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Organ-on-a-chip: key industry insights, challenges, and opportunities from 100+ NSF I-Corps interviews

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Organ-on-a-chip (OoC) is a rapidly advancing technology with significant potential to revolutionize healthcare, drug discovery, and personalized medicine. OoC technologies offer cost-effective and ethical platforms that enable the acquisition of physiologically relevant data and enhance our understanding of human disease mechanisms and drug responsiveness. Over the past decade, numerous academic start-ups and spin-offs have sought to translate foundational research on OoC platforms from the lab bench to commercial and real-world applications. However, industry adoption of these systems has been limited, resulting in a marginal impact on personalized medicine and drug discovery – two key application areas for OoC technology. The U.S. National Science Foundation Innovation Corps (NSF I-Corps™) program, an entrepreneurial training program, provides a means to assess the commercialization potential of academically developed technologies, such as, for instance, OoC, by encouraging in-depth discussions with over 100 key stakeholders and potential customers within relevant areas. Our research group participated in the Fall 2024 cohort of the NSF I-Corps program, conducting 100+ (*i.e.* 102) interviews with OoC experts, clinicians, and professionals across the pharmaceutical and biotech industries. This perspective article summarizes our collective effort and the insights gained from this program, offering valuable knowledge for the OoC community. Overall, the vision of our NSF I-Corps interviewees highlighted the urgent need for OoC standardization, reproducibility, reliability, scalability, as well as ease of usability along with regulatory acceptance. Moreover, these interviews highlighted a critical gap between academic innovations and commercial applications, emphasizing the importance of bridging collaboration between the two entities. This perspective further explores the current commercialization potential of OoC technologies and outlines the key hurdles that must be addressed for OoC technologies to achieve broader adoption in drug discovery and personalized medicine.

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1. Introduction

Organ-on-a-chip (OoC) technologies are a subcategory of microphysiological systems (MPS) that are designed to host engineered human tissues and organ models in a biomimetic microenvironment.[1] These technologies enable precise control over cell–cell interactions, extracellular matrix (ECM) composition, fluidic perfusion, mechanical forces, as well as diffusion of biological factors and molecules for accurate modeling of human physiology and disease states.[2] OoC technologies have gained widespread notoriety due to their significant potential to benefit the scientific community by offering a more physiologically relevant, cost-effective, and ethical platform for studying various disease mechanisms, organ functionality, personalized medicine, and drug testing.[3,4] In recent years, there has been a significant surge in the development of various OoC platform technologies, each modeling different organs. Several academic research laboratories have launched start-ups, aiming to translate these foundational research tools into the pharmaceutical and biotech sectors, capitalizing on their promising advantages for practical applications.[5,6] However, a key question still remains: could the push to commercialize OoC systems and platform technologies be ahead of its time?

Our lab has been a pioneer in the development of several tissue-on-a-chip technologies, specifically tumor-on-a-chip (ToC) platform technologies, through the use of stem or patient-derived cells for accurate disease modeling and drug testing applications.[7–15] With over a decade of experience in

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developing OoC and specifically ToC systems, our lab became interested in scientifically answering fundamental and hypothesis-driven questions into areas where there is a strong market demand for OoC technologies. To accomplish this, our team embarked on a seven-week journey through the U.S. National Science Foundation Innovation Corps (NSF I-Corps™) program to gain insight into the commercialization trajectory of OoC technologies and our developed ToC platforms. The NSF I-Corps program is an intensive entrepreneurial training program designed to facilitate the transition of NSF-funded research from academia to industry. At its core, the NSF I-Corps program leverages an experiential, iterative, hypothesis-based learning approach to provide academic researchers, scientists, and engineers with first-hand experience in customer discovery, allowing them to gain direct insight into the current market ecosystem of their proposed technological innovation.[16] The program guides teams to focus on identifying and understanding the needs and pain points of potential customers, rather than simply promoting or 'selling' their prospective product. It encourages the use of open-ended, unbiased questions to uncover the real challenges faced by customers in their respective fields. Participation in the program requires the formation of a team of three to five members, with each member assuming the role of either entrepreneurial lead, technical lead, or industry mentor. Teams are tasked with interviewing at least 100 potential industry stakeholders and customers to test their innovation's hypothesized market segments, customers, key partners, competitors, and value propositions.[16,17] Through this experience, participants can develop and refine their technology's business model and, more importantly, discover whether a significant need exists

Ronin-Mae Komarnisky

Ronin-Mae Komarnisky earned her BS and MS degrees in Biomedical Engineering from Arizona State University. She is currently a research scientist in Dr. Mehdi Nikkhah's laboratory, working on the fabrication of microfluidic disease-on-a-chip models for applications in personalized medicine. She served as the Co-Entrepreneurial Lead for the National Science Foundation (NSF) I-Corps team, participating alongside Shaun Wootten, Nathan Friedman, and Mehdi Nikkhah to understand the commercialization potential of organ-on-a-chip technologies.

Shaun Wootten

Shaun Wootten is a Ph.D student in Dr. Mehdi Nikkhah's lab at Arizona State University, where his research focuses on biofabrication methodologies for organ-on-a-chip and microfluidic models. He brings over eight years of R&D industry experience, with a strong background in the commercialization of biomedical technologies. He served as the Entrepreneurial Lead for the NSF I-Corps team and is a member of the International Microphysiological Systems Society (IMPSS).

Nathan Friedman

Nathan Friedman is the Chief Executive Officer of HemaSense and founder of Morphologic, where he leads early-phase medical device development and commercialization. He previously spent nearly two decades at W. L. Gore & Associates, focusing on medical device innovation, product development, and technology strategy. Nathan holds a BS in Mechanical Engineering and Materials Science from Rensselaer Polytechnic Institute. His interests center on fostering entrepreneurship and advancing early-stage innovation across diverse industry sectors, with a particular focus on translating novel technologies into high-impact businesses. He served as the Industry Mentor of the NSF I-Corps team.

Mehdi Nikkhah

Mehdi Nikkhah is currently a Professor of Biomedical Engineering at Arizona State University. He completed his postdoctoral fellowship at Harvard Medical School and earned his Ph.D. at Virginia Tech. His research interests focus on integrating micro- and nano-scale technologies, innovative biomaterials, and biology to better understand the mechanisms of human disease progression and to develop regenerative medicine strategies for treating organ and tissue failure. His lab is among the pioneers in disease-on-a-chip modeling, particularly tumor-on-a-chip technologies, with numerous notable publications and patents. He served as the Technical Lead of the NSF I-Corps team.

for their proposed technologies and innovations, thereby helping teams effectively determine the best path forward, whether that be launching a start-up, licensing their technology, pursuing additional technical research, or ceasing the commercial pursuit altogether.

Within the NSF I-Corps program, we aimed to test and refine our business model hypothesis surrounding our proposed OoC, and particularly ToC, technology platform. We hypothesized that pharmaceutical research scientists focused on preclinical anti-cancer drug discovery would utilize a microfluidic OoC (ToC) platform to increase the number of effective drug candidates moving into human clinical trials. To test this hypothesis, as per the program's directive, our team conducted interviews with potential customers, competitors, and partners within our hypothesized target market segments. During the seven-week program, a total of 102 interviews were conducted, either in person or virtually *via* Zoom video conferencing, using a flexible, exploratory interview strategy to naturally elicit the challenges, needs, and perspectives of stakeholders across the OoC commercial ecosystem. Each interview ranged between 30 to 60 minutes, and interview notes, customer archetypes, and tested hypotheses were recorded in AirTable Ascent, a project management software tool provided by the NSF I-Corps program. For further qualitative data analysis, we utilized Taguette, a free, open-source software tool, to manually track and organize interviewee insights. An inductive coding approach was used to identify and categorize recurring themes and patterns related to perceived translational challenges that appeared across the 102 interviews, as outlined in Table 1. The questions asked in each interview were tailored to the weekly learning objectives of the NSF I-Corps program as well as to

