The Biospecimen Management Crisis at Sites and Beyond: Unraveling the Hidden Complexities of Oncology Clinical Trials

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The views expressed within this paper are those of the individual authors and the Biospecimen Management Consortium (BMC) and do not reflect the views of the affiliated institutions. The institutions listed below are current members of the BMC.

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Abstract

Introduction

With an increase in clinical trial complexity, biospecimen management has become more challenging than ever before. Increased complexities combined with a lack of efficient systems generate waste with financial and ecological impact. The burden of appropriate specimen management at the site level is becoming increasingly unsustainable as acuity and regulations collide.

Materials and Methods

A site survey was distributed to AACI-affiliated institutions in June of 2025. Questions focused on site operations and biospecimen management aimed to address key challenges and priorities.

Results

Of 92 AACI-participating Cancer Centers, 50 responded to the electronic survey between June 23, 2025 through July 15, 2025. Common challenges were identified across participating sites. Highest priority issues for sites included discrepancies between protocol and lab manual documents, tight processing windows, lab-related queries, and kit management.

Conclusions

The excessive waste of time, money and resources related to clinical research biospecimen management demand immediate action. Sponsors, central lab vendors and clinical research sites are all operating in a vacuum, often trying to solve the same problems by creating stop-gap, non-standardized and paper-based solutions, ultimately

wasting precious time, resources and money. Immediate recommendations for best practice by sponsors and central labs include developing study tools that sites can use for specimen management. Sponsors and central labs should develop flexible kit designs and supply streams that don't overburden sites or generate unnecessary waste. Protocol documents and lab manuals must be aligned before they're provided to sites. Most importantly the patient experience must be considered when designing clinical trials, especially the cadence and complexity of specimen collections. Stakeholder alignment across the biospecimen ecosystem is essential to ensure appropriate, responsible, sustainable and efficient operations that serve our patients rather than burden them.

Introduction

Biospecimen management plays a vital role in the advancement of medical research, drug development, and precision medicine, especially in oncology clinical trials. However, managing biospecimens effectively presents numerous challenges, from storage and logistics to ethical considerations. The complexities and challenges within biospecimen management at clinical research sites highlight an urgent need for change with wider collaboration across the clinical research enterprise before the conduct of clinical trials becomes unsustainable.

The acuity of oncology clinical trials, especially in the setting of precision medicine, is scaling to new levels, becoming increasingly more challenging to operationalize efficiently at research sites[1,4]. The complexity of some Phase III clinical trials rises to the same level of intensity of early Phase I oncology clinical trials with significant impact to site resources. Oncology clinical trial patients are often required to stay for hours after the completion of their treatments, potentially overnight, in order to complete the expected biospecimen collections. These added late and overnight requirements strain the already overtaxed hospital systems, placing increased demands on site staff, hospital nursing, research laboratories, and ultimately the patients to accommodate these off-hours requirements. Community hospitals or smaller healthcare settings may be disproportionately impacted and excluded from participating in many new trials because of the increased site burden and lack of robust resources.

As sites struggle to support the increasing requirements with rising trial complexity, the documents and supplies sent to sites to support the respective clinical trials often lack congruency, containing conflicting information or ambiguity that translates to lost efficiency, increased noncompliance, and overall fiscal impact to sponsors and sites alike. During the conduct of a clinical trial, industry sponsors will provide sites with the study protocol, a corresponding laboratory manual and study-specific kits that contain the necessary supplies for biospecimen collection processing and shipments. While protocol

documents will outline the expected collections associated with a clinical trial, the details for the collections regarding supplies, set up, processing, storage and shipment, are outlined separately in a laboratory manual or flow chart, often generated by an external vendor, contracted by the study sponsors. Frequently, the laboratory manuals and flow charts do not match the details found in the protocol, including tube type, collection timing, cohort, and other important collection details. Additionally, these supplemental laboratory documents are not updated in a timely manner when protocol amendments are released. This discordance often translates to undue hardship for the clinical research sites who are then required to reconcile differences to support the patients they have on study[3].

