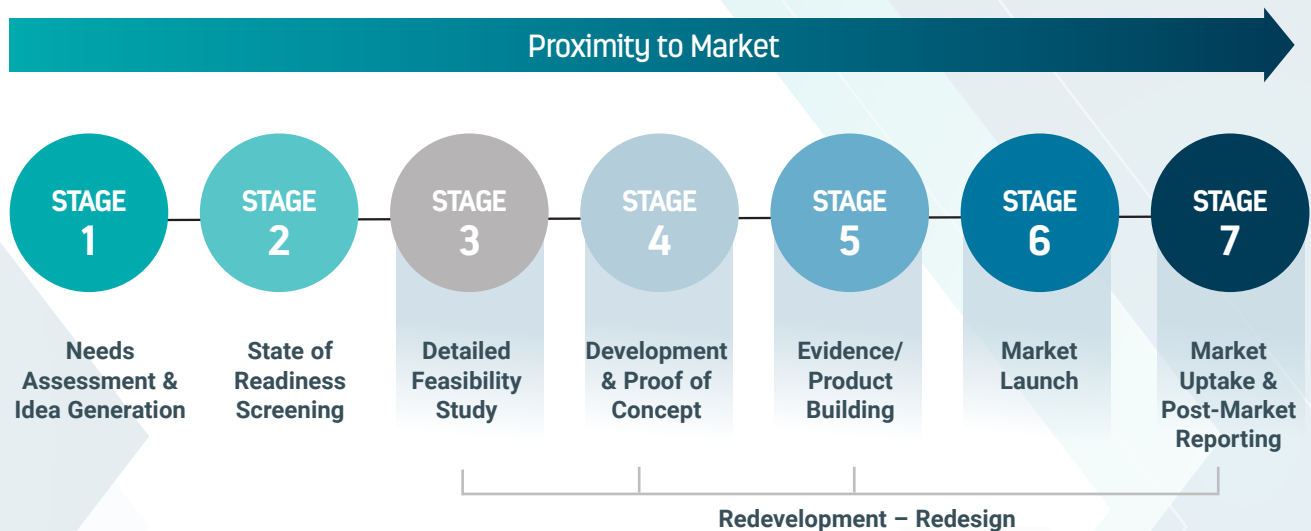


Figure 5. Digital Health Roadmap, adapted from Oxford AHSN³¹

MTPConnect Adaptive Regulation for Digital Health

Mapping the four case study companies against this roadmap indicates they are all at different stages of product development. Atmo Biosciences is at Stage 3/4, Vitalic Medical is at Stage 4/5, Cardihab is at Stage 5, and ResMed is at Stage 7. A benefit of this case study design is that each company's development activities can be compared across stages. Also, mapping these companies shows a representative cross-section within and across stages. Taken together, the case studies enable a quasi-longitudinal assessment of how digital health companies are engaging with regulatory requirements during the product development process.

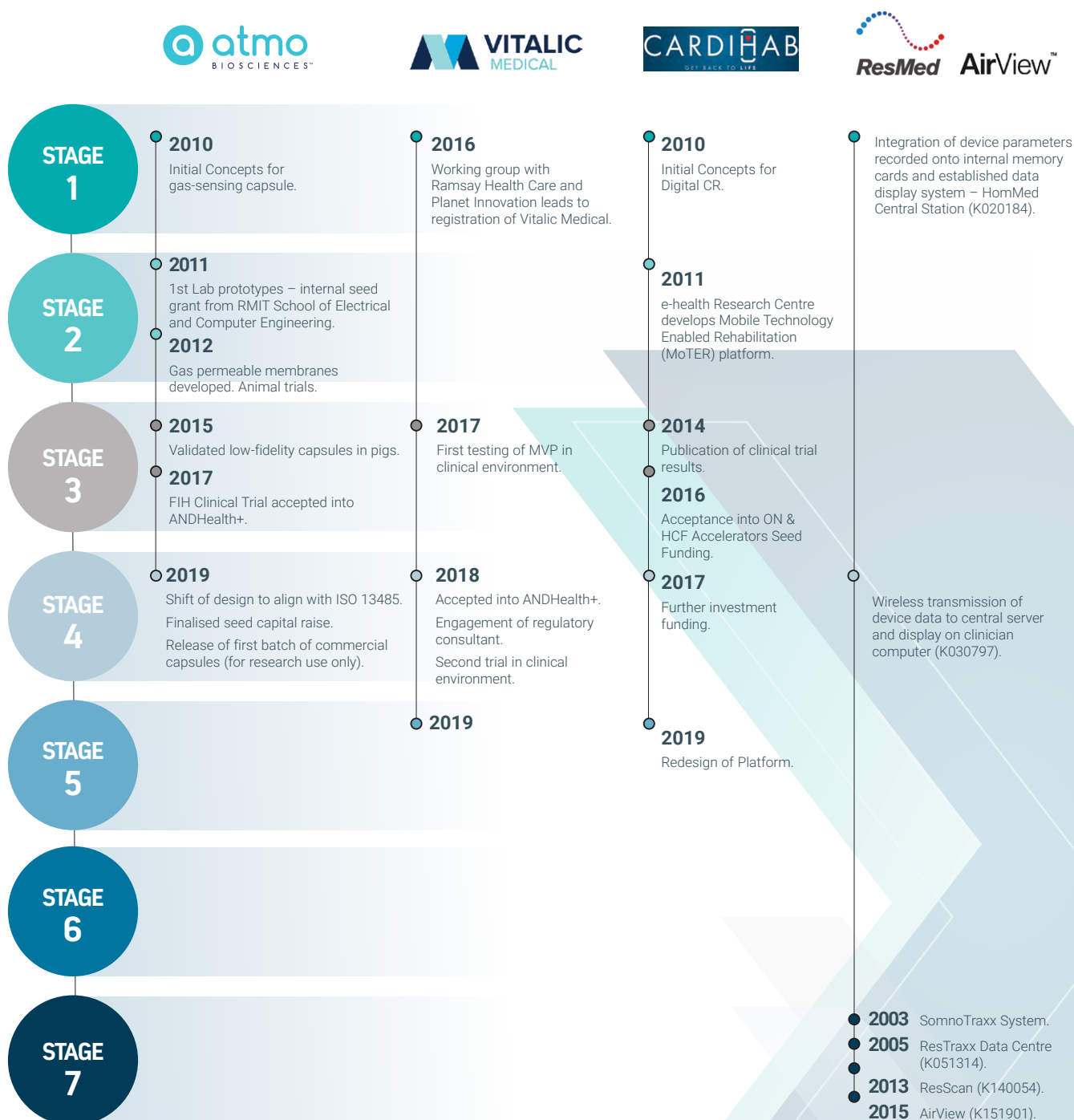


Figure 6. Detailed development history of case study companies included in this report

Enhancing Australia's Regulatory System

4. Enhancing Australia's Regulatory System

Integrating findings from the four case studies presented in the previous section with interviews from the industry, consumer, regulatory and policy lenses reveals the following opportunities to:

- 1) enhance firms' regulatory strategies and capabilities, including best practice approaches to regulatory engagement, and clarify how developers can be better supported in achieving best practice;
- 2) more effectively integrate regulatory with other key strategies of the firm – most notably product development and commercialisation strategies; and
- 3) enhance the Australian regulatory framework through the integration of additional adaptive mechanisms.

In isolation, each of these three strategic adjustments can improve outcomes for some of the key stakeholder groups. In combination, all stakeholder groups should see improvements in the performance of the digital medical devices that reach markets and patients.

4.1 Enhancing firm regulatory strategies and capabilities

New and emerging companies are heavily focussed on the product/technology that will permit them to enter their market of choice, creating an internal focus usually only overcome with experience. Yet, for most companies, being proactive in regulatory engagement is critical, as any lack of, or delay in engagement can lead to expensive rework and redevelopment. Proactive regulatory engagement early in the development process, on the other hand, drives progress. Approaching regulation with a strategic mindset is critical, as plotting a regulatory path is not so much about clearing or avoiding a hurdle, but rather a way of ensuring legal compliance, gaining market access, instilling investor and customer confidence and achieving a competitive advantage. Finally, potential misalignments between technical, commercial and regulatory drivers during development can be mitigated by appropriate investment in regulatory resources. These points are summarised in Figure 7 and discussed in the subsequent sections.

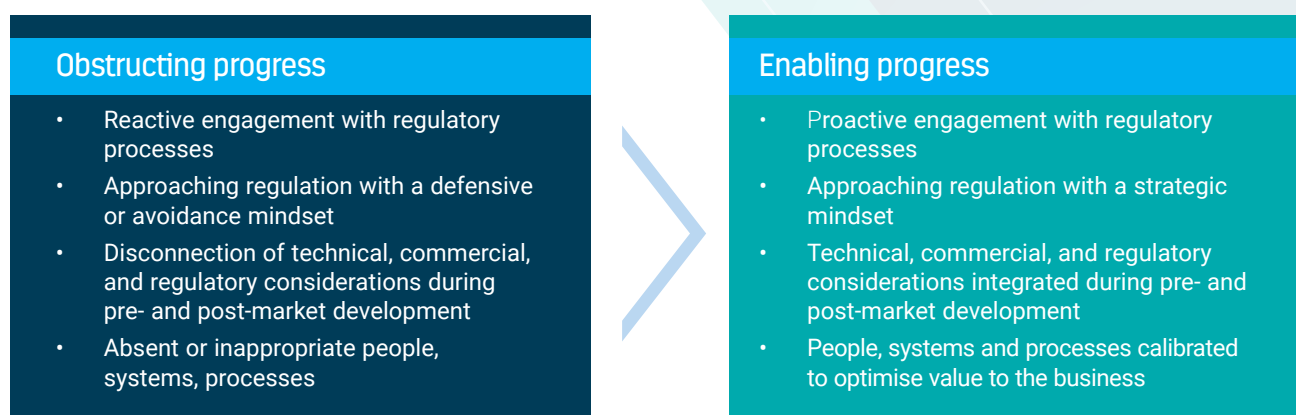


Figure 7. Strategies for efficient and effective development of DHTs

4.1.1 Proactive and early regulatory engagement

Almost all study participants agreed that regulatory requirements need to be considered proactively and managed early in the development process; specifically, as proof-of-concept is achieved. For more mature companies, there is often a clear demarcation between research and development, and internal policies and procedures dictate when regulatory expertise is needed, and documentation commences (e.g. ResMed; see also Section 4.4.1).

For smaller firms, particularly those that are inexperienced, regulatory engagement is often triggered by questions presented by external stakeholders (e.g. funders or potential customers asking questions about regulatory status). By not proactively dealing with regulatory requirements, they risk significant redevelopment and (re)documentation, which can have dire consequences, particularly for a resource-constrained start-up in their race to market as progress is slowed and costs build:

"When they're doing their initial design and manufacture, they don't realise the data capture and documentation of that is actually critical and if they get that wrong it's very expensive to go back to go forward ... It kills companies."
Industry – industry body (P01)

4.1.2 Approach regulation with a strategic mindset

Acknowledging that regulatory approval is a legal requirement for the manufacture and sale of medical devices, participants repeatedly emphasised that regulatory compliance should be viewed as a strategic advantage. A clearly articulated regulatory strategy, developed alongside other strategic considerations, has flow-on effects for attracting investment and reimbursement:

"In an area where your IP is likely to be in your code, and your secret sauce is probably not patentable, your regulatory clearances and your evidence stack are really critical to your defensible competitive position, which is therefore directly tied to your valuation and investability." Industry – industry body (P10)

"Reimbursement [is] intimately tied to regulatory. ... So I look at the regulatory very much in conjunction with the reimbursement. Because I could get something approved, and then if there's no reimbursement code for it in the US, it's going to go nowhere. If I have to forge my own path to get a reimbursement code, that's years in the making."
Product developer (P18)

Viewing regulatory considerations through a strategic lens also allows for better alignment with technical and commercial considerations during the development process. This could streamline corporate processes, reduce cost and speed up product development.

4.1.3 Integrate technical, commercial and regulatory considerations

The case studies clearly demonstrate that regional market entry, therapeutic indication and regulatory classification determine which features and functions are included or withheld from products during development and, crucially, the sequencing for when this occurs.

To accelerate a path to market, companies often adopt a 'stripping-back-and-bolting-on' approach. This is where a 'stripped-back' version of the product, featuring the most critical design features (from a commercial and regulatory perspective), is built first, and regulatory approval/inclusion is sought. Additional features, functionalities and indications are then 'bolted on' after regulatory approval and market launch:

"You don't necessarily have to develop all of it. You might only have to develop half of it and then you can do a 510(k), then keep going with the other half of it. You can go and change other features of it. There's nothing wrong with changing stuff after you've submitted a 510(k), as long as [it] is still substantially the same device." Product developer (P16)

However, companies must carefully manage the addition of new features, functions and fixes to ensure they extract market value and remain compliant with regulatory obligations:

"So for software in particular you need to plan your changes and your releases so that by the time you get the approval, you have some time to sell that product and have some income from some product. In the meantime, you work on the next release or version. Again, you incorporate all the changes, you submit them and it's the next release. So some companies they have like two software releases per year. If it's more than that, they're probably not well organised." Industry – industry body (P07)

A firm's capacity to competently manage pre- and post-market obligations depends on the maturity levels of their quality and regulatory systems, as well as access to regulatory expertise. This creates a strong link to the experience, learning and knowledge within the firm, which are built over time. However, education and awareness programs can fast-track the knowledge-building process for new and emerging firms if coordinated at an industry level.

4.1.4 Calibrating people, processes and systems to optimise value to the business

The ability to access regulatory expertise and institute appropriate quality and regulatory procedures within firms is key to successfully navigating regulatory requirements. Our data suggests that larger firms with more experience are more likely to have access to in-house regulatory expertise and have mature systems and processes, with new product development conducted under a certified QMS.

"You just need to have systems in place. I cannot emphasise that enough." Industry – industry body (P07)

Because the development of digital medical devices is far less formulaic than it is for drugs, it is difficult to define a one-best-way in terms of development and regulation. Flexibility is critical to success for all stakeholders. As such, companies were seen to build flexibility into their QMS so that procedures can be adjusted to accommodate differences in jurisdictional requirements and regulatory classification. However, a challenge for all firms is to continue to adapt their existing systems and expertise to incorporate new resources and competencies for developing digital health (e.g. improving cybersecurity capabilities):

"We've been in the med device world for so long we have very mature systems in some areas, but in other areas, you know, when it comes to cybersecurity and things like that, we're just getting into the world of what that means and what systems we have to have, and we're building up our capabilities." Product developer (P08)

Resource constraints for start-ups and smaller firms mean that they can struggle to access the necessary people and implement the right processes at the right time:

"... it requires having a bunch of expertise that they don't necessarily have at that point ... and there aren't tools available from our regulators that assist them to run through that process. It's almost like they have to at that early stage engage with specialist consultants to assist them, and that's not necessarily affordable." Industry – regulatory affairs (P11)

For emerging firms, developing regulatory capabilities is described as a 'journey' whereby experience enables calibration of internal systems and processes that deliver the best value for the business – from a technical, commercial and regulatory perspective:

"There's kind of this curve. You've got these newer companies that don't have a clue, they're just chugging along, completely oblivious. Then, when they do get that clue, and often times it's at the end of a regulatory action, the FDA comes in and gives them a 483 or whatever. Then the pendulum completely swings in the other direction, and they totally overdo it, letter of the law, and then realise that's not sustainable, we can't run a business just doing it because it says it has to be done, we really have to be thoughtful about it. So then you kind of come to this realisation that there's a purpose for all of the things that we do, and if we're not realising the benefit of that, either we're doing it wrong or we don't understand, or we're overdoing it. That's kind of that journey." Product developer (P08)

Finally, in the future, developers can look for opportunities to use digital tools and regulation technology (regtech), including blockchain and AI, to automate aspects of change tracking and documentation.³²

"Finally, something that blockchain could be useful for! Because this would all happen in the background, so I'm changing X, Y and Z. My initial approval was to work within this framework, I'm allowed to change the colour from the red colour family! Blockchain says 'we've changed this, it's within that, notify, ledger done, move on'. ... So coming back to aligning speeds right, it's got to be in a way that aligns. So, we've got to use digital tools to help us to do the certification processes." Industry – research organisation (P09)

4.2 Enhancing Australia's regulatory framework

There are additional opportunities for collaboration between regulators and developers to enhance Australia's regulatory framework for DHTs, both in terms of overcoming the potential for misalignment between development and regulatory processes and for mutual learning.

Considering the case studies and stakeholder findings alongside the adaptive regulatory mechanisms described earlier, Table 3 summarises existing enablers, opportunities and possible enhancements for adaptive regulation of DHTs.

Table 3. Enablers, opportunities and possible enhancements for adaptive regulation of DHTs in Australia

Existing enablers	Opportunities for improvements	Possible enhancements
Risk-weighted & outcomes-based		
Australia's risk-weighted and outcomes-based regulatory framework (i.e. principles rather than rules, and based on certification of manufacturers) are regulatory design features enabling flexibility to accommodate novel DHTs and services.	While the framework incorporates adaptive mechanisms, there are opportunities to build awareness and understanding amongst industry participants (especially new entrants) as to how it can be navigated. This could better leverage the inherent flexibility of Australia's regulatory framework.	<p>Education and awareness campaigns.</p> <p>New modes of engagement with manufacturers/industry to facilitate more streamlined and efficient regulatory oversight, reflecting elements of the FDA's precertification or breakthrough devices where appropriate.</p> <p>Enhancement of information and guidance available through the TGA, including online sources.</p>
Adaptive authorisation		
Developers describe already adopting a quasi-adaptive registration strategy ('stripping back and bolting on') in Australia given the system is based on certification of manufacturers before they can apply for product/device approval; this suggests an adaptive approach is already possible within Australia's existing framework.	Opportunities to improve alignment between speed of iterative change and regulatory compliance. With post-market obligations in particular, industry can be helped to better understand the circumstances in which notification or resubmission for regulatory assessment is required and to streamline the documentation of ongoing changes.	<p>Working with manufacturers (developers) who are certified before products are developed or authorised.</p> <p>Potential for simplified versions of products on market to generate real-world evidence, then supporting registration for additional indications or user groups.</p> <p>Clarity from regulators about appropriate use of advanced digital technology (e.g. blockchain or AI) and regtech, to facilitate automated traceability and documentation of iterative change.³³</p>
Harmonisation		
Australia's harmonisation with EU and participation in initiatives like IMDRF is recognised and highly valued by industry.	<p>Australia is rarely the first choice point-of-market entry; often due to market size but also because registration is <i>perceived</i> to take longer.</p> <p>Influenced by the lack of a tailored authorisation option for DHT developers, such as is available in the US; the faster pathway is perceived to be the EU first, then the US and then Australia (although this may change with MDR). A review of approval times is included in Appendix C-5.</p>	<p>Continued alignment with other international frameworks may make Australia more attractive as a first point of entry.</p> <p>This could be aided by interactive elements of the FDA precertification and other peer-to-peer collaborative programs to enable developers to put into place systems to satisfy multiple jurisdictional requirements. This could further enhance US developer mobility given the strong community of digital health developers already established in the US and the attraction of that market for Australian developers.</p>

Possible enhancements to the regulatory framework focus on education and awareness; developing new modes of engagement; enhancing online communication; leveraging collaboration; and boosting international competitiveness.

4.2.1 Education and awareness

The development of educational campaigns focused on new entrants and informing existing participants of ongoing changes to regulation and guidance was identified as a necessity. Many participants spoke very positively about new outreach efforts conducted by the TGA.

“TGA has improved a lot in terms of transparency, education, and accessibility. A lot of educational material presentation is just free of charge, publicly available on TGA’s website. They also have a portal dedicated to start-ups, SME Assist which is very good.” Industry – industry body (P07)

Strong education programs are supported by interactive dialogue. It was also identified that there is scope to build on this via tailored educational programs.

“... solid communication to the industry, knowing that there are a lot of people coming from outside health and don’t understand it. So, we have got to do Health Regulation 101, and that is going to have to be just all the time. That could be a web-based training, but it is going to have to be all the time. ‘So, you think you are going to have a Health Tech company?’ That sort of stuff. Through to the idea of an established pathway and guidance with steps that you need to come through. That needs to happen.” Industry – research organisation (P06)

A move to enhance education and awareness to reduce knowledge gaps signals strategic intent by the TGA to shift from the role of assessor to that of enabler and being actively involved in supporting developers to navigate the regulatory pathway. This may include developing a range of communication strategies targeted at new entrants such as:

1. optimising the usability and navigability of the online information provided by the TGA;
2. identifying, synthesising, and promulgating a range of appropriate good and best-practice examples of conformity assessment proposals or technical documentation that can be supplied as guidance;
3. supporting software developers to create appropriate artefacts to assist assessments of safety and security through either guidance documents, roadmaps, workshops or resources, or a combination thereof; and
4. modelling and promoting the value uplift of regulatory approval.

Approaches that support building value through regulatory engagement are technology co-design with the TGA, augmented by an ‘engage early, engage often’ program that better integrates regulatory considerations into the design and development of new and improved technologies.

4.2.2 Novel modes of industry engagement

Participants were positive about SME Assist and suggested ways that it can be extended including:

1. a ‘concierge-like’ service to help navigate the regulatory process with non-binding advice and information aimed at leading developers through the process;
2. ensuring training and guidance is not ‘one size fits all’ but instead tailored for relevance to developers at different development stages and with different experience and resource levels;
3. official regulatory representation at pitch nights and start-up events. Facilitating two-way exchange so that developers are not ‘scared of the regulator’ and the ‘regulator learns about what is coming’ in terms of potential technologies in development; and
4. promoting the availability of early consultation for ‘boundary-pushing’ products and services, allowing developers and regulators to collaborate on charting a regulatory path.

“Is it possible for those more boundary pushing applications to have some kind of early stage consultative process about how are we going to classify it? What’s the regulatory review going to be like? What’s the evidence going to look like? How are we going to maintain that product? If it’s a machine learning algorithm that continues to learn, how are we going to put a system around that to make sure that it doesn’t go sort of out of bounds?” Industry – regulatory affairs (P12)

"You don't necessarily need an extensive engagement, but you need to be able to talk to someone fairly quickly, so what is the best way?" Product Developer (P14)

Accessibility makes a good partner to flexibility. Facilitating communication is essential to an effective education process at industry level.

Elements of the FDA's precertification program could be considered for Australia. Currently limited to SaMD, this program is a tailored mechanism that facilitates engagement between the regulator and industry/manufacturers during the development and regulatory review process. The FDA precertification program potentially facilitates streamlined regulatory oversight of software-based medical devices developed by manufacturers who have "demonstrated a robust culture of quality and organizational excellence (CQOE) and are committed to monitoring real-world performance".³⁴ Using tailored approaches that support development in a regulated environment, and certifying these developers, strengthens the evidence base available to the regulator in the approval process. Specifically, the goals of the program are to:

1. establish trust that developers have a culture of quality and organisational excellence;
2. leverage transparency of organisational excellence and product performance across the entire life cycle;
3. use a tailored streamlined pre-market review; and
4. leverage unique post-market opportunities available in software to verify the continued safety, effectiveness, and performance in the real world.³⁴

Further, from a commercial and investor viewpoint, the precertification program provides more certainty of regulatory approval timelines, potentially reducing the regulatory risk and cash flow impacts of delayed approvals for future products. The program supports commercialisation by going beyond regulatory approval and regulator validation to providing commercial certainty and encouraging new product development and deployment within a supported investment/financial framework.

These improvements can help ensure that less experienced firms are not disadvantaged by what is termed 'liability of newness', and can help established firms to avoid 'path-dependence' in their own processes that can create inefficiencies and slow product development.

4.2.3 Enhance online communication

Comprehensive information is available via the TGA website; however, presentation and communication could be improved to better support developer and consumer navigation. Clear online communication will help developers better identify classification and the regulatory pathway as well as the documentation required for regulatory submission.

Suggestions for improvement included easily accessible flowcharts and templates for preparing documentation for submission:

"It'd be really easy if someone had a flow chart and all the documents there ... that would be considered applicable for satisfying this requirement. I think it could be much easier and save companies lots of money." Product developer (P18)

Examples of templates, process flows and flow charts developed by others have been identified, and while the need for flexibility precludes the use of fixed templates, examples of good or best practices would be valuable.

Manufacturers have also suggested they do not always understand their post-market notification and resubmission obligations, indicating this as an important area for improving the accessibility of information regarding ongoing requirements (e.g. what changes require resubmission or notification).

4.2.4 Collaboration between developers and regulators

Increased collaboration and communication with developers has been validated in other jurisdictions to increase the speed of patient access to novel drugs and devices. While collaboration and support mechanisms are already available from the TGA through pre-submission meetings, the FDA was highlighted as particularly accessible:

"You'll never get formal permission, but you can at least go to the office that's going to be doing your assessment and have a one or two hour meeting that's pre notified and say okay here's our product; here's what we want to do; this is why we want to do it, and here's our clinical evidence strategy – and see what they say. And you can minute that meeting and then you include those minutes in your submission." Industry – regulatory affairs (P12)

"It's a novel device, it's new, so you basically take your case to the FDA and say, 'What do you think? We think it might be this class. If it's this class what would the design of the study look like? The primary end point is going to be this'... and then the FDA gives their comments." Product developer (P18)

This also has implications for clinical pathways:

"They decided their first step would be that it would be for clinicians' use only ... so that made them scale back their regulatory application. Then within that they also presented the study design, the FDA were very specific about numbers and capturing a full broad range of subjects with all sorts of signs and symptoms of respiratory disease." Product developer (P18)

Formal pre-development meetings can help both the applicant and TGA gain a common understanding of the technology itself, clarify the documentation required to evaluate the application, resolve any arising issues and manage timelines and resources as part of planning for the submission.

Aligned with the meetings, the 'stripping-back-and-bolting-on' approach to regulatory approval described in the case studies indicates that a quasi-adaptive authorisation approach is already possible within Australia's existing regulatory framework. However, for developers to leverage adaptive authorisation strategies fully, ongoing collaboration with regulators is necessary. For example, developers and regulators can identify pathways where 'stripped back' versions of products could be released on market (for limited applications or user groups/sub populations). Specified time on market to gather real-world evidence may be used to further identify safety, performance, and quality. Here, consultation with the regulator could help clarify the evidence required and how it could be collected safely and securely. That data can then be used to gradually expand applications, functions and user groups, and provide better evidence of the benefits delivered by product/services:

"Real-world data collection capabilities of software as medical device products create a quite unique opportunity to add value in the post-market monitoring and support ... I think the regulators need to be thinking about how do we collect that data? How do we interpret that data?" Industry – industry body (P01)

As regulatory technologies become available to automate change documentation and reporting requirements, consultation with regulators may also be required to ensure that the regulatory artefacts generated are appropriate.³²

Another alternative could be for the regulator to work with manufacturers (developers) before their respective products are developed, and before the manufacturers are ready to apply for conformity assessment certification. This approach could be better suited to the iterative design and development and the type of validation used for digital health, providing more streamlined and efficient regulatory oversight of digital health medical devices. The FDA's Breakthrough Devices Program has similar benefits. Indeed, the shift to more collaborative regulation by the FDA for breakthrough designation includes options of obtaining feedback through sprint discussions, discussions on data development plans and requests for clinical protocol agreement.²⁰ Similar collaborative engagement could be trialled by the TGA.

4.2.5 Boosting international competitiveness

Differentiation of a jurisdictional regulatory framework is seen as being less competitive than alignment and harmonisation, which provides an opportunity to promote Australia's harmonised and adaptive regulatory framework. For example, in 2018 the TGA introduced the Priority Review designation for medical devices, a program with similar intent to other priority review programs offered by leading regulators such as the FDA and EMA, and the TGA accepts approvals from comparable regulators (see Appendix C-1-4).

"The biggest plus I would say is the fact that Australia is aligned with the major markets. It's good that Australia has aligned itself with one of the two and to me Europe seems to be better, because it has those pluses with the risk classification system. The central requirements, which are generic and can be applied to any technology. So that flexibility I think it's better than the US system. I would say it is a plus of the Australian system." Industry – industry body (P07)

However, alignment is still an issue that affects competitiveness of the Australian medical device industry. For example,

one product developer discussed a product that was considered a wellness app in the US as it didn't treat or diagnose. Therefore, it was deemed not to fall within the purview of the FDA. However, in another jurisdiction, the regulator viewed it as a component of the device that it works with and classified it as a Class II medical device. This has implications for a competitive strategy and patient access in other markets:

"Variations from [one] regulatory authority to the next can create big disparities in device classification, market access ... and we have to ask ourselves, is it worth it?" Product developer (P08)

A regulatory affairs consultant also highlighted these inconsistencies:

"There are a number of Class I devices in Australia and Europe that are Class II devices under the FDA system. And not so much vice versa. I mean, the classification system is different ... where it's easier in one market than the other." Industry – regulatory affairs (P12)

As such, the FDA approach of providing tailored guidance could be considered for Australia, with a greater focus on guidance and meetings during the development process. This would have the potential to:

1. enable developers to put in place systems that would satisfy both Australian and US requirements;
2. make Australia a more competitive place for digital health developers; and
3. encourage greater two-way flow of communication and technologies between Australia and the US, encouraging the strong community of US developers to engage more with the Australian community.

However, careful consideration would need to be given to how further harmonisation could be achieved without increasing regulatory burdens.

4.3 Barriers to enhancements

A critical element in implementing any strategy variation is the additional resourcing to support time expended, staffing, training, communication and coordination activities. The FDA options discussed here are supported by a robust federal budget authority for several FDA Centers. For the TGA, a similar shift towards greater collaboration and engagement with inexperienced and emerging developers would be resource-intensive. Under the current TGA business model, these additional activities cannot be resourced, as it supports most operations through user fees alone. Sources of additional funding may need to be identified to develop the required implementation stages of ideation, design, implementation, business model innovation, cultural change and communication. The return on investment would potentially be in creating a world-leading sector that attracts local and international developers, the increased value and return on their development efforts, an expanding industry and improved healthcare outcomes for patients.

