Click Therapeutics

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Mehmet Oz, MD
Administrator
Centers for Medicare & Medicaid Services
U.S. Dept. of Health & Human Services
7500 Security Boulevard
Baltimore, MD 21244

Thomas Keane, MD, MBA
Assistant Secretary for Technology Policy
National Coordinator for HIT
U.S. Dept. of Health and Human Services
330 C St SW, Floor 7
Washington, DC 20201

Submitted via email at ostp-ai-rfi@nitrd.gov

**Re: Request for Information; Health Technology Ecosystem [CMS-0042-NC] RIN 0938-AV68**

Dear Administrator Oz and Assistant Secretary for Technology Policy Keane,

Thank you for the opportunity to respond to the Request for Information regarding the Health Technology Ecosystem issued by the Centers for Medicare & Medicaid Services (CMS) and the Assistant Secretary for Technology Policy (ASTP). We appreciate the opportunity to inform federal policy and help the Administration ensure that the evolving U.S. health technology infrastructure is designed to recognize, support, and incentivize the development and adoption of cutting-edge health technology solutions.

## Click Therapeutics

Founded in 2012 and headquartered in New York, NY, Click Therapeutics develops, validates, and commercializes software as prescription medical treatments for people

T. 1-332-222-4177
info@clicktherapeutics.com
80 White St 3rd floor,
New York, NY 10013

with unmet medical needs. Operating at the intersection of biology and technology, Click combines neuroscience with the power of software, creating a new way to treat disease. With a strong focus on clinical rigor, Click specializes in software-as-a-medical-device (SaMD) treatments that are clinically validated mobile applications regulated by the U.S. Food & Drug Administration (FDA). Among other accomplishments, earlier this year, Click Therapeutics received a de novo clearance from FDA for the first digital therapeutic for the preventative treatment of episodic migraine in the United States. Click's digital treatment portfolio includes:

- 6+ RCTs assessing digital therapeutic safety and effectiveness versus gold standard clinical outcome measures.
- 3 FDA Class II SaMD authorizations, along with 3 FDA breakthrough device designations.
- Software-based solutions addressing neurological or behavioral components of diseases across psychiatry, neurology, oncology, immunology, and cardiometabolic disease, with more therapeutic areas in development.
- An Artificial Intelligence (AI)-enabled platform for developing and deploying patient-centric digital therapies.

Click Therapeutics is paving the way for a healthcare system where digital treatments—whether in combination with medication as Software-Enhanced (SE) Medicines or alone as prescription digital therapeutics—can reduce suffering on a global scale.

## Software-Enhanced Medicines (SE Medicines)

The integration of sophisticated software technologies with traditional pharmaceutical interventions offers immense potential to address our healthcare system's key challenges. Among the most promising innovations in this domain are Software-Enhanced Medicines (SE Medicines), a novel, emerging therapeutic class designed to synergistically combine software with conventional pharmaceuticals, such as small molecule drugs or biologics. This integration is not merely adjunctive; rather, the software is an integral component designed to enhance therapeutic outcomes, improve patient safety profiles, or significantly increase patient adherence to prescribed treatments.

The transformative potential of SE Medicines aligns directly with the goals of a modernized, patient-centric health technology ecosystem. These innovative therapies offer a clear pathway towards highly personalized medicine, enabling real-time

adjustments to treatment regimens based on individual patient data and responses. Furthermore, SE Medicines foster improved patient engagement by empowering individuals with tools and information to actively participate in their care. This approach is pivotal for managing complex and chronic conditions, where tailored interventions and sustained patient involvement are critical for success.

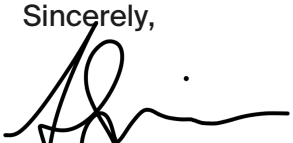
**Summary of Recommendations**

To effectively integrate SE Medicines into the health technology ecosystem and unlock their full potential, this submission will detail several key recommendations:

- The establishment of clear and distinct definitions for SE Medicines to differentiate them from other digital health tools;
- The development of cohesive cross-center policies that incentivize SE Medicine development and utilization, prepared in collaboration between CMS, ASTP/ONC, and the FDA;
- The introduction of modernized, data-driven reimbursement models that benefit from the real world data generation capabilities of SE Medicines; and
- The development of a robust data infrastructure, emphasizing interoperability and security, to support the seamless functioning of SE Medicines within the broader healthcare system.

These recommendations, elaborated in the document sections below, aim to provide a comprehensive roadmap for fostering the growth and responsible adoption of software-enhanced medicines.

Sincerely,



**Click Therapeutics**
Austin C. Speier
Chief Strategy Officer

## I. Integrating Software-Enhanced Medicines into the Health Technology Ecosystem

### A. Defining Software-Enhanced Medicines & Related Concepts

A clear and consistent lexicon is fundamental for effective policymaking in the rapidly evolving field of digital health. To ensure that policies adequately address the specific attributes of software-enhanced medicines, precise definitions are necessary. We propose the following definitions to delineate SE Medicines and related concepts:

| Term | Core Definition | Key Characteristics/Examples |
|---|---|---|
| **Software-Enhanced Medicine (SE Medicine)** | A drug-software combination product where the software component is integral to the drug's value proposition, potentially affecting its labeling, safety, efficacy, or adherence. The software is co-packaged or co-prescribed with a specific branded medication. | Designed to enhance a specific drug's action or use; software targets unique needs of the medication and its patient population; creates an "SE formulation" of the drug; software component often built on PDT principles. Example: A medication for depression co-packaged with a software application that provides cognitive behavioral therapy tailored to the drug's mechanism and monitors symptoms to optimize dosing. |
| **Prescription Digital Therapeutic (PDT)** | Software-based interventions that deliver evidence-based therapeutic interventions directly to patients to prevent, manage, or treat a medical disorder or disease. PDTs require | Clinically validated to demonstrate safety and effectiveness; subject to regulatory oversight; can be used independently or in conjunction with other therapies, e.g., as an adjunct to pharmacotherapy generally (vs. a specific branded medication). Example: Click's CT-132 for the preventive treatment of episodic migraine (DEN240064), authorized |

| | | |
|---|---|---|
| | a prescription and are authorized by the FDA. | for adjunctive use alongside acute and/or other preventive treatments for migraine. |
| **Software as a Medical Device (SaMD)** | Software intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device. The software itself is the medical device. | Can run on general-purpose computing platforms (e.g., smartphones); may be used with other products, including medical devices; can diagnose conditions, suggest treatments, inform clinical management. Examples: Software that analyzes MRI images to detect stroke[1]; software that determines drug dosage based on patient data.[1] PDTs and the software component of an SE Medicine typically qualifies as SaMD. |

Notably, SE Medicines are not merely software adjunct to a drug; they are conceived as an integrated therapeutic offering where the software component is developed in conjunction with a specific drug to achieve a synergistic effect or to address challenges associated with the drug's use, such as adherence or side effect management.

Failure to distinctly recognize SE Medicines could lead to the misapplication of policies designed for standalone software or less integrated digital tools, potentially stifling innovation or creating inappropriate regulatory burdens. Clear definitions, as provided above, can guide CMS and ASTP/ONC towards considering specific policy tracks that acknowledge the unique drug-software interplay inherent in SE Medicines, such as how real-world data derived from SE software can inform new value-based contracting models or how SE software can improve adherence using a personalized, medication-specific approach.

### B. Educating Stakeholders on Key Benefits of Software-Enhanced Medicines

Software-Enhanced Medicines offer a multitude of benefits that align with the overarching goals of improving patient outcomes, enhancing healthcare efficiency, and empowering patients. These advantages stem from the synergistic integration of pharmaceutical action with tailored software functionalities:

- **Enhanced Personalization and Efficacy:** SE Medicines enable a level of treatment individualization previously unattainable. Software components can adapt interventions in real-time based on patient-specific data, leading to treatments that are fine-tuned to each patient's unique physiological and behavioral profile. This data-driven personalization can significantly improve clinical efficacy by helping ensure therapeutic relevancy to the individual patient, such that the right treatment is delivered at the right time.
- **Improved Medication Adherence:** Non-adherence to medication is a pervasive challenge in healthcare, leading to suboptimal outcomes and increased costs. SE Medicines can address this by incorporating features such as reminders, usage tracking, educational content, and behavioral support mechanisms delivered directly to the patient. Studies on AI-based tools, which can be a component of SE Medicines, have demonstrated improvements in medication adherence ranging from 6.7% to 32.7% compared to control interventions.[2] Such software can provide a "complete visual picture of patient medicine-taking behavior".[3]
- **Enhanced Safety and Side Effect Mitigation:** The software element of an SE Medicine can play a crucial role in monitoring for potential adverse effects associated with the drug component. It can alert patients and providers to early warning signs and, in some cases, mitigate or buffer against safety issues, for instance, by guiding dose adjustments or providing timely supportive interventions.
- **Augmented Drug Label and Value:** A unique and significant benefit of SE Medicines is the potential for data generated by the software component, when rigorously studied in conjunction with the drug, to be incorporated into the drug's official labeling. This can provide a more comprehensive understanding of the drug's real-world performance, its effects in specific subpopulations, or optimal usage strategies, thereby enhancing its overall value proposition to prescribers and payers.[4]
- **Increased Patient Engagement and Autonomy:** By providing interactive tools, personalized feedback, and accessible information, SE Medicines can empower patients to take a more active role in managing their health conditions. This

increased engagement can lead to better self-management skills and a greater sense of control over their treatment journey, aligning with initiatives to improve patient autonomy.[5]