In addition to the protocol and laboratory manual documents supplied to sites, sponsors will also supply sites with study-specific lab kits. However, central labs lack a cost-effective flexible kit configuration that can be rapidly implemented for different cohorts or amendment-driven changes, leading to confusion in the biospecimen collections and increasing the risk of protocol non-compliance. When shipping kit supplies to sites, sponsors and vendors often may disregard the sheer volume and types of supplies shipped, causing undue burden on the sites to reconcile, store or discard the supplies[2,4]. When sites cannot utilize or store the supplies due to the large quantity provided, they are forced to discard excess supplies, generating costly fiscal and environmental waste. The quantity and consistency of supplies discarded can generate financial losses ranging from $50,000 to $200,000 per study for sponsors with substantial ecological impact.

With the challenges associated with protocol complexity, lengthy hours to support research collections, continued changes with protocol amendments, and a broken supply system, sites are forced to create study-specific tools to fill the gaps presented to them with each study that opens. There has been a longstanding and increasing expectation placed on sites to solve operational problems that are not within their control, which places unfair responsibility on site Principal Investigators (PIs) to maintain oversight and avoid noncompliance that is seemingly impossible with the current structure.

To address the challenges identified, the Biospecimen Management Consortium (BMC) was formed in June of 2024 as an independent, non-profit organization. The BMC strategically addresses persistent challenges in biospecimen management, including the lack of best practices, standardization and quantifiable data across the clinical trial ecosystem. In recognition of the fact that one stakeholder alone cannot solve these challenges, the BMC includes broad membership from key stakeholders in the biospecimen management enterprise, including clinical trials sponsors, clinical research

sites, and research vendors. To help define the problem, the BMC launched a site survey and has developed key recommendations as possible solutions.

Materials and Methods

To capture the challenges of biospecimen management at the site level, members of the BMC created an electronic 16-question survey through a secure Microsoft Forms SharePoint link. Survey questions focused on site and lab structure at individual sites, patient and study volume, and current challenges experienced at each site related to biospecimen management. A QR code was distributed to American Academy of Cancer Institutes (AACI)-affiliated Cancer Centers at the AACI-CRI annual meeting in June of 2025 and then disseminated via email to participating sites following the annual meeting.

Survey questions included the following:

- Does your site have a dedicated clinical research laboratory?
- What is your clinical research laboratory model?
- Who is responsible for sample processing at your site?
- Does your site create internal study-specific tools to manage sample collections (e.g. lab templates)?
    - If "Yes" to the above, what are you utilizing these tools for?
- Approximately how much time does your site spend responding to biospecimen-related queries weekly?
- What information do you need from sponsors before specimen collection?
- What information from sponsors do you need after samples have been shipped?
    - If other to the above, please specify
- Approximately what percentage of kits does your site waste per month?
- Would you prefer the option to customize supply kits (e.g. opt out of needles, etc.)?
- How would you prefer items such as needles, vacutainers, shippers, tissue processing reagents (e.g. formalin) to be provided?
- Is your site allowed to utilize pre-paid airway bills?
- Please rate the items below in order of importance at your site, 1-5 with 1 being most important requiring immediate intervention. List 0 for any items that are not an issue for your site
    - Kit management/waste
    - Study-specific tools for sample management
    - Discrepancies between protocols and lab manuals
    - Sample Tracking and Chain Custody
    - Sample Requisitions (electronic vs paper vs other)

- Sample storage (space limitations)
- Shipping Restrictions
- Processing Windows too tight (ie. Within 15min of collection)
- Access to too many portals for tracking and management
- Other issue not listed
    - If unlisted, specify

Results

Of 92 AACI-participating Cancer Centers, 50 responded to the electronic survey between June 23, 2025, through July 15, 2025. The majority of responding sites (86%) indicated that they had their own dedicated clinical research laboratory to support the clinical research collections within their Cancer Centers. Common challenges were identified across participating sites including the need for study-specific tools, better kit inventory management and collaboration with sponsors, excessive time associated with laboratory query resolution, and clarity needed from sponsors regarding operational considerations prior to study activation.

To support the increasing complexity of the clinical trials opening at sites, 80% of respondents indicated that they are creating their own internal study-specific tools to manage study collections. These tools may include study templates to aid with processing instructions to simplify point-of-collection processing for the laboratory technicians, kit inventory management tools, and internally- developed chain of custody documents. Additionally, response time to laboratory-related queries weekly was surveyed. While 66% of responding sites indicated that time was variable for entry, 30% indicated that they spent two hours or more weekly resolving these queries.

