Maximising Strategic Development for Digital Medicines and Therapeutics

The realm of digital medicine is one that is always moving. As regulatory agencies try to keep up with the changing landscape, how can companies get the best out of new digital medicines and therapeutics?

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The market for digital health products is large and rapidly expanding. At the end of 2020, there were over 350,000 unique digital health applications being marketed to users (1). In 2021, over $37.9 billion in new capital was invested in digital health startups, up nearly 75% from $21.7 billion in 2020 (2).

Digital innovations are now being developed across the spectrum of healthcare, as the industry seeks to address critical gaps in care, remove geographic barriers, and create access to underserved patient populations.

To keep pace with these exciting innovations, the FDA and other regulatory agencies have expanded their focus. In September 2020, the FDA launched the Digital Health Center of Excellence and, over the past few years, has issued an array of new guidances for developers of Digital Medicines. Despite this focus on defining the regulatory pathways for Digital Medicines, these regulations are still in flux, and significant questions remain unanswered, with 'grey' areas where regulations may be only applied using 'discretionary enforcement' (3). This presents developers with both challenges and opportunities and a variety of development options that could lead to fundamentally different products being developed.

Ultimately, the success of any digital health product will be determined by the alignment between the data generated from the product development programme, the applicable regulations, and the go-to-market strategy. When considering the range of potential investments that may be needed to develop and successfully launch a product, making well-informed strategic decisions at each step of the process is critical.

To understand some of the potential challenges and opportunities digital developers may encounter, we first need to outline the hierarchy of digital health products, identify the regulations applied at each level, and define how these different products are commercialised.

Digital Health Products

'Digital health' can be used to refer to any digital product, including: technologies, platforms, and systems that engage consumers for lifestyle, wellness, and health-related purposes; technologies that capture, store, or transmit health data; and/or those that support life science and clinical operations. The overwhelming majority of digital health products are applications that can be downloaded and installed on a computer, mobile phone, or other device. There are an estimated 350,000 health applications that are now available for download from online marketplaces such as Apple's App Store or Google Play. The majority of these applications (55%) are focused on diet, exercise, and weight-loss training. Disease-specific apps that allow patients to track symptoms, schedule appointments with physicians, and connect with other resources to learn more about their condition make up a substantial proportion of the other digital health products, comprising roughly 22% of the applications available for download.

These products are not required to be cleared by the FDA and are not subject to FDA regulations.

In most cases, non-regulated digital health products have simple commercialisation models in which the products are developed and paid for by the end users, or in which the products are given to users for free and data from users is captured and sold to a third party. However, a few digital health companies have developed more sophisticated commercialisation models.

Digital Medicine and Digital Therapeutics

While the regulatory and commercial environments for digital health products are relatively straightforward, the environments for 'digital medicine' and 'digital therapeutics' products are significantly more complex.

Digital medicine and digital therapeutic products that meet the definition of a medical device are classified from a regulatory perspective as either 'Software as a Medical Device' or, in the case of devices that have embedded software, 'Software in a Medical Device'. The term 'mobile medical app' (MMA) is also used to classify products and is commonly used to describe digital medicine or digital therapeutic products; MMAs are defined either as an accessory to a regulated medical device or an application that transforms a mobile platform into a regulated medical device. While there is significant overlap between these terms, there is one key distinction: by definition, all MMAs will also be considered digital medicine products, but not all digital medicine products are mobile. For example, digital medicine products that are embedded into a non-mobile machine (e.g., an MRI machine) are not classified as MMAs.

There is another regulatory complexity worth noting; specifically, a segment of digital health products for which the FDA exercises 'enforcement discretion'. Although there are regulations that apply to the clearance and promotional claims of the device, the FDA has stated it will not actively enforce compliance. The FDA has published guidance to clarify that discretionary enforcement will be used for software functions that may meet the definition of a medical device but that are deemed to present a 'minimal risk' to patients. These 'minimal risk' digital products include apps that: a) help patients/users self-manage their disease or condition without providing specific treatment suggestions; or b) automate simple tasks for healthcare providers.

Acknowledging those caveats, the remainder of this article will focus on the segment of fully regulated digital medicines and digital therapeutic products for which substantive development programmes are required.

To more precisely define the term, digital medicine products are a subset of digital health products which include clinically validated software and/or hardware products that either measure or intervene in the service of human health.

'Digital Therapeutics' represent a subset of digital medicine products that deliver evidence-based therapeutic interventions that are uniquely capable of preventing, managing, or treating a medical disorder or disease. These products are only available via a prescription. Although there is substantial investment in the space with hundreds of clinical studies evaluating products, to date there have only been a handful of prescription digital therapeutics fully cleared by the FDA. These include Somryst®, a downloadable application developed by Pear Therapeutics and cleared as a treatment for insomnia, and EndeavorRx™, an application developed by Akili Labs and cleared as a treatment for paediatric patients diagnosed with ADHD.

As all digital medicine or digital therapeutic (DTx) products are

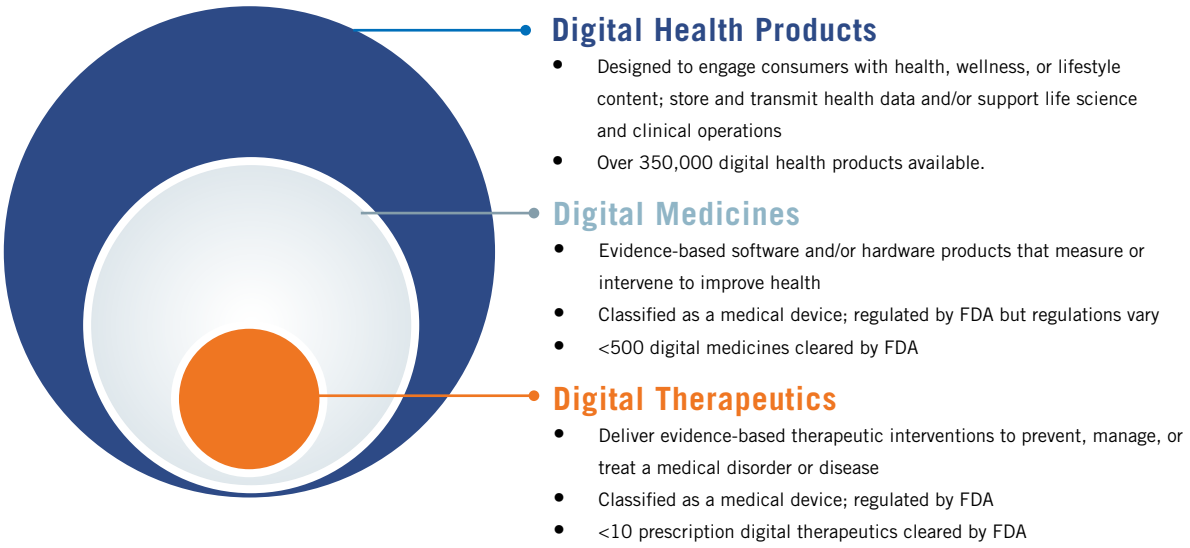

Figure 1: Adapted from Digital Therapeutic Alliance / Digital Medicine Society

considered medical devices, they must have clinical evidence to support their promotional claims. However, the types of claims that each product can make are fundamentally different.

By definition, digital medicine products can claim to measure specific disease markers or intervene in the management of a disease, but these devices cannot claim a specific therapeutic benefit. For instance, LivongoHealth® – which provides targeted programs, and an app, for people living with diabetes, obesity, or hypertension – describe the benefits users can receive ("Improve your habits to help lower your risk of developing Type 2 diabetes", "Track your health trends to work toward reaching your health goals"). But Livongo does not make direct claims on the specific health benefits that could be achieved (i.e., magnitude of the glycemic lowering).

By contrast, DTx claims are focused on the clinical impact of the intervention. To illustrate, EndeavorRx states that 73% of children report an improvement in their attention after using its product. Somryst shows a 45% reduction in the severity of insomnia symptoms and a 52% reduction in the amount of time spent awake at night. These are substantial efficacy claims that are similar to other prescription therapeutics.

To gain FDA clearance, both digital medicine and digital therapeutic products must have thoughtfully designed and well-structured development programmes. However, the size of the programmes may vary significantly. Determining the optimal size of the development programme to support an ideal set of claims requires strategic thought and, ultimately, an understanding of how the product will be commercialised.

Distinct Pathways to Commercialisation

On the commercialisation front, there are multiple go-to-market strategies that are available for digital medicine and digital therapeutic products. Since these products are regulated and require clinical evidence to be generated, reimbursement becomes a potential option. As more digital medicines and digital therapeutics have garnered FDA clearance, commercial insurers, such as Express Scripts, have designed and implemented 'digital formularies' that provide reimbursement for a select group of clinically validated applications. More recently, in February 2022, the Center for Medicare and Medicaid Services created a new Healthcare Common Procedure Coding System code for "prescription digital behavioural therapy", which is expected to further expand the reimbursement of digital interventions (5).

Commercial success for any of these products will ultimately depend on the design and execution of a clinical programme that balances regulatory requirements and go-to-market opportunities with unmet needs and commercial drivers. This means that key decisions must be identified and made early in the development process in order to develop a compelling clinical programme. As noted, this obviously requires foresight and planning. Fortunately, there are strategic frameworks and driving questions that can help developers identify, inform, and make these pivotal decisions.

Determining the Ideal Product Development Strategy

Any new product development strategy can be defined by a series of questions and trade-off decisions that begin with identifying and prioritising the specific problem a product can solve – i.e., what is the unmet need that the product will address? Subsequent trade-off decisions are then made: Who will be the prioritised customers? What benefits will the product provide for these targeted customers? How will these benefits be differentiated from existing and/or new competition? How will customers access and purchase the product? How can the product be priced and the investments made in development ultimately be monetised? Most importantly, developers of innovative digital medicine products must answer the following question: What evidence must be generated to demonstrate the product's value, and what claims must be made to motivate targeted customers to purchase the product?

The answer to the last question will ultimately define the amount of capital and time needed to successfully develop a product. But, as noted, answering this question requires an understanding of how potential regulations will be applied and what claims the product will ultimately be able to make. It also requires that developers identify and prioritise who they expect will pay for the product early in the development process. The claims that might motivate a payer will likely be fundamentally different from those that would motivate an end-user, and determining the priority between these claims will be important.

Considering the evolving landscape and the level of innovation in the space, market research is likely a key tool to

Key Questions for Digital Medicine Developers:

- What is the unmet need your product is intended to address?
- Who will be your targeted customer?
- What benefits will your product provide for these targeted customers?
- How will these benefits be differentiated from existing and/or new competition?
- How will customers access and purchase your product?
- How can you price your product and ultimately monetise the investments made in development?
- What evidence must be generated to demonstrate your product's value and what claims will you need to make to motivate targeted customers to purchase your product?

help confirm if a product will be considered for reimbursement. If it will, how are payers currently evaluating and calculating economic value? What clinical or real-world data will be required to develop a compelling value proposition for digital intervention? If reimbursement is not available, how much will end-users be willing to pay for the product? Are there other intermediaries that could realise value? How could expanding the product's claims or target population fit into the product's lifecycle management strategy?

The answers to these questions will help developers determine what claims will be needed to demonstrate value and drive utilisation – and the type of clinical endpoints that should be prioritised in the development programme. They can also help inform the scope of the development programme that will be needed and ultimately the level of investment that will be required to bring the product to market. However, in this rapidly evolving and innovative space, the answers are not always clear.

By establishing the Digital Health Center of Excellence and authoring updated guidance documents, the FDA has demonstrated that it recognises the incredible potential of digital products to impact and improve the health of consumers. Yet much is still in flux.

Especially for early-stage companies seeking to build a digital medicine or digital therapeutic product, it may be difficult to gauge the quantity of evidence that regulators will ultimately require. It's important to engage early and often with the FDA, to determine how regulators might evaluate a product and what types of evidence they will want to see. Developers who don't have an experienced regulatory or commercial leader on staff should seek external advice and consider bringing strategic development experts into the process early in the product's lifecycle; these experts can help guide development, navigate interactions with regulatory authorities, and reduce unnecessary risks and inefficiencies. That expertise can make all the difference in developing a commercially successful product.

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In 2020, **Robb Lawrence** joined **Premier Consulting** as Senior Vice President of Commercial Strategy with responsibility for Premier Consulting's new suite of commercial strategy solutions. He spent the ten years prior to joining Premier as a health-care entrepreneur, building companies designed to bring new and innovative pharma products. He founded and served as CEO of two virtual specialty pharma companies, TLC Therapeutics, LLC (TLC) and Tropical Disease Therapeutics, LLC (TDT), both of which were built around co-development partnerships with larger global pharma companies. Prior to founding TLC and TDT, he launched and managed the day-to-day operations of Salient Consulting, a boutique strategy consulting practice focused on strategic product development and go-to-market strategies for novel medicines. He began his career in biopharmaceuticals at Merck and Company, where he held a variety of sales and marketing roles and played a key role in the successful launch of Merck's Diabetes Franchise (Januvia® and Janumet®). He received a Master's in Business Administration from Duke University's Fuqua School of Business, US, and a Bachelor of Arts from Wake Forest University, US.

Dr Shauna Swanson has eight years of industry experience in drug discovery and clinical development, including more than three years of regulatory experience with **Premier Consulting**. She has experience leading project teams to support development of products across many therapeutic areas and at all stages of development. Her recent focus has been on regulatory pathways for prescription digital therapeutics and other digital health products, especially those being developed for patients with rare diseases. Dr Swanson has a Regulatory Affairs Certification in global drug development. Dr Swanson earned her PhD in Microbiology and Immunology from the University of North Carolina, US, in 2014, where she focused on identifying mechanisms of antibiotic resistance and evaluating new therapeutic approaches. She has also worked as a scientist at Synereca, a small, UNC-based start-up company, leading the microbiology research team and collaborating closely with the chemistry team developing new antibiotics to treat antibiotic-resistant infections, and at bioMérieux, a global *in vitro* diagnostics company, where she designed and oversaw clinical studies to support the 510(k) premarket submission and CE-marking of three new diagnostic assays.