Discussion and Conclusion

5. Discussion and Conclusion

The speed of development and iterative improvement, the generation and utilisation of data, new entrants from outside the medical industries and new pathways to market access are creating specific regulatory challenges for DHTs.

5.1 Matching product development, commercialisation and regulatory strategies

One of the key findings of the case studies is that many of those developing DHTs do not prepare well enough for the entire process – until they hit roadblocks. There are three distinct areas developers need to build a strategy around from the beginning of the development of their technology. They are:

1. product development;
2. commercialisation; and
3. regulatory.

Unfortunately, while many developers create a product development plan at the outset, many neglect a commercialisation strategy until they encounter financial roadblocks and some may not create a regulatory strategy at all. If all three strategies are established and interconnected at the outset, progress to market can be streamlined, making it more rapid and less costly.

The commercialisation strategy can also be assisted by key industry partners and industry bodies, including MTPConnect and ANDHealth. MTPConnect operates two Medical Research Future Fund (MRFF) programs, BioMedTech Horizons and Biomedical Translation Bridge. These competitive granting programs are open to supporting digital health projects and have a strong translation and commercialisation imperative. A third MRFF program, the Researcher Exchange and Development within Industry (REDI) initiative, aims to drive the growth and capabilities of the MTP sector workforce to improve commercialisation outcomes and is being delivered by MTPConnect in partnership with a range of leading sector participants. MTPConnect will deliver an additional program, the Targeted Translation Research Accelerator (TTRA), to provide a new integrated research program to improve the management and treatment of diabetes and cardiovascular disease in Australia. ANDHealth's programs, including B.R.I.G.H.T. Future for Digital Health in Victoria, masterclasses Dominate: Digital Health and ANDHealth+, are designed to enhance the competitive skills of DHT companies and accelerate their commercialisation on a global scale.

Federal and state governments and their departments also have a role to play in designing education and awareness programs. Where industry-wide issues are identified, there is scope for policies and programs at both state and federal levels to promote progress and enhance pathways.

5.2 Adaptiveness in regulation

While policy cannot be designed to predict technological disruption, it can be broad enough in its scope and implementation to deliver proactive and rapidly responsive regulation with the ability to capture and assess new data and support increasingly effective evidence-based decision-making. The 'adaptiveness' of regulation can be viewed as an extension of reactive regulation, which is determined by disruptive forces. To promote discussion, we have plotted adaptive regulation along a spectrum ending speculatively in anticipatory and pre-emptive regulation – regulatory concepts that do not yet exist, but would culminate in the perfect adaptability to the increasing pace of technological and environmental change. In some industries, the application of predictive machine learning and AI to regulation has taken 'regtech' to the next level and opened the door to anticipatory regulation. However, balancing risk-weighted and outcomes-based regulation keeps an anticipatory approach to regulation of digital medical devices in the realms of possibility, but not a current reality.

It is premature to discuss extensively pre-emptive regulation – potentially AI-based, incorporating vital data and statistics from relevant global bodies, blended with extensive technology trends and patterning data, to make decisions about technologies before they emerge. This may seem over-the-horizon thinking, but as Microsoft co-founder Bill Gates warned: "We always overestimate the change that will occur in the next two years and underestimate the change that will occur in the next 10. Don't let yourself be lulled into inaction."³⁵

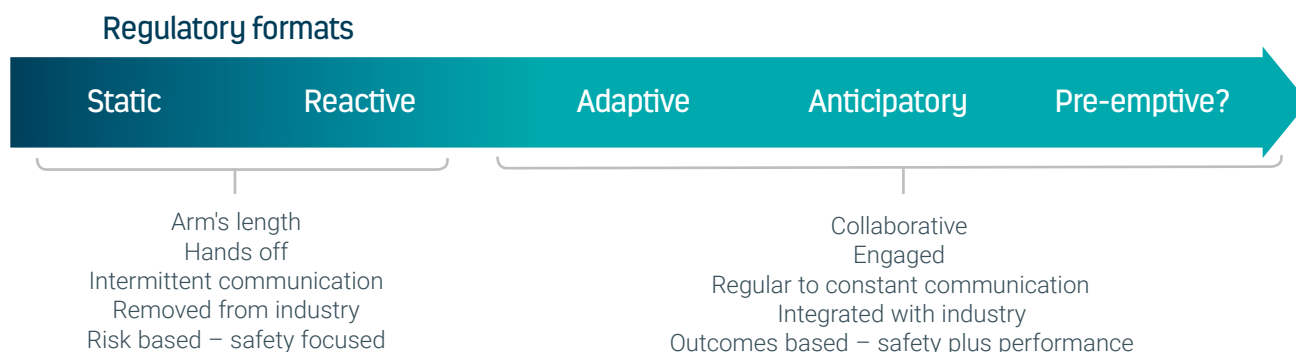


Figure 8. Scale of regulatory adaptiveness

With flexibility and adaptation in mind, the TGA is collaborating with developers, industry representatives and research institutions to identify enabling factors, barriers and constraints in the current regulatory framework. With this framework founded on a broad-principles and risk-based approach, the TGA is developing new guidelines through discussion papers and consultation to clarify how novel digital technologies are covered and supported. Similar changes are occurring in other international regulatory frameworks, such as the EU with the adoption of the MDR and the FDA with their review and restructure of the Center for Devices and Radiological Health (CDRH) and technology life cycle approach embodied in the Digital Health Innovation Action Plan and 21st Century Cures Act.

While there are gaps in awareness, comprehension and problems with technology fit, all stakeholders should take responsibility to increase the awareness of which DHTs are regulated as therapeutic goods.

A move to enhance education and awareness to reduce these knowledge gaps signals strategic intent by the TGA to shift from the role of assessor to that of enabler: being actively involved in supporting developers navigate the regulatory pathway. This could include developing a range of communication strategies targeted at new entrants.

However, under its current business model, the TGA does not have the resources to support the additional time, staffing, training, communication and coordination activities required to support its intent. Sources of additional funding may need to be identified to develop the stages of implementation of strategic intent: design, implementation, business model innovation, cultural change and communication. A world-leading sector that attracts local and international developers would be an excellent return on investment.

Yet, "healthcare innovations are delivered at the speed of life".ⁱⁱ Regardless of how efficient, robust and supportive Australia's regulatory system for digital health is, development timeframes of any healthcare technology where clinical testing and validation are required is limited to the speed with which the human body and disease-causing factors respond. The use of surrogate endpoints in pharmaceutical interventions provides a partial solution and could be considered for digital therapeutics but they still require extensive validation and post-market confirmation, often through additional or ongoing clinical trials.

Experienced developers understand these timeframes and actively build regulatory processes into their product development cycles from the outset. They are enacting risk-based assessments during the commercialisation process, from proof of concept to prototyping, to build regulatory requirements into protocols and development strategies.

Feedback from other stakeholders also suggests that the information asymmetry between knowledgeable industry participants and representatives and regulators is rapidly narrowing. Established companies increasingly view regulatory approvals as fundamental to increasing value and de-risking to attract and encourage new investment. Engaging with, and integrating regulatory processes, protocols and approval gates early and effectively into the product development process and the developer's entire business model, helps to speed up investment, market release and patient access.

ⁱⁱ Dr Peter Kambouris.

Just as technology developers are required to consistently review and invest in their capabilities for change and improvement, regulators also need to assess their business model and the existing and future capabilities required to deal with rapid technological, social and environmental change. Developing these capabilities is as important as enhancing the communication pathways to industry. Yet developing dynamic capabilities takes substantial time, resources and the tolerance for – and ability to learn from – failure en route to success.

Resourcing constraints are the enemy of innovation and improvement and will limit the adaptiveness of the regulatory process for digital medical devices. The strategic intent for change and commitment to meaningful industry engagement are evident in the TGA and provide a promising foundation for the collaborative building of Australia's future adaptive regulatory framework for digital health.

Appendix A

Project Methodology

A-1 Qualitative research design

A qualitative research design incorporating desktop research, case studies and in-depth interviews was used to develop a rich and contextually grounded account of how Australian digital health stakeholders currently understand and engage with existing therapeutic regulatory frameworks. The research included two phases.

A-1-1 Phase 1

Phase 1 involved desktop research into the existing therapeutic regulatory framework in Australia and other leading markets, including the US and Europe. This phase drew on publicly available documents (e.g. slide decks, position papers, strategic plans); peer-reviewed scientific literature; and online content from industry bodies, national regulators and governments. We collated definitions of digital health used in the peer-reviewed literature, industry, government bodies and national regulators, and compared regulatory frameworks across key markets. The outcomes of Phase 1 were: a) clarification of broad similarities and differences across jurisdictions in their approach to the regulation of digital therapeutics; and b) development of a spectrum of digital health that clarifies different technology types and whether or not they fall within the domain of a regulated therapeutic good.

A-1-2 Phase 2

Phase 2 involved applied research into how digital health industry stakeholders are engaging with existing regulatory frameworks. Firstly, we undertook case studies of four Australian companies developing and commercialising novel DHTs. The case studies drew on semi-structured interviews with company managers, regulatory affairs personnel and developers, as well as a review of relevant documents and online sources. Case companies were selected to provide some diversity and representativeness on the basis of size, current stage of product development, maturity and anticipated or regulated risk classification of their products. The sampling strategy enabled an initial longitudinal assessment of how digital health companies are engaging with regulation during pre- and post-market product development processes. This allowed us to identify potential points of alignment and misalignment between regulatory, technical, and commercial considerations during the development processes.

Subsequently, to broaden and deepen the case study insights, we conducted additional in-depth interviews with stakeholders across the four lenses described in Figure 2. This enabled us to contextualise and deepen our interpretation of the cases. In total, 19 interviews of between one and two hours' duration were conducted across the four lenses. Participants from the product developer lens belonged to the case study companies. Throughout the body of the report, participants from each stakeholder group are de-identified via use of code P01 to P19. All interviews were transcribed verbatim. Both the interview and documentary data were subject to coding and thematic analysis via the NVivo qualitative data analysis computer software package.

The goal of qualitative inquiry is to capture participants' subjective understandings and experiences of the social phenomena under study. In line with this standpoint, the case studies do not represent objective evaluations of systems and processes, rather participants' own descriptions of their approaches and experiences in navigating the regulatory process for DHTs.^{36–38}

Appendix B

What is Digital Health?

B-1 Literature search

A search of both the US National Library of Medicine's PubMed database (comprising more than 29 million citations for biomedical literature from MEDLINE, life science journals, and online books) and Clarivate's Web of Science Core Collection shows the number of citations with 'digital health' in the title or abstract remained relatively low until the early 2010s, and has been increasing almost exponentially since the early 2000s (see Figure 9).

The PubMed database was searched using the term 'digital health' in the Title or Abstract fields.

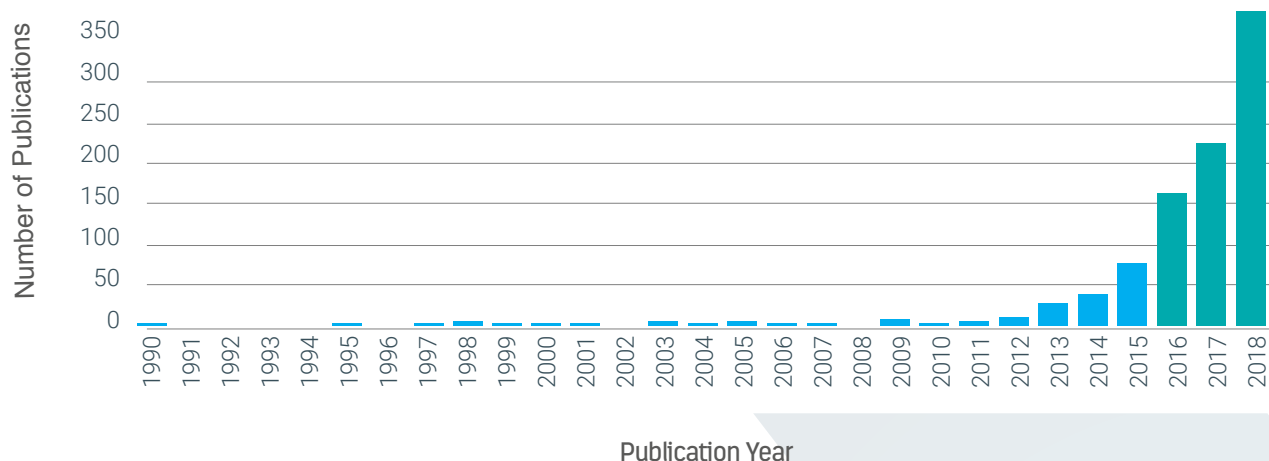


Figure 9. Number of publications in PubMed with 'digital health' in title or abstract, by publication year³⁹

Similar results were obtained by searching 'digital health' in the Topic field in Web of Science.

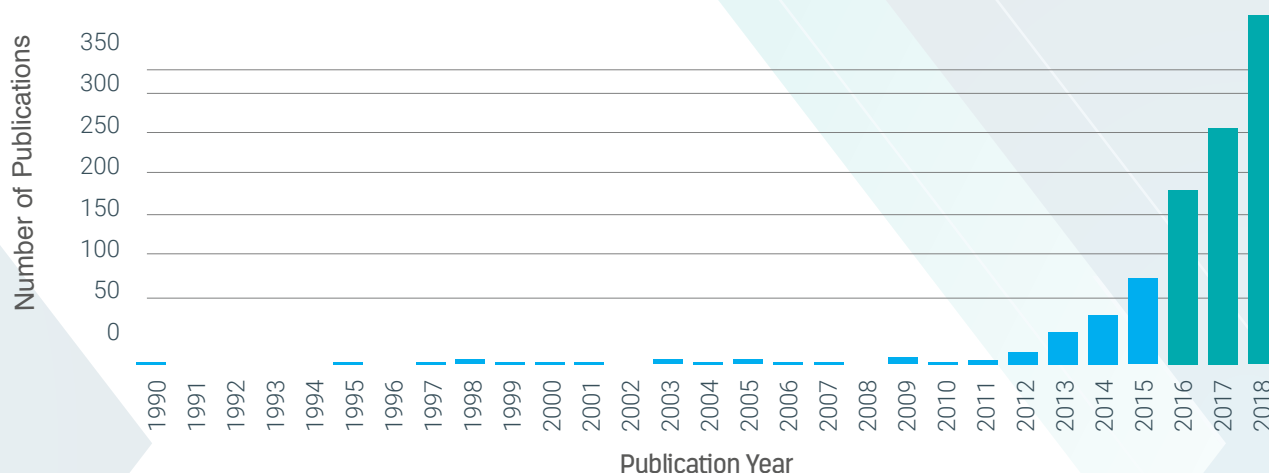


Figure 10. Number of publications in Web of Science with 'digital health' in the topic, by publication year⁴⁰

B-2 ICMJE

The International Committee of Medical Journal Editors (ICMJE) is a working group of general medical journal editors who provide recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals. Current members are: *Annals of Internal Medicine*, *British Medical Journal*, *Bulletin of the World Health Organization*, *German Medical Journal*, *Ethiopian Journal of Health Sciences*, *Iranian Journal of Medical Sciences*, *JAMA*, *Journal of Korean Medical Science*, *New England Journal of Medicine*, *New Zealand Medical Journal*, *PLOS Medicine*, *The Lancet*, *Medical Journal of Chile*, *Danish Medical Journal*, the US National Library of Medicine and the World Association of Medical Editors. ICMJE requires registration of clinical trials in a public registry at or before the time of first patient enrolment as a condition of consideration for publication (<http://www.icmje.org/recommendations/>). This policy has had a profound impact on clinical trial registrations at ClinicalTrials.gov⁴¹

B-3 Literature review

Table 4. Review of literature in the PubMed database with 'digital health' in the title or abstract, and published in ICMJE member journals

Citation	Study description and applied definitions of digital health
Alipanah et al., 2018. ⁴²	<p>Investigated adherence to tuberculosis treatment interventions to determine which approaches led to improved TB treatment outcomes. Adherence interventions included digital health interventions, which were adherence interventions (including directly observed therapy offered by providers, reminders and tracers, incentives and enablers, patient education, staff education) implemented via mobile electronic devices (SMS, Video Observed Therapy [VOT], medication monitors).</p> <p>DHTs are considered to be treatment interventions implemented by mobile electronic devices.</p>
Lee & Kesselheim, 2018. ⁹	<p>An analysis of the benefits and risks of the FDA's precertification pilot program for digital health software.</p> <p>Digital health software is considered to be innovative medical software meeting the definition of a device (an article intended to diagnose or treat a disease [or other condition] or to affect the structure or function of the body, provided the article does not achieve its purpose through chemical action or by being metabolised).</p>
Miller et al., 2018. ⁴³	<p>Examines the effect of Mobile Patient Technology for Health-CRC (mPATH-CRC) on the rates of colorectal cancer (CRC) screening. mPATH-CRC is an iPad application displaying a CRC screening decision aid that lets patients order screening tests and sends automated follow-up messages. The mPATH-CRC intervention increased CRC screening.</p> <p>DHTs are considered mobile apps to improve patient outcomes.</p>
Blumenthal, 2017. ⁴⁴	<p>Discusses the value of digitised patient health data in the current era of AI and machine learning.</p> <p>DHTs are considered to be electronic health records.</p>
Agboola, Bates & Kvedar, 2016. ⁴⁵	<p>Outlines benefits of DHTs for improving patient outcomes, but also safety concerns raised from apps incorrectly recommending dosage and misidentifying skin cancer lesions. Argues digital health should not be viewed as a distinct modality of care, instead as a tool bridging gaps in existing care delivery systems and the need to better understand potential increased harm from digital health innovations.</p> <p>Digital health is the use of advanced electronic communication and monitoring technologies to exchange health information.</p>
Levine, Lipsitz & Linder, 2016. ⁴⁶	<p>Investigates trends in seniors' use of DHT in the US digital health modalities: the use of the internet to fill prescriptions, contact a clinician, address insurance matters and research health conditions.</p> <p>Despite seniors representing the sickest, most expensive and fastest growing segment of the US population, few seniors surveyed used DHTs.</p> <p>DHTs are considered the use of the internet for health-related activities.</p>
Wilson & Drozda, 2013. ⁴⁷	<p>Discusses the benefits of implementing unique device identification (UDI), such as enhancing post-market surveillance, tracking devices across healthcare settings, supporting safe and accurate device use, creating a standard for device documentation, enhancing recall management, and improving efficiency and healthcare cost savings.</p> <p>Digital health is considered health information technologies such as electronic health records and electronic device tracking.</p>

B-4 Industry, government and organisational review

Table 5. Definitions and descriptions of digital health from Australian industry, government departments and select international organisations

Industry organisation or government department	Definition or description of digital health
Australian Government Australian Digital Health Agency (ADHA)	<p><i>"Digital health is about connecting you to better healthcare and Australia to a healthier future."</i>⁴⁸</p> <p>Other aspects of digital health include: "Genomics, precision medicine, AI-based decision support, and epidemiological applications of 'big data' ... 'smart' medical devices that incorporate DHTs to enable new and better ways of monitoring health and delivering care."⁴⁹</p>
Australian Government Department of Health	<p><i>"Digital health is the electronic management of health information to deliver safer, more efficient, better quality healthcare. The Commonwealth's digital health initiatives include My Health Record, Telehealth and the Healthcare Identifiers Service."</i>⁵⁰</p>
World Health Organization	<p><i>"The use and scale up of digital health solutions can revolutionize how people worldwide achieve higher standards of health, and access services to promote and protect their health and well-being."</i>⁵¹</p> <p>The WHO's <i>Global Strategy on Digital Health 2020-2025</i> states <i>"digital health is understood to mean 'the field of knowledge and practice associated with the development and use of digital technologies to improve health'. This definition encompasses eHealth"</i>.⁵²</p>
ANDHealth	<p>According to its white paper <i>Digital Health: Creating a New Growth Industry for Australia</i>,⁵³ ANDHealth follows the FDA definition of digital health (see Table 6).</p> <p>ANDHealth also describe digital health as representing "a technological evolution that spans the entirety of the healthcare paradigm, from prevention and diagnosis, to management and treatment. Digital health transforms the way frontline healthcare services are created, delivered and measured by putting patients at the centre of their own health and care. This creates a new focus on 'healthcare consumers' and 'the empowered patient' as a driver of improved health outcomes."⁵⁴</p> <p><i>"A complete digital health ecosystem includes the development of innovative evidence-based products and services that change the clinical outcome for healthcare consumers, and in doing so change the efficiency and effectiveness of the healthcare system as a whole."</i>⁵³</p>

B-5 National therapeutic regulator review

Table 6. Definitions and descriptions of regulated DHTs from leading national therapeutic goods regulators

National therapeutic goods regulators	Definition or description of digital health
TGA	<p>During a TGA webinar on <i>"The role of the TGA in digital health"</i>, Dr Lee Walsh, Technical Lead (Digital Health) presented definitions and descriptions of digital health from the Australian Government's Australian Digital Health Agency (above), the FDA, and Wikipedia. Dr Walsh also explained that <i>"it's actually quite hard to define, but it's a term that's used very commonly these days and it's used to refer to a lot of different technologies ... the whole concept of it is that it's about connecting medicine using information, digital technologies, smart devices, all these things to improve healthcare."</i>⁵⁵</p> <p><i>"What we're really worried about is, are any of these products medical devices? ... when they come to life and come to market and they have a use that <u>meets the definition of a medical device</u>, they are captured under the legislation and we regulate it."</i>⁵⁵</p>
FDA	<p>According to the FDA, <i>"the broad scope of digital health includes categories such as mobile health (mHealth), health information technology (IT), wearable devices, telehealth and telemedicine, and personalized medicine ... Providers and other stakeholders are using digital health in their efforts to: reduce inefficiencies, improve access, reduce costs, increase quality, and, make medicine more personalized for patients. Patients and consumers can use digital health to better manage and track their health and wellness related activities."</i>⁵⁶</p> <p>On 6 December 2017, the FDA Commissioner, Scott Gottlieb, M.D., stated <i>"We know that consumers and health care providers are increasingly embracing digital health technologies to inform everyday decisions. From fitness trackers to mobile applications tracking insulin administration, these digital tools can provide consumers with a wealth of valuable health information."</i>⁵⁷</p> <p>A presentation by Marisa Cruz, M.D., Senior Medical Advisor, Digital Health, states that <i>"FDA regulation of digital health products" is "tailored, risk-informed regulatory oversight", "FDA oversight limited to digital health products that <u>meet the definition of a medical device</u>", and "recent legislation excluded medical device data systems and general wellness apps from definition of a medical device".</i>⁵⁸</p>
EMA & Notified Bodies	<p>According to the European Commission, <i>"Digital health and care refers to tools and services that use information and communication technologies (ICTs) to improve prevention, diagnosis, treatment, monitoring and management of health and lifestyle. Digital health and care has the potential to innovate and improve access to care, quality of care, and to increase the overall efficiency of the health sector."</i>⁵⁹</p> <p>However, unlike other jurisdictions mentioned, in the EU therapeutic goods are not regulated by a single agency. The EMA is a centralised authorisation procedure to regulate human medicines (any substance or combination of substances presented for the treatment or prevention of disease in human beings), however medicines may also be authorised by national agencies.⁶⁷ <i>"Notified Bodies are responsible for assessing medical devices (MDs) and diagnostics (IVDs)."'</i>⁶⁰</p> <p><i>"A notified body is an organisation designed by an EU country to assess the conformity of certain products before being placed on the market. These bodies carry out tasks related to conformity assessment procedures set out in the applicable legislation ... conformity assessment is a service to manufacturers in an area of public interest."</i>⁶¹</p> <p><i>"In the EU, digital health technologies such as medical apps or wearable sensors can fall within the scope of the medical devices directives. These directives provide the basic definition of a medical device and lay down the technical and procedural obligations that must be followed by the manufacturer of a medical device prior to affixing a CE mark to the product."</i>⁶² Also, <i>"manufacturers of digital health applications must carefully examine new MDR [Medical Devices Regulation] requirements for CE-marked technologies prior to any type of commercial distribution to determine where they fall into the ... definition of a 'medical device' under the new regulation".</i>⁶³</p>

B-6 Medical device definitions

B-6-1 Australia

According to Section 41BD of the Therapeutic Goods Act (1989)⁶⁴

“What is a medical device

(1) A medical device is:

- (a) any instrument, apparatus, appliance, software, implant, reagent, material or other article (whether used alone or in combination, and including the software necessary for its proper application) intended, by the person under whose name it is or is to be supplied, to be used for human beings for the purpose of one or more of the following:
 - (i) diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease;
 - (ii) diagnosis, monitoring, treatment, alleviation of or compensation for an injury or disability;
 - (iii) investigation, replacement or modification of the anatomy or of a physiological or pathological process or state;
 - (iv) control or support of conception;
 - (v) in vitro examination of a specimen derived from the human body for a specific medical purpose;and that does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but that may be assisted in its function by such means; or
- (aa) any instrument, apparatus, appliance, software, implant, reagent, material or other article specified under subsection (2A); or
- (ab) any instrument, apparatus, appliance, software, implant, reagent, material or other article that is included in a class of instruments, apparatus, appliances, software, implants, reagents, materials or other articles specified under subsection (2B); or
- (b) an accessory to an instrument, apparatus, appliance, software, implant, reagent, material or other article covered by paragraph (a), (aa) or (ab); or
- (c) a system or procedure pack.

Note: Declarations under subsection (3) exclude articles from the scope of this definition. Declarations under section 7 can also have this effect: see subsection 7(4).

- (2) For the purposes of paragraph (1)(a), the purpose for which an instrument, apparatus, appliance, software, implant, reagent, material or other article (the **main equipment**) is to be used is to be ascertained from the information supplied, by the person under whose name the main equipment is or is to be supplied, on or in any one or more of the following:
 - (a) the labelling on the main equipment;
 - (b) the instructions for using the main equipment;
 - (c) any advertising material relating to the main equipment;
 - (d) technical documentation describing the mechanism of action of the main equipment.
- (2A) The Secretary may, by notice published in the Gazette or on the Department's website, specify a particular instrument, apparatus, appliance, software, implant, reagent, material or other article for the purposes of paragraph (1)(aa). The notice is not a legislative instrument.
- (2B) The Secretary may, by legislative instrument, specify a particular class of instruments, apparatus, appliances, software, implants, reagents, materials or other articles for the purposes of paragraph (1)(ab).

- (3) The Secretary may, by order published in the *Gazette* or on the Department's website, declare that a particular instrument, apparatus, appliance, software, implant, reagent, material or other article, or that a particular class of instruments, apparatus, appliances, software, implants, reagents, materials or other articles, are not, for the purposes of this Act, medical devices.

Note: A declaration under this section does not stop articles from being therapeutic goods.

- (4) A declaration under this section takes effect on the day on which the declaration is published in the *Gazette* or on the Department's website or on such later day as is specified in the order.

accessory, in relation to a medical device covered by paragraph 41BD(1)(a), (aa) or (ab), means a thing that the manufacturer of the thing specifically intended to be used together with the device to enable or assist the device to be used as the manufacturer of the device intended." ⁶⁵

B-6-2 US

The FDA's oversight is similarly limited to digital health products that meet the definition of a medical device. If a product is labelled, promoted or used in a manner that meets the definition of a medical device in section 201(h) of the Federal Food, Drug & Cosmetic (FD&C) Act, it will be regulated as a medical device.

According to the FDA, "A device is:

an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

- recognized in the official National Formulary, or the US Pharmacopoeia, or any supplement to them,
- intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and
- which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term "device" does not include software functions excluded pursuant to section 520(o)."⁶⁶

Section 520(o) was added to the FD&C Act on 13 December 2016 and describes software functions excluded from the definition of a device in 201(h) of the FD&C Act. Recent guidance from the FDA interprets this amendment (focusing on 520(o)(1)(A)-520(o)(1)(D), describing the following software functions that do not meet the device definition:¹¹

- Software functions intended for administrative support of a health care facility,
- Software functions intended for maintaining or encouraging a healthy lifestyle,
- Software functions intended to serve as electronic patient records, and
- Software functions intended for transferring, storing, converting formats, displaying data and results.

B-6-3 EU

In the EU, directives provide the basic definitions of a medical device. Directives are issued by the European Parliament and then adopted by EU member states as domestic law. However, on 5 May 2017 Regulation (EU) 2017/745 on Medical Devices (MDR) and Regulation (EU) 2017/746 on In-Vitro Diagnostic Medical Devices (IVDR) were adopted, changing the legal framework for medical devices. The MDR has a transitional period of four years and will fully apply from 26 May 2021. The IVDR has a transitional period of five years and will fully apply from 26 May 2022.

During the transitional period, manufacturers can opt to place medical devices on the market under the applicable EU Directives (93/42/EEC, 98/79/EC and 90/385/EEC) or under the new Regulations if they fully comply with these.⁶⁷ Further, "in contrast to Directives, Regulations do not need to be transposed into national law. The MDR and the IVDR will therefore reduce the risks of discrepancies in interpretation across the EU market."⁶⁸

According to Article 2 of Regulation (EU) 2017/745:

“medical device’ means any instrument, apparatus, appliance, software, implant, reagent, material or other article intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury or disability,
- investigation, replacement or modification of the anatomy or of a physiological or pathological process or state,
- providing information by means of in vitro examination of specimens derived from the human body, including organ, blood and tissue donations, and which does not achieve its principal intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its function by such means.