From an operations perspective, respondents were asked to comment on challenges associated with sponsor communications, specifically what information was needed from sponsors prior to specimen collection. A close distribution of accurate processing windows (29%), sample stability (25%), courier selection (25%), and substitution options (22%) were selected. Additionally, sites indicated that they need more information related to confirmation of receipt (57%) and confirmation of sample integrity (32%) after samples are shipped from the sites to a central laboratory.

Sponsor-provided study kit waste was evaluated with 22 sites indicating more than 30% of their kits were destroyed monthly. Twelve sites did not track kit waste at all. Additional challenges related to sponsor-provided study kits included the lack of kit customization based on site needs with 94% of respondents indicating that they'd prefer the option to customize kit supplies and opt out of unnecessary supplies, like needles. Furthermore,

66% of sites indicated that they'd prefer to receive specialized items in bulk supply based on their individual needs to reduce overall waste.

Finally, sites were asked to rank items in order of importance. The top three issues selected as the most important included discrepancies between protocols and lab manuals (70%), processing windows too tight (46%), and kit management/waste (42%), respectively.

Discussion

Common challenges such as the need for study-specific tools, efficient and effective kit inventory management, collaboration with sponsors, excessive time required for laboratory query resolution, and clarity needed from sponsors regarding operational considerations prior to study activation were highlighted in the AACI-CRI site survey that was distributed to participating Cancer Centers in June of 2025.

Study-specific tools were highlighted on the site survey and noted that the vast majority of participating sites (80%) create their own study tools to fill a gap in provided materials. Sponsor-provided laboratory manuals and study protocols are often vague, may contain conflicting information, and don't present information in a way that is operationally feasible for site staff to efficiently and compliantly process samples once they are received, especially as amendments are released. As a result, sites are often forced to consolidate information from the protocol and laboratory documents into a tool that site staff can use when processing samples. Even then, sites are still responsible for filling gaps in provided documents to ensure that samples can be appropriately handled per protocol requirements. This translates to additional staff time, the potential for increased study delays, and risk to data and sample integrity if the sites don't catch gaps in provided sponsor materials[4].

The lack of usable materials provided to sites highlights a costly and broken system, where 80% of respondents (40 sites) are creating their own tools. If 40 sites are generating these tools for the same study across the country, sponsors will be charged for the same effort to make the same tool 40 times. This wasted effort drives up clinical trial costs. Site Principal Investigators (PIs) are responsible for the accurate and compliant usage of specimens, inclusive of their processing and data. However, sites consistently do not receive what is needed to generate accurate, reliable sample-driven data. More efficiently, sponsors could elect to create flexible study-specific tools to meet the needs of sponsors, sites and vendors alike.

Additionally, sites highlighted the need for better, well controlled study kit management to avoid excessive waste. Specifically, 22 sites indicated more than 30% of their kits were destroyed monthly. Sites are generally unable to customize kit needs, which results in

unnecessary waste once kits are received at the site level. Similarly, sites often receive more kits than they can use or receive the wrong types of kits that must then be discarded. For example, sites may not be able to use laboratory kit needles, but sponsors and lab vendors send these supplies regardless of site preferences or limitations. The extra needles received at the site must be sorted out of individually boxed kits and discarded in a secure manner, separate from normal trash. This additional and time-consuming process results in wasted effort at the site that requires staff to filter through each of the received kits, throwing away supplies as soon as they are received. Since the waste generated from unusable kits is often not suitable for routine trash, sites are often required to pay an additional fee for safe removal of sharps (needles or glass slides) or other chemical-based supplies. In this example, sites are throwing sponsor dollars away due to a lack of awareness, communication and inflexible systems, further driving up clinical trial costs and wasting precious resources at participating sites.

Data from the survey also highlighted the resources needed from sites to resolve lab-related queries. Queries are often received through multiple portals, faxes, or emails, highlighting an inefficient system that absorbs site resources, limiting the effort that can be used to process samples and contribute to clinical trial data. Of participating centers, 30% of respondents indicated that their site(s) spend at least 2 hours each week resolving lab queries. Many of the queries generated are automated, irrelevant queries that have no meaningful impact on data, and are dispersed across antiquated systems. To protect resources and ensure efficient operations, effective solutions must be explored.

A need for sponsor collaboration was highlighted in several responses throughout the survey, with respondents calling almost equitable attention to accurate processing windows, sample stability, courier selection and substitution options. Oftentimes, sites must utilize the limited trial resources provided when patients are enrolling to clinical trials, filling gaps internally when resources are not made available. Lab manuals often conflict with protocol documents, lab kits don't contain the correct supplies, or the lab manual is outdated because of a protocol amendment with the site left to figure out how to collect, process and/or ship specimens on a new IRB approved document with no supporting information, supplies, or tools available at the time of implementation.

Additionally, tight processing windows established by central laboratory vendors or study sponsors are often so strict that they are not feasible in many clinics, certainly not in many community hospital settings. Strict processing windows (e.g. "must process within 10 minutes of collection") may prohibit feasibility at many sites and non-academic medical centers that don't have access to the same resources. Additionally, samples that require late-night or around-the-clock collections may also prohibit participation at sites

unaffiliated with inpatient hospitals, thereby impacting enrollment, diversity, and large-scale data extrapolation. Patients who would otherwise be willing to participate in clinical trials are thereby excluded because of operational challenges associated with their treatment center. Sponsors must be encouraged to allow for substitution options, increase sample stability and expand processing windows to allow for feasible options and wider flexibility in order to increase efficiencies and expand enrollment potential, including enrollment to community sites and the underrepresented populations they serve.

Increased communication, transparency and planning with sponsor partners is essential in a path forward. Currently, sites receive little feedback regarding the samples that are sent to central labs. Respondents noted that confirmation of receipt and sample integrity are necessary when sending samples to sponsors and central laboratories, yet sites receive little to no confirmation when patient samples are received centrally.

A recurring theme in this survey highlighted systems that work for industry sponsors but not for clinical research sites. With the implementation of ICH E6(R3), sponsors are told they "should not place unnecessary burden on participants and investigators[5]," which positions sites uniquely and urges a paradigm shift. It is considered the sponsor's responsibility to ensure sites have the capabilities that are needed to support a trial efficiently, compliantly and effectively, which stems from providing accurate and timely protocol documents, including those that impact sample collections. Sites are unnecessarily burdened every time an amendment is IRB approved without an updated lab manual, or any corresponding laboratory kits. Sites are additionally burdened when the laboratory manual, provided laboratory kits and IRB approved protocol documents do not match. Participants are burdened when labs must be repeated because a sponsor-provided document was wrong, or a tube wasn't provided in the laboratory kit. Participants are further burdened when they are hospitalized for a mid-night collection that is ultimately wasted because the processing instructions were incorrect.

A paradigm shift is needed to move biospecimen management to an essential component in the design and execution of clinical trials, treating it as importantly as the data it generates. Furthermore, ICH E6(R3) now explicitly considers biospecimens and their metadata to be part of essential trial records, therefore requiring robust data tracking and traceability, and treating them as we would treat any other trial data. A sustainable solution must be explored for all stakeholders – one that includes research sites and their participants, not just industry partners.

Conclusions and Recommendations

The results of the site survey were not surprising and bring to the forefront the excessive waste of time, money and resources related to clinical research biospecimen management demand immediate action and reform. While the survey results are limited to oncology-focused, AACI-affiliated institutions in the United States, a broader site-focused survey is warranted globally across additional disease groups. Special attention in a follow-up survey should be given to community research sites to determine the impact and potential exclusion of community sites and underrepresented populations because of challenges related to biospecimen management.

The issues highlighted in the survey may benefit from several strategic solutions. Guidance is needed regarding best practices for sample documentation practices, inclusive of chain of custody and processing requirements. While ICH E6(R3) has taken the step to include biospecimens as essential trial records, guidance is limited as to what metadata should consistently be captured and for which biospecimens (e.g., biospecimens supporting primary or secondary endpoints, vs. those used for exploratory testing). In addition, Sponsors should be encouraged to provide flexible study tools that can be used at the sites to support collections and processing. As noted in the survey data, 40 sites reported creating their own study tools; if sites repeat this for every trial they have open for the same study at different institutions, sponsors are being charged for the same site effort, used to make the same tools forty-times. This effort is a waste of resources that can drive up clinical trial costs and should be addressed by sponsors during trial design.

Another potential solution to improve clinical trial costs includes collaboration and communication between sponsors and sites to develop sustainable, flexible laboratory kit supