CELL & GENE THERAPY INSIGHTS

Innovation Insights

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"This is not a sustainable model."

Healthcare Providers call for sector-wide standards & collaboration to solve widespread cell & gene therapy challenges at hospitals and sites of care

Joe DePinto & Robert Richards

Cell and gene therapies (CGTs) are on the cutting edge of medicine, but their current production and delivery complexity is pushing many Healthcare Providers to a breaking point. CGT operational systems and processes are so numerous and unnecessarily varied that the growth of the field is at risk. At a recent advisory council attended by 16 leading cell and gene therapy healthcare professionals, providers and administrators voiced an urgent need for standards and simplicity to make the growth of CGT sustainable. Among the greatest challenges – workflows and systems that are not standardized; large amounts of uncompensated time lost to data entry and system trainings; low staff morale and high attrition risk due to the need to prioritize processes and training over time with patients; IT and cybersecurity vulnerabilities related to the proliferation of too many portals and digital systems; and excessive operational variability and training requirements for CGT clinical trials that may only enroll a limited number of patients per site. These challenges arise from many different types of CGT products, in all phases of development. Healthcare professionals stated that these operational challenges will limit CGT's ability to scale, may prevent some medical centers from taking on new CGT clinical studies, and will likely become unsustainable as the field provides therapies for more common diseases with larger patient populations. Collaboration among the entire sector, with a special emphasis on the needs of Healthcare Providers and the patients they serve, is urgently required to develop necessary standards and harmonized approaches – and reduce complexity.

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Cell and gene therapies (CGTs) are on the cutting edge of medicine. But in the healthcare settings where patients are treated these transformative therapeutics, the supporting operational systems and infrastructure for CGTs have not kept pace. Hospitals are critical not only to the care of CGT patients, but to the production and delivery of these transformative therapeutics – and growing complexity is making all aspects of CGT care more difficult. Healthcare Providers (HCPs) say that ongoing CGT production and delivery complexity is pushing them to a breaking point and puts further growth of the sector at risk.

[1]

At a recent Clinical Advisory Council attended by 16 veteran cell and gene therapy healthcare professionals from the University of Pennsylvania and other leading academic institutions and organizations across the United States, providers and administrative leaders gathered to share CGT challenges experienced across hospitals and sites of care. The attendees included leading physicians, nursing managers, cell pharmacy decision-makers, and hospital IT and technology strategists, all experienced in working with multiple types of cell and gene therapies at all stages of clinical and commercial development. All share a common commitment to CGT patients and their mission of delivering these life-changing therapies.

With more than 200 years of collective experience in CGT among the attendees, the goal of this initial session was to surface challenges that are common across HCPs and institutions. (Future advisory councils will focus further on solutions, as well as collaborative discussions with biopharmaceutical manufacturers.)

The Clinical Advisory Council, hosted by Vineti, revealed a set of common, urgent challenges in healthcare settings that present a call to action for to the CGT sector. Here are some of the most significant, as described by advisory council attendees:

- Workflows and operational systems are not standardized for critical steps across the CGT patient and product journeys, introducing extra work, unnecessary complexity, and risk.
- HCPs are losing excessive amounts of uncompensated time to "back office" work, including duplicative IT audits and risk assessments, one-off system trainings for each individual CGT product, and repetitive, high-risk manual data entry that all lead to delays in offering therapies.
- Clinical staff is overwhelmed by the need to prioritize processes and training over time with patients, resulting in low morale and attrition.
- IT and cybersecurity vulnerabilities are arising from the proliferation of too many individual manufacturer portals and digital systems.
- CGT clinical trials are bogged down in excessive operational variability and training requirements that require large amounts of clinical staff time but may ultimately enroll only a limited number of patients per clinical site.

The challenges related to use of these therapies are present in both research and commercial settings but are proving to have a greater effect on commercial products. The reason for this is that centers will keep more therapies that have

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similar indications on formulary in the event that one company has a long lead time manufacturing. This, coupled with the probability that some CGTs will advance to second-line therapy amid market competition to offer them, will put pressure on centers to site-certify. Research-phase products don't have those pressures, as the number of patients that can be put on trial is smaller, which in turn reduces the risks of complexity at scale.

In this white paper, we will outline the findings of the Clinical Advisory Council, beginning with a detailed look at current trends in CGT as described by council attendees, followed by the key challenges described by the advisory council and some recommended solutions. The goal of this white paper is to surface CGT challenges being described across hospitals and sites of care, in the interest of encouraging the CGT sector to collaborate on solutions. Independent industry-wide organizations, such as the independent, non-profit Standards Coordinating Body for Regenerative Medicine, have already initiated efforts to work with biopharmaceutical manufacturers in support of HCPs. We hope that this paper will provide information to accelerate such efforts.