The following products shall also be deemed to be medical devices:

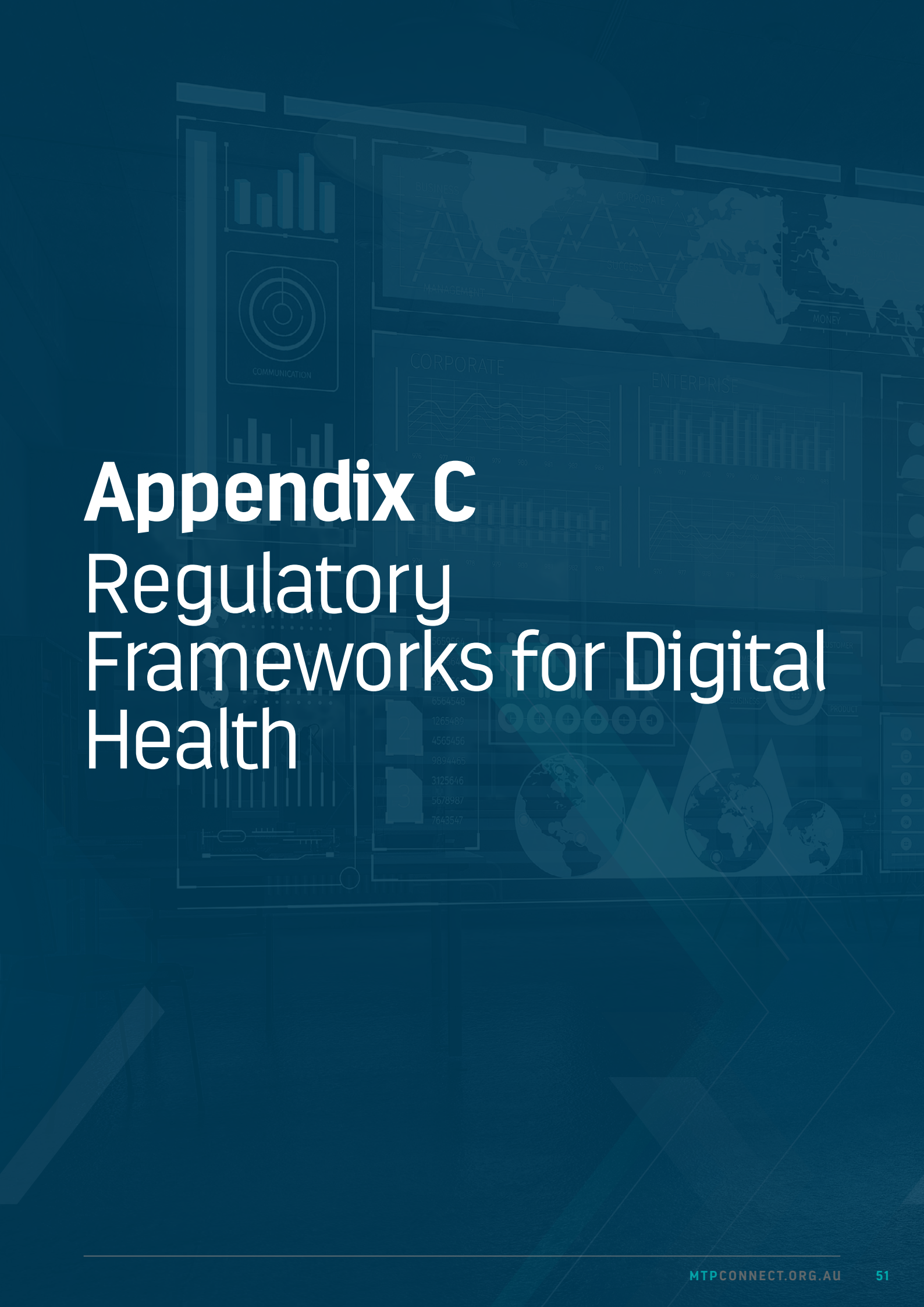
- devices for the control or support of conception;
- products specifically intended for the cleaning, disinfection or sterilisation of devices as referred to in Article 1(4) and of those referred to in the first paragraph of this point.”⁶⁹

B-6-4 Comparison across legislations

The following table compares the broad descriptions of medical devices across the three jurisdictions examined.

Table 7. Comparison of selected phrases in the legislated definitions of medical devices

	Section 41BD Therapeutic Goods Act (1989)	Section 210(h) Food, Drug & Cosmetic Act (1938) with major amendments including the Medical Device Amendments Act (1976) and 21st Century Cures Act (2016)	Article 2 of Regulation (EU) 2017/745
Broad description:	any instrument, apparatus, appliance, software, implant, reagent, material or other article ... whether used alone or in combination ... including the software necessary for proper application	an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article	any instrument, apparatus, appliance, software, implant, reagent, material or other article
Broad intended use:	diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease	in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease	diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease
Distinctions from drugs and other pharmacological actions:	does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means	does not achieve its primary intended purposes through chemical action and which is not dependent upon being metabolised	does not achieve its principal intended action by pharmacological, immunological or metabolic means
Mention of software:	software included in definition, but also noting the TGA's website states "The TGA does not regulate health and lifestyle apps and software that do not meet the definition of a medical device" ¹⁰	does not include software functions for administrative support of a health care facility, maintaining or encouraging a healthy lifestyle, electronic patient records, or for transferring, storing, converting formats, displaying data and results	software included in broad description, but also noting the act states software for general purposes in a healthcare setting or software for lifestyle and wellbeing purposes is not a medical device

The background is a dark blue gradient with faint, semi-transparent white graphics. These include various business-related icons and charts: a bar chart, a target icon labeled 'COMMUNICATION', a world map with labels like 'BUSINESS', 'CORPORATE', 'MANAGEMENT', 'SUCCESS', and 'MONEY', and several line and bar charts labeled 'CORPORATE' and 'ENTERPRISE'. There are also some circular icons and a list of numbers.

Appendix C

Regulatory Frameworks for Digital Health

C-1 Australia and the TGA

All products for which therapeutic claims are made by the manufacturer must first be included in the Australian Register of Therapeutic Goods (ARTG) prior to being imported, exported, or supplied for use in Australia. Class I and Class I IVD medical devices must complete a self-assessed conformity assessment, which is included along with the application for auto-inclusion in the ARTG. All other products of higher regulatory classifications are required to submit a conformity assessment to be assessed by the TGA. A successful assessment will deliver a conformity assessment certificate, which device sponsors are required to include with their application for ARTG inclusion. Further audits may be required for some products and a final decision for inclusion is provided by the TGA.

“Australia is fantastic in terms of being local, and we’re connected here, and we can do clinical trials relatively easily here. So that’s all very good and very useful.” Product developer (P17)

The TGA takes a total life cycle approach to medical device regulation and regulates all DHTs that fall under the definition of a medical device. All medical devices are required to comply with the general Essential Principles of safety and performance as set out in Section 41BH of the Therapeutic Goods Act (see Appendix C-1-1).⁶⁵

In Australia, medical devices are classified into one of the following classes: Class I, I (measuring), I (sterile); Class IIa; Class IIb, IIb (sterile); Class III or Active Implantable Medical Device (AIMD) based on a selection of risk factors, for instance, whether the device is intended to be implanted and the level of regulatory control deemed appropriate.⁷⁰

Device sponsors submit evidence from manufacturers that the minimum conformity assessment procedures required for the class of device have been followed. The TGA is flexible in allowing for several combinations of assessment documentation for each regulatory class, each of which corresponds to separate conformity assessment pathways (see Appendix C-1-2).¹²

Documentation and evidence required for all medical devices increases with regulatory classification, with higher regulatory classes of device requiring documentation that may include the delivery of a technical and device design dossier.

For devices higher than a Class I designation, once a conformity certificate is received from the TGA, sponsors of digital medical devices can apply for inclusion in the ARTG and upon acceptance and provision of an ARTG inclusion may begin to supply their product in Australia.⁷¹

In addition to its role in assessing conformity assessment applications, the TGA is also listed as a notified body with the ability to issue MRA CE certificates under EU directive 93/42/EEC Medical Devices to selected Australian manufacturers.⁷²

C-1-1 Australian Essential Principles

Six general Essential Principles apply to all devices:⁶⁵

- the use of a medical device must not compromise health and safety;
- the design and construction of a medical device must conform with safety principles;
- medical devices are to be suitable for the intended purpose;
- long-term safety;
- medical devices are not adversely affected by transport or storage; and
- the benefits of medical devices are to outweigh any undesirable effects.

Further Design and Construction Principles may apply to DHTs including those relating to the safety and performance profiles of their:

- chemical, physical and biological properties;
- infection and microbial contamination;
- construction and environmental properties;
- measuring function;
- protection against radiation;
- connection to an energy source;
- accompanying information to patients or clinicians; and
- clinical evidence.

C-1-2 Conformity assessment procedures

According to the Australian Guidelines for Medical Devices,¹² under review at the time of writing, there are a number of conformity assessment procedures that can be used depending on the regulatory class of the medical device. Tables 9 and 10 in Appendix C-3 outline the minimum conformity assessment procedures for each class, as well as compare them directly to the EU procedures.

C-1-3 TGA submission documentation

Market authorisation requires that applicants provide some or all of the following pieces of evidence for review by the TGA.^{91,93}

- a self-certification declaration (for Class I, non-sterile, non-measure devices)
- evidence of compliance with the applicable conformity assessment procedures (this may include evidence of third-party certification)
- technical documentation demonstrating how the Essential Principles have been met, including:
 - a documented and detailed risk analysis
 - evidence of compliance with relevant standards (such as IEC 62304 or equivalent)
 - clinical evidence
 - copies of information provided with the device (labels, instructions for use, packaging, patient information documents)
 - post-market surveillance plans

The evidence required depends on a number of factors, including:

- the regulatory classification of the device,
- whether a device is supplied sterile or has a measuring function,
- whether a device is selected for an application audit, and
- whether applicants are self-certifying (for Class I, non-sterile, non-measure devices) or making use of third-party certification (comparable overseas regulator evidence or TGA conformity assessment certification, see Appendix C-1-4).

C-1-4 Comparable Regulatory Approvals

The TGA considers specific evidence and dossiers issued by the following overseas regulators:⁹¹

- Certificates issued by Notified Bodies designated by the medical device regulators of European member states, under the medical device regulatory frameworks of the EU;
- Decisions of the FDA;
- Approvals and licences issued by Health Canada;
- Pre-market approvals from Japan, issued by the Ministry of Health, Labour and Welfare, Pharmaceutical and Medical Devices Agency, or Registered Certified Body, as applicable;
- Certificates and reports issued under the Medical Device Single Audit Program, where Australian regulatory requirements have been covered and certified in the audits;
- ISO 13485:2016 certificates issued by a certification body that is also a Notified Body designated under the IVDD 98/79/EC (for IVD inclusion applications only until 26 May 2022); and
- ISO 13485:2016 certificates issued by a body that is an accredited body that is a signatory to the Multilateral Recognition Arrangement of the International Accreditation Forum (IAF MLA) (for IVD inclusion applications only until 26 May 2022).

C-1-5 Australia and Europe – stakeholder perspectives

“The European system has these essential principles and the Australian one as well, because we are aligned with Europe. Which are kind of generic. And compliance is done to a set of standards, to the generic essential principles of safety and performance ... Australia is aligned with the major markets. ... It's good that Australia has aligned itself with one of the two and to me Europe seems to be better, because it has those pluses with the risk classification system. The central requirements, which are generic and can be applied to any technology. So that flexibility I think it's better than the US system.” Industry – industry body (P07)

C-2 US and the FDA

The FDA takes a risk-based approach to the regulation of DHTs that fall within the definition of a medical device.

Unless an exemption applies, the FDA requires that a manufacturer introducing a new medical device or a new indication for use of an existing medical device obtain either a Section 510(k) pre-market notification clearance or a pre-market approval (PMA) before introducing it into the US market. The type of marketing authorisation is generally linked to the classification of the device.

The FDA classifies medical devices into one of three classes (Class I, II or III) based on the degree of risk the FDA determines to be associated with a device and the level of regulatory control deemed necessary to ensure the device's safety and effectiveness (see Table 8). The FDA has a list of over 1,700 distinct types of devices, which they have classified, described and organised under Title 21 of the Code of Federal Regulations (CFR), Parts 862–892.⁷⁴ Split into 16 medical specialty 'panels', such as cardiovascular devices or immunology devices, most medical devices can be classified according to the list by finding the matching description of the device or an equivalent.

Table 8. FDA classifications of medical devices and associated regulatory pathways and activities ^{4,75,76}

Regulatory Classification	Risk	Pathway	Required Documentation
Class I	Low	General controls, most exempt from Pre-market notification (510(k))	No need for proof of safety or efficacy, nor clinical trials
Class II	Moderate	General controls and special controls Pre-market notification (510(k))	Demonstrates performance as expected. Likely not requiring clinical trials
Known Class III with predicate device (minor change from existing device)	Significant	General controls Pre-market notification (510(k))	If substantial similarity to previous predicate devices, may be able to under 510(k) rather than full PMA
Known Class III without predicate device	Significant	Pre-market approval (PMA)	Demonstrate sufficient scientific evidence that it is safe and effective in its intended use, incl. high quality randomised controlled trials
New Class III	Significant	Pre-market approval (PMA)	Demonstrate sufficient scientific evidence that it is safe and effective in its intended use, incl. high quality randomised controlled trials

C-2-1 Exempt devices

Most Class I medical devices are exempt from undertaking a 510(k) pre-market notification procedure. Exemptions of certain Class I devices (and certain Class II devices) are listed in the classification regulations of 21 CFR and also have been collected together in the Medical Device Exemptions document. However, regardless of exemption, all Class I medical devices must be manufactured under a quality assurance program, be suitable for their intended use, be adequately packaged and properly labelled, and have their establishment registration and device listing forms on file with the FDA.

C-2-2 Non-exempt devices

Clearance processes for other classes of devices (apart from those exempt) is achieved primarily through three streams: 510(k) pre-market notification, pre-market approval (PMA), or De Novo.

C-2-3 Pre-market notification – 510(k)

A 510(k) must demonstrate that the device is substantially equivalent to one legally in commercial distribution in the US: (1) before 28 May 1976; or (2) to a device that has been determined by the FDA to be substantially equivalent.⁷⁷

The FDA determines substantial equivalence if the device, when compared to a predicate device, has the same intended use and same technological characteristics, or has the same intended use and different technological characteristics and can demonstrate that it is at least as safe and effective as the predicate device.⁷⁷

510(k) is required prior to any commercial distribution of a medical device, when there is a change to a currently marketed device that could significantly affect its safety or efficacy or when the device is intended to be marketed for a new or different intended use.⁷⁷

Alongside the pathway of internal review of applications, the FDA also created the Accredited Persons Program under the FDA Modernization Act of 1997 (FDAMA), which allows the primary review of applications for eligible Class I and II devices to be conducted by accredited organisations prior to final FDA certification.

C-2-4 Pre-market approval – PMA

Products requiring PMAs are new or novel Class III devices that pose a significant risk of illness or injury, or devices found not substantially equivalent to Class I and II predicates through the 510(k) process.

PMA submissions under Title 21 Code of Federal Regulations (CFR) Part 814 require device description, alternative practices and procedures, marketing history, summary of non-clinical and clinical studies, including any investigations conducted under an investigational device exemption, along with conclusions from the studies (see Appendix C-2-6). The submitted study designs, study conduct, clinical and non-clinical data analysis should be completed under all applicable FDA guidance documents, industry standards and recommended practices in order for the applications to be accepted and device-specific guidance documents should be used in the design of all study protocols.⁷⁸

C-2-5 De Novo

Regulations for the De Novo process are currently being finalised by the FDA, though this process offers a pathway to classify devices for which there is no marketed predicate device available and which are classified as Class I or Class II. These devices are still subject to both general and special controls and must be submitted along with reasonable assurance and appropriate clinical and/or non-clinical data that ensures the device is safe and effective for its intended use.

C-2-6 Clinical studies

Clinical studies conducted within the US must comply with Good Clinical Practices regulations, including an Investigational Device Exemption (IDE) filed prior to the start of clinical testing.

There are two main types of clinical studies that support a PMA: traditional feasibility studies and pivotal studies. Traditional feasibility studies are commonly used to capture preliminary safety and efficacy information on a near final or final device design to adequately plan an appropriate pivotal study.

Pivotal studies are designed to collect definitive evidence of the safety and effectiveness of a device for a specified intended use.

The FDA also allows IDEs for early feasibility medical device clinical studies, including first in human studies. "Early feasibility studies allow for early clinical evaluation of devices to provide proof of principle and initial clinical safety data. These studies may be appropriate early in device development when clinical experience is necessary because nonclinical testing methods are not available or adequate to provide the information needed to advance the development process."⁹⁰ Early feasibility studies take place before the device design has been finalised.

According to the FDA, a sponsor of a significant risk device study must submit a complete IDE application to the FDA. This application must include information demonstrating that there is reason to believe that the risks to human subjects from the proposed investigation are outweighed by the anticipated benefits to subjects and the importance of the knowledge gained, that the investigation is scientifically sound, and that there is reason to believe the device as proposed for use will be effective.

C-2-7 Additional FDA pathways and programs

Medical Device Development Tool – MDDT

A pathway to qualify devices to be used specifically as tools in medical development for either:

- Clinical Outcome Assessment – measuring how patients feel or function using either patient-reported or clinician-reported scales;
- Biomarker Testing – detecting or measuring an indicator, biologic process or pharmacological response to a treatment; or
- Non-clinical assessment model – a non-clinical test or model such as an in vitro 'bench', animal, or computational model, that measures or predicts device function or performance in a living organism.⁷⁹

Breakthrough Devices Program

The FDA has also recently introduced a Breakthrough Devices Program.²⁰ This program expedites development, assessment, and review of devices and device-led combination products that provide for more effective treatment or diagnosis of life threatening or irreversibly debilitating diseases or conditions. The statutory standards and application processes for PMA, 510(k) clearance, and De Novo marketing authorisation are still preserved but this pathway is designed to expedite the process. Devices seeking application under this pathway must also meet at least one of the following subsequent criteria:

- (a) represent breakthrough technology; (b) no approved or cleared alternatives exist; (c) offers significant advantages over existing approved or cleared alternatives; (d) device availability is in the best interests of patients.

Software precertification pilot program – pre-cert program

This pilot program was designed and developed specifically for and in consultation with digital health companies to address the observation that "FDA's traditional approach for the regulation of hardware-based medical devices is not well suited for the faster, iterative design and development, and type of validation used for software device functions, including SaMD".³⁴ Nine companies developing health software currently participate. The program facilitates companies' applications through the existing pathways of 510(k), PMA and De Novo using an expedited process based on a precertification of manufacturing standards and quality management systems. These include both the existing US Quality System Regulations at 21 CFR 820, as well as the recognition of standards, some of which are also recognised by the TGA and the EU:

- ISO 13485:2016 Medical devices – Quality management systems – Requirements for regulatory purposes;
- ISO/IEC/IEEE 12207:2017 Systems and software engineering – Software life cycle processes;
- IEC 62304:2006 Medical device software – Software life cycle processes;
- ISO 14971:2007 Medical devices – Application of risk management to medical devices;
- ISO 9001:2015 Quality management system – Requirements.

C-2-8 FDA – stakeholder perspectives

"In the US you have this predicated system ... when you go to their classification database or approval database you see a list of standards applicable to that. So they're trying to standardise as well, the assessment process. So that's a big difference ... Another is the risk classification. The US classification system is per category, so they have regulations for different categories of products and there is a risk class aligned to those." Industry – industry body (P07)

"[for Europe] you get to put your CE mark on it, you're good to go, whereas in the United States you [have] to build a pretty comprehensive dossier, you have to submit that to the regulator, they had to be able to review it and confirm you did all the right testing and the right validations, and that that product was substantially equivalent to something already on the market. So, the burden there was much higher..." Product developer (P08)

C-3 Europe and Notified Bodies

The EU's Medical Device Regulation (MDR) went into effect in May 2017 and replaces the Medical Device Initiative (93/42/EEC) and the Directive on active implantable devices (90/385/EEC). Manufacturers have been given until May 2021 to meet the new directive.

The section most pertinent to DHTs under MDR 2017 is the definition of active medical devices (see Appendix C-3-1).

For device manufacturers of software or mobile applications, the definition of a medical device or in-vitro diagnostic medical device is regulated by the respective Directives 93/42/EEC or 98/79/EC. For borderline cases, the MEDDEV Guidance 2.1/6, entitled "Guidelines on the qualification and classification of stand-alone software used in healthcare within the Regulatory Framework of Medical Devices", released in January 2012, is the most relevant document and provides practical advice to manufacturers, organisations and public authorities on how to determine when a software falls under the definition of a medical device or of an *in-vitro* diagnostic medical device. Such criteria apply also to mobile applications.⁸⁰

European regulatory classification of medical devices is split into four main categories: Class I, Class IIa, Class IIb and Class III. Under MDR 2017 Class I will be split into a further three categories of those that are placed on the market in sterile condition, have a measuring function, or are reusable surgical instruments (as per Section 2, Article 52, Item 7).⁸¹

Tables 9 and 10 below describe the minimum applicable conformity assessment procedures for each class under the EU 2017 MDR. These tables also compare the minimum procedures with the Australian reference, given the fact that the conformity assessment procedures in both jurisdictions are based on meeting essential principles of safety and performance (see Section 2.2.2). Requirements specific to Australia are underlined while requirements specific to the EU are italicised.

Table 9. Non-IVD medical devices^{65, 73, 81, 82}

Device classification	Minimum applicable CA procedure	Australian reference	EU 2017 MDR reference
Class I	Declaration of Conformity Procedures	Part 6	Annex IV
Class I with measuring function and/or sterile and/or reusable	Declaration of Conformity + Production Quality Assurance Procedures OR Declaration of Conformity + Full Quality Assurance Procedures N.B. The QMS requirements may be limited to control of the special characteristics (e.g., of the sterilisation process)	Part 6 + Part 4 OR Part 6 + Part 1 excluding Clause 1.6	Annex IV + Annex XI, Part A OR Annex IV + Annex IX, Chapter 1
Class IIa	Full Quality Assurance Procedures OR Verification Procedures OR Production Quality Assurance Procedures	Part 1 excluding Clause 1.6 OR Part 3 OR Part 4	Annex IX, Chapter 1 OR Annex XI, Part B OR Annex XI, Part A

Device classification	Minimum applicable CA procedure	Australian reference	EU 2017 MDR reference
Class IIb	Full Quality Assurance Procedures OR Type Examination Procedures + Verification Procedures OR Type Examination Procedures + Production Quality Assurance Procedures	Part 1 excluding Clause 1.6 OR Part 2 + Part 3 OR Part 2 + Part 4	Annex IX, Chapter 1 OR Annex X + Annex XI, Part B OR Annex X + Annex XI, Part A
Class III and AIMD*	Full Quality Assurance Procedures + Examination of Design OR Type Examination Procedures + Verification Procedures OR Type Examination Procedures + Production Quality Assurance Procedures	Part 1 including Clause 1.6 OR Part 2 + Part 3 OR Part 2 + Part 4	Annex IX including Chapter 2 OR Annex X + Annex XI, Part B OR Annex X + Annex XI, Part A
System or Procedure Packs or custom-made medical device	Procedures for Medical Devices Used for a Special Purpose	Part 7	Annex XIII
Class III Implantable custom-made medical device	<i>Procedures for Medical Devices Used for a Special Purpose + Production Quality Assurance Procedures (EU 2017 MDR only)</i> OR <i>Procedures for Medical Devices Used for a Special Purpose + Full Quality Assurance Procedures</i>	—	<i>Annex XIII + Annex XI, Part A</i> OR <i>Annex XIII + Annex IX, Chapter 1</i>

* AIMD as a separate classification has been removed in the EU 2017 MDR.

The authors thank the TGA for assistance in constructing this table.

Table 10. IVD medical devices^{65, 73, 81, 82}

Device classification	Minimum applicable CA procedure	Australian reference	EU 2017 IVDR reference
<u>Class 1</u> Class A	Declaration of Conformity Procedures	Part 6A	Annex IV
<i>Class A with sterile (EU 2017 MDR only)</i>	<i>Full Quality Assurance Procedures with limited QMS to control sterility</i> OR <i>Production Quality Assurance Procedures with limited QMS to control sterility</i>	—	<i>Annex IX, Chapter 1</i> OR <i>Annex XI</i>
<u>Class 1 (in-house)</u>	<u>Declaration of Conformity Procedures</u>	<u>Part 6A</u>	—
<u>Class 2</u> Class B	Full Quality Assurance Procedures OR <u>Declaration of Conformity Procedures + Production Quality Assurance Procedures (Australia)</u> <i>Production Quality Assurance Procedures (EU)</i>	Part 1 excluding Clause 1.6 OR Part 6 + Part 4	Annex IX, Chapter 1 OR Annex XI
<u>Class 2 (in-house)</u>	<u>Declaration of Conformity Procedures</u>	<u>Part 6A</u>	—
<u>Class 3</u> Class C	Full Quality Assurance Procedures OR Type Examination Procedures + Production Quality Assurance Procedures	Part 1 excluding Clause 1.6 OR Part 2 + Part 4	Annex IX, Chapter 1 OR Annex X + Annex XI
<u>Class 3 (in-house)</u>	<u>Declaration of Conformity Procedures</u>	<u>Part 6A</u>	—
<u>Class 4</u> Class D	Full Quality Assurance Procedures + Examination of Design OR Type Examination Procedures + Production Quality Assurance Procedures	Part 1 including Clause 1.6 OR Part 2 + Part 4	Annex IX including Chapter II OR Annex X + Annex XI
<u>Class 4 (in-house)</u>	<u>Full Quality Assurance Procedures</u> OR <u>Procedures applying to Class 4 in-house IVD medical devices</u>	<u>Part 1 including Clause 1.6</u> OR <u>Part 6B</u>	—

The authors thank the TGA for assistance in constructing this table.

Unlike the FDA and TGA, the EU does not have a centralised assessor and certifier for medical device market approval. Owing to the complexity of a union involving numerous territories, the EU member states and the European Economic Area (EEA) countries have designated third-party assessors called Notified Bodies (NB) to ensure manufacturers' compliance to the safety and performance of medical products. NB may be authorised to assess products according to their technical competence, so it is important for manufacturers to select appropriate NB for the assessment of their device according to needs.

There are currently 57 NB under directive 93/42/EEC Medical Devices including the TGA (the TGA is able to issue MRA CE certificates to selected Australian manufacturers).

C-3-1 MDR active device

MDR 2017/745 Article 2 paragraph 4 states:

“‘Active device’ means any device, the operation of which depends on a source of energy other than that generated by the human body for that purpose, or by gravity, and which acts by changing the density of or converting that energy.

Devices intended to transmit energy, substances or other elements between an active device and the patient, without any significant change, shall not be deemed to be active devices.

Software shall also be deemed to be an active device.”⁶⁹

C-3-2 EU Notified Bodies – stakeholder perspectives

“They’re all commercial entities, yeah. If you don’t understand that, they are not like the FDA, TGA or Health Canada. They are commercial entities in there to make a profit.” Industry – industry body (P07)

“European regulation contact, it’s really – I mean you’re never contacting the base regulators because they’re the regulation makers back in the European Parliament. It’s the notified – the Notified Bodies are essentially the public face of that system. So it’s dealing with the Notified Bodies. And you absolutely do that for every device application you’ve got.” Industry – regulatory affairs (P12)

“It’s easier working with a Notified Body. They will try and assist you to get it CE marked and get it through. They will basically give you every opportunity to meet those regulations and support you to do that.” Product developer (P18)

C-3-3 CE mark – stakeholder perspectives

“When it comes to getting devices on the market the European method was a lot easier. Much, much easier, and the people that would come into your facility, so you’d have a Notified Body that would come in periodically and make sure that you knew what you were doing, they would check out the work that you did, they might look at the technical file for the product, but was one person and they had a limited range of technical skills in the background, whereas when you sent it in to the FDA they’d take the bio-compatibility part and give to either a materials expert or a bio-c expert, and then they would take your mechanical testing and give it to another expert, so it was much more thoroughly scrutinised.” Product developer (P08)

“When you’re really tiny, and with the FDA you kind of get one chance. If they’re not happy with your submission they’re just not happy, whereas with the CE they’ll come back to you going, ‘we’re not happy about this, have you got another document that could show this?’ But the FDA just go, ‘No, we’re not happy.’” Product developer (P18)

C-4 IMDRF

The IMDRF is a group of national medical device regulators established to accelerate international medical device regulatory harmonisation, fostering global convergence, leveraging resources, and making available safe and effective medical devices globally. Current member countries include Australia, Japan, South Korea, China, Singapore, the US, Canada, Russia, the EU and Brazil. A number of recently completed and ongoing work items are particularly pertinent to DHTs.

For example, the IMDRF has released a series of documents to establish a common framework for identifying types of SaMD and associated risks and controls,⁸³ including definitions of SaMD,⁸⁴ Application of Quality Management System to SaMD,⁸⁵ and Clinical Evaluation of SaMD.⁸⁶

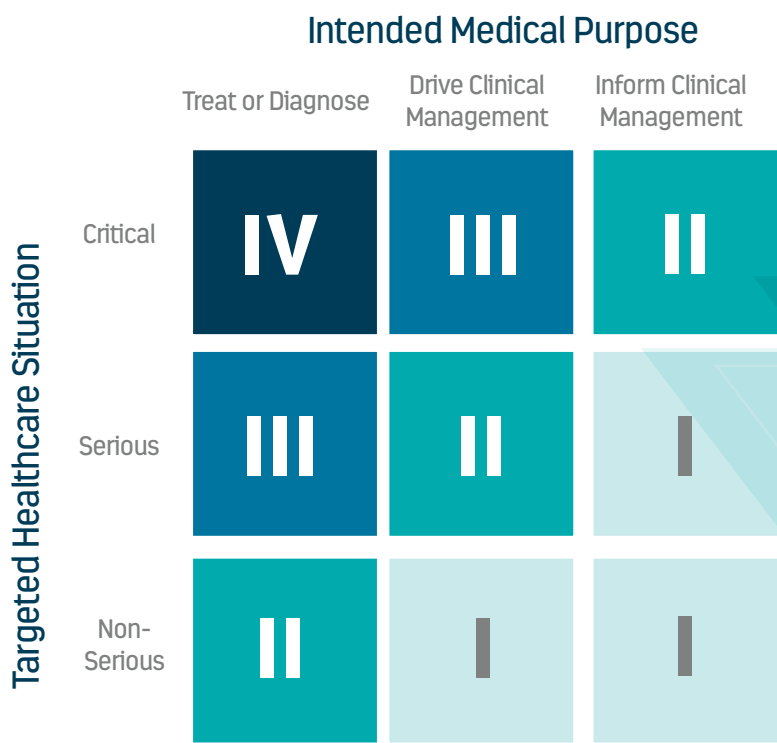


Figure 11. New categories for SaMD from IMDRF⁸³

C-5 Regulatory approval times – FDA & TGA comparisons

The TGA publishes processing times for completed conformity assessment applications in annual performance statistics reports.⁸⁷ We collated the data presented in these reports (July 2014 to July 2018) for conformity assessment approvals and approvals for inclusion in the ARTG and compared them to data from the FDA on pre-market approvals (PMA) and pre-market notifications (510(k)).

TGA reports included a total of 872 conformity assessment applications were completed. TGA processing times for new devices and variations are listed in Table 11, in working days. Median times were refined to an estimation of weeks to allow comparisons with FDA data. Total completed applications for inclusion in the ARTG were 25,546, including 12,422 Class I inclusions only requiring self-assessment by the device sponsor.

Table 11. TGA conformity assessment applications (2014–2018)

	2014–2015 July–June	2015–2016 July–June	2016–2017 July–June	2017–2018 July–June
Applications completed	208	187	204	273
Mean review time (working days)	130	133	129	131
Median review time (working days)	173	178	167	189
Median review time (weeks)	35	36	33	38

Table 12. TGA completed applications for ARTG inclusion (2014–2018)

	2014–2015 July–June	2015–2016 July–June	2016–2017 July–June	2017–2018 July–June
Class I	2497	2690	2431	4804
Class I measuring	74	48	50	64
Class I sterile	265	253	255	240
Class IIa	1382	1206	1178	1191
Class IIb	760	716	682	568
Class III	372	249	471	373
Class III Joint	364	355	203	88
AIMD	46	19	87	34
IVDs	623	420	245	243
TOTALS	6383	5956	5602	7605
TOTALS (not including Class I self-assessment)	3886	3266	3171	2801

FDA approvals across the time period (July 2014 to July 2018) were 141 PMAs⁸⁸ and 12,184 510(k) including De Novo 510(k) classifications.⁸⁹ Approval times were calculated from the listed start dates of application review and end dates of application approval and totalled as calendar days elapsed. Median times were refined to an estimation of weeks to allow comparisons with TGA data.

Table 13. FDA Pre-market authorisations (2014–2018)

	2014–2015 July–June	2015–2016 July–June	2016–2017 July–June	2017–2018 July–June
PMA applications received	36	39	44	22
Mean review time (calendar days)	401	355	351	299
Median review time (calendar days)	357	307	266	276
Median review time (weeks)	51	44	38	39

Table 14. FDA Pre-market notifications 510(k) (2014–2018)

	2014–2015 July–June	2015–2016 July–June	2016–2017 July–June	2017–2018 July–June
PMA applications received	3080	3017	3110	2977
Mean review time (calendar days)	150	158	154	142
Median review time (calendar days)	124	134	131	116
Median review time (weeks)	18	19	19	17

The data for review times between the TGA and FDA cannot be directly compared, as the Australian framework is primarily based on certification of the manufacturer (except for Class III devices, which require a third-party design/type examination) whereas the US system is primarily based on the product. Also, Australia separates the pre-market approval and market authorisation steps.⁹² However, for a broad comparison of the two approval systems, it can be seen from the chart in Figure 12 that the total median approval times for TGA certification applications, including for examination of the design/type of a device (Class III devices only), falls between those of FDA PMA and 510(k) approval times, with TGA review times tending towards FDA PMA approval timeframes. Note in this chart, TGA N = 872, FDA PMA N = 141, and FDA 510(k) N = 12,184.

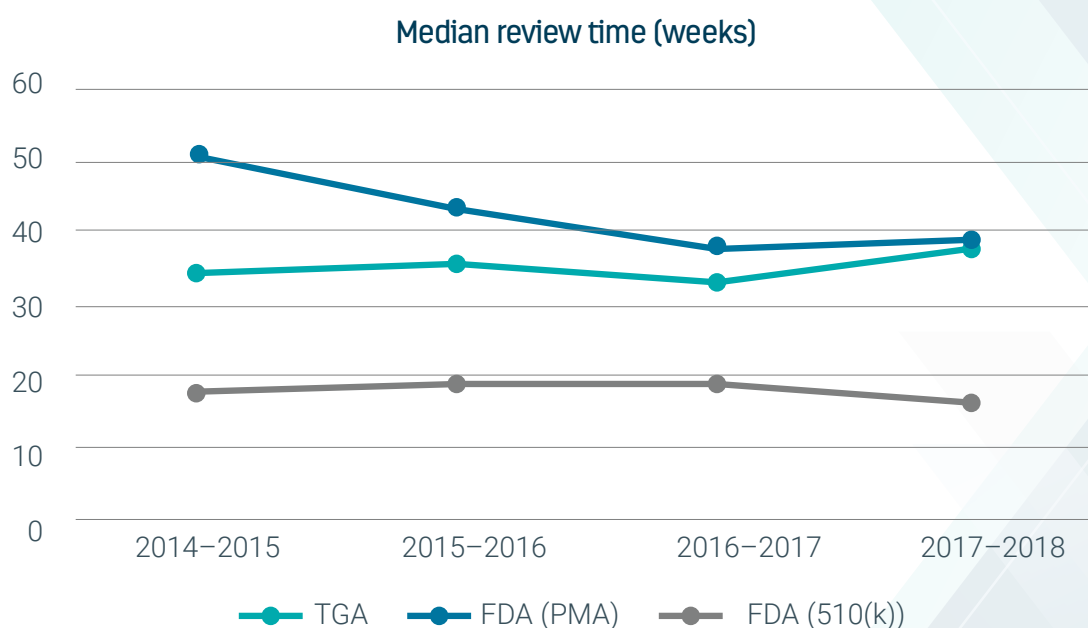


Figure 12. TGA and FDA comparison of review times

A medical professional in a white coat is shown from the chest up, holding a patient's hand. The image is overlaid with a teal grid and various medical data visualizations, including an ECG line, a circular gauge, and a temperature scale. The text 'Appendix D Adaptive Regulation' is prominently displayed in the center.

Appendix D

Adaptive Regulation

D-1 A review of adaptive regulation

'Adaptive regulation' is a term used to describe two different ways of ensuring regulation keeps pace with contextual change, and can apply to all sectors that are regulated.

In the first instance, adaptive regulation is used to refer to **"a structured regulatory process that enables learning and modification of policy over time via adjustments informed by data collection and analysis"**.⁶ In this interpretation, the legislative, policy and/or regulatory frameworks themselves are amended. Such changes are based on evidence and analysis of policy outcomes and can occur as a reaction to, or for prevention of poor or misaligned policy outcomes.

Second, adaptive regulation is used to describe the concept of a regulatory system that is **"planned to adapt, i.e. that its adaptive quality is designed from the outset"**.⁶ The legislation, policy and regulation is designed to be broad enough in scope to allow for a multitude of technologies to be assessed, as opposed to a more precise regulatory scope that categorises individual technologies into defined groups and seeks to codify types of technology use. The regulation can also be designed to incorporate adaptive features and mechanisms through a planned allowance for emergent and disruptive innovations. Examples of adaptive regulatory features and mechanisms for therapeutic products highlighted in existing peer-review literature and industry reports are synthesised in Table 15.

Table 15. Adaptive regulation features and mechanisms^{7,18,32}

Features and Mechanisms	Description
Outcomes-based	Regulatory approval shifts from a focus on specific manufacturing inputs to achieving broadly defined outcomes. Regulations specify what outcomes are required rather than how to achieve them, which enables flexibility in how outcomes are met.
Risk-weighted	Regulatory obligations vary according to the level of risk posed by the specific product and service, alongside the capabilities and regular reviews of the manufacturers themselves.
Harmonisation through collaboration	Aligns regulations internationally and nationally by engaging stakeholders across the ecosystem to collaborate in regulatory design.
Adaptive authorisation	A single, binary decision is replaced with a series of approval stages. Initial limited marketing authorisation (e.g. can be used for specific indication for specific subpopulation) is granted based on a reduced level of evidence. This is followed by iterative phases of evidence gathering to better define the product's benefits/risks. This approach enables the technology developer to gain evidence in 'real-world' scenarios rather than through clinical trials.
Experimentation and co-design	Utilises mechanisms such as 'regulatory sandboxes'. Sandboxes involve regulators partnering with industry and users/consumers/patients to 'experiment' with novel products, services, and business models in a controlled, safe, and transparent environment. May involve time-limited exemption from the standard regulations alongside monitoring to ensure consumers will not be negatively affected. Assists regulators in: a) understanding how disruptive technologies work, and b) co-designing rules and regulations with industry partners that are 'fit-for-purpose'.

Thus, regulation can be adaptive through either regular review, or adaptive by design. These two approaches to adaptive regulation can also apply at different levels of legislation, policy and regulation (see Figure 13).

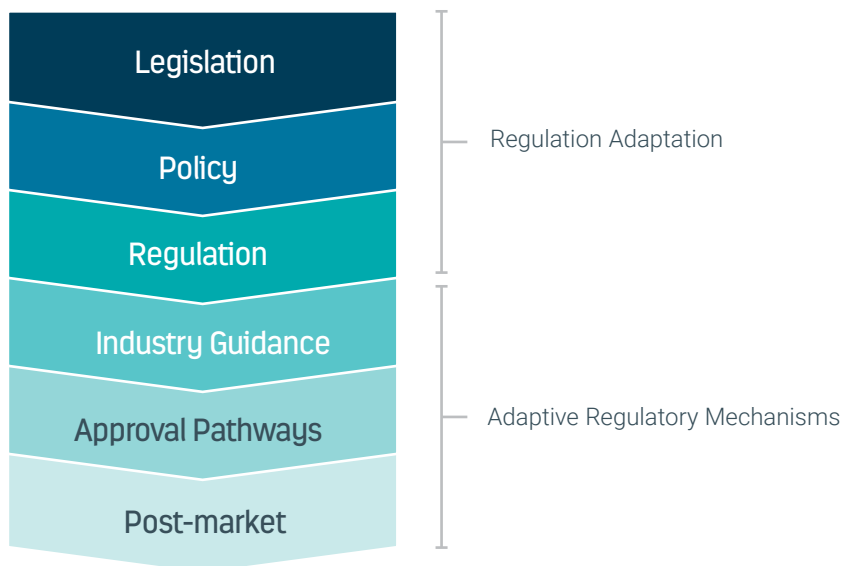


Figure 13. Levels of adaptive regulation

The two concepts of adaptive regulation are not mutually exclusive. Regulation can be regularly reviewed and changed (adaptive regulation through periodic review and improvement), and that change could be towards a broader, more flexible, collaborative, risk-weighted, and/or outcomes-based approach to regulating (adaptive regulation through design).

References

1. MTPConnect. *Sector Competitiveness Plan*, (2020) <https://www.mtpconnect.org.au/images/2020%20MTPConnect%20Sector%20Competitiveness%20Plan.pdf> Last Accessed 11 December 2020.
2. Tseng, J., Samagh, S., Fraser, D. & Landman, A. 'Catalyzing healthcare transformation with digital health: Performance indicators and lessons learned from a Digital Health Innovation Group', *Healthcare* **62** (2018).
3. IRGC. *Planning Adaptive Risk Regulation, Conference Report*, (2016), Lausanne <https://irgc.org/wp-content/uploads/2018/09/IRGC-Conference-Planned-Adaptive-Regulation-Summary-Report-final-WEB.pdf> Last Accessed 11 December 2020.
4. Van Norman, G.A. 'Drugs and devices: comparison of European and US approval processes', *Journal of the American College of Cardiology: Basic to Translational Science* **1**, 399–412 (2016).
5. Fenwick, M., Kaal, W.A. & Vermeulen, E.P. 'Regulation tomorrow: what happens when technology is faster than the law?' *American University Business Law Review* **6**, 561–594 (2016).
6. Bennear, L.S. & Wiener, J.B. 'Adaptive Regulation: Instrument Choice for Policy Learning Over Time', (2019) <https://www.hks.harvard.edu/sites/default/files/centers/mrcbg/files/Regulation%20-%20adaptive%20reg%20-%20Bennear%20Wiener%20on%20Adaptive%20Reg%20Instrum%20Choice%202019%2002%2012%20clean.pdf> Last Accessed 11 December 2020.
7. Eggers, W.D., Turley, M. & Kishnani, P. 'The future of regulation: Principles for regulating emerging technologies', (2018) <https://www2.deloitte.com/insights/us/en/industry/public-sector/future-of-regulation/regulating-emerging-technology.html> Last Accessed 2 May 2019.
8. Walker, W.E., Marchau, V.A. & Swanson, D. 'Addressing deep uncertainty using adaptive policies: Introduction to section 2', *Technological Forecasting and Social Change* **77**, 917 (2010).
9. Lee, T.T. & Kesselheim, A.S. 'U.S. Food and Drug Administration Precertification Pilot Program for Digital Health Software: Weighing the Benefits and Risks', *Annals of Internal Medicine* **168**, 730–732 (2018).
10. TGA. *Regulation of Software as a Medical Device*, (2018) <https://www.tga.gov.au/regulation-software-medical-device> Last Accessed 16 December 2020.
11. US FDA. *Digital Health Innovation Action Plan* (2017) <https://www.fda.gov/media/106331/download> Last Accessed 9 December 2020
12. TGA. *Australian regulatory guidelines for medical devices (ARGMD)*, (2011) <https://www.tga.gov.au/sites/default/files/devices-argmd-01.pdf> Last Accessed 12 April 2019.
13. TGA. 'What Classification is my Medical Device?', (2019) <https://www.tga.gov.au/sme-assist/what-classification-my-medical-device> Last Accessed 10 April 2019.
14. US FDA. *Digital Health Innovation Action Plan* (2020) <https://www.fda.gov/media/106331/download> Last Accessed 9 December 2020.
15. National Institute for Health and Care Excellence (NICE). *Evidence Standards Framework for Digital Health Technologies*, (2019) <https://www.nice.org.uk/about/what-we-do/our-programmes/evidence-standards-framework-for-digital-health-technologies> Last Accessed 11 October 2019.
16. IMDRF. About IMDRF, (2019) <http://www.imdrf.org/about/about.asp> Last Accessed 11 April 2019.
17. IMDRF. Work Items, (2019) <http://www.imdrf.org/workitems/work.asp> Last Accessed 11 April 2019.
18. Eichler, H.G. et al. 'Adaptive licensing: taking the next step in the evolution of drug approval', *Clinical Pharmacology & Therapeutics* **91**, 426–437 (2012).
19. MOH. 'MOH Launches First Regulatory Sandbox to Support Development of Telemedicine', Singapore Ministry Of Health, (2018) <https://www.moh.gov.sg/news-highlights/details/moh-launches-first-regulatory-sandbox-to-support-development-of-telemedicine> Last Accessed 2 May 2019.
20. US FDA. Breakthrough Devices Program. Guidance for Industry and Food and Drug Administration Staff, (2018) <https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM581664.pdf> Last Accessed 3 April 2019.
21. Vitalic Medical. 'How It Works', (2019) <https://vitalicmedical.com/> Last Accessed 11 April 2019.
22. Australian Institute of Health and Welfare 2018. *Australia's hospitals 2016–17 at a glance*. Health services series no. 85. Cat. no. HSE 204. Canberra: AIHW.
23. Varnfield, M. et al. 'Smartphone-based home care model improved use of cardiac rehabilitation in post myocardial infarction patients: results from a randomised controlled trial', *Heart* **100**, 1770–1779 (2014).
24. ResMed. Form 10-K, United States Securities and Exchange Commission, (2018) <https://www.sec.gov/Archives/edgar/data/943819/000094381918000013/0000943819-18-000013-index.htm> Last Accessed 11 December 2020.

25. ResMed. AirView (TM) Patient Management System, (2019) <https://www.resmed.com/au/en/healthcare-professional/products/monitoring-and-data-management/airview-patient-management-system.html> Last Accessed 11 December 2020.
26. NASA. 'Technology Readiness Levels Demystified', (2010) https://www.nasa.gov/topics/aeronautics/features/trl_demystified.html Last Accessed 12 April 2019.
27. US Department of Defense. *Technology Readiness Assessment (TRA) Deskbook*, (2009) <https://apps.dtic.mil/dtic/tr/fulltext/u2/a524200.pdf> Last Accessed 28 May 2019.
28. Blank, S. 'It's Time to Play Moneyball: The Investment Readiness Level', (2013) <https://steveblank.com/2013/11/25/its-time-to-play-moneyball-the-investment-readiness-level/> Last Accessed 10 October 2019.
29. Oetting, E.R. et al. 'Assessing Community Readiness for Prevention', *International Journal of the Addictions* **30**, 659–683 (1995).
30. Stanley, L.R. *Community Readiness for Community Change*, Tri-Ethnic Center for Prevention Research, Colorado State University, Fort Collins, CO (2014) https://tec.colostate.edu/wp-content/uploads/2018/04/CR_Handbook_8-3-15.pdf Last Accessed 11 December 2020.
31. Oxford Academic Health Science Network. *Oxford AHSN's Digital Health Roadmap*, (2017) <https://www.oxfordahsn.org/news-and-events/news/new-digital-health-roadmap-provides-tools-to-turn-ideas-into-products/> Last Accessed 10 October 2019.
32. Ernst & Young. *The upside of disruption: Megatrends shaping 2018 and beyond* [online] Ernst & Young Global Limited, (2018) https://staging-area.info/EY/ey_report_v14_v04E_INTERACTIVE.pdf Last Accessed 29 March 2019.
33. Australian Government Productivity Commission. *Regulation in the Digital Age. Shifting the Dial. 5 Year Productivity Review. Supporting Paper No. 13*. Canberra, Australia, (2017).
34. US FDA. 'Developing a Software Precertification Program: A Working Model', (2019) <https://www.fda.gov/media/119722/download> Last Accessed 31 October 2019.
35. Gates, B., Myhrvold, N., Rinearson, P. & Domonkos, D. *The Road Ahead*. Viking Penguin, New York, NY, (1995).
36. Sandberg, J. 'How do we justify knowledge produced within interpretive approaches?' *Organizational Research Methods* **8**, 41–68 (2005).
37. Denzin, N.K. & Lincoln, Y.S. *Collecting and Interpreting Qualitative Materials*. Thousand Oaks, CA: Sage Publications Ltd, (2008).
38. Stake, R. E. *Qualitative Case Studies*. In N. K. Denzin & Y. S. Lincoln (Eds.), *The Sage handbook of qualitative research* (443–466), Sage Publications Ltd, (2005).
39. National Library of Medicine. PubMed, (2019) <https://www.ncbi.nlm.nih.gov/pubmed> Last Accessed 9 April 2019.
40. Clarivate Analytics. Web of Science, (2019) <https://www.webofknowledge.com/> Last Accessed 9 April 2019.
41. Zarin, D.A., Tse, T. & Ide, N.C. Trial Registration at ClinicalTrials.gov between May and October 2005. **353**, 2779–2787 (2005).
42. Alipanah, N. et al. 'Adherence interventions and outcomes of tuberculosis treatment: A systematic review and meta-analysis of trials and observational studies', *PLOS Medicine* **15**, e1002595 (2018).
43. Miller, D.P., Jr. et al. 'Effect of a digital health intervention on receipt of colorectal cancer screening in vulnerable patients: A randomized controlled trial', *Annals of Internal Medicine* **168**, 550–557 (2018).
44. Blumenthal, D. 'Realizing the value (and profitability) of digital health data', *Annals of Internal Medicine* **166**, 842–843 (2017).
45. Agboola, S.O., Bates, D.W. & Kvedar, J.C. 'Digital health and patient safety', *JAMA* **315**, 1697–1698 (2016).
46. Levine, D.M., Lipsitz, S.R. & Linder, J.A. 'Trends in seniors' use of digital health technology in the United States, 2011–2014', *JAMA* **316**, 538–540 (2016).
47. Wilson, N.A. & Drozda, J. 'Value of unique device identification in the digital health infrastructure', *JAMA* **309**, 2107–2108 (2013).
48. Australian Government Australian Digital Health Agency. 'What is Digital Health?', (2019) <https://www.digitalhealth.gov.au/> Last Accessed 11 December 2020.
49. Australian Digital Health Agency. 'Digital Health Beyond My Health Record', Australian Government, (2019) <https://www.digitalhealth.gov.au/about-the-agency/digital-health-space/digital-health-beyond-my-health-record> Last Accessed 10 April 2019.

50. Australian Government Department of Health. *Digital Health*, (2019) <http://www.health.gov.au/internet/main/publishing.nsf/Content/eHealth> Last Accessed 10 April 2019.
51. World Health Organization. *Digital Health*, (2020) <https://www.who.int/health-topics/digital-health> Last Accessed 11 December 2020.
52. WHO. *Global Strategy on Digital Health 2020-2025*, (2019) https://www.who.int/docs/default-source/documents/gsdhdaa2a9f352b0445bafbc79ca799dce4d.pdf?sfvrsn=f112ede5_42 Last Accessed 11 December 2020.
53. ANDHealth. *Digital Health: Creating a New Growth Industry for Australia*, (2018) https://andhealth.com.au/wp-content/uploads/2019/04/Digital-Health_Creating-a-New-Growth-Industry-for-Australia.pdf Last Accessed 11 December 2020.
54. ANDHealth. 'ANDHealth Release Digital Health: Creating a New Growth Industry for Australia', (2018) <https://andhealth.com.au/andhealth-release-digital-health-creating-a-new-growth-industry-for-australia/> Last Accessed 11 December 2020.
55. TGA. Webinar Recording: The role of the TGA in digital health, (2019) <https://www.tga.gov.au/node/874464> Last Accessed 10 April 2019.
56. US FDA. Digital Health, (2019) <https://www.fda.gov/medical-devices/digital-health-center-excellence/what-digital-health> Last Accessed 10 April 2019.
57. US FDA. Statement from FDA Commissioner Scott Gottlieb, M.D., 'Advancing new digital health policies to encourage innovation, bring efficiency and modernization to regulation', (2017) <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm587890.htm> Last Accessed 10 April 2019.
58. Cruz, M., *Emerging Digital Health Technologies*. FDA Center for Devices & Radiological Health. Digital Health Program, <https://www.fda.gov/media/122896/download> Last Accessed 10 April 2019.
59. European Commission. *eHealth: Digital Health and Care*, (2019) https://ec.europa.eu/health/ehealth/overview_en Last Accessed 10 April 2019.
60. MedTech Europe. 'Notified Bodies', (2020) <https://www.medtecheurope.org/new-medical-technology-regulations/notified-bodies/> Last Accessed 11 December 2020.
61. European Commission. 'Notified Bodies', (2019) <https://ec.europa.eu/growth/single-market/goods/building-blocks/notified-bodies/> Last Accessed 10 April 2019.
62. Hogan Lovells. *Digital Health: The issues you need to consider to leverage its full potential in 2018*, (2018) <https://www.hoganlovells.com/en/publications/digital-health-the-issues-you-need-to-consider-to-leverage-its-full-potential-in-2018> Last Accessed 10 April 2019.
63. Buttrn, S, *CE Marking of Digital Health Technologies: Stricter Rules for Medical Device Software Under the EU MDR*, NAMSA, (2018) <https://namsa.com/mdr-stricter-rules-medical-device-software/> Last Accessed 10 April 2019.
64. TGA. 'What is a Medical Device?' (2019) <https://www.tga.gov.au/what-medical-device> Last Accessed 15 September 2020.
65. Therapeutic Goods Act 1989, Cth. (1989).
66. US FDA. *Medical Device Overview*, (2018) <https://www.fda.gov/medical-devices/classify-your-medical-device/how-determine-if-your-product-medical-device> Last Accessed 10 April 2019.
67. European Medicines Agency. Medical Devices, (2019) <https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices> Last Accessed 10 April 2019.
68. European Commission. 'Factsheet for Manufacturers of Medical Devices', Ref. Ares(2018)3873669 – 20/07/2018, (2018) <https://ec.europa.eu/docsroom/documents/31201> Last Accessed 10 April 2019.
69. In Article 2, REGULATION (EU) 2017/745 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC, (2017).
70. TGA. The regulation of medical devices, (2011) <https://www.tga.gov.au/behind-news/regulation-medical-devices> Last Accessed 12 April 2019.
71. TGA. Searching the Australian Register of Therapeutic Goods (ARTG), (2018) <https://www.tga.gov.au/searching-australian-register-therapeutic-goods-artg> Last Accessed 12 April 2019.
72. European Commission. LIST OF BODIES NOTIFIED UNDER DIRECTIVE : 93/42/EEC Medical devices, (2019) http://ec.europa.eu/growth/tools-databases/nando/index.cfm?fuseaction=directive.pdf&refe_cd=93%2F42%2FEEC&requesttimeout=900 Last Accessed 12 April 2019.
73. Therapeutic Goods Act 1989. Medical Devices—Information that Must Accompany Application for Inclusion. Determination 2018. Compilation date: 10 April 2019. <https://www.legislation.gov.au/Details/F2019C00353> Last Accessed 20 October 2020.

74. US FDA. Device Classification Panels, (2018) <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051530.htm> Last Accessed 12 April 2019.
75. Kaplan, A.V. et al. Medical device development. *Circulation* **109**, 3068–3072 (2004).
76. Van Norman, G.A. 'Drugs, devices, and the FDA: Part 2: An overview of approval processes: FDA approval of medical devices', *Journal of the American College of Cardiology: Basic to Translational Science* **1**, 277–287 (2016).
77. US FDA. Premarket Notification 510(k), (2018) <https://www.fda.gov/medical-devices/premarket-submissions/premarket-notification-510k> Last Accessed 12 April 2019.
78. US FDA. Premarket Approval (PMA), (2019) <https://www.fda.gov/medical-devices/premarket-submissions/510k-third-party-review-program> Last Accessed 12 April 2019.
79. US FDA. *Qualification of Medical Device Development Tools. Guidance for Industry, Tool Developers, and Food and Drug Administration Staff*, (2017) <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/qualification-medical-device-development-tools> Last Accessed 12 April 2019.
80. European Commission. Manual on Borderline and Classification in the Community regulatory framework for Medical Devices Version 1.18, (2017) <https://ec.europa.eu/docsroom/documents/26785/attachments/1/translations/en/renditions/pdf> Last Accessed 12 April 2019.
81. European Parliament. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC (Text with EEA relevance.), (2017) <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0745#d1e4765-1-1> Last Accessed 12 April 2019.
82. EU Medical Device Regulation. Conformity assessment compared to the MDD, (2019) <http://eumdr.com/conformity-assessment-compared/> Last Accessed 12 April 2019.
83. IMDRF. 'Software as a Medical Device: Possible Framework for Risk Categorization and Corresponding Considerations' (2014) <http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-140918-samd-framework-risk-categorization-141013.pdf> Last Accessed 12 April 2019.
84. IMDRF. 'Software as a Medical Device (SaMD): Key Definitions', (2013) <http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-131209-samd-key-definitions-140901.pdf> Last Accessed 12 April 2019.
85. IMDRF. 'Software as a Medical Device (SaMD): Application of Quality Management System', (2015) <http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-151002-samd-qms.pdf> Last Accessed 12 April 2019.
86. IMDRF. 'Software as a Medical Device (SaMD): Clinical Evaluation', (2017) http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170921-samd-n41-clinical-evaluation_1.pdf Last Accessed 12 April 2019.
87. TGA. Annual performance statistics reports, (2018) <https://www.tga.gov.au/annual-performance-statistics-reports> Last Accessed 20 May 2019.
88. All Releasable PMA data, (2019) <http://www.accessdata.fda.gov/premarket/ftparea/pma.zip> Last Accessed 21 April 2019.
89. US FDA. 510(k) Premarket Notification Database, (2018) <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm> Last Accessed 20 May 2019.
90. US FDA. *Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies. Guidance for Industry and Food and Drug Administration Staff*, (2013) <https://www.fda.gov/media/81784/download> Last Accessed 1 October 2020.
91. TGA. Use of Market Authorisation Evidence From Comparable Overseas Regulators / Assessment Bodies for Medical Devices (Including IVDs), (2019) <https://www.tga.gov.au/publication/use-market-authorisation-evidence-comparable-overseas-regulators-assessment-bodies-medical-devices-including-ivds> Last Accessed 15 September 2020.
92. TGA. *Report on TGA Processes and Timeframes for the Regulation of Medical Devices and Access to Market. International Benchmarking*, (2019) <https://www.tga.gov.au/sites/default/files/medical-device-application-processing-times-report.pdf> Last Accessed 15 September 2020.
93. TGA. Supporting documentation for inclusion of a medical device, (2019) <https://www.tga.gov.au/supporting-documentation-inclusion-medical-device> Last Accessed 1 October 2020.

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