Digital Health Technologies: Definitions, Regulatory Framework, and Considerations

Policy Brief

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Background

Digital health technologies are relatively novel health care interventions with a rapidly growing market presence.[1-3] The first mention of the term *digital therapeutic* in a peer-reviewed publication was in 2015[4]; between 2015 and 2019, the number of studies of digital therapeutic interventions registered on ClinicalTrials.gov increased nearly 5-fold, from 12 to 58.[5] As of 2021, over 25 digital therapeutic products have been granted market authorization worldwide,[6,7] with more than 150 digital health technologies in earlier stages of development.[2,8]

The growth of digital health technologies can be attributed to several factors: the COVID-19 public health emergency which led to rapid adoption of remote health care practices such as telehealth and remote patient monitoring[9-13]; the relatively fast development period and low cost for software-based health applications compared with pharmaceuticals or medical devices[5,8,14,15]; and significant investments in digital health technologies by pharmaceutical companies and venture capital firms.[5,12-14]

Proponents of these technologies describe many benefits of digital health interventions that traditional health care practices cannot provide. Digital health interventions may:

- Improve access to care, particularly for rural and underserved communities[9,16,17]
- Provide access to care in fields where there are provider shortages (e.g., behavioral health treatments)[10,17-19]
- Provide access to care when individuals may be reluctant to seek in-person care due to stigma (e.g., substance use disorder treatment; behavioral health conditions)[10,16,18-20]
- Allow individuals to play a more active role in their treatment, increasing engagement and adherence[21-23]
- Allow patient data tracking and data sharing with health care providers (e.g., blood glucose levels, medication adherence)[10,14,16,22]

Potential harms associated with these technologies include issues related to data (e.g., not keeping patient data secure, selling patient data without notification),[6,16,24,25] offering inaccurate or ineffective information or treatment,[24,26] and problems related to software defects.[14,22,25] A review of the US Food and Drug Administration (FDA) medical device recall database (January 2002 through the first quarter of 2020) found the primary cause of recalls was software-related issues.[25,26] Recalls were issued because of security vulnerabilities, as well as failures in timing of patient alerts or miscalculation of medication dosing.[25-27]

The November 2024 New York State Department of Health's (NYSDOH) Evidence Based Benefit Review Advisory Committee (EBBRAC) meeting will focus on 2 digital health technologies: Freespira, a digital therapeutic used to treat panic disorder and posttraumatic stress disorder (PTSD) in adults,[28,29] and CanvasDx, which uses an artificial intelligence (AI) software platform to aid in the diagnosis of autism in young children.[30-32] In preparation for this EBBRAC meeting featuring health technology assessment presentations for Freespira and CanvasDx, NYSDOH staff asked the Center for Evidence-based Policy (Center) to prepare an additional report for the EBBRAC focused on 3 key questions (KQs).

Key Questions

KQ1. How are digital health technologies defined?

KQ2. How does the FDA regulate digital health technologies?

a. How do regulations for digital health technologies compare with regulations of other health care interventions (e.g., pharmaceuticals, medical devices)?

KQ3. What should NYSDOH staff and EBBRAC members know when considering coverage policies for digital health technologies?

Methods

Center researchers constructed search strategies for Ovid MEDLINE and Scopus to identify published studies, commentaries, and reports to address the KQs. Our search strategies used a combination of controlled vocabulary terms and keywords to describe digital therapeutics, software as a medical device, regulation, legislation, and device approval. We used citation chaining in Scopus to identify additional relevant publications.

We also searched federal government websites (e.g., Federal Register, Regulations.gov, and FDA) for laws, regulations and legal guidance, as well as websites of relevant organizations (e.g., Digital Medicine Society, Digital Therapeutics Alliance, International Medical Device Regulators Forum) for policies and analyses related to digital health technologies and their regulation. A complete list of sources and search strategies are provided in Appendix A.

Findings

KQ1: Definitions of Digital Health Technologies

Digital health is a broad term that encompasses multiple categories of technology, only some of which are regulated by the FDA.

The FDA defines *digital health technologies* as products that "use computing platforms, connectivity, software, and sensors for health care and related uses."[33, para. 3] Some digital health products, such as telehealth platforms or health information technology such as electronic health records and consumer health interfaces (e.g., patient portals such as MyChart) are not regulated by the FDA.[16,34] Mobile health applications used by consumers without clinician involvement, or wearable devices that track health information without clinician engagement, are also not regulated by the FDA.[16,34]

Digital health technologies that do meet the requirements for FDA review are classified as *software as a medical device* (SaMD).[35] The FDA uses the definition of SaMD created by the International Medical Device Regulators Forum (IMDRF): The definition of SaMD is "software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device."[35,36, p.6]

Incorporated into the IMDRF SaMD definition is the notion of a *medical device*, which they also define:

> Medical device means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:
> - Diagnosis, prevention, monitoring, treatment or alleviation of disease
> - Diagnosis, monitoring, treatment, alleviation of or compensation for an injury
> - Investigation, replacement, modification, or support of the anatomy or of a physiological process
> - Supporting or sustaining life
> - Control of conception
> - Disinfection of medical devices
> - Providing information by means of in vitro examination of specimens derived from the human body
>
> And does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.[36, p.6-7]

Digital therapeutics is not a term used officially by the FDA, but the term is used extensively by producers of SaMD, researchers, and health organizations.[6,16,37,38] In 2023 the International Organization for Standardization (ISO) published a definition of *digital therapeutics* that has been adopted by many: "health software intended to treat or alleviate a disease, disorder, condition, or injury by generating and delivering a medical intervention that has a demonstratable positive therapeutic impact on a patient's health."[38, p.1,39]

Notably, the definition of digital therapeutic does not encompass diagnosis of a disease or condition.[38,39] Of the 2 digital health technologies EBBRAC plans to review at an upcoming meeting, CanvasDx (used to aid in *diagnosis* of autism spectrum disorder) is not considered a digital therapeutic, while Freespira (used as an adjunct *treatment* for panic disorder and PTSD) is considered a digital therapeutic.

KQ2: FDA Regulation of Digital Health Technologies

The 21st Century Cures Act of 2016 required the FDA to categorize certain digital health technologies as medical devices and to use the medical device regulatory framework to review the technologies.[5,40,41] The FDA regulates SaMD under its medical devices framework through the Center for Devices and Radiological Health.[42] The FDA uses a risk-based framework (see Figure 1) to classify medical devices and to determine potential regulatory pathways.[21,43]

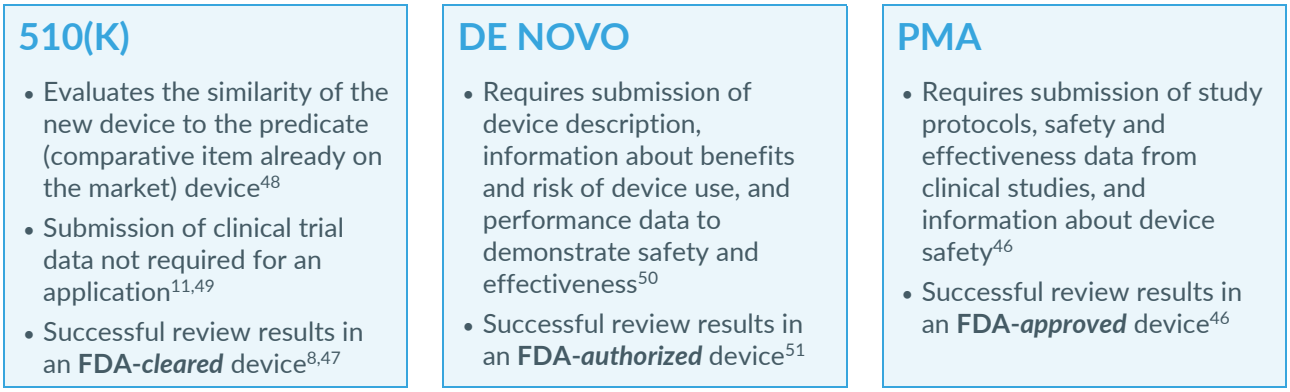
Figure 1. FDA Medical Device Classifications

CLASS I DEVICES	CLASS II DEVICES	CLASS III DEVICES
• Low-risk devices (e.g., bandages, tongue depressors)[43] • Regulated only through general controls such as device registration and listing, sound production practices, and premarket notification[43]	• Intermediate-risk devices (e.g., infusion pumps, catheters)[43] • Require premarket notification and review through either the De Novo or 510(k) pathway[43]	• High-risk devices used to sustain or support life (e.g., pacemakers, high-frequency ventilators)[43] • Regulated through PMA pathway which requires submission of clinical evidence of safety and effectiveness[21,43]

Abbreviations: FDA: US Food and Drug Administration; PMA: premarket approval.

Based on a device's risk classification, the FDA regulates medical devices through 3 pathways: the 510(k) pathway, the De Novo pathway, and premarket approval (PMA).[44] Certain devices may also be eligible for the Breakthrough Devices Program, which speeds up FDA review under certain circumstances.[45] While devices that go through the 510(k) pathway are considered FDA-***cleared*** devices, and devices that go through the De Novo pathway are considered FDA-***authorized*** to be marketed, only devices that go through PMA are considered FDA-***approved*** devices.[46,47]

Figure 2. FDA Regulatory Pathways for Medical Devices



Abbreviations: FDA: US Food and Drug Administration; PMA: premarket approval.

510(k) Pathway

The 510(k) pathway allows medical device manufacturers to receive marketing approval for their device by demonstrating that their product is "substantially equivalent" to one or more approved FDA devices.[48] According to the FDA website, a device is:

> ...substantially equivalent if, in comparison to a predicate [comparative product] it:
> - Has the same intended use as the predicate; and
> - Has the same technological characteristics of the predicate; or
> - Has the same intended use as the predicate; and
> - Has different technological characteristics and does not raise different questions of safety and effectiveness; and
> - The information submitted to FDA demonstrates that the device is as safe and effective as the legally marketed device.[48, para.6]

The FDA's approach to determining substantial equivalence has been questioned by researchers and academics.[52,53] After serious adverse events with transvaginal placement of surgical mesh led to an FDA warning about the devices in 2008, the FDA asked the Institute of Medicine to review the 510(k) clearance process for medical devices.[52,53] The report was issued in 2011 and recommended FDA terminate the 510(k) process and develop a new regulatory framework for Class II medical devices.[53, p.7-8] The Institute of Medicine's conclusions were challenged,[54,55] and the FDA instead began a process to "strengthen and modernize" the 510(k) program.[56,57] A 2018 report by the FDA described steps the agency had taken to improve the 510(k) review process.[58] Efforts included issuing guidance to clarify the 510(k) review process[58,59]; implementing a quality check on all 510(k) submissions[58,60]; creating a template to improve consistency and thoroughness of 510(k) application reviews[58]; eliminating the use of the 510(k) pathway for high-risk Class III medical devices[58]; and removing more than 1,000 devices from the list of devices eligible to be used as predicate device.[58]

A challenging area for the 510(k) pathway has been the relationship between device recalls and predicate devices.[61-63] Two studies published in 2023 found that significant proportions of 510(k) device applications relied on predicate devices that had existing recalls, and when approved, the new devices were more likely to have a higher probability of recall.[62,63] New guidance issued by the FDA in 2023 asks manufacturers to avoid using predicate devices that have been recalled and submit flow charts to explain their choice of predicate device.[57]

More recent research has questioned whether the medical device review process adequately protects patients from harm.[61,64] A 2024 study by See and colleagues looked at the clinical evidence used to authorize cardiovascular devices recalled by the FDA between January 2013 and December 2022.[61] The study found that of the 157 devices recalled during that period, a majority of the devices (71%) had been cleared through the 510(k) pathway.[61] Only 30 recalled devices had documentation of premarket clinical testing before approval.[61] Only 22 of the recalled devices had FDA required postmarket studies, and 14 of those studies had reported delays in producing results.[61]

For devices submitted via the 510(k) pathway, the FDA operates a third-party review program as a voluntary alternative review process.[65] Under third-party review, manufacturers can submit their application to an accredited third-party organization which reviews the manufacturer's submission and provides a recommendation to FDA staff.[65] Staff from the FDA review the documentation and review organization recommendation and make the final decision on whether to clear the device.[65]

For a 510(k) pathway review, FDA staff or an accredited third-party review organization evaluates the similarity of the new device to the predicate device[48]; submission of clinical trial data is *not* required for a 510(k) pathway application.[49]

Devices reviewed though the 510(k) pathway are considered FDA-**cleared** devices.[8,47]

De Novo Pathway

The De Novo pathway was created by the Food and Drug Administration Modernization Act of 1997 with a goal of fostering device innovation by creating a middle path between the existing 510(k) pathway and the requirements of a PMA application.[21,66]

According to a 2021 FDA rule, a De Novo request requires submission of a "device description, classification summary information, benefits and risks of device use, and performance data to demonstrate reasonable assurance of safety and effectiveness."[50] The FDA has issued little guidance on standards for this "performance data,"[67] particularly compared to the guidance issued for new drug approvals.[8,49,68]

Devices reviewed through the FDA De Novo pathway are considered FDA-**authorized** to be marketed.[51]

Premarket Approval (PMA)

The FDA regulates Class III devices through the PMA pathway, the most rigorous regulatory pathway for medical devices.[46] The PMA pathway requires submission of data to demonstrate safety and effectiveness of the medical device, including submission of study protocols, safety and effectiveness data from all clinical studies, and information about device failures and patient

complaints.[46] The PMA review process involves 4 steps: a filing review and acceptance of the application; a substantive review of the submission; a panel review; and notification of the FDA decision.[69]

Time to Approval

A study that compared medical device approvals from 1997 through 2023 found the mean decision time for 510(k) pathway submissions was 150 days; for the De Novo pathway it was 338 days; and for the PMA pathway it was 399 days.[66] For reference, the average review time by the FDA for a new drug application (NDA) for a pharmaceutical is 6 to 10 months (180 to 300 days).[70]

Breakthrough Devices Program

The FDA operates a breakthrough devices program that speeds up FDA review of PMA, De Novo and 510(k) marketing authorizations, under certain conditions.[45] Manufacturers can apply for breakthrough device designation under the following conditions:

- …The device provides for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions; and
- The device also meets at least one of the following:
  - Represents a breakthrough technology;
  - No approved or cleared alternatives exist;
  - Offers significant advantages over existing approved or cleared alternatives; or
  - Device availability is in the best interest of patients.[45]

A device is considered a *breakthrough technology* when "the device represents a novel technology or novel application of an existing technology that has the potential to lead to a clinical improvement in the diagnosis, treatment (including monitoring of treatment), cure, mitigation, or prevention of the life-threatening or irreversibly debilitating disease or condition."[71, p.13]

Manufacturers granted breakthrough device designation are able to access additional consultation with FDA staff and are given priority in the review schedule.[45,72] Critics of the breakthrough devices program assert that the system offers many benefits to manufacturers including attracting funding and enhancing marketing efforts, but the process may lead to less certainty in the effectiveness and safety of products.[72]

FDA Medical Device User Fees

In 2002, Congress directed the FDA to collect fees from medical device companies when a device application is submitted for review.[73] The stated goal of the fee system is to "increase the efficiency of regulatory processes with a goal of reducing the time it takes to bring safe and effective devices to the US market."[73] However, advocates have argued that the fees have "gradually resulted in a fundamentally dangerous shift in the relationship between the FDA and the regulated pharmaceutical and medical-device industries, such that the agency now views these companies as partners and customers rather than regulated industries."[74] Concern about "regulatory capture," where a special interest is prioritized above the general public, is widespread amongst critics of the FDA in both pharmaceutical and medical device arenas.[75-78]

Table 1. FDA Medical Device Review Fees by Pathway[73]

Regulatory Pathway	Standard Fee, $	Small Business Fee, $
510(k)	21,760	5,440
De Novo	145,068	36,267
PMA	438,560	120,890

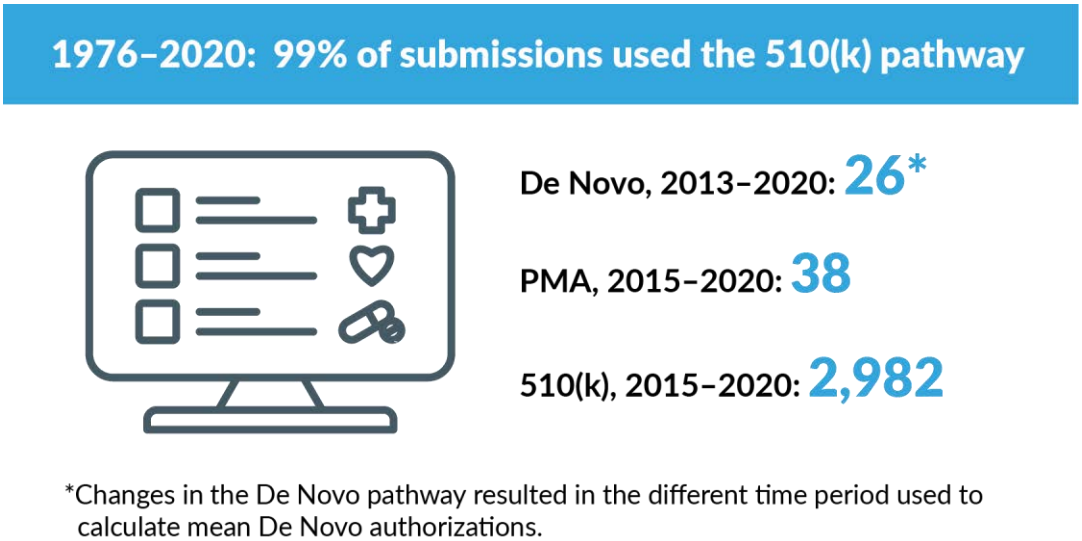
Abbreviations. FDA: US Food and Drug Administration; PMA: premarket approval.

KQ2a: Regulation of Digital Health Technologies vs. Other Care Interventions

As described above, SaMD digital health technologies are regulated by the FDA in the same way as medical devices, and the requirements for medical device authorization vary based on the risk class of the device and the authorization pathway the device qualifies for.[43] The PMA pathway is the only one requiring submission of data demonstrating safety and effectiveness, and is the pathway used least often.[79] Furthermore, Congress has directed the FDA to take a "least burdensome" approach to medical device evaluations.[69]

A 2021 study looked at all FDA medical device approvals, including regular medical devices and SaMD, from 1976 through 2020 and found that 99% of submissions used the 510(k) pathway which relies on similarity to predicate devices and does not require the submission of any efficacy data.[80] The authors calculated the mean number of device authorizations annually for each pathway between 2015 and 2020: the mean number of PMA device approvals was 38 while the mean number of 510(k) device clearances was 2,982.[80] Due to changes in the De Novo pathway during the study period, the authors used a different time period to calculate the mean annual De Novo device authorizations; between 2013 and 2020, a mean of 26 De Novo device applications were authorized.[80]

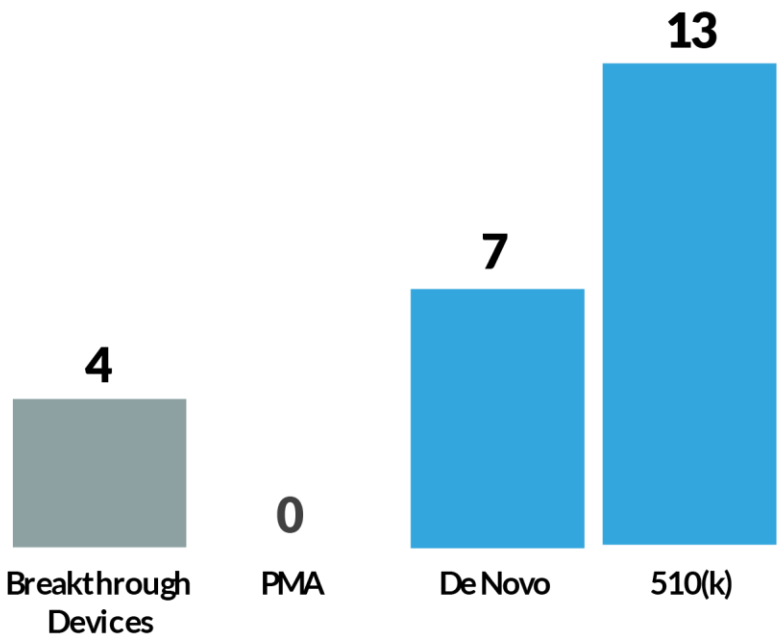
Figure 3. FDA Medical Device Approvals by Pathway, 1976 to 2020[80]



Abbreviations. FDA: US Food and Drug Administration; PMA: premarket approval.

A 2023 study by Kumar and colleagues identified 20 prescription digital health technologies reviewed by the FDA as of November 29, 2022, and categorized them by FDA review pathway.[81] As shown in Figure 4, no digital therapeutics were reviewed through the PMA pathway. Thirteen devices (65%) were cleared through the 510(k) pathway, while 7 (35%) used the De Novo pathway; 4 (20%) received Breakthrough Devices Program expedited review.[81]

Figure 4. FDA Authorization of Prescription Digital Therapeutics by Review Pathway[81]



Note. Study did not identify which pathway was used by the 4 devices receiving breakthrough device designation. Abbreviations. FDA: US Food and Drug Administration; PMA: premarket approval.

The Digital Therapeutic Alliance (a trade organization; see section on Industry Advocacy for more information), along with product manufacturers and advocates, claim that because the FDA authorizes or clears digital health products there is a reason to have confidence in the products.[6,9,16,37] However, researchers have pointed out that the FDA does not have for medical device market authorizations the clear standards for evidence required for pharmaceuticals.[1,49,82] Whereas pharmaceuticals require phase 3 clinical trials that include effectiveness, safety, and pharmacokinetic evaluation,[15] clearance through the 510(k) pathway does not require submission of *any* clinical effectiveness data,[11,49] and the agency has not published standards for the performance data required in the De Novo pathway.[49,83] A meeting of prominent behavioral health providers in 2021 issued a statement encouraging the adoption of digital mental health treatments in the US health system, but also noted that as currently operated, "FDA clearance which focuses on safety and minimal effectiveness thresholds does not provide adequate information for decision makers."[84, p.679]

KQ3: Coverage Policy Considerations For Digital Health Technologies

The policy environment surrounding digital health technologies is complicated and rapidly evolving. During research for this background paper, we identified several themes that may be of interest to NYSDOH staff and EBBRAC members: evolving FDA regulations, industry efforts to ensure adoption of digital therapeutics, concerns about the quality of evidence available to evaluate the technologies, and the creation of the Peterson Health Technology Institute (which conducts systematic reviews of digital health technologies).

FDA Regulations

FDA officials have acknowledged that digital health technologies will require new regulatory approaches, and the FDA will have to develop new processes to address the use of AI and machine learning, along with the necessity of frequent software updates.[40,85-87] To address this need, the FDA has piloted a new type of certification for digital health, created a new digital health unit within the agency, and established an advisory committee to assist with policy setting.

In 2017, the FDA piloted a Digital Health Software Precertification (Pre-Cert) program intended to establish a pathway for validating the software design, testing, and monitoring process of a manufacturer.[88-91] The program would then offer those manufacturers validated as high-quality a streamlined regulatory review process for their products.[27,91] The FDA concluded the Pre-Cert program in 2022 with a report acknowledging the agency did not have the statutory or regulatory authority to implement the program and would need legislative action to move forward[92]: "Based on these observations from the pilot, FDA has found that rapidly evolving technologies in the modern medical device landscape would benefit from a new regulatory paradigm, which would require a legislative change."[92, p.4]

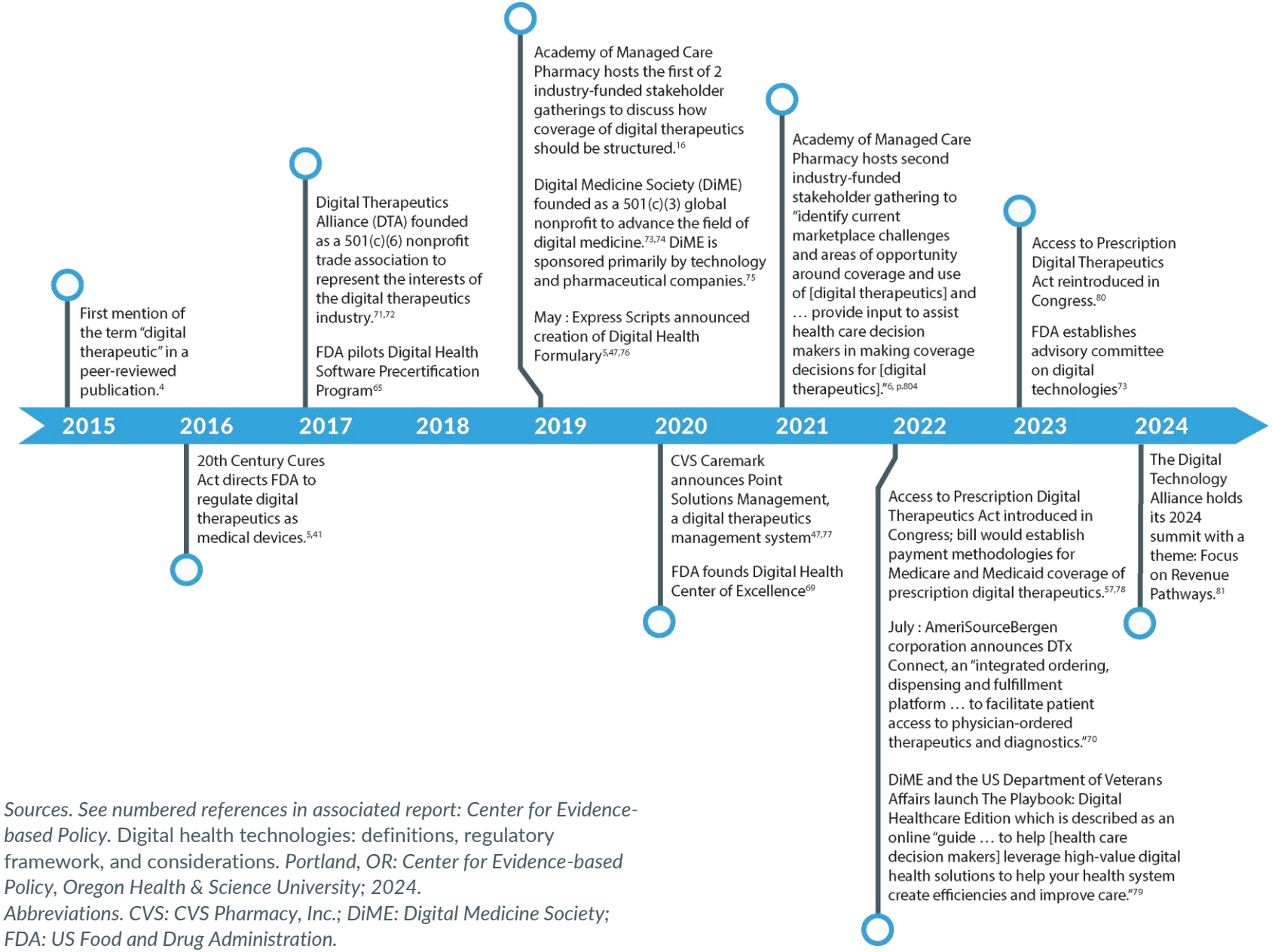
In 2020, the FDA founded the Digital Health Center of Excellence (DHCoE) as part of the Center for Devices and Radiological Health to coordinate digital health work within the agency.[93] The DHCoE has 4 goals[93]:

- Empower digital health stakeholders to advance health care
- Innovate regulatory approaches to provide efficient and least burdensome oversight
- Share knowledge to increase understanding and advance best practices
- Connect and build partnerships to accelerate digital health advancements

Staff at the DHCoE provide recommendations about how the FDA should regulate digital health technologies, but they are not responsible for reviewing product submissions or making marketing authorization decisions.[93]

In October 2023, the FDA established an advisory committee on digital health technologies to assist the agency in setting policy for these technologies.[94] In August 2024, the committee members were announced, 9 individuals with what the FDA describes as "minimal conflicts of interest."[95] The FDA also solicited applications from individuals with industry ties to join a pool of industry experts who may be called to serve as nonvoting members of the advisory committee on relevant topics.[96] The first meeting of the Digital Health Advisory Board will be held in November 2024 to discuss the use of generative AI in medical devices.[97]

Figure 5: Developments in the Digital Therapeutics Marketplace from 2015 to 2024



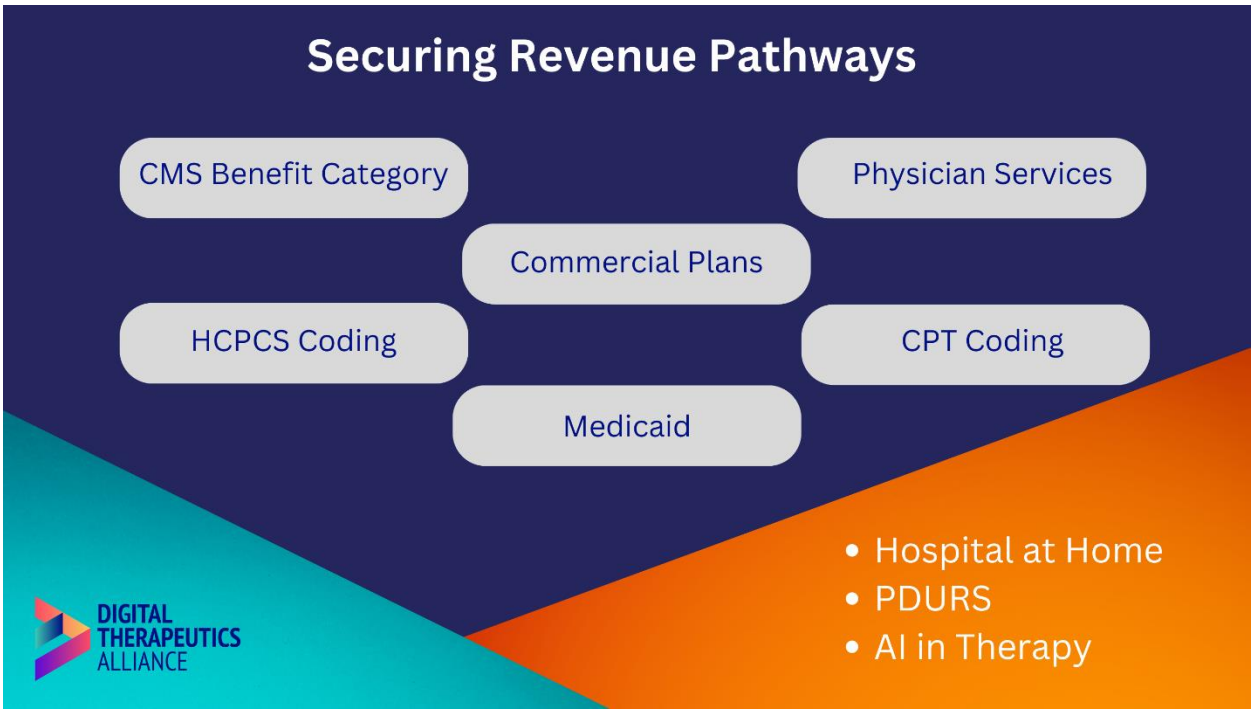
Sources. See numbered references in associated report: Center for Evidence-based Policy. Digital health technologies: definitions, regulatory framework, and considerations. *Portland, OR: Center for Evidence-based Policy, Oregon Health & Science University; 2024.*
Abbreviations. CVS: CVS Pharmacy, Inc.; DiME: Digital Medicine Society; FDA: US Food and Drug Administration.

Industry Advocacy

The evolving digital therapeutics industry has benefited from significant funding from venture capital funds, as well as pharmaceutical and technology companies.[5,12-14] Venture capital funding of digital health care products reached a peak in 2021 of almost $30 billion dollars, and declined to $15 billion in 2022.[12] In 2023, the global digital therapeutics market size was valued at $6.77 billion but is projected to grow to $43.88 billion by 2032.[98] The significant infusion of funding has allowed industry leaders to actively pursue multiple strategies to ensure market penetration of their technologies. Figure 5 depicts significant developments in the digital therapeutics marketplace from 2015 to 2020.

The last event in the timeline, the Digital Technology Alliance 2024 summit, shows how the interest group has focused on securing market access through insurance coverage.[99] The summit report stated "the [digital therapeutics] industry is looking positive and [the Digital Technology Alliance] is laser focused on establishing revenue pathways with the following:" (see Figure 6).[99]

Figure 6. Digital Technology Alliance 2024 Summit Wrap[99]



Abbreviations. CPT: Current Procedural Terminology; HCPCS: Healthcare Common Procedure Coding System; PDURS: Prescription Drug Use-Related Software.

One area of debate is how to categorize digital health technologies as a benefit class: should they be considered a pharmaceutical benefit, a medical benefit, or a different class entirely?[6,16,100] The Academy of Managed Care Pharmacy has suggested that pharmacists have expertise that could be used effectively to evaluate digital health technologies, and that existing state Drug Utilization Review (DUR) boards or Pharmacy and Therapeutics (P&T) Committees could review coverage considerations as a committee.[6,16] Other authors have mentioned that health technology assessment groups could serve as review bodies for digital health technologies.[8,100] IPD Analytics, however, has advised that instituting a formal digital therapeutics review process

similar to a P&T committee "would be an enormous undertaking for payers because of the sheer volume of [digital therapeutics] programs available and the inconsistent quality of clinical evidence supporting their use."[49, p.14]

Quality of Evidence

A major concern for health care decision makers has been the quality of evidence available to assess the effectiveness and safety of digital health technologies.[3,17,81,84,100] The 2023 study by Kumar and colleagues looking at prescription digital therapeutics by FDA approval pathway also included a retrospective, cross-sectional analysis of the clinical studies conducted on prescription digital therapeutics authorized or cleared by the FDA as of November 29, 2022.[81] The study included all clinical studies referenced in FDA documents and all studies listed on manufacturer websites, as well as reports identified by searching ClinicalTrials.gov and PubMed.[81]

The authors identified 117 clinical studies on the 20 authorized prescription digital therapeutics.[81] Of the studies, only 45 (39%) were randomized controlled trials (RCTs) and 82 (70%) did not use any blinding.[81] In addition, 81 studies (69%) were funded by the manufacturer.[81] The 117 studies included 179 outcome measures, of which 149 (83%) were clinical outcome measures and 21 (12%) were non-clinical outcomes such as patient satisfaction.[81] The median length of follow-up duration was 12 weeks (interquartile range: 7.5 to 24.0).[81]

Overall, only 2 of the 20 prescription digital therapeutics included in the study were evaluated in at least 1 RCT that met the authors' definition of a high-quality trial: a randomized, blinded, multicenter study with a clinical outcome measure that met the primary endpoint.[81] Two-thirds of the studies reviewed were postmarket studies which have "less rigorous standards of evidence" than premarket studies."[81, p.1559] The authors also noted high-English-language-proficiency requirements in the studies, exclusion of older adults, and lack of reporting of race and ethnicity data.[81]

Following publication of the Kumar and colleagues study, the Digital Therapeutics Alliance trade association challenged the assertions made in the article, arguing that the author's conclusions were misleading.[101] They emphasized that Kumar and colleagues had documented that 90% of the technologies reviewed had been studied in at least one RCT, 60% had a trial conducted with blinding, 100% met at least 1 clinical primary endpoint, and 75% were multicenter trials.[101]

The Digital Therapeutics Alliance also advocates for relying less on clinical trials and more on "real-world evidence."[101,102] Real-world evidence is assembled by using data gathered from sources such as electronic health records, claims and billing records, and data generated by the digital therapeutic technology itself.[103,104] They argue that real-world evidence may provide more accurate information about how a given intervention functions in the "real world" compared with the artificial setting of a clinical trial.[103,105] However, real-world evidence does have limitations, including higher risk of bias, along with data privacy and confidentiality issues.[103,105,106] Use of real-world evidence also creates opportunities for data manipulation.[107]

Concerns about the quality of evidence led the United Kingdom's National Institute for Care and Excellence (NICE) to develop an "evidence standards framework for digital health technologies." Manufacturers seeking coverage of technologies within the UK health system are expected to

follow the evidence standards framework, which is also used to make informed decisions when evaluating digital therapeutics.[108]

Peterson Health Technology Institute

In 2023, the Peterson Center on Healthcare, a philanthropic organization focused on health care, launched the Peterson Health Technology Institute (PHTI) as an independent nonprofit organization for conducting health technology assessments of digital health solutions.[109,110] The PHTI partnered with the Institute for Clinical and Economic Review (ICER) to develop a framework for evaluating digital health solutions; the framework considers evidence of clinical effectiveness, economic impact, health equity, and data privacy and security.[1,111] The PHTI intends to serve as an unbiased resource for patients, providers, payers, technology developers, and investors who need information about the clinical effectiveness and economic impact of digital therapeutics.[112]

The first completed PHTI assessment addresses digital diabetes management solutions and was published in March 2024.[113] According to a summary of findings on their website, the PHTI assessment found that[113]:

> …digital diabetes management solutions in the remote patient monitoring and behavior and lifestyle modification categories do not deliver meaningful clinical benefits, and they increase healthcare spending relative to usual care. The evidence showed that improvements in glycemic control for patients using digital diabetes management solutions were minimal and short term.

Coverage of the report in the health care press was extensive,[114-121] and the Digital Technology Alliance issued a response to the report criticizing PHTI for: including only a sample of digital diabetes management solutions in its report; using a predictive economic model rather than claims analysis; not including endocrinologists in their review panel; and focusing their analysis solely on reduction in HbA1c rather than other relevant outcomes (e.g., reductions in hypoglycemic and hyperglycemic events).[122]

The second PHTI assessment, on digital health products for adults with musculoskeletal conditions such as low back, knee, hip, shoulder and neck pain, was published in June 2024.[123] The assessment found that some virtual musculoskeletal solutions provided clinically meaningful improvements in pain and function compared to usual care, and that depending on price, coverage of these interventions may be warranted.[123]

The third PHTI assessment, on digital hypertension solutions, was published in October 2024.[124] The assessment found that products focused on medication management deliver clinically meaningful improvements in blood pressure and may produce long-term net savings due to improved health which offset the cost of the intervention.[124] Other solutions considered in the report include blood pressure monitoring systems that transmit data to clinicians and solutions focused on patient behavior change; these interventions were found to less effective and unlikely to offset upfront costs of implementation.[124]

Future planned reports from PHTI include digital hypertension management tools and digital health technologies for depression and anxiety.[120]

Conclusions

Digital health technologies are a new and rapidly evolving area of health care technology, with significant financial investment driving development of products and encouraging payer and provider adoption of the products. Current FDA regulatory processes have not kept pace with the technological development and the agency is still addressing how best to regulate these products.

Concerns about the evidence base to demonstrate effectiveness and safety of products continues. Most digital therapeutics are cleared through the FDA's 510(k) pathway which does not require the submission of any evidence of effectiveness. The PHTI assessment program is one attempt to address the challenge of insufficient evidence for evaluating these technologies. The policy landscape is also notable for the significant industry advocacy and significant financial resources devoted to obtaining insurance coverage of these products.

This report was prepared as a background primer to accompany health technology assessments for 2 specific digital health technologies. This report is limited, in that it is not a comprehensive review of all aspects of FDA regulations. For example, details of how the FDA plans to address AI and machine learning components of SaMD, frequent product updates, or use of real-world evidence, have not been addressed.

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Appendix A. Methods

Sources Searched

Researchers from the Center for Evidence-based Policy used keywords such as *digital therapeutics*, *software as a medical device*, *regulation*, *legislation*, and *device approval* to search the sources listed below. No date limits were applied, but search results were limited to publications available in English language.

Bibliographic Databases

- Ovid MEDLINE
- Scopus

Policy Sources

- AcademyHealth
- Alliance for Health Policy
- Center on Budget and Policy Priorities
- Center for Public Health Law Research
- Commonwealth Fund
- Kaiser Family Foundation (KFF)
- Mathematica
- Pew Charitable Trusts
- RAND Corporation
- Robert Wood Johnson Foundation
- Urban Institute

Professional and Trade Organization Sources

- American Medical Association
- American Public Human Services Association
- Digital Medicine Society (DiME)
- Digital Therapeutics Alliance
- International Medical Device Regulators Forum

Regulatory Body Sources

- Health Resources and Services Administration
- Regulations.gov
- United States Federal Register
- United States Food and Drug Administration (FDA)
- United States Government Accountability Office (GAO)

Search Strategies for Bibliographic Databases

Ovid MEDLINE ALL

1 (digital adj3 therapeut*).ti,ab,kw.
2 digiceutical?.ti,ab,kf.
3 (software adj3 medical device?).ti,ab,kw.
4 samd.ti,ab,kf.
5 or/1-4
6 government regulation/
7 "united states food and drug administration"/
8 device approval/
9 product labeling/
10 exp legislation, medical/
11 lj.fs.
12 regulat*.ti,kf.
13 "food and drug administration".ti,ab,kw.
14 fda.ti,ab,kf.
15 usfda.ti,ab,kf.
16 (approv* adj2 (device? or guid* or path* or process*)).ti,ab,kw.
17 (label?ed or labe?ling).ti,ab,kf.
18 (law* or legal* or legislat*).ti,ab,kf.
19 or/6-18
20 clinical decision rules/
21 exp clinical protocols/
22 consensus/
23 exp consensus development conferences as topic/
24 critical pathways/
25 decision making, shared/
26 exp guidelines as topic/
27 health planning guidelines/
28 consensus development conference.pt.
29 consensus development conference, NIH.pt.
30 guideline.pt.
31 practice guideline.pt.
32 guideline?.ti,kf.

33 ((committee or executive) adj2 (recommendation* or statement* or summar*)).ti,kw.

34 (consensus adj2 (document* or paper* or recommendation* or report* or statement*)).ti,kw.

35 (joint adj2 (document* or recommendation* or statement*)).ti,kw.

36 ((policy or position) adj2 (paper* or statement*)).ti,kw.

37 ((clinical or critical or practice) adj2 (pathway? or standard?)).ti,kw.

38 or/20-37

39 medicaid/

40 "centers for medicare and medicaid services, u.s."/

41 dual medicaid medicare eligibility/

42 medicaid*.ti,ab,kf.

43 or/39-42

44 and/5,19

45 and/5,38

46 and/5,43

47 or/44-46

48 exp animals/ not humans/

49 47 not 48

50 limit 49 to english language

Scopus

1	TITLE-ABS-KEY (digital W/3 therapeut*)
2	TITLE-ABS-KEY (digiceutical*)
3	TITLE-ABS-KEY (software W/3 "medical device*")
4	TITLE-ABS-KEY (samd)
5	(TITLE-ABS-KEY (digital W/3 therapeut*)) OR (TITLE-ABS-KEY (digiceutical*)) OR (TITLE-ABS-KEY (software W/3 "medical device*")) OR (TITLE-ABS-KEY (samd))
6	TITLE (regulat*)
7	TITLE-ABS-KEY ("food and drug administration")
8	TITLE-ABS-KEY (fda)
9	TITLE-ABS-KEY (usfda)
10	TITLE-ABS-KEY (approv* W/2 (device* OR guid* OR path* OR process*))
11	TITLE-ABS-KEY (labeled OR labelled OR labeling OR labelling)
12	TITLE-ABS-KEY (law* OR legal* OR legislat*)
13	(TITLE (regulat*)) OR (TITLE-ABS-KEY ("food and drug administration")) OR (TITLE-ABS-KEY (fda)) OR (TITLE-ABS-KEY (usfda)) OR (TITLE-ABS-KEY (approv* W/2 (device* OR guid* OR path* OR process*))) OR (TITLE-ABS-KEY (labeled OR labelled OR labeling OR labelling)) OR (TITLE-ABS-KEY (law* OR legal* OR legislat*))
14	(TITLE-ABS-KEY (digital W/3 therapeut*)) OR (TITLE-ABS-KEY (digiceutical*)) OR (TITLE-ABS-KEY (software W/3 "medical device*")) OR (TITLE-ABS-KEY (samd))) AND ((TITLE (regulat*)) OR (TITLE-ABS-KEY ("food and drug administration")) OR (TITLE-ABS-KEY (fda)) OR (TITLE-ABS-KEY (usfda)) OR (TITLE-ABS-KEY (approv* W/2 (device* OR guid* OR path* OR process*))) OR (TITLE-ABS-KEY (labeled OR labelled OR labeling OR labelling)) OR (TITLE-ABS-KEY (law* OR legal* OR legislat*)))
15	((TITLE-ABS-KEY (digital W/3 therapeut*)) OR (TITLE-ABS-KEY (digiceutical*)) OR (TITLE-ABS-KEY (software W/3 "medical device*")) OR (TITLE-ABS-KEY (samd))) AND ((TITLE (regulat*)) OR (TITLE-ABS-KEY ("food and drug administration")) OR (TITLE-ABS-KEY (fda)) OR (TITLE-ABS-KEY (usfda)) OR (TITLE-ABS-KEY (approv* W/2 (device* OR guid* OR path* OR process*))) OR (TITLE-ABS-KEY (labeled OR labelled OR labeling OR labelling)) OR (TITLE-ABS-KEY (law* OR legal* OR legislat*))) AND (LIMIT-TO (SRCTYPE , "j") OR LIMIT-TO (SRCTYPE , "d")) AND (LIMIT-TO (LANGUAGE , "English"))