CURRENT TRENDS IN CGT

On the scientific side, growth in the CGT sector is rapid and multi-dimensional. There are currently more than 5,000 unique therapeutic products in development [2], and more than 2,260 clinical trials ongoing worldwide [3]. The newest wave of treatments represents "CGT 3.0," building on the dendritic cell and CAR-T cell breakthroughs that have already received regulatory approvals over the last 12 years. Many of the newest approaches rely on manipulating a broader range of cells – such as allogeneic cells from donors or starting material from solid tumors – that are often even more complex to collect, manage, and dose than those used in CAR-T treatments. (Figure 1).

Advisory council attendees described growing patient volumes for both clinical-phase and commercial products that mirror this overall CGT sector growth. More than 60 percent of attendees said their institution experienced increased clinical trials and trial patient volumes in 2021 over 2020 (Figure 2) [1]. More than 75 percent said their institution experienced a similar increase

FIGURE 1

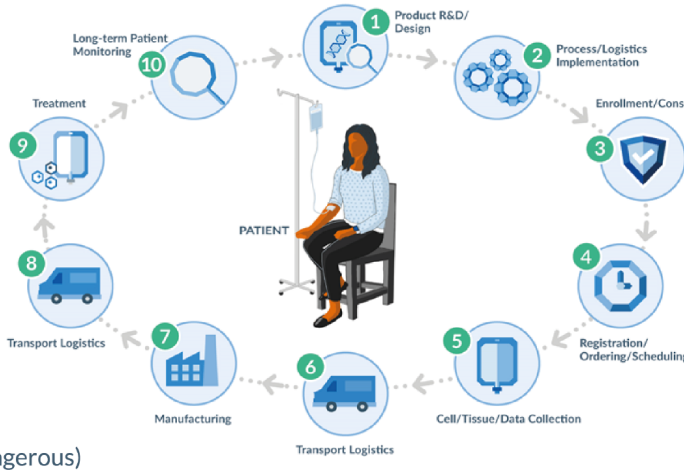
Complexities for healthcare providers

Operational complexities in CGT

Many considerations for clinical sites, including the patient-specific supply chain

Key raw material: human cells (patient and/or donor)

- Variability in the human biology of patients and the cellular starting material
- Complexity
  - GMP starting material is collected in medical centers (regulated process)
  - Multiple locations for collections, depending on cell type
  - Large number of clinical stakeholders
- Circular, patient-centric supply chain
- Unique handling requirements for cells, product
- Increased patient safety risk (mix-ups are extremely dangerous)
- "Real-time" nature of supply chain



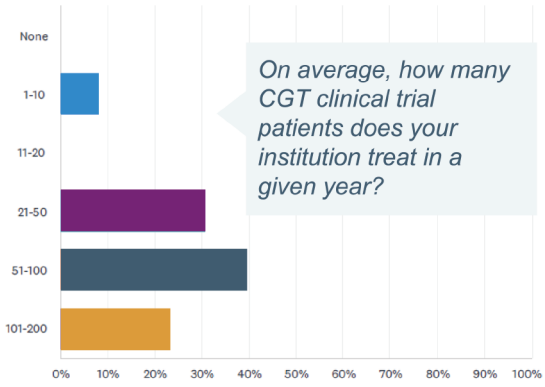
The unique, patient-specific nature of cell and gene therapies introduces a wide variety of new requirements and workflows for Healthcare Providers and sites of care.

FIGURE 2

Growing patient volumes in cell and gene therapy

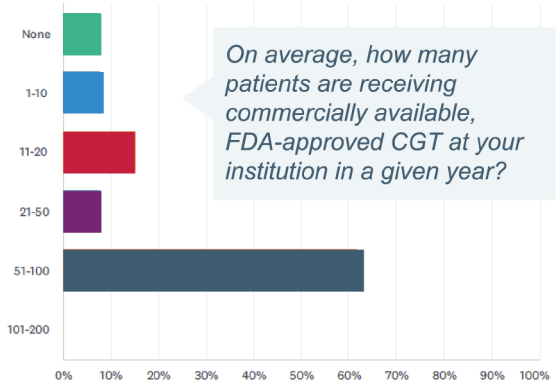
Growth in clinical trials and patient volumes

- 62% of Advisory Council attendees experienced increased clinical trials and patient volumes for clinical trials this year over last year
- Nearly 70% of attendees' institutions treat 20-100 patients per year
- Most support 10-50 clinical trials per year



Growth in patients treated with commercial products

- Five approved products, some with multiple indications
- 62% of attendees are treating 50-100 patients per year
- 77% indicate that patient volumes have increased over last year



Institutions saw growth in the numbers of both clinical trial and commercial patients over the past year [1].

for patients treated with commercial CGTs [1]. This growth has taken place despite the COVID-19 pandemic, which has periodically affected CGT's progress at some medical centers (Figure 3) [4]. However, healthcare professionals have collaborated to find ways to continue their commitment to CGT patients amid the pandemic, with one such consortium stating that the

> "COVID-19 pandemic should not serve as reason to defer CAR T cell therapy for patients truly in need of a potentially curative therapy." [5]

The healthcare professionals attending the advisory council came from a wide variety of roles, specialties, and backgrounds – including physicians, cell pharmacy specialists, apheresis specialists, and program leaders or healthcare technology strategists.

The diversity of roles on the advisory council reflects the realities of CGT care. Healthcare teams serving CGT patients are often sizable and represent a wide variety of skills and specialties – a reflection of the complexity of providing CGT care.

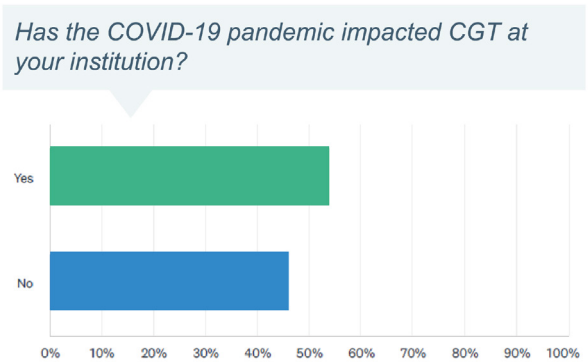
CGT care teams at sites of care can involve dozens of team members. Advisory council attendees described at least 15 specialized roles involved in CGT clinical trials, and at least

FIGURE 3

Effects of COVID-19

COVID affected CGT in 2021, but less than expected

- Institutions adapted quickly
- Clinical trial enrollment was temporarily paused
- Some elective procedures delayed or patients less willing to come on-site for treatment
- Travel restrictions and staff leave played a role



Institutions providing CAR-T cell therapies have worked hard to adapt and serve CGT patients amid the pandemic [1].

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16 involved in CGT commercial products [1]. Roles for both clinical and commercial phases are outlined in the following table (Figure 4).

The clinical and operational complexities of CGT procedures necessitate these large and varied care teams. Some advisory council attendees stated that all the above roles were required to provide CGT patient care at their institutions.

In addition to large-sized teams, the set of professionals involved in key functions can also vary from one hospital to another. Cell shipments, for example, may be handled by one set of specialists at one center and a different set at another – introducing more variability to already complex processes (Figure 5).

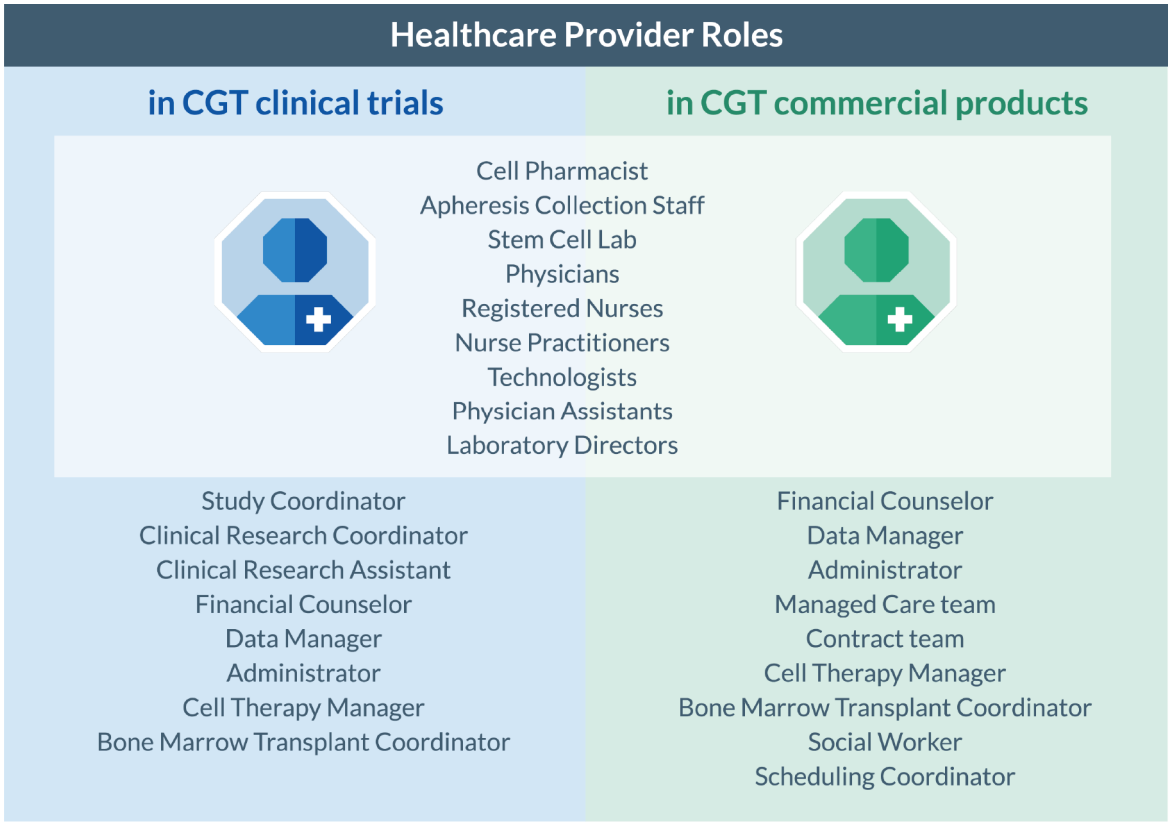
The effects of CGT requirements on HCP staffing (large teams are needed, from a wide variety of specialties), along with the high-touch work that comes with a nascent sector (patient populations that are still relatively small require support from large care teams that are learning as the field develops), have significant implications. Clinical teams must use the correct operational systems, workflows, and processes every time to ensure safe, high-quality care. But ensuring this consistency among many specialists from different backgrounds, all of whom are providing many different CGT treatments to many different patients, can be extremely difficult and time-consuming.