Table 1 Summary of the codes and definitions derived from inductive qualitative analysis of interviewee responses, outlining the thematic challenges that emerged from the NSF I-Corps interviews. Representative quotes are featured to illustrate the recurring challenges identified across NSF I-Corps interviewee responses

Code	Definition	Example quotation from interviews
Platform design complexity	Concerns relating to the complexity of OoC platforms in terms of channel and culture chamber designs, geometries, and component integration (*i.e.*, pumps and sensors), which may limit widespread industry adoption and commercialization	"The design should be simple, robust, and fool-proof"
Material and cell source variability	Concerns regarding inconsistencies in biological materials, chemical reagents, or cell/tissue sources, which reduce the reproducibility and reliability of OoC-generated data	"Cell sourcing is an issue, especially for scaling up. There is an unknown black box of regents and tissues"
High-throughput compatibility	Concerns the lack of high-throughput capabilities or integration with automated systems for drug screening applications or workflows	"They [OoC platforms] often lack high-throughput handling"
Resistance to technology adoption	Concerns relating to the resistance of industry to adopt new *in vitro* systems due to legal, operational, cultural, or workflow barriers	"Pharma is very conservative. It is an unknown system to them, so the risk is high"
Design for manufacturability and scalability	Concerns related to the ability to design and manufacture OoC platforms at scale	"Scaling up is a notable issue. There is a need and push for increasing and improving manufacturing needs"
Regulatory and quality control	Concerns regarding OoC alignment with regulatory expectations and approval. Refers to uncertainty or lack of clear regulatory guidelines and quality control measures to ensure OoC reproducibility and reliability	"An SOP is not enough… Good quality control checks should be in place to ensure the product is producing the same result every time"
Usability	Concerns regarding the ease-of-use and interoperability of OoC technologies. Encompasses concerns regarding operational issues that may deter utilization and integration into established industry workflows	"A baseline analyst should be able to use this technology"
Reproducibility and reliability	Concerns regarding the reproducibility and reliability of OoC technologies and OoC-generated data between devices, platforms, end-users, and laboratories	"Reproducibility and reliability. Make sure the chip doesn't leak frequently. Have a device that looks clean. Build the customer's confidence"
Standardization	Concerns the need for consistent terminology, definitions, and robust, standardized protocols, materials, and processes that determine the technological and biological performance of OoC systems	"Real standardization is needed across microfluidics and OoC"
Validation and qualification	Concerns the need for robust validation and qualification of OoC technological systems to demonstrate physiological relevancy within their predefined context of use to satisfy regulatory and end-user requirements	"Investors are interested in a product with a strong data package. Regulatory hurdles must be considered and addressed early on"

the interviewee's background, experience, skill set, and field of work. However, questions our team commonly utilized throughout the interview process included the following:

- *What are the biggest challenges in bringing drug candidates to the market, specifically moving from the preclinical to the clinical testing stage?*
- *What kinds of improvements or research tools would help accelerate the drug development pipeline?*
- *In your opinion, what is currently preventing the use of microfluidic OoC devices in pharmaceutical and biotech industry settings?*
- *What criteria do pharmaceutical/biotech companies look at when deciding to acquire a new in vitro system?*
- *What criteria does the company use when purchasing in vitro systems? How do they commonly discover or learn about these systems?*
- *What are some ways to establish a relationship with a pharmaceutical/biotech company?*

This perspective article aims to elucidate and distill key insights and understandings gathered from our interviews with over 100 key stakeholders involved in microfluidic and OoC technologies for specific applications in the pharmaceutical, biotech, and clinical sectors. It is important to clarify that this perspective is not intended as an in-depth review of OoC technologies, but rather aims to share the valuable insights, recommendations, and lessons on OoC commercialization that our team collected during the seven-week NSF I-Corps program. To reiterate, the interviews conducted through the NSF I-Corps program were qualitative and investigative by design. Moreover, given the confidential nature of the pharmaceutical and biotech industries, several discussions were kept at a high level to protect sensitive information related to research and business operations. Despite these limitations, however, this perspective offers a unique take on the translational potential of OoC technologies by incorporating direct industry feedback along with commercialization insight. Translating any laboratory innovation from bench to market is a challenging endeavor. Successful translation requires both technological refinement and a deep understanding of the innovation's market needs, target customers, value propositions, and financial feasibility. By reflecting on our NSF I-Corps lessons and findings, this perspective illuminates the current perception, needs, and opportunities in OoC commercialization. As such, this perspective aims to provide a resource for both new and seasoned OoC developers and researchers seeking to enter the market and advance the industry adoption of these promising technologies.

2. OoC: a promising technology for drug discovery

In the past few years, drug discovery and personalized medicine have been widely regarded as the most promising commercial avenues for OoC technologies, largely driven by the pharmaceutical industry's need for more efficient approaches to bringing new therapeutics to market. Drug research and development is a long and arduous process plagued by high costs and extreme failure rates.[18] Despite increased research and development (R&D) investment, the total number of annual new drug approvals has steadily declined over the past two decades.[19,20] Approximately 90% of new drug candidates that enter phase I clinical trials ultimately fail, often due to insufficient clinical efficacy, adverse side effects, or uncontrollable toxicity.[21,22] These failures stem largely from reliance on ineffective *in vitro* and *in vivo* models – namely animal models and 2D cell culture systems.[18,22] Despite their significant contributions in the development of novel therapeutics and enhancing our general understanding of disease, animal models are inherently poor predictors of drug safety and efficacy due to their inability to accurately recapitulate human physiology and pathology.[22] Moreover, the use of animal models is costly, labor-intensive, and carries significant ethical concerns in experimentation. Alternatively, 2D cell culture assays are cheaper, faster, offer high-throughput capabilities, and, unlike animal models, can leverage human cell lines for better physiological relevance.[23] However, these systems are largely unable to provide the essential cell–cell and cell–ECM interactions necessary to recapitulate the *in vivo* diseased microenvironment.[24] These simplified *in vitro* systems often lack native-like cell morphology and organotypic structure as well as essential features such as spatial organization, vascularity, and perfusion.[25] Overall, the inherent limitations of these gold-standard platforms, combined with the significant attrition rates in clinical trials and a decline in new therapeutics approved by the United States Food and Drug Administration (FDA), underscore the urgent need for innovative approaches and improved investigational research tools.[18,26]

At its core, the field of OoC emerged from the growing need for more predictive, physiologically relevant platforms capable of overcoming the limitations of current *in vitro* and *in vivo* systems used in modeling human diseases and advancing drug discovery.[1] OoC technologies are defined as microscale cell culture platforms that integrate microfluidics, biology, advanced biomaterials, and tissue-engineering to establish dynamic three-dimensional (3D), biomimetic human tissue constructs *in vitro*.[27] Since the publication of the first "lung-on-a-chip" model in 2010, numerous OoC technologies have been developed, leading to new discoveries in fundamental biology, tissue and organ functionality, and disease pathophysiology.[28,29] OoC platforms can be designed to simulate various biomechanical forces and molecular gradients, in addition to enabling the integration of numerous cell types (*i.e.*, stromal, immune, and vascular cells). Additionally, these platforms can incorporate biosensors, actuators, and fluorescent biomarkers to enable real-time quantitative data collection and monitoring of cell viability, behavior, and functionality.[25,30] These features enable OoCs to replicate the *in vivo* tissue environments under both healthy and diseased states with unprecedented precision.[3,31] The field of OoC has rapidly evolved over the years, with recent advancements notably expanding the technology's relevance and utility within various areas of pharmaceutical development and biomedical research. For instance, organoid-on-a-chip platforms, emerging from the synergistic combination of organoid and microfluidic technology, harness the finely controlled microenvironment of OoC systems with the advanced physiological mimicry of human organoids to establish more sophisticated, functionally relevant 3D models with improved perfusion, organization, and maturation for patient-specific and personalized drug screening applications.[32] OoC models with vascularization and incorporated immune system components (*e.g.*, macrophages, neutrophils, monocytes), on the other hand, have enhanced the modeling of complex diseases and biological responses, such as for inflammatory conditions like periodontal disease.[33,34] Multi-organ systems, another technological advancement, have garnered increased interest within drug screening and toxicology assessment, as these systems aim to simulate systemic drug interactions that occur *in vivo*.[35] Despite these significant developments and advancements, the commercial application of OoC technologies continues to fall behind other traditional models. Organoids, for example, are widely used within pharmaceutical drug development due to their high-throughput capabilities.[36] Meanwhile, animal models and 2D assays, or simplified 3D assays (*e.g.*, cell-embedded hydrogels), continue to dominate preclinical research and drug discovery as these platforms are required by regulatory agencies prior to human clinical trials.[37]

Recent regulatory tailwinds have increased recognition of OoC as a viable alternative to animal models. In 2022, the FDA Modernization Act 2.0 presented a pivotal shift in regulatory policy regarding drug discovery.[38] This legislation paved the way for minimizing and potentially eliminating the requirement of *in vivo* animal testing, permitting the use of computer models and cell-based assays like organoids and OoCs as alternative preclinical models – opening new avenues for integrating OoC technologies into the drug development pipeline.[38] Taking advantage of the promising attributes and advancements of OoC technologies, in addition to its high market potential and increasing recognition by the FDA as a promising research tool, many academic groups have spun out companies to commercialize unique OoC systems, aiming to deliver on the promise of these platforms to reducing, replacing, or refining (the 3R's) animal use in drug discovery and personalized medicine.[5]

Through our stakeholder and customer discovery interviews during the NSF I-Corps program, an urgent and critical need for advanced biomedical research tools that accurately predict the safety and efficacy of new pharmaceutical compounds was strongly affirmed. Most of the interviewees with prior background and knowledge of OoC recognized the significance and impact of these technologies, as well as the need for these systems to enable more accurate and predictive drug testing and discovery. For instance, several interviewees noted the significance of OoC platforms designed to recapitulate the human immune system, suggesting that these platforms could enable the development of new vaccines. Other interviewees suggested that an off-the-shelf OoC platform with a robust data package could potentially save them years of development time spent on making their own models internally. Research scientists and regulatory personnel within the pharmaceutical and biotech industry consistently highlighted species-to-species translatability, poor predictive accuracy, and ethical concerns as key pain points pertaining to the use of the current gold-standard murine animal models and 2D assays. According to several pharmaceutical scientists interviewed, some key pain points they encounter in the drug development pipeline are a result

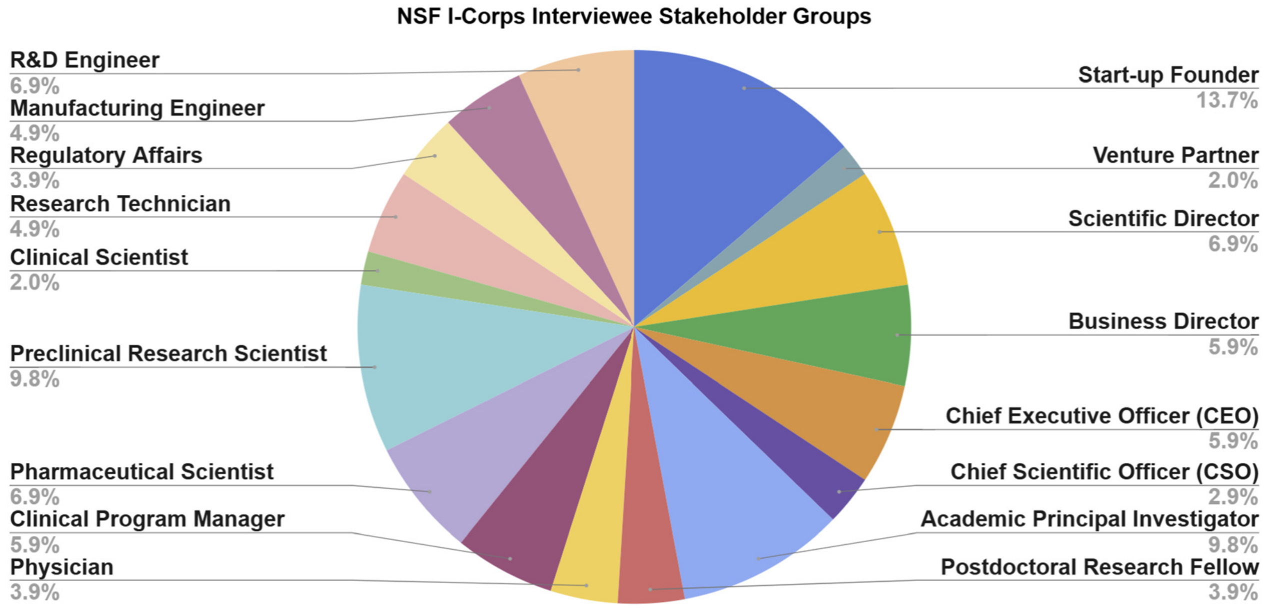

Fig. 1 Breakdown of roles and positions from 102 NSF I-Corps interviews featuring key stakeholders within OoC development, academia, pharmaceutical drug development, contract research organizations (CROs), and biotech start-up space.

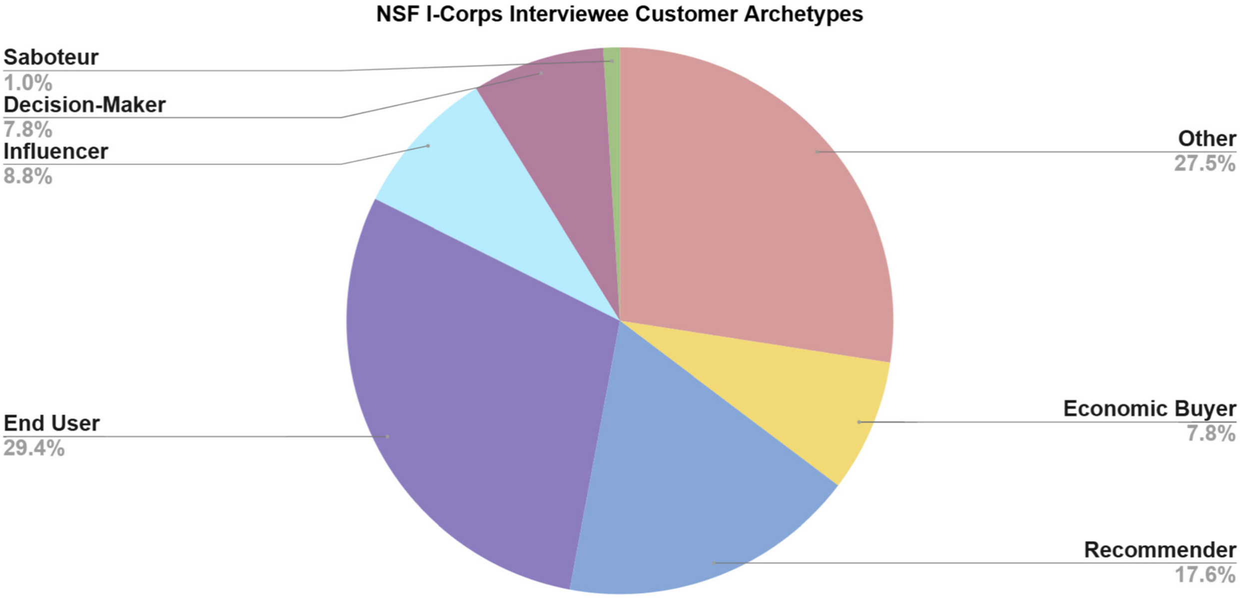

Fig. 2 Organization of NSF I-Corps interviewees into different customer archetypes: saboteurs, decision-makers, influencers, economic buyers, recommenders, end-users, and others. Interviewees categorized as "others" were professionals who either had start-up experience but were not working directly with microfluidic or OoC technology, professors in other academic fields not related to microfluidic or OoC technology, or interviewees who otherwise had little to no knowledge or experience with microfluidics.

of poor *in vitro* and *in vivo* models, emphasizing that studies conducted using 2D assays and small animal models almost never translate to humans. One interviewee noted two critical limitations of the gold-standard systems: current 2D cell culture assays lack flow, which can cause the loss of critical pharmacokinetic information, and small animal models prompt the development of multiple versions of the same pharmaceutical compound since the intended target (*e.g.*, receptors) of the compound changes between *in vivo* models, which significantly slows down the drug development process. Despite the promise of OoC technologies to circumvent and address these critical limitations, the pharmaceutical and biotech sectors have been slow to adopt these systems.

3. Chasing bubbles: barriers to adoption

While the disruptive potential of OoC technologies is evident, their limited adoption in the pharmaceutical and biotech industries prompts a closer investigation into the barriers obstructing their path toward successful commercialization. As noted earlier, during the NSF I-Corps program, 102 individuals, including research scientists, academic researchers, physicians, venture capitalists, start-up founders, and industry professionals were interviewed. The interviewees spanned the pharmaceutical, biotech, and microfluidic industry sectors, representing a diverse range of roles, including scientists, business directors, regulatory affairs specialists, engineers, and academic principal investigators. The diversity offered a comprehensive perspective on the current landscape of OoC technology as seen in Fig. 1. From these professional roles, the interviewees were categorized into different customer types, including end-users, decision-makers, influencers, economic buyers, recommenders, saboteurs, and others (Fig. 2). The exact number of interviewees per stakeholder group and per customer archetype are shown in Tables S1 and S2, respectively.

Following the NSF I-Corps program's objective to actively engage in customer discovery to determine if a viable

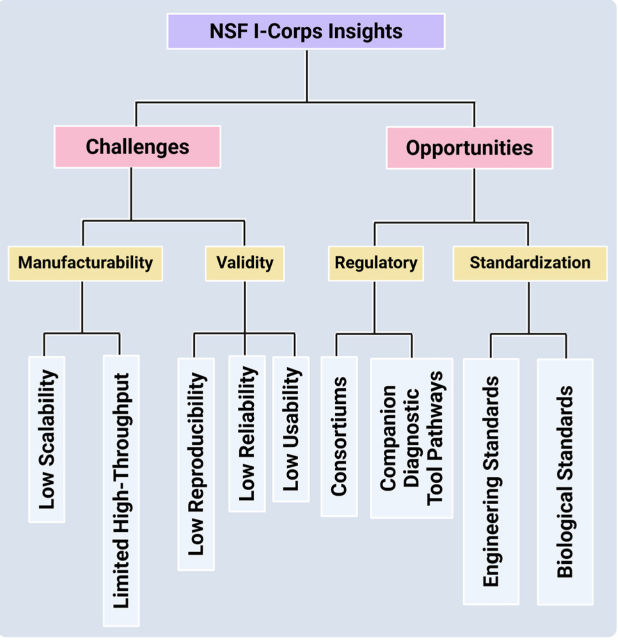

Fig. 3 Breakdown of common challenges and areas of opportunity reported by NSF I-Corps interviewees within the OoC space. When asked about common challenges with OoC systems and current barriers to adoption, the responses of the NSF I-Corps interviewees were categorized as "challenges" and "opportunities". Created in **https://BioRender.com**.

commercial need exists, the interviews were not centered around the team's proposed OoC platform. Rather, the interviews were structured to elicit the interviewee's perspectives regarding the current capabilities of OoC technologies and their role in today's drug discovery, disease modeling, and personal medicine landscape. Insights from our customer discovery interviews, facilitated during the NSF I-Corps program, echoed critical barriers preventing industry and clinical adoption while also illuminating actionable steps that can be taken to propel OoC toward successful and impactful commercialization. Based on these conducted interviews, barriers that are impeding the integration of OoC technologies into the drug discovery and development workflow can be succinctly summarized as: minimal reproducibility and reliability, poor usability, low scalability and high-throughput capabilities, and the lack of regulatory validation and standardization (Fig. 3). To illustrate role-based differences and similarities in these perceived barriers, a cross-stakeholder comparison of recurring challenges inhibiting OoC commercialization and adoption has been generated and depicted in a heatmap, using GraphPad Prism, as shown in Fig. 4. Raw counts of interviewees within each stakeholder group who discussed each thematic challenge are shown in Table S3. This analysis revealed that, across stakeholder groups, the most frequently cited barriers to OoC translation and commercialization include limited platform usability and insufficient reproducibility and reliability, both in terms of the platform itself and the data generated. Other top areas of concern emphasized across roles pertained to OoC standardization, validation, and qualification.

3.1 Insights into barriers to adoption

Throughout the program, NSF I-Corps interviewees with prior background or experience in microfluidics OoC technology were asked about what they perceive to be the current challenges inhibiting the application of OoC technologies in pharmaceutical, biotech, academic, and clinical research settings. Among interviewees, the lack of widespread industry and clinical application was noted to be due to concerns with platform reproducibility and reliability, ease of use, and extensive validation to demonstrate clinical relevancy and equivalency. Traditionally, pharmaceutical companies are conservative and risk-adverse in their approach to drug discovery and development, a strictly regulated process that requires comprehensive preclinical and clinical testing to demonstrate drug efficacy and safety.[39,40] Similarly, the clinical sector and biotech companies require robust data packages documenting reproducibility, reliability, and key performance metrics of new biomedical research tools and systems prior to purchase.[41] As such, these sectors are hesitant to invest in new technological systems, including OoC technologies, without extensive testing and validation,