- **Potential for Cost-Effectiveness:** Through improved clinical outcomes, enhanced medication adherence, and a potential reduction in costly downstream events such as hospital readmissions or emergency department visits, SE Medicines offer the prospect of being highly cost-effective.[6] For example, digital disease management interventions have been shown to drive a 45% reduction in major adverse cardiovascular events (MACE) and a 50% reduction in 30-day readmission rates for patients post-acute myocardial infarction (AMI).[7] A specific cost-effectiveness analysis of a prescription digital therapeutic for hypertension in Japan demonstrated an incremental cost-effectiveness ratio (ICER) of ¥1,199,880 ($10,434) per quality-adjusted life-year (QALY) gained, well within accepted thresholds.[8]
- **Data Generation for Real-World Evidence (RWE) and Research:** SE Medicines are inherently data-generating technologies. Further, as validated SaMD, SE Medicine software generally yields data that is reliable, interpretable, and consistent across healthcare settings. The software component can capture a wealth of information on patient usage patterns, adherence, patient-reported outcomes (PROs), and physiological responses in real-world settings. This data, when collected and analyzed with appropriate privacy and security safeguards, can be invaluable for continuous product improvement, the generation of robust RWE to support value-based care arrangements, and furthering clinical research.[9]

It is vital for stakeholders to understand that SE Medicines deliver unique value and are not interchangeable with general wellness applications, digital health tools or even standalone Prescription Digital Therapeutics (PDTs). The defining characteristic of an SE Medicine is the intrinsic link between its software component and a *specific* pharmaceutical product. The software is purposefully designed and often co-developed to augment the action of that particular drug, manage its specific side effects, or improve adherence to its prescribed regimen. This deep integration means that the clinical evaluation, regulatory oversight, and reimbursement considerations for SE Medicines will necessarily differ from those for digital tools that are not tied to a specific medication. For instance, the safety and efficacy profile of an SE Medicine is a composite of both the drug and the software acting in concert. This distinction is paramount for crafting policies that accurately reflect their unique nature.

## II. Specific Responses to RFI Queries

### A. Enhancing Patient and Caregiver Experience (RFI Section B: Questions PC-1 to PC-14)

Software-Enhanced Medicines (SE Medicines) are uniquely positioned to address many of the patient and caregiver needs identified in this section of the RFI.

- **PC-1 (Patient Needs for Health Management/Care Navigation Apps), PC-2 (Access to Health Information in One Location), and PC-4 (Missing Features in Current Apps):**
  - SE Medicines can directly meet patient needs by offering integrated digital tools that support disease self-management and provide personalized health guidance, directly linked to their prescribed medication regimen. For instance, an SE Medicine could include features for medication and symptom tracking, dose optimization guidance based on patient inputs, educational modules about their condition and treatment, and tools to communicate relevant information to their caregivers or healthcare providers.
  - SE Medicines inherently provide access to crucial health information—specifically related to their medication and its management via the software—in a single, unified platform. This contrasts with the often-fragmented experience patients have when trying to piece together information from various sources.
  - A significant missing feature in many current health apps is the deep, evidence-based integration with specific pharmaceutical therapies that SE Medicines provide. Generic health apps may offer general advice, but SE Medicines deliver support and interventions tailored to the nuances of a particular drug and the patient population for whom it is indicated.
- **PC-5 (How CMS Can Encourage Interest and Adoption of Digital Health Products for Medicare Beneficiaries/Caregivers):**
  - CMS can significantly encourage interest in and adoption of SE Medicines by publicly recognizing their unique value in improving health outcomes and quality of life for Medicare and Medicaid beneficiaries. This is particularly relevant for managing chronic conditions (e.g., diabetes, cardiovascular disease, COPD) and mental health disorders, which are prevalent in these populations.
- **PC-5, Part a (Role of CMS in Reviewing or Approving Digital Health Products):**
  - While the FDA is the primary agency responsible for the review and

authorization of drugs and medical devices (including SE Medicines), CMS plays a critical role in determining coverage and reimbursement for its beneficiaries. CMS should publicly communicate its coverage approach for FDA-authorized SE Medicines, and in particular the evaluation of added clinical benefit claims associated with the software component of SE Medicines.[10] This CMS validation, subsequent to FDA review, would enhance trust and encourage appropriate utilization among patients and providers.

- **PC-7 (Collecting Real-World Data on Impact):**
  - SE Medicines are inherently designed to collect valuable real-world data regarding patient use, medication adherence, patient-reported outcomes, and physiological responses linked to treatment. CMS should support initiatives, and potentially offer incentives, for leveraging this data—with robust privacy and security safeguards—to assess the real-world impact of SE Medicines on health outcomes, patient experience, and healthcare costs within Medicare and Medicaid populations. Such data can also be instrumental in informing value-based care arrangements and refining treatment guidelines.
- **PC-8 (Readily Available and Valuable Health Data),PC-8, Part a (Valuable but Hard to Access Data), and PC-9 (Blue Button 2.0 API):**
  - SE Medicines can make highly valuable health data, which is often hard to access systematically, readily available to patients and their caregivers. This includes granular data on medication adherence patterns, daily symptom reports, and physiological measurements directly correlated with medication intake and software interaction. This information empowers patients in their self-management and facilitates more informed discussions with their healthcare providers. Data from SE Medicines can complement existing CMS data sources, such as the Blue Button 2.0 API, by providing a richer, more continuous view of the patient's health journey, particularly concerning medication use and its immediate effects. SE Medicines offer a unique opportunity to bridge the information gap that often exists between the act of medication intake and the patient's daily experiences and outcomes—data that is frequently missing or siloed in traditional healthcare interactions.

### B. Empowering Providers with Innovative Solutions (RFI Section C: Questions PR-1 to PR-14)

Provider adoption is critical for the successful integration of SE Medicines into patient care. CMS policies can significantly influence this adoption.

- **PR-1 (How CMS Can Encourage Providers to Leverage Digital Health Products):**
  - CMS can encourage provider adoption of SE Medicines by clearly articulating their clinical benefits, such as improved patient outcomes, enhanced medication adherence, and the potential for more personalized treatment adjustments. Demonstrating how SE Medicines can streamline aspects of care, for example, through remote monitoring of medication effects or patient-reported symptoms, can also be persuasive.[11] Crucially, establishing clear and adequate reimbursement mechanisms for the provider time and effort involved in prescribing, educating patients about, and managing SE Medicines is paramount.[10]
- **PR-2 (Obstacles to Development and Utilization of Innovative Applications):**
  - Key obstacles hindering the development and utilization of SE Medicines include regulatory uncertainty regarding combination products, the lack of standardized data exchange protocols tailored to SE Medicine-generated data, and inadequate or unclear reimbursement pathways for the software component. CMS should collaborate with the FDA and ASTP/ONC to provide greater clarity on regulatory expectations for SE Medicines and actively promote interoperability standards that support their seamless integration into clinical workflows.
- **PR-4 (Changes Needed for Third-Party Digital Products to Access Administrative Workflows):**
  - The software components of SE Medicines, when designed with appropriate security, authentication, and consent mechanisms, could potentially interface with administrative workflows. For example, SE Medicines could facilitate prescription verification or provide adherence data (with patient consent) to support reporting requirements for providers participating in value-based care models, thereby reducing administrative burden.
- **PR-5 (Support for Various FHIR APIs):**
  - CMS's strong support for Fast Healthcare Interoperability Resources (FHIR) APIs is highly commended. It is essential to emphasize that robust FHIR implementation is critical for SE Medicines to integrate effectively with Electronic Health Records (EHRs) and other health IT systems.[12] This integration enables seamless and secure data flow, such as transmitting prescribing information from the EHR to the SE Medicine software and returning patient-generated data (e.g., adherence metrics, PROs) from the SE Medicine back to the EHR for provider review.[13]
- **PR-8 (Simplifying Clinical Quality Data Responsibilities):**

- SE Medicines have the potential to simplify clinical quality data responsibilities for providers. By automating the collection of certain data points relevant to clinical quality measures—such as medication adherence rates, patient-reported outcomes, or physiologic parameters directly related to medication efficacy—SE Medicines can reduce the manual data entry burden on providers and support more accurate and timely reporting for quality improvement programs.

Providers are often hesitant to adopt new technologies if they are perceived as cumbersome, fail to integrate with their existing EHR systems, or add uncompensated workload. While SE Medicines offer significant clinical benefits, their integration into practice involves prescribing, patient education, and potentially monitoring new streams of data. If CMS policies (relevant to PR-1, PR-5) actively promote interoperability (e.g., via FHIR for EHR integration) and establish clear billing codes and reimbursement for SE Medicine-related services[10], it would substantially lower these adoption barriers. This would make providers more inclined to leverage these innovative therapies, ultimately benefiting patients.

### C. Aligning Payer Policies with Therapeutic Innovation (RFI Section D: Questions PA-1 to PA-7)

Payer policies are a critical determinant of patient access to innovative therapies like SE Medicines. CMS can lead by example and provide guidance to other payers.

- **PA-2 (How CMS Can Encourage Payers to Accelerate API Implementation):**
  - CMS should continue to strongly encourage, and where appropriate, offer incentives for, payer implementation of secure, standards-based APIs, particularly FHIR APIs. For SE Medicines, robust payer APIs are vital for facilitating the exchange of outcomes data and adherence information. This data exchange can underpin innovative value-based agreements between SE Medicine manufacturers and payers, where reimbursement is linked to demonstrated performance.[14]
- **PA-5 (Simplifying Clinical Quality Data Responsibilities for Payers):**
  - Data generated by SE Medicines, such as medication adherence metrics, patient-reported outcomes, and engagement levels with the therapeutic software, can provide payers with valuable, near real-time insights for their quality improvement initiatives and population health management programs. Access to this data can help payers identify at-risk populations, measure the effectiveness of interventions, and tailor support services.

- **Payer Section:**
    - It is strongly recommended that CMS offer programs and incentives that can act as examples to encourage favorable coverage from payers for FDA-authorized SE Medicines. This guidance should recognize the unique value proposition of SE Medicines as integrated therapeutic solutions and acknowledge their FDA authorization status, including of any added clinical benefit claims (e.g., favorable pricing or formulary positioning for added clinical benefits, and better reimbursement rates to plans/payers achieving superior SE Medicine utilization).
    - CMS should actively encourage and support the development and implementation of innovative payment models for SE Medicines, including value-based contracts.[14] Given that SE Medicines can generate rich datasets on usage and outcomes, they are particularly well-suited for arrangements where reimbursement is tied to achieving pre-defined clinical or economic endpoints.

Payer reluctance often stems from uncertainty about the cost-effectiveness of new technologies and the absence of established billing and reimbursement mechanisms.[15] As a major payer, CMS's actions have a profound influence on the broader payer landscape. If CMS establishes incentive programs for SE Medicines within Medicare and Medicaid and spearheads the development of specific HCPCS codes for the software components and associated services,[10] it would send a powerful signal to private payers regarding the legitimacy, value, and expectation of coverage for these therapies. This can create a positive cascade, encouraging wider payer adoption and thereby facilitating improved patient access to SE Medicines.

### D. Fostering a Vibrant Ecosystem for Technology Developers (RFI Section E: Questions TD-1 to TD-19)

A supportive policy environment is essential to stimulate innovation and investment in the development of SE Medicines.

- **TD-1 (Steps CMS Can Take to Stimulate Developer Interest in Building Digital Health Products for Medicare Beneficiaries and Caregivers):**
    - The most significant stimulants for developer interest are clear, predictable regulatory pathways and viable reimbursement models. If developers perceive a clear route to market and a sustainable business model for SE Medicines within the Medicare population, investment and innovation will follow.[16]
    - CMS could further stimulate interest by identifying and highlighting priority

therapeutic areas where SE Medicines could bring substantial value to Medicare beneficiaries. Examples include chronic conditions highly prevalent in this population, such as diabetes, heart failure, chronic obstructive pulmonary disease (COPD), and various mental health conditions where improved adherence and personalized management would be beneficial.

- **TD-2, Part a (What Additional CMS Data Would Be Most Valuable Through APIs):**
  - Appropriately de-identified and aggregated CMS claims data or population health data, made available through secure APIs, could help SE Medicine developers identify unmet clinical needs, understand treatment patterns, and design SE Medicines that are better tailored to the specific needs and characteristics of Medicare beneficiaries. Robust privacy and security protections must be paramount in any such data-sharing initiative.
- **TD-4 (How CMS Can Encourage the Use of Open, Standards-Based APIs):**
  - CMS should strongly endorse and, where feasible, mandate the use of open, standards-based APIs, particularly FHIR. These standards are fundamental for SE Medicines to achieve interoperability with the broader health IT ecosystem, including EHRs, pharmacy systems, and patient portals.[17] This reduces development friction, lowers integration costs, and enhances the clinical utility of SE Medicines.
- **TD-7 (Effectiveness and Limitations of USCDI):**
  - The United States Core Data for Interoperability (USCDI) is a valuable foundational standard. It is recommended that ASTP/ONC consider expanding USCDI to include data elements specifically relevant to the functionality and outcomes of SE Medicines and PDTs.[13] This could encompass standardized adherence metrics, patient-generated data derived from software interactions (e.g., responses to digital assessments), and specific outcome measures pertinent to software-based therapeutic interventions. Such an expansion would significantly improve the quality and consistency of data exchange related to SE Medicine performance.
- **TD-8 and TD-9 (Improvements to Health IT Certification Criteria):**
  - Health IT certification criteria, particularly for EHRs, should be updated to include robust support for integrating or exchanging data with FDA-authorized SE Medicines and PDTs. This could involve specific criteria for secure API connections (e.g., leveraging SMART on FHIR), standardized representation of SE Medicine-generated data within the EHR, and workflow support for prescribing, monitoring, and managing SE Medicines.
  - Consideration should be given to a "lite" certification pathway or specific,

focused certification modules for the software components of SE Medicines if they are not adequately covered under existing SaMD guidance. Such a pathway would concentrate on critical aspects like interoperability, security, and privacy, ensuring these components meet essential standards without imposing overly burdensome requirements that might stifle innovation.

We recommend that CMS and ASTP/ONC provide a clear "playbook"—comprising explicit guidance on preferred standards (e.g., FHIR, an expanded USCDI), well-defined certification criteria that specifically consider SE Medicines, and clear expectations for API implementation—it would significantly de-risk the development process. This predictability reduces ambiguity and lowers development costs, making the market more attractive and encouraging investment in SE Medicines that are designed for interoperability and alignment with national health IT strategy from their inception.

### E. Driving Value-Based Care through Software-Enhanced Medicines (RFI Section F: Questions VB-1 to VB-15)

SE Medicines are inherently aligned with the principles of value-based care (VBC) due to their focus on outcomes, adherence, and data generation.

- **VB-1 (Incentives for APMs to Leverage Digital Health Products):**
  - CMS should consider specific incentives for Accountable Payment Models (APMs) to incorporate FDA-authorized SE Medicines that have demonstrated improvements in clinical outcomes, medication adherence, or cost savings relevant to the APM's specific quality and cost targets (e.g., reduced hospitalizations for heart failure, better glycemic control in diabetes, improved functional status in patients with depression).[8]
  - The data generated by SE Medicines can provide APMs with the necessary metrics to measure performance against their targets and demonstrate the value delivered by incorporating these innovative therapies.
- **VB-3 (Essential Health IT Capabilities for Successful Participation in Value-Based Care Arrangements):**
  - Essential health IT capabilities for leveraging SE Medicines in VBC include robust interoperability for seamless data exchange between SE Medicine software, EHRs, and APM analytics platforms; secure and compliant patient data management systems; and user-friendly tools for providers to easily prescribe SE Medicines, monitor patient engagement and outcomes, and integrate SE Medicine-derived insights into care plans.
- **VB-4 (Essential Data Types for Successful Participation in Value-Based Care**

**Arrangements):**

- Data derived directly from SE Medicines is highly valuable for demonstrating value within APMs. This includes objective medication adherence data, patient-reported outcomes (PROs) collected systematically via the software, physiological data linked to drug use (if the SE Medicine integrates with sensors), and metrics on patient engagement with the therapeutic software components. This data can provide a more holistic and timely view of treatment effectiveness than traditional episodic data collection.

- **VB-5 (How Current Certification Criteria Support Value-Based Care) and VB-6 (Health IT Capabilities Not Currently Addressed by Certification):**
  - Current health IT certification criteria may not adequately address the unique data types and functionalities offered by SE Medicines. Updates are needed to ensure that certified EHRs can effectively ingest, display, and utilize data from SE Medicines to support VBC objectives. Capabilities not currently well-addressed include standardized APIs for SE Medicine data, tools for visualizing SE Medicine-derived adherence and outcome trends, and decision support that incorporates SE Medicine data.
- **VB-11 (Interoperability Challenges in Value-Based Care):**
  - A key interoperability challenge for SE Medicines in VBC is the lack of standardized data exchange formats for SE Medicine-specific data elements. CMS and ASTP/ONC should advocate for and support the development and adoption of FHIR-based implementation guides tailored to SE Medicines, ensuring that data related to their use and impact can be shared reliably and meaningfully across the care continuum.

Value-based care models (relevant to VB-1) are predicated on achieving better patient outcomes and managing healthcare costs more effectively. SE Medicines are specifically designed to contribute to these goals by improving treatment outcomes and adherence, and they possess the inherent capability to generate the data needed to substantiate these contributions. However, current APMs and health IT certification criteria (relevant to VB-5) may not be optimally structured to specifically incorporate or incentivize the use of SE Medicines. By suggesting how APMs can offer targeted incentives for SE Medicine utilization and how certification programs can better support SE Medicine data integration, comments can illustrate to CMS how these advanced technologies can be leveraged more effectively to achieve VBC objectives. This involves recognizing the unique and valuable data types that SE Medicines provide (relevant to VB-4) and ensuring that health IT systems are capable of exchanging and utilizing this data (relevant to VB-11).

## III. Addressing Key Ecosystem Considerations for Successful Integration of Software-Enhanced Medicines

The successful integration of SE Medicines into the U.S. health technology ecosystem requires careful attention to several critical areas: recognizing the value of FDA regulatory authorization, reimbursement modernization, and aligning manufacturer incentives.

### A. Regulatory Pathways and FDA Collaboration

A clear, predictable, and efficient regulatory framework is foundational for innovation and patient access to SE Medicines.

- Current FDA Landscape for SE Medicines/SaMD:
  The software component of an SE Medicine is typically regulated by the FDA as Software as a Medical Device (SaMD), while the drug component follows established pharmaceutical approval pathways.[1] This dual nature necessitates careful coordination in development and regulatory review. The FDA provides several pathways for SaMD authorization, including the 510(k) premarket notification (for devices substantially equivalent to an existing legally marketed device), the De Novo classification request (for novel, low-to-moderate risk devices without a predicate), and Premarket Approval (PMA) (the most stringent pathway, typically for high-risk devices).[18]

  Of particular relevance to SE Medicines is the FDA's draft guidance on "Regulatory Considerations for Prescription Drug Use-Related Software" (PDURS).[19] This guidance clarifies how the FDA intends to apply its drug labeling authorities to software outputs that are disseminated by or on behalf of a drug sponsor and are textually related to the drug product. Since SE Medicines often involve software that provides information, guidance, or data directly related to the use of the co-packaged drug, the PDURS guidance is a key document shaping their regulatory considerations. It underscores that the end-user output from such software may be considered a form of prescription drug labeling.
- **Recommendations for CMS/ONC to Support Regulatory Clarity:**
  - It is recommended that CMS and ASTP/ONC maintain close and ongoing collaboration with the FDA. This collaboration should ensure that CMS coverage policies and ASTP/ONC health IT certification criteria are well-aligned with the FDA's regulatory framework for SE Medicines, SaMD, and PDURS. Specifically, FDA authorization should be a key criterion for

determining coverage eligibility and for inclusion in certified health IT systems.
    - CMS and ASTP/ONC should encourage the FDA to develop and finalize clear, specific guidance on the evidence requirements for SE Medicines. This guidance should particularly address how developers can robustly demonstrate the "added clinical benefit" of the software component when combined with a pharmaceutical.[20] Clarity on endpoints, study designs, and data expectations for establishing this synergistic value is crucial.
    - There is a need for streamlined and efficient FDA review processes for combination products like SE Medicines, where both drug and software components are assessed.[18] CMS and ASTP/ONC can support FDA efforts in this area by highlighting the importance of timely access to innovative combination therapies for their beneficiaries.

While the FDA holds the authority for regulating medical products, the policies enacted by CMS and ASTP/ONC significantly shape the market viability and practical adoption of these products. Misalignment between FDA regulatory status and CMS/ONC policies can create substantial barriers. For example, if an SE Medicine receives FDA authorization but CMS lacks a clear policy for coverage of its added clinical benefit claims, or if ASTP/ONC certification criteria do not facilitate its integration into EHRs, its utility and reach will be severely limited. Therefore, comments to the RFI should emphasize the critical need for continuous, explicit collaboration and policy harmonization among these agencies to create a coherent and supportive ecosystem for SE Medicines.

### B. Reimbursement Modernization for SE Medicines

Adequate and appropriate reimbursement is arguably the most critical factor for the widespread adoption and sustained availability of SE Medicines.

- **Challenges in Current Reimbursement:**
  A significant challenge is that PDTs and the software components of SE Medicines often do not fit neatly into existing Medicare and Medicaid benefit categories, leading to coverage ambiguity.[10] Payers, including CMS, may exhibit hesitancy due to a perceived lack of sufficient long-term efficacy and cost-effectiveness data for these novel interventions, inconsistent coverage policies across different plans, and the absence of tailored billing codes specifically designed for digital services.[15] Furthermore, providers face challenges with billing for their time associated with SE Medicines and integrating these new modalities into their financial workflows.[15]

- **Recommendations for CMS/ONC:**
    - A primary recommendation is for CMS to take a leading role in establishing clear, predictable, and nationally consistent coverage and reimbursement pathways for FDA-authorized SE Medicines. It is anticipated that SE Medicines, when authorized by FDA as a co-packaged combination product with a single new National Drug Code (NDC) specific to the combination, may be reimbursed under existing benefit categories. However, this single, combined reimbursement should reflect the value of both the drug and software components to outcomes. Clarity on CMS coverage policies for SE Medicines would be immensely beneficial to accelerating the category.
    - CMS should urgently establish a clear and predictable reimbursement pathway for the essential clinician services associated with FDA-authorized Software-Enhanced (SE) Drugs by issuing guidance that crosswalks payment to the existing Remote Therapeutic Monitoring (RTM) framework, specifically asking CMS to confirm that CPT codes 98975 (for setup and education), 98980 (for the first 20 minutes of monthly management), and 98981 (for each additional 20 minutes) are the appropriate codes for billing and should be reimbursed at parity with their RTM counterparts, given the functional equivalence of the clinical work involved.
    - CMS is encouraged to actively champion and pilot value-based contracting (VBC) models for SE Medicines.[14] Given that SE Medicines can generate substantial data on patient engagement, adherence, and outcomes, they are well-suited for VBC arrangements where reimbursement is linked to the achievement of pre-defined clinical improvements or cost savings.

Innovation in therapeutic modalities like SE Medicines can be significantly stifled if the pathway to reimbursement is opaque, overly burdensome, or fails to recognize the value delivered. Manufacturers invest substantial resources in the research, development, and clinical validation of SE Medicines based on the potential for market access and fair compensation.[16]

If major payers like CMS do not provide clear and adequate reimbursement mechanisms, the financial viability of these innovative products is undermined. This, in turn, discourages further research and development and prevents potentially beneficial therapies from reaching patients who could benefit from them. Therefore, strong and specific recommendations to CMS regarding the creation of these pathways are critical to fostering the entire SE Medicine ecosystem.

This includes not only decisions about coverage but also the development of appropriate coding systems and payment methodologies that accurately reflect the unique value and operational aspects of SE Medicines.

### C. Adapting Existing Policies and Incentives to Encourage Manufacturers to Prioritize SE Medicines

Evolving a robust ecosystem of software-enhanced therapies, where SE Medicines are routinely developed and deployed for all key indications, will require broad support from developers and manufacturers of these innovative therapies. This will require careful consideration of how existing policy and incentive structures may need to be adapted to encourage SE Medicine development and adoption.

- **Modify the Medicaid Drug Rebate Program (MDRP) to Protect Against "Best Price" Penalties.**
  - The current "Best Price" rule poses a significant risk for SE Medicines. If the software component is offered at a low cost or as part of a value-based arrangement to a single commercial payer, it could collapse the Best Price for the entire drug-software bundle, leading to massive rebate liabilities.
  - CMS could issue guidance to create a new definition for SE Medicines within the MDRP, allowing for the submission of a "multiple Best Price." This would permit manufacturers to report one Best Price for the standalone drug and a separate, value-adjusted price for the SE Drug bundle when used under specific arrangements, similar to the flexibilities recently allowed for value-based purchasing (VBP) contracts. This would de-risk investment and encourage innovative contracting based on the value the software provides.
- **Establish a Favorable Pathway for SE Drugs Under the Inflation Reduction Act (IRA).**
  - Manufacturers need assurance that the significant R&D investment in the software component will be recognized and not penalized under the IRA's negotiation and rebate provisions.
  - CMS could issue guidance stating that for the purposes of the Drug Price Negotiation Program, an FDA-authorized SE Medicine will be evaluated as a distinct therapeutic approach. The program already recognizes drug-drug combination products can be a distinct therapy for price negotiation purposes; this would extend such treatment to cover drug-device combination products, particularly in the case of SE Medicines. The demonstrable clinical benefits of the software component (e.g., improved adherence, better outcomes, reduced

side effects) would be a primary factor in determining that the SE Medicine should be accounted for separately from the drug-only constituent part.

- **Implement a "Technology Kicker" for the CPI-U Inflation Rebate.**
  - This would provide manufacturers with greater pricing flexibility and reward the ongoing costs of maintaining and updating the software component of an SE Medicine.
  - For qualifying SE Medicines, CMS could modify the calculation for the inflation rebate required under the IRA. For example, instead of the rebate being triggered when a drug's price increase exceeds the Consumer Price Index for All Urban Consumers (CPI-U), the threshold could be set at **CPI-U + 1.5%**. This "kicker" would acknowledge the added value and maintenance costs of the technology, allowing for modest price adjustments without triggering steep financial penalties.
- **Create a Value-Based Purchasing (VBP) "Safe Harbor" Specifically for SE Medicines.**
  - SE Medicines are perfectly suited for VBP arrangements because their software components naturally generate the data needed to measure outcomes and adherence. A streamlined pathway would reduce the administrative burden and legal uncertainty for manufacturers wanting to enter into such contracts.
  - CMS could define a VBP "safe harbor" model for SE Medicines. If a manufacturer's contract with a payer meets the pre-defined criteria (e.g., payment is tied to metrics like medication adherence above a certain threshold or achievement of a specific clinical biomarker, both measured by the software), it would be deemed compliant with CMS regulations, including Best Price reporting rules.
- **Offer an Expedited "Coverage with Evidence Development" (CED) Pathway.**
  - Speed to market and earlier revenue generation are powerful motivators. An accelerated pathway to initial reimbursement would significantly de-risk the development of SE Medicines.
  - For SE Medicines that receive FDA authorization and demonstrate a high potential for clinical benefit, CMS could offer an expedited pathway to temporary coverage under a CED model. This would allow for reimbursement while the manufacturer collects the large-scale, real-world data required for a permanent National Coverage Determination (NCD), bridging the gap between regulatory approval and full market access.

Initiatives such as the above can help recognize the significant effort required to develop, validate and maintain therapeutically active software subject to FDA regulations and compliance requirements. Creating a supportive array of incentives that favor SE Medicine development promises to meaningfully accelerate the category and sooner realize its potential to improve patient outcomes while enhancing cost-effectiveness throughout the healthcare system.

## IV. Conclusion and Recommendations

### A. SE Medicines are Essential to Advancing American Health

Software-Enhanced Medicines (SE Medicines) represent a significant and promising opportunity to rapidly advance therapeutic innovation. They offer the potential to bring tangible benefits to patients through more personalized and effective treatments, improved medication adherence, and enhanced safety. For providers, SE Medicines can offer new tools to manage complex conditions and gain deeper insights into patient responses. For the healthcare system at large, they hold the potential for improved outcomes and greater cost-effectiveness. The Request for Information from CMS and ASTP/ONC presents a critical juncture. The policies developed in response to this RFI will play a determinative role in either hindering or significantly accelerating the development, adoption, and positive impact of these transformative technologies within the United States.

### B. Summary of Key Recommendations

To harness the full potential of SE Medicines and ensure their successful integration into the U.S. health technology ecosystem, this submission puts forth the following overarching recommendations:

1. **Recognize and Define SE Medicines:** Formally acknowledge Software-Enhanced Medicines as a distinct category of therapeutic intervention, with unique characteristics and considerations separate from general digital health tools or standalone pharmaceuticals. This requires clear, consistent definitions to guide policy.
2. **Streamline and Align Policy:** Foster robust and ongoing collaboration between CMS, ASTP/ONC, and the FDA to ensure that policies and pathways for SE Medicines are clear, efficient, and harmonized across agencies. This includes recognizing FDA authorization, providing clarity on evidence requirements for

demonstrating the value of the integrated software component, and developing policies that favor SE Medicine development.

3. **Modernize Reimbursement:** Establish predictable, transparent, and adequate coverage, coding, and payment models for FDA-authorized SE Medicines. This must address both the drug and the software components, address clinical workflow considerations, and should actively encourage and support value-based contracting approaches that reward demonstrated outcomes.
4. **Champion Interoperability and Security:** Incentivize and promote robust, standards-based interoperability (e.g., via FHIR APIs and an expanded USCDI) to enable seamless data exchange between SE Medicines, EHRs, and other health IT systems. Concurrently, ensure stringent cybersecurity standards and data privacy protections to maintain patient trust and safety.

### C. Conclusion

We thank CMS and ASTP/ONC for the opportunity to comment on this RFI. We appreciate your thoughtful and thorough consideration of the comments and recommendations presented herein.

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