CGT CHALLENGES

The wide variety of specialists providing CGT care is reflective of a wider, fundamental operational challenge facing CGT – excessive variability between products and the processes underlying them. Health care professionals

FIGURE 4

Healthcare Providers in cell and gene therapies



Some roles focus specifically on clinical-phase or commercial products, while others work with CGTs at all phases of development [1].

FIGURE 5

Common tasks, multiple specialists

Schedules the apheresis	Tracks the progress of shipment	Administers CGT Treatments
• Apheresis coordinator, apheresis staff • Nursing coordinator • RN • Donor services • APPs • Apheresis nurse manager • Cell therapy coordinator	• CGT Coordinator • RN coordinator • QA • Physician Assistant • Nursing team • Cell collection/Cell therapy lab • Specialty Lab Director • Lab tech, lab manager • Pharmacists, Admin staff • Nurse coordinator	• Provider/nursing staff • Stem cell lab • Pharmacist • PA/NP with MD support as indicated (if APP not credentialed) • APP or RN • Nurse practitioner • MD • Inpatient nurses, inpatient service (MD, APP, fellow)

From one institution to another, essential CGT operations may be managed by different types of specialists [1].

repeatedly described how the field's supporting operational workflows and technologies, from cell collection protocols to digital portals for product ordering and tracking, often introduce more complexity than they solve. This challenge is largely driven by differences from one product to the next – differences that healthcare professional described as often unnecessary.

Repeatedly, advisory council attendees described working with a confusing jumble of digital and manual systems and processes as they juggled multiple CGT therapies and patients. Some HCP advisors expressed concerns that operational complexity puts patient access at risk. These challenges, they said, threaten to become blockers when CGT products for larger patient populations become widely available. HCPs attending the advisory council spotlighted five specific challenges as the most urgent for providers and patients.

Challenge 1. Workflows & systems that are not standardized for critical steps across the patient journey

These steps include but are not limited to cell collection, cell and product labeling, treatment order placement, and scheduling of cell collections and/or final patient treatments. The process of getting patient to apheresis varies from company to company. Some companies' products are sent out fresh, requiring more coordination of steps such as authorization, case agreements (managed care), hospital review (clearance) prior to collection. Those products that are frozen have more flexibility, but that flexibility puts the institution at risk. For example, an institution may not have a single case agreement executed with the payer. They have to decide whether to continue with collection and recognize that the optics of collection tell everyone that the center is ready to start the episode of care. Complexities in this area alone vary when diving deeper – manufacturing lead times, apheresis/stem cell processing availability, benefits investigation (if needed), pharmaceutical companies varying policies on the collection process (some companies manufacture everything you send, some only use what they need), and the impact to the patient in the event of a failure.

Chain of Identity and Chain of Custody, two required patient- and product-related traceability workflows, are mandated by regulators [6,7] but can be implemented in highly variable ways, HCPs said. To help alleviate

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this tracking burden, some manufacturers have moved towards the use of digital workflow and supply chain orchestration systems, with such digital systems in wider use for commercial products than for clinical-phase therapies. (Figure 6).

However, HCPs described how these digital systems can be of limited assistance if they introduce more variability than they prevent. Some manufacturers choose to implement unique stand-alone systems, which often involve manual processes. Others still rely on paper-based systems, especially for clinical trials, which involve even more manual processes and data entry. Difficulties can quickly arise as care teams try to navigate between multiple systems across multiple therapies and diverse patients, often requiring some mix of digital and manual data entry and management. Duplicate data entry is a common, time-consuming daily task, with HCP teams forced to enter patient and/or treatment data into multiple systems 'all day, every day' [1].

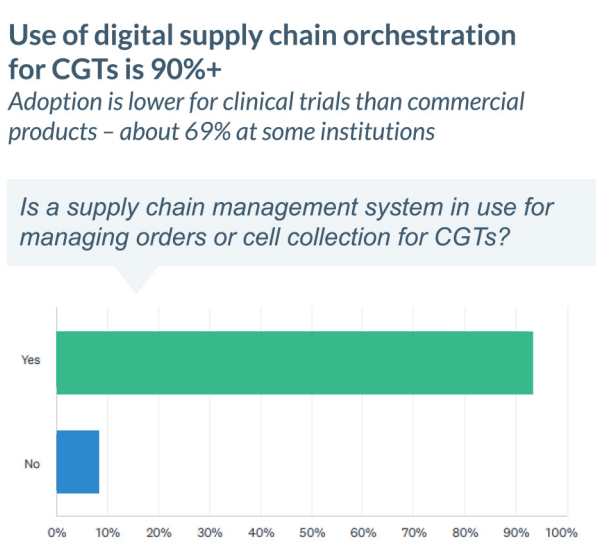
> We have heard of scope creep – you know, the project gets bigger and bigger and bigger. So, portal creep – as every company comes online, there's another portal, right? So sooner or later, that's going to be unsustainable.
>
> *–Vineti Clinical Advisory Council, 2021*

[1]

In addition to an over-proliferation of disparate systems and workflow tools, HCPs said that excessive variability has been introduced for processes and Standard Operating Procedures (SOPs) that should have commonality, such as cell collection. Care teams are forced to navigate between multiple processes that are sometimes only slightly different from one another, they said, which can be worse than managing large differences. Small differences between systems and processes, they said, are harder to remember and track, creating risk for both patients and the institution.

FIGURE 6

Digital supply chain orchestration systems



Digital systems are now widely used, especially for commercial CGTs [1].

Challenge 2. Excessive amounts of uncompensated time lost to numerous system trainings for each individual CGT workflow & repetitive, error-prone manual data entry

Many CGT care teams are inundated with time-consuming administrative tasks. Providers repeatedly described how their days are consumed by trainings for each CGT, along with repetitive processes related to data entry, site qualifications, tutorials, and surveys. As products are commercialized, CGT pharma companies have a site certification process that generally consists of legal reviews, IT work and installations (which often includes a specialized, proprietary CGT management portal), audits of institutional policies/procedures, a REMS program, and more. The site certification process is intense and can take months to complete. Beyond that, there is

ongoing work, including operational changes made by the biopharma company (such as portal upgrades, SOP revisions) that affect the sites of care with ongoing training requirements. However, this step-up in work is not always accompanied by increased staffing or gains in efficiency. Some hospital executives may see CGT as a niche field because of its cost and early commercial nature. This, along with the need to break-even, may make resourcing for CGT a challenge.

> We have to throw people at problems... and [we] have sat in on so many meetings where we have MDs, and pharmacists, and a whole host of other individuals sitting in a room with an Excel file up on the wall, people sorting through their phones, trying to find emails, trying to find confirmation numbers. And it is on a weekly basis, or biweekly, depending where we have all these people together, trying to piece these disparate pieces of information together in order to provide the quality of care that the patients deserve.
>
> *–Vineti Clinical Advisory Council, 2021*

[1]

Different clinical trial manufacturers may use different electronic data collection systems and require data collection that may be onerous for the clinical staff. Many different electronic data collection systems require unnecessary tutorials, participants said. The problem is not only about the complexity of the job, but also all the additional administrative tasks associated with each individual therapy. This represents not only a resource strain, but also often uncompensated time.

As part of commercial site certification, centers have been asked by biopharmaceutical manufacturers to address these administrative activities by identifying an individual designated as an "authorized representative," or AR, who must juggle large amounts of patient-and product-related information, audits, and numerous portals, bearing an increasing burden as the number of CGTs and portals grows. This workload will quickly become unsustainable for those staff members assigned to manage it.

Challenge 3. Clinical staff are overwhelmed by the need to prioritize processes & training over time with patients, resulting in low morale & staff attrition.

HCP staff bear the brunt of CGT variability and operational challenges. With many care teams inundated with time-consuming administrative tasks, time is taken away from patient care and leads to a need to further invest in resources (staff) to be able to deliver care. The high "back office" workload and related stress, HCPs said, can lead to staff turnover, which in turn requires new staff members to be recruited and trained.

> We have an army of people that are trained in navigating other people's systems, rather than focusing on the quality of care for the patient.
>
> *–Vineti Clinical Advisory Council, 2021*

[1]

Many of the advisory council participants described operations-related staffing problems as one of their greatest challenges. Medical centers are bearing an excessive burden and too much risk, providers said, which is an unsustainable model. Not only are staffing needs increased, but members of the care team experience stress, confusion, inefficiency, and burnout, ultimately leading to attrition.

HCPs stressed that they want to help people, not spend time logging tasks or entering the same data into multiple systems manually. Advisory council attendees expressed hope

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that if clinical researchers could be consulted early during study design, there could be alignment between the needs of the company and the institution, which would allow for appropriate scale when a product is commercialized.

> Ultimately it impacts patient experience. Patients deserve full transparency and high-quality care without Herculean efforts to connect data and capabilities.
>
> *–Vineti Clinical Advisory Council, 2021*

[1]

Challenge 4. IT & cybersecurity vulnerabilities related to the proliferation of too many portals and digital systems.

Hospitals and healthcare organizations already face daunting cybersecurity requirements and challenges. Patient data and PHI are protected by regulations such as the Health Insurance Portability and Accountability Act (HIPAA) [8] in the U.S. and the General Data Protection Regulation (GDPR) in the EU [9]. In addition, hospitals and sites of care working in CGT must often comply with Good Manufacturing Practices (GMP) regulations, and related rules governing electronic systems such as Title 21 CFR Part 11 and Annex 11 [10].

Such requirements are meant to protect a sector based on sensitive, high-value personal health information and facing frequent security threats. The FBI, Homeland Security, Dept of Health and Human Services warned hospitals of an increased and imminent threat from hackers in the last year [11]. Pharma and biotech companies suffer more data breaches than those in any other industry, with 53% of them resulting from malicious activity [12] .

> ...from a probability standpoint, you're statistically increasing the risk of vulnerability with each and every portal that you have to deal with more and more and more.
>
> *–Vineti Clinical Advisory Council, 2021*

[1]

In this environment of already-heightened risk, the proliferation of CGT systems and manufacturer portals becomes even more overwhelming for sites of care. Healthcare professionals said there is an increase in cybersecurity risk and vulnerabilities with each portal that is used – too many people accessing data, requiring user IDs, and requiring training, all of which puts digital systems at greater risk of an access break and puts patient information safety at risk. In addition, varied processes of requesting access to a biopharmaceutical company's portal, along with the management of staff who have access (which is typically left to those who may not understand the risks associated with portal access), increases the likelihood that a potential breach will occur.

> (For) every therapy that comes to market, we go through another training of portals, another cost, and another IT risk assessment. So these things just continue to subtly creep upwards. And they are going to be rate-limiting steps in Centers' ability to offer CGTs.
>
> *–Vineti Clinical Advisory Council, 2021*

[1]

Challenge 5. Excessive operational variability & training requirements for CGT clinical trials that require large amounts of staff training and 'back office' time but ultimately enroll only a limited number of patients per clinical site

Given the nascent nature of CGTs, most products are still clinical phase. And, HCPs said, early science is often accompanied by early, unproven, unwieldy operational approaches.

Providers described clinical-phase CGTs as inherently more difficult to implement because they are sponsor-dependent, and their systems are still often paper or are email-based. They said that some small biotech sponsors may also make the process more complex than necessary out of lack of experience with CGT products. Effective coordination and operations often require significant manual intervention by disparate care teams and departments.

[1]

Overall, HCPs stated that for clinical studies, the time and resource investments upfront often take a heavy toll on staff – and ultimately may enroll only a few patients. If not resolved during clinical phase, these complexities can extend through to commercial, putting an institution's ability to continue offering the therapy at risk if the long-term investment proves to be unsustainable. A more standardized approach to clinical trial workflows and processes would go a long way towards making CGT studies tenable – and making commercialized products viable in the long run.

Across the board, HCPs shared that these operational challenges in CGT trigger a wide range of unintended negative outcomes across sites of care:

- Patient experience is reduced due to the care team's ongoing need to prioritize "back office" tasks over spending time at the bedside. Patient access may be reduced if operational complexity makes it too difficult or too costly for institutions to treat more CGT patients.
- Staffing needs are increased when operational complexity, manual data entry requirements, and IT concerns require attention from more healthcare professionals for each patient and product. At the same time, biopharmaceutical manufacturers are recruiting experienced CGT staff from sites of care, adding further pressure to staffing concerns.
- HCPs experience stress, confusion, inefficiency, and an excessive amount of repetitive administrative work, leading to burnout and driving up attrition.
- The transition from clinical phase to commercial is more difficult when one set of research-phase complexities must be replaced by an entirely new set of different but even more complex commercial processes.
- Scaling CGTs to more patients can be limited by operational complexity and administrative costs. Larger institutions are currently better able to recruit greater numbers of patients, but also must choose which clinical trials and commercial products make the best use of staff time and resources. Smaller centers may not have the resources to manage complex

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CGT workflows for larger numbers of patients.

- As a result, development of new therapies and overall sector growth may be hampered. Institutions may be limited in the number of therapies that can be administered. Adoption and participation in clinical trials may be reduced due to the difficulties of running CGT trials.
- To reduce variability and control costs, centers will select what therapies are on formulary, which has the potential to limit access to patients **(Figure 7)**.

Sector growth may be especially challenging in oncology as CGT moves from autologous blood cancer products to other approaches that have the potential to treat greater numbers of patients, such as allogeneic products and products intended to treat solid tumors. Solid tumor CGT products, for example, often have very complex starting material collections, are more likely to require multiple dosing, and the patient populations for some solid tumor indications are larger than seen in blood cancers.

CGT SOLUTIONS

Organizations working towards standards and solutions

- Association for the Advancement of Blood and Biotherapies (AABB)
- The American Society for Transplantation and Cellular Therapy (ASTCT)
- The Standards Coordinating Body for Regenerative Medicine (SCB)

HCPs are keenly aware of the unique requirements of CGTs and have no expectations that all complexity can be removed. It is also important to note that this particular advisory council session brought clinical leaders together to surface challenges occurring across institutions, with subsequent sessions to focus more deeply on specific solutions. However, the discussions of challenges also

FIGURE 7

Summary – key challenges

Challenges with current systems

- Complex web of systems - multiple systems and portals in use for a single patient/product journey and each therapy
- Mixed manual and digital systems increase errors and require duplicate entry
- Systems are not integrated and interoperable
- No transparency and real-time visibility
- Security and data privacy risks

- Rely heavily on dedicated staff and person-to-person communication
- Clinical trials use paper and email-based systems and processes
- Ease of use varies from system to system

Operational challenges

- Lack of standardized processes, requirements, and systems across therapies/trials
- Capacity and scheduling availability/constraints for each step
- Tracking and accessing COI and COC from "vein-to-vein"
- Clinical to commercial transition requires process changes
- Range and number of highly trained HCP personnel required to treat CGT patients
- Roles and touch points - 100s of them - vary across treatments and institutions
- Scaling complex inefficient systems is difficult and expensive
- Clinical trials require specialized staff, more documentation, redundant audits, and rely on inexperienced stakeholders

Top challenges in CGT, as identified by healthcare professionals.

yielded a set of specific improvements that would make the CGT field more sustainable for sites of care. Here are five of the advisors' top recommendations.

- **Standardize workflows and digital systems.** Harmonize processes, systems, and SOPs wherever possible. Connect disparate digital systems to reduce manual data entry and duplicative record-keeping. Key areas recommended for standardization and harmonization are listed in the table below. **(Box 1)**

- **Simplify the clinical phase, and plan for commercial early.** Many HCPs said that clinical trial operations are not sufficiently streamlined to make most studies efficient or enable a smooth transition to the commercial phase. Providers hope to see process improvements embedded in early-phase trials so that scaling is simpler, and they encouraged clinical-phase manufacturers to connect with HCPs and build solutions proactively before challenges arise. Centers that participate in CGT clinical studies would also benefit from being able to start the trial assessment earlier, which would simplify site certification requirements more quickly. Without such changes, they said, centers may start declining to participate in a greater number of trials.

> Get to the manufacturers early in their processes during development and remind them that eventually, if they want to scale up and scale out that they're going to have to work in a standardized ecosystem.
>
> *–Vineti Clinical Advisory Council, 2021*

[1]

- **Root out and eliminate small differences.** HCPs repeatedly said that in many cases, small operational distinctions between systems, tools, and products are harder to monitor and may, in some cases, present greater risks to both treatment viability and patient outcomes.

> If it is the same, keep the same. If it can be the same, keep the same. If it is similar, we have a tendency to overlook it. And if it is different, it should be wildly different. It should be able to be identified… Whatever needs to be different needs to be different and explained for us to really appreciate that.
>
> *–Vineti Clinical Advisory Council, 2021*

[1]

BOX 1

Summary – top solutions

- Common key processes should be standardized. These include order placement for CGT treatments, chain of identity, chain of custody, in-process cell and product labelling, and apheresis-based cell collection.
- All manufacturer portals are currently separate from and redundant with the EMR. Integrate CGT systems with EMRs.
- The system landscape is complex and disparate. Information does not flow consistently, requiring significant manual intervention and data entry. Integrate CGT data with a variety of 'back office' hospital workflow, including payor approval, conversion to IRB, and billing.
- Standardize data entry portals, data entry SOPs, audits, and regulatory oversight.
- Create one system that manages clinical processes, no matter if the product is commercial or part of a clinical trial. Portals are not the way to move forward. Each company trains institutions as part of their site certification process – it would be easier if adding portals were more 'plug and play'.

Important solutions to make CGTs sustainable for sites of care, as identified by healthcare professionals.

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- **Reduce costly, demoralizing "back office" demands on providers and staff.** Creating standards, reducing training needs, reducing manual processes and duplicative data entry, and simplifying digital systems will go a long way towards improving HCP morale and opening up more time for patients. If manufacturers aren't willing to make these changes, they should help cover the administrative and staffing costs of CGT, some healthcare professionals said.

- **Solve CGT challenges proactively for allogeneic and solid tumor products.** In the CGTs that are already relatively established, such as the CAR-T products for lymphoma, some HCPs said that solving so many operational challenges this far along in the development of the field feels overwhelming. In less established indications, however, the time to standardize, harmonize, and simplify is now. This is especially important in solid tumor indications, which are often multi-dose treatments with especially complex cell collections and larger patient populations.

CONCLUSION

Healthcare Providers in cell and gene therapies are dedicated to the success of the field and the patients they serve. But for their commitment to yield even greater results over time, urgent action is required on the part of the entire sector.

Systems, workflows, and processes must be standardized and harmonized wherever possible. Disparate systems must be integrated to reduce duplicative manual data entry and the risk of error. Clinical trials should start with eventual commercial processes in mind, and not try to differentiate unnecessarily on workflows and SOPs. Such changes begin now, in advance of allogeneic CGT treatments, products for solid tumor indications, and other approaches for larger patient populations.

Above all, Healthcare Providers should be treated as up-front design partners in the development of CGT systems and workflows. They are working with multiple therapies and diverse group of patients every day. Their perspectives will prevent problems early and allow the entire field of cell and gene therapies to scale and reach more patients.

> Instead of asking 200 transplant centers to conform, maybe these companies can join hands together... and start to standardize and harmonize amongst themselves.
>
> —*Vineti Clinical Advisory Council, 2021*

[1]

As a starting point, we encourage the sector to join the work of key organizations working to create sustainable systems for CGT. Here are three places to start:

- The American Society for Transplantation and Cellular Therapy is conducting an "80/20 Taskforce" to address the roughly 80 percent of operational requests from biopharmaceutical manufacturers that ASTCT members find to be duplicative.

- The FDA-funded work of the independent, non-profit Standards Coordinating Body includes multiple cross-sector standards advancement projects in areas of importance to Healthcare Providers and sites of care, including cell collection, Chain of Identity, and patient data management. Please consider connecting with the SCB and lending your expertise to an SCB working group.

- The Association for the Advancement of Blood and Biotherapies offers multiple resources and workstreams to streamline

the working relationships between HCPs and biopharmaceutical researchers and manufacturers. Learn more at AABB's Biotherapies resources hub.

The successful adoption of cell and gene therapies into mainstream medicine requires ongoing collaboration with healthcare professionals and sites of care. By surfacing challenges across institutions providing CGT care, we hope to encourage the development of new solutions that will ultimately create more patient access to this transformative field of medical science.

BIOGRAPHIES

JOE DEPINTO brings more than 28 years of executive leadership in biotech, pharmaceuticals, specialty pharma, and cell therapy to Vineti. He joins us from Cardinal Health, where he served as the President of Specialty Solutions, leading one of the fastest-growing businesses within the Fortune 14-ranked company. Prior to Cardinal Health, Joe's roles included leadership positions at top pharmaceutical companies, including Johnson & Johnson and Lilly. His core leadership competencies include leading all aspects of strategy, drug development, investor relations, and commercialization with multiple global launches. He also previously served in executive roles at Sunesis Pharmaceuticals, Dendreon, ImClone, and Abraxis.

ROBERT 'ROBB' RICHARDS has over 20 years of experience in oncology, initially with a private practice in Southern New Jersey, and more recently the University of Pennsylvania Health System. He comes to Penn after serving as the IT Manager for the Center for Cancer and Hematologic Disease in Cherry Hill, Regional Cancer Care Associates (RCCA) in New Jersey, Division Chief Operating Officer, and RCCA corporate VP and Chief Information Officer. He has provided oversight in the integration of the South Jersey medical oncologists onboarding to Penn Medicine while working with the Cell Therapy and Transplant program (CTT) and has been the lead in overseeing operationalizing/implementation of CAR-T cell therapy for commercial use. He is currently the Administrative Director of the Cell Therapy and Transplant program at Penn Medicine, with oversight of both commercial and research work, and its expansion in the Penn system. Robb received his BS from Drexel University and both his MS and MBA at St Joseph's University and specializes in oncology informatics.

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AUTHORSHIP & CONFLICT OF INTEREST

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