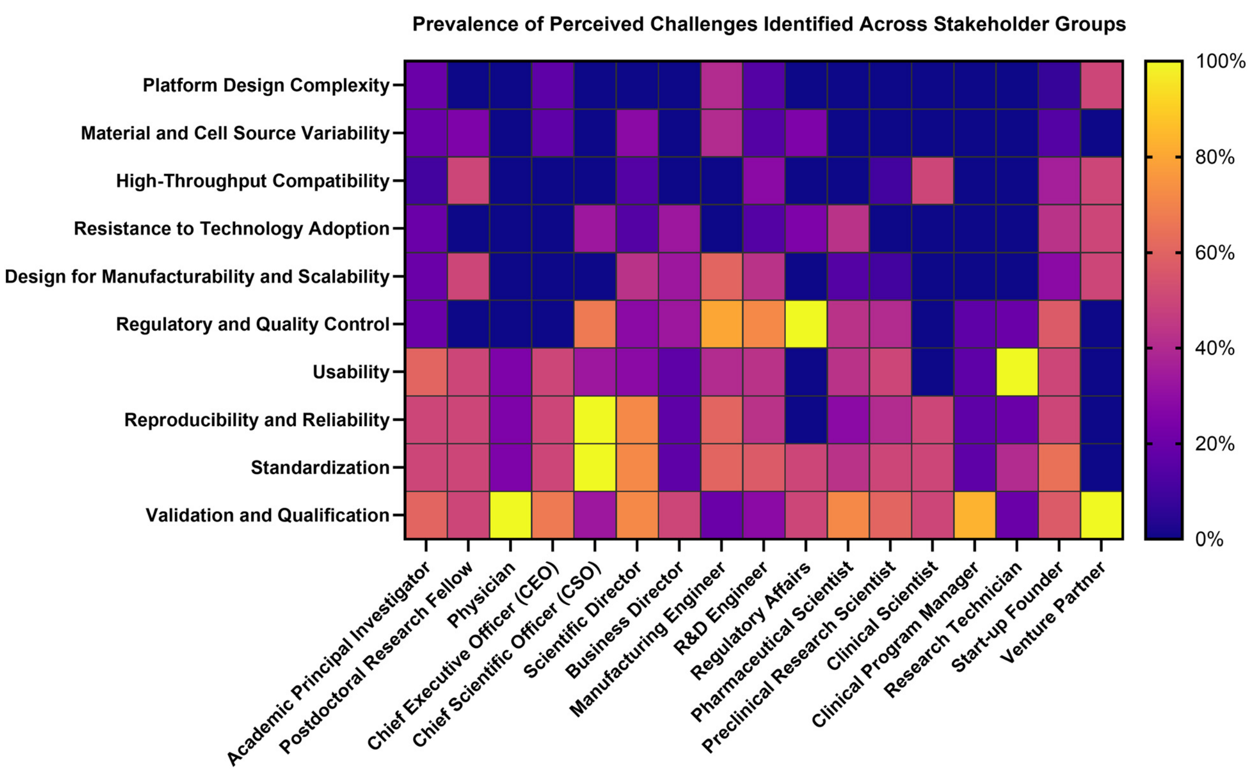

Fig. 4 Heatmap comparing key challenges across different stakeholder groups interviewed during the NSF I-Corps program. The rows of the heatmap correspond to common challenges (*e.g.*, high-throughput compatibility, usability, standardization) noted throughout the interviews, and columns depict the roles and positions of NSF I-Corps interviewees (*e.g.*, academic principal investigators, research technicians, start-up founders). Color intensity corresponds to the percentage of interviewees within each stakeholder group citing a challenge as a barrier to OoC commercialization and adoption.

which demonstrates robust reproducibility and reliability of the new platforms.

In the context of OoC, reproducibility concerns the extent to which the system can produce the same result under identical experimental conditions, while reliability concerns the ability of the model to consistently perform as designed. Interviewees suggested that the reproducibility threshold exhibited by *in vitro* screening and culture platforms should, at minimum, exceed 90% of the coefficient of variation (CV). Currently, it has been reported that OoC systems exhibit high variability between users and across laboratories.[42] Inconsistencies in reproducibility and reliability typically observed in OoC systems are driven, in part, by variations in cell and tissue sources, culture conditions, chemical reagents, materials, platform design complexity, and experimental procedures.[43] To achieve high levels of reproducibility and reliability, it was pointed to and suggested that robust quality control measures and well-defined acceptance criteria must be implemented to ensure uniformity across devices, users, and laboratories. Several key customer types, including end-users, decision makers, and recommenders, strongly emphasized the importance of implementing quality control measures in all aspects of the design, development, and fabrication processes to align OoC systems with industry and regulatory demands for reproducibility and reliability.[42,44] The lack of standardization in OoC technologies complicates the reproducibility and reliability of these systems across different laboratories, making data utilization for regulatory approval more challenging. Beyond the technical challenges impairing reproducibility and reliability, standardization initiatives must also address the ethical concerns inherent to OoC technologies. The use of human-derived cell lines and tissues, such as primary cells, stem cells, immortalized cells, and patient-derived tumor biopsies, introduces additional hurdles for ensuring both responsible use and regulatory compliance. The technology's reliance on these materials raises concerns regarding cell and tissue sourcing, patient consent, and data privacy and ownership.[45,46] As such, establishing clear guidelines for ethical sourcing, informed consent, and data management is essential to ensure the safety, efficacy, and responsible use of OoC in personalized medicine, drug discovery, disease modeling, and other biomedical applications.[45,47] This undertaking requires careful consideration of the ethical and legal frameworks that will govern the downstream utilization of OoC platforms in the commercial sectors, including the development and implementation of clear policies regarding data ownership, usage, and intellectual property rights to uphold transparency, accessibility, and protect vulnerable patient and donor populations from exploitation.[46]

In conjunction with reproducibility and reliability limitations, as well as ethical considerations, ease of use concerns are another significant barrier to OoC utility in industry, academic, and clinical settings. Platform usability is crucial for customer adoption, retention, and the generation of reproducible and reliable data. Academic groups are the primary developers of OoC systems, designing more sophisticated platforms for improved replication of *in vivo* conditions of a plethora of tissues and diseases. However, increased design complexity typically lends itself to more specialized equipment setup and operation requirements, reducing overall platform usability and translatability to the industry and clinical sectors.[48] Academic research scientists and principal investigators developing OoC platforms are often highly specialized and trained on their own platforms. As a result, transferring this technology into industry and clinical spaces, and even between academic laboratories, is still a challenging and time-consuming undertaking. End-users, including industry research scientists and research technicians, with experience using OoC and microfluidic platforms within their work discussed their own difficulties with grasping the nuanced handling techniques required for OoC systems. One interviewee reported that they spent most of the time "chasing bubbles" within the platform due to the high design complexity of the microchannels. The learning curve that research scientists and technicians encounter when utilizing OoC platforms was a recurring theme within the NSF I-Corps interviews. Despite expressed interest in incorporating these systems into their workflow, interviewees frequently cited the complexity of microfluidic channel designs and the specialized handling techniques required for cell injection, culture, and imaging as major barriers to adoption. Several interviewees also reported that the lack of standardized operating procedures (SOPs) and, in some cases, overly complex protocols, make moving between different OoC platforms exceedingly difficult. Other end-users noted that the incompatibility of OoC platforms with existing laboratory equipment or automated systems posed further challenges to routine utilization. Collectively, these issues slow the pace of adoption and transfer of OoC technologies from academic to industry settings.

To reiterate, the steep learning curve associated with OoC platforms remains a significant barrier to their widespread utilization within the pharmaceutical and biotech industries. Fortunately, OoC developers can leverage several strategies to help mitigate this barrier.[27,49] Such strategies include designing user-friendly, plug-and-play platforms compatible with standard laboratory instrumentation, providing end-users with easily accessible, robust protocols, and offering hands-on training workshops. However, several microfluidic and OoC start-up founders interviewed during the NSF I-Corps program noted that a significant amount of time, effort, and resources are still required to provide customer support to end-users. Such efforts included sending personnel to train inexperienced users, developing workshops, and troubleshooting experimental protocols. Despite these efforts, however, some start-up founders continue to encounter usability issues with long-standing customers, prompting a handful of start-up founders to reconsider the direct sales of their devices and transition their business model and vision to a more service-based model, such as through contract research organizations (CROs). For instance, one interviewee's start-up provided hands-on training for their microfluidic 3D tissue culture system to industry end-users. However, despite training users within the start-up's laboratory, users still encountered some challenges and handling discrepancies when they returned to their own laboratories to use the platform. As a result, the start-ups planned to develop a CRO branch to improve collaboration with pharmaceutical industry partners. However, it is important to note that transitioning from a sales-oriented start-up to a CRO consists of its own challenges, such as requiring substantial infrastructure, resources, and personnel to meet the expectations and needs of potential customers.[25] Several industry professionals noted that unless standardized protocols are introduced across the board, OoC platforms will continue to struggle to translate from academic prototypes to user-friendly, industry-ready platforms.

3.2 Insights into technical challenges

There are several inherent technical challenges that significantly hinder the commercialization and adoption efforts of OoC technologies. Commonly cited technical challenges, during the interviews, concerned the overall manufacturability of OoC systems. Most OoC systems suffer from limited scalability, low throughput, and generally lack automation, which not only impacts mass production, but also contributes to poor reproducibility, reliability, and usability of OoC platforms. Limited scalability and throughput pose significant challenges for pharmaceutical companies, which require the ability to screen thousands of compounds efficiently to make critical, rapid decisions at each stage of the drug discovery and development process.[50] The current microfabrication methodologies (*i.e.*, soft-lithography) employed by academic laboratories primarily rely on the use of polydimethylsiloxane (PDMS). PDMS offers a unique combination of gas permeability, optical transparency, and biocompatibility, rendering it a preferred choice for microfabrication in the field.[51–53] The use of PDMS is well-established for OoC device fabrication. While appropriate for academic research, PDMS exhibits several limitations that make it unsuitable for large-scale manufacturing. These shortcomings include inadequate structural support for specialized applications, limited scalability for high-throughput production, and, most notably, is prone to drug adsorption and leaching, which can impair pharmaceutical drug discovery and screening applications.[54–56] Microfabrication techniques using PDMS are often not optimal for mass production as they are time-consuming and require specialized infrastructure and microfabrication equipment.[48,57] As a result, industry professionals strongly recommend seeking out alternative manufacturing methodologies, such as CNC machining, 3D printing, and precision injection molding to circumvent the limitations of OoC fabrication techniques.[58–60] While alternative manufacturing methodologies can optimize the scalability of OoC technologies, it should be stated that more advanced manufacturing techniques are typically associated with high start-up costs, making it difficult to implement design changes following initial productization of OoC platforms.[25,48] Interviews with start-up founders and venture capitalists emphasized the importance of minimizing research risks prior to commercialization to bolster confidence, trust, and reliability. Therefore, it is crucial to substantially finalize design requirements, user requirements, and perform usability, feasibility, and verification and validation studies prior to start-up launch.

Best practices and recommendations from interviewees focus on interfacing and collaborating with manufacturing experts, end-users, and regulatory bodies early in the design and development process of innovative OoC systems. Doing so can help ensure the proposed OoC platforms are aligned with manufacturing requirements and constraints without compromising user needs and simplicity. By clearly defining user needs and desired outcomes early in the design process, the geometrical complexities of OoC systems can be minimized to improve overall manufacturability, potential for high throughput, and usability. The manual handling of OoC devices naturally creates more sources of variation and inconsistencies. The lack of integration with current robotic liquid-handling systems further exacerbates issues with high-throughput experimentation, as many OoC platforms are not designed for automation. Some of the end-users recommended leveraging automation and integration with artificial intelligence (AI) and machine learning (ML) to design more robust platforms with improved means of data extrapolation and analysis. While automation was more frequently mentioned as a critical element for improving consistency and throughput, some interviewees shared a common recognition of the potential for AI and ML algorithms to reduce variability and streamline the management, analysis, and interpretation of large, complex datasets generated by OoC platforms. Insights shared by scientific directors and research scientists alike noted a critical need for more advanced analytical methodologies to expedite real-time data acquisition, image processing, and analysis for purposes relating to drug toxicity assessments, predictive analytics, disease modeling, and novel drug or biomarker discovery.[49,61,62] This sentiment becomes increasingly critical as OoC platforms continue to evolve into more comprehensive systems, generating more complex and multidimensional datasets.[62,63] Naturally, the integration between OoC and AI/ML algorithms is envisioned to expand the impact and power of OoC technologies. However, further development in this area raises additional considerations about the infrastructure, data management systems, and computational resources necessary to seamlessly integrate and support combinational OoC and AI/ML platforms. Some interviewees remarked that the tremendous power between the pairing of AI/ML and OoC will only be realized if the underlying data and processes are also robust. As such, focused efforts will also be needed to standardize data collection, storage, and user interfaces, as well as to develop high-quality, ethical, and robust training datasets. Infrastructure, standardization, and regulatory requirements necessary to achieve AI/ML with OoC integration will ultimately shape whether these analytical tools are embedded within OoC platforms and distributed directly to end-users or provided as part of an in-house service model. Additional insights from interviewees revealed that pharmaceutical companies and clinicians do not prioritize the complexity or innovation behind a technological system when adopting a platform for their workflow. Rather, they are far more concerned with the overall capabilities of a platform, prioritizing the reproducibility, quality, and relevancy of the data generated. Therefore, OoC developers should first and foremost focus on establishing a simple and user-friendly OoC platform that consistently meets end-users' needs without forgoing the platform's manufacturability, reliability, and usability.

3.3 Insights into value proposition

One notable challenge reported by interviewees is the need for extensive validation of OoC systems within their context of use, demonstrating, through data, the advantages of OoC technology over existing models within their intended application. While the advantages of OoC systems over traditional 2D cell culture assays are well documented and supported in literature, skepticism from pharmaceutical and biotech companies regarding the predictive power of these systems remains.[64,65] Indeed, research scientists, microfluidic OoC experts, and pharmaceutical professionals interviewed during the NSF I-Corps program agree that OoC's most promising commercial application lies within drug discovery and personalized medicine. However, interviewees also suggested that OoC models, at their current stage, are not poised to completely replace existing animal models. Even with the passage of the FDA Modernization Act 2.0, it is unlikely for industry to completely negate the use of animal models within the preclinical drug development process.[66] As a result, it is imperative for OoC developers and academic research scientists to validate the performance of their OoC devices within their intended specific application, and against current state-of-the-art models, to further bolster their value proposition.[66] To achieve this, interviewees suggested that efforts toward conducting studies that focus on comparing the predictive power and equivalency of OoC data to conventional preclinical models (*i.e.*, animal models and 2D cell-based assays) or data from human clinical trials will be necessary. Performing such studies will increase industry trust and confidence in OoC technologies for use as an accurate and reliable tool for predicting biological response.[67]

Another insight that emerged from the NSF I-Corps interviews is the importance of clearly defining the value proposition of OoC technologies. To remain competitive, pharmaceutical companies need to make decisions quickly to move more potential drug candidates to market and reduce downstream costs.[5,68] While OoC systems offer a more physiologically relevant and cheaper alternative to current models, offering a more cost-effective technological platform is not a compelling enough value proposition to drive the adoption and integration of OoC systems. Any proposed OoC system requires a well-defined, measurable outcome, with high reproducibility and reliability. It is therefore crucial that OoC developers who seek to commercialize their OoC systems gain a clear and informed understanding of their potential customer's specific problem and needs, ensuring that their technology is solving an existing problem rather than trying to force their technology to provide a solution to a non-existent problem.

4. Moving forward: future directions for OoC commercialization

Identifying and engaging with opportunities to address the aforementioned barriers is now a key priority for OoC developers seeking to bolster the commercial application of these technologies. The responses from the NSF I-Corps program regarding the current challenges for OoC systems and their commercialization underscores the growing realization that standardization is essential for unlocking the full potential of OoC systems within drug discovery and personalized medicine. Standardization can help improve the reproducibility, reliability, validity, and interoperability of OoC platforms in addition to easing regulatory hurdles. Achieving standardization will require extensive collaboration with key stakeholders, including regulatory and federal bodies, funding agencies, developers, end-users, and suppliers. Such collaboration is essential for creating guidelines that standardize experimental design, data management, qualification and validation, and key terminology and definitions across different areas of application. Furthermore, standardization will involve outlining criteria and recommendations for materials, hardware, platform dimensions, inlet and outlet interfaces, and biological components in the design and fabrication of OoC systems for industry, drug discovery, and preclinical and clinical use. The lack of such standards not only impedes the compatibility of OoC platforms with standard laboratory equipment, limiting high-throughput experimentation, but also slows progress toward creating highly robust and reproducible OoC systems and results. Ultimately, beyond enhancing usability and integration into laboratory workflows, standards are crucial for ensuring the adoption and regulatory acceptance of any new technological systems, particularly for drug research and development.

4.1 Standardization: a catalyst for commercialization

Standardization emerged as a central theme throughout the NSF I-Corps interviews, consistently identified as a key factor for unlocking the full commercial potential of OoC technologies. As such, there is a critical need for the establishment of clear international standards, such as those by the International Organization for Standardization (ISO) and the Organization for Economic Co-operation and Development (OECD), to support the development, qualification, validation, and regulatory acceptance of OoC technologies, thereby solidifying their efficacy and reliability.[46] The implementation of international standards will be essential for addressing critical gaps impeding OoC standardization, including the lack of consensus regarding OoC terminology, manufacturing and design processes, performance criteria, and biological components.[46,69] Aside from ensuring reproducibility and interoperability, international standards are necessary for data generated by OoC technologies to be reproducible, comparable, and acceptable across international regulatory jurisdictions. This is especially critical in the context of drug discovery and development, where inconsistencies in data generation and reporting can subsequently lower trust and confidence in data generated using OoC technologies, thus further slowing adoption by pharmaceutical and biotech companies. Therefore, it is crucial to set international standards that define how data generated by OoC systems is processed, validated, reported, and exchanged. Efforts by the ISO and OECD are currently underway to help address these needs. In 2024, the creation of ISO/TC 276/SC 2, which focuses on standardization of microphysiological systems and OoC, marked a significant milestone in ongoing global OoC standardization efforts and plays a key role in addressing the aforementioned standardization gaps.[70] In conjunction with the actions taken by the ISO to standardize OoC platforms, the OECD has taken steps to harmonize data reporting for *in vitro* systems through the implementation of OECD Harmonized Template 201: Intermediate Effects, which can be leveraged for the reporting of data derived from OoC platforms.[69] Additionally, to support the regulatory acceptance of *in vitro* methods, the OECD has developed a guidance document on Good *In Vitro* Method Practices (GIVIMP), designed to help researchers enhance the reliability and reproducibility of data generated by *in vitro* systems.[69,71] This document outlines best scientific and technical practices related to *in vitro* work and development, including guidance on standard operating procedure development, experimental design, and reporting criteria, which can be directly applied to OoC development.[69] Despite initial progress, a focused and concerted effort by international regulatory agencies is still required to establish robust standards that guarantee the reproducibility, usability, interoperability, and reliability of OoC technologies and OoC-generated data to enable their regulatory acceptance and adoption, and ultimately their successful commercialization. OoC developers and researchers are strongly encouraged to familiarize themselves with and incorporate best practices and guidelines from standard-setting organizations, such as the OECD and ISO, into their R&D processes in order to accelerate the translation of their technologies to market.

4.2 Bridging the gap: what's needed to achieve standardization

During the NSF I-Corps program, several pharmaceutical research scientists remarked that the application OoC systems has been severely limited within the United States, with only a few notable companies (*i.e.*, Roche, Novo Nordisk, AstraZeneca) reporting instances of use.[6] The United States FDA has stringent regulatory requirements surrounding preclinical drug development models, diagnostic companion tools, and clinical research tools. These regulatory requirements often hinder widespread industry application of OoC technologies. Europe, however, is currently making significant strides toward OoC standardization. As of 2024, the European Commission's Joint Research Centre (JRC), in collaboration with the European Committee for Electrotechnical Standardization (CENELEC) and the European Committee for Standardization (CEN), worked to establish the Focus Group Organ-on-Chip (FGOoC) to outline the roadmap toward OoC technology standardization.[72] This effort seeks to establish global standards for OoC technologies, recognizing the importance of international collaboration in accelerating OoC regulatory acceptance and commercial adoption. More recently, key regulatory and standardization organizations within the United States, such as the FDA and National Institute of Standards and Technology (NIST), have begun taking significant steps toward creating OoC guidelines and standards, acknowledging that the absence of such standards is limiting the technology's broader impact.[73] As of April 2025, the FDA has taken significant action to promote the use of new approach methodologies (NAMs), such as computational modeling and OoC systems, within investigational new drug (IND) applications.[74] To support this effort, the FDA unveiled a roadmap detailing the agency's plan to reduce the use of animal models in preclinical drug safety studies over the next 3–5 years, beginning with monoclonal antibody therapy development.[74] This initiative involves fostering strategic partnerships with the Department of Veterans Affairs, the National Institute of Health (NIH), and other agencies to support the development, validation, and adoption of these methodologies to streamline the development of safer, more effective therapeutics.[74] Overall, these initiatives will not only improve the drug development pipeline but also represent a major advancement toward regulatory recognition of innovative technologies like OoC systems, thereby broadening areas of application, encouraging industry-wide adoption, and signaling a potential increase in market demand for OoC systems.

Notably, early engagement with regulatory authorities can help streamline the validation and qualification process for OoC systems as well as foster increased recognition of OoC as viable *in vitro* systems for clinical and drug discovery applications. The development and subsequent commercialization of MatTek's EpiDerm™, a 3D tissue model designed to replicate the human epidermis for dermal toxicology testing, serves as a noteworthy example for how early engagement can help establish regulatory guidelines and validate *in vitro* systems for clinical and industry use.[75,76] Coordination with the European Centre for the Validation of Alternative Methods (ECVAM), a unit within the European Commission's JRC, enabled EpiDerm™ to engage in formal validation studies to assess and demonstrate its predictive capabilities.[76] In turn, these early validation studies supported the technology's inclusion in OECD Test Guidelines no. 431 and no. 439, allowing this technology to be formally recognized as an acceptable alternative to animal models for skin irritation and corrosion testing.[75] Consortiums and scientific organizations can help facilitate this engagement with regulatory bodies and policymakers, bridging the gap between academia, industry, and regulatory agencies to establish standards and guidelines for OoC development. Several consortiums across Europe and the United States, such as Organ-on-Chip in Development (ORCHID), Unlocking the Data Content of Organ-on-Chips (UNLOOC), and TEX-VAL Tissue Chip Testing Consortium, for instance, have emerged to validate OoC platforms as well as establish consensus between academia, industry, and regulatory agencies to create qualification frameworks and promote the broader use of OoC technologies.[77–79] Numerous scientific societies, most notably the International MPS Society (iMPSS) and European Organ-on-Chip Society (EUROoCs), have also been established to support the education of the scientific community on OoC systems, foster collaboration between industry and academia, and further OoC research and development.[80,81] Such societies can play a key role in driving innovation, advocating for regulatory support, and increasing awareness and education of OoC systems. Overall, the establishment of consortiums and scientific societies are an effective step in forming the necessary partnerships and collaboration to facilitate OoC standardization and propel the creation of innovative OoC solutions. Recognizing the benefits of partnerships, the FDA announced its intention to collaborate with the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) to coordinate validation and standardization efforts for NAMs, including OoC systems, as part of its effort to scale back the use of animal testing.[74] Currently, the FDA offers Drug Development Tool (DDT) Qualification programs that can help support OoC developers wanting to gain regulatory acceptance.[74,82] These programs can be leveraged to help ease barriers to industry adoption from a regulatory standpoint. One such program includes the Innovation Science and Technology Approaches for New Drugs (ISTAND) program, which focuses on assessing the qualification of innovative drug development tools that have potential use in drug research and development.[74,83,84] These programs may be used to formalize the qualification and acceptance of OoC systems within clear, well-defined contexts of use, thereby boosting industry and regulatory confidence in data generated by OoC systems in IND applications. For OoC technologies to make a significant commercial impact and deliver on their long-standing potential to revolutionize drug discovery and personalized medicine within the United States, the standardization efforts must be accelerated. To accomplish this, it is imperative that OoC developers, academic institutions, and key influencers (*i.e.*, clinicians, manufacturers, engineers, research scientists, business personnel) actively engage with regulatory and federal agencies to establish standardized guidelines, recommendations, and best practices to expedite regulatory acceptance and industry adoption.

In practice, a successful standardization initiative would first begin by establishing a network of key stakeholders, including federal regulatory agencies, non-governmental organizations (NGOs), CROs, academia, and industry, that collaboratively work to identify high-impact use cases where OoC could best be leveraged to address safety and efficacy questions within the areas of drug discovery and personalized medicine. At this stage, workshops will be critical for aligning stakeholder priorities, familiarizing regulatory agencies with OoC technologies, and developing validation and qualification pathways.[74,85] As previously discussed, such efforts are currently underway with governmental agencies like the FDA and NIH organizing workshops focused on implementing strategies to phase out animal testing.[74] Following this, efforts will need to be dedicated toward investing in the development of OoC technologies, by collaborating with research and funding agencies, to design and execute use case validation studies that will help define performance metrics for reproducibility, reliability, predictive accuracy, and physiological relevance among other critical endpoints.[86] The need to qualify and validate different OoC technologies against current industry standards is critical. However, direct comparison against industry standards and between technology platforms becomes increasingly difficult to achieve as each system differs in format, cell source, and experimental parameters.[5] Therefore, attention must be equally directed toward assessing data reproducibility across independent laboratories and to developing standardized biological protocols for cell sourcing, tissue formation, culture conditions, and engineering standards for platform fabrication to ensure interoperability, high-throughput capabilities, and usability.[74,86] As more data and insights emerge from these qualification and validation efforts, the development of standards and regulatory guidance will continue to evolve, enabling regulatory bodies to issue clear guidelines on how OoC technologies can be implemented within the pharmaceutical, biotech, and clinical sectors. Ongoing efforts dedicated to training, education, and communication across stakeholders, ensuring that both scientists and regulatory personnel are familiar with and open to the use of alternative drug development tools, will be pivotal to achieving both regulatory acceptance and successful standardization of OoC technologies.

4.3 Collaboration: defining the roles, responsibilities, and implementation

To translate the envisioned standardization initiative into practice, it is necessary to identify practical implementation steps in addition to clarifying the roles of key stakeholders, particularly those within academia and industry, in the standard-setting process. Drawing from insights gathered from our NSF I-Corps interviews and Europe's leadership in coordinated OoC standardization efforts, advancing OoC standardization should begin with the standardization of OoC terminology, definitions, and classifications to support clear communication and discussion amongst key players within the OoC ecosystem.[69,72] Following the established consensus on OoC terminology, the next step toward standardization focuses on first qualifying OoC platforms for specific contexts of use (*e.g.*, drug efficacy testing, cardiotoxicity screening) and subsequent standardization of experimental protocols, particularly in regard to cell/tissue sourcing, culture conditions, critical endpoint assays, and performance metrics. To ease implementation, these actions should align with existing and emerging qualification pathways such as the FDA's ISTAND program.[84] Establishing experimental protocols will enable downstream studies to validate each OoC system within its intended context of use, ensuring the reproducibility and reliability of data across different platforms, laboratories, and organizations.[72] In this regard, the standardization of materials, manufacturing processes, design, and additional engineering criteria should parallel experimental protocol development. Engineering standards are essential for reducing variability, supporting interoperability, and enabling usability and scalability. However, premature standardization may impede OoC innovation and will therefore be most effective once experimental procedures and protocols are optimized. These steps will require coordinated efforts to align user-specific requirements and intended applications with international standard-setting bodies such as ISO and OECD. Simultaneously, establishing standardized practices for data reporting, processing, and management will further support regulatory acceptance and enable seamless integration of OoC-generated data with AI and ML algorithms, furthering OoC scalability, usability, and impact.[72] Finally, it is also important to ensure that all legal, regulatory, and ethical aspects central to OoC development and commercialization are carefully considered throughout the standardization process.

Each stakeholder group within the OoC ecosystem plays a significant role in advancing standardization efforts to address the persistent barriers impeding the commercialization of this technology. Academic researchers have played a major role in the initial developmental efforts of OoC technology. However, OoC industry developers and start-ups are emerging as additional key players in OoC innovation and R&D activities. As such, OoC developers in both academia and industry are well-positioned to collaborate in leading the development, qualification, and validation of OoC technologies. By leveraging existing standards in place by international standard-setting organizations, such as those established by the ISO and OECD, academic and industry OoC researchers and developers can work jointly to develop robust systems, experimental designs, protocols, and reporting practices that ensure that the generated data are reliable, reproducible, and biologically relevant for regulatory use and applications in drug discovery and personalized medicine. Utilizing guidelines suggested by the ISO/TC 276/SC 2 and the GIVIMP guidance document, for instance, may be a highly beneficial starting point.[70,71] As advised by our NSF I-Corps interviewees, namely start-up founders and key opinion leaders in the OoC space, academic researchers should adopt an "entrepreneurial mindset" that guides their research and development processes. More specifically, researchers must ensure that their technological systems address a clear, well-defined question or unmet need that end-users cannot sufficiently resolve using existing models. To successfully translate and commercialize their technology, OoC developers should prioritize solving a specific pain point experienced by their targeted customer segments. Otherwise, OoC researchers, and specifically academic developers, run the risk of creating a solution for a non-existent need or problem. Therefore, it is critical for OoC developers to proactively engage and collaborate with potential end-users (*e.g.*, physicians, pharmaceutical and biotech companies, teaching hospitals, research scientists, and technicians) to guide their technological development. As suggested by the underlying premise of the NSF I-Corps program and recommendations from interviewees, this approach will not only enhance the translational capacity of OoC technologies but also inform the qualification and validation activities necessary to align performance metrics with intended use cases. Academic partnerships with industry will be immensely helpful in translating OoC platforms into scalable, manufacturable products that meet regulatory demands and standards. Such partnerships can also ensure OoC platforms are interoperable with existing laboratory infrastructure, thereby increasing usability and high-throughput capabilities. Industry, specifically pharmaceutical and biotech companies, will also play a complementary role in validating OoC platforms within commercialized settings. Funding organizations, in coordination with regulatory and federal agencies, can accelerate the translation of OoC technologies by incentivizing collaboration between academia and industry, the development of open-access databases, and by supporting qualification and validation studies. Standard organizations and regulatory agencies, alongside consortiums and scientific organizations, will play a pivotal role in facilitating cross-collaboration efforts to align priorities and create consensus amongst key stakeholders. They will also be crucial in establishing workshops and training programs to support broader education and familiarization of relevant industry and regulatory personnel with the transformative potential of OoC technologies, a key component in both facilitating seamless technology transfer and advancing their application and adoption within pharmaceutical development and personalized medicine.

5. Conclusion

In summary, the insights of 100+ industry experts, potential end-users, and start-up founders, facilitated through our NSF I-Corps program, highlight several critical challenges hindering commercialization and the broader impact of OoC technologies. As discussed, the barriers that impede industry application of OoC technologies include the lack of standardization, limited scalability, the lack of automation, low throughput, and issues with reproducibility, reliability, robustness, and usability. Most critical, however, is the minimal effort put toward OoC technology validation and qualification, which is crucial for demonstrating OoC technologies as a viable, improved alternative to conventional modeling and screening platforms. Ultimately, bridging the gap between academic innovation and widespread industry adoption requires addressing these challenges through collaboration with regulatory agencies to advance standardization efforts and build confidence in OoC technologies.

For OoC experts and developers interested in increasing OoC adoption and advancing OoC technologies to market, it is crucial to minimize the engineering and research risks associated with an OoC system prior to commercialization. Establishing a robust, reproducible, and reliable OoC platform can significantly improve commercialization success and utility. However, identifying a key end-user, with a pressing unmet need, is essential for commercial viability. Collaboration between academia and industry is essential for developing OoC solutions that address real industry needs. An OoC platform should answer a critical problem, providing a specific measurable outcome with high reproducibility and reliability to be used as a diagnostic or screening platform. Developers need to set realistic expectations for their OoC technology and avoid overpromising or selling its capabilities. Instead, experts and developers must focus on demonstrating platform validity and value for end-users. By strategically addressing the presented challenges and opportunities for advancement, as highlighted through the NSF I-Corps program, OoC experts, developers, and key stakeholders accelerate industry adoption and regulatory acceptance, enabling diverse and impactful utilization of these technologies within healthcare, drug discovery, and personalized medicine. Despite these challenges, a promising future lies ahead of OoC technologies. Indeed, these technologies are rapidly gaining recognition for their significant transformative capabilities across pharmaceutical R&D and personalized medicine, attracting increasing interest and investment from regulatory bodies and pharmaceutical companies alike. Overcoming the presented challenges are the next crucial steps that OoC researchers and pioneers must take to unlock the full commercialization potential of OoC systems.

Author contributions

Ronin-Mae Komarnisky: conceptualization, visualization, writing – original draft. Shaun Wootten: conceptualization, visualization, writing – original draft. Nathan Friedman: writing – review & editing. Mehdi Nikkhah: conceptualization, funding acquisition, project administration, resources, supervision, writing – review & editing.

Conflicts of interest

There are no conflicts of interest to declare.

Data availability

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The data supporting this perspective have been included as part of the SI. Original interview notes are not publicly available due to interviewee privacy and confidentiality considerations. Anonymized interview notes may be shared upon request by contacting the corresponding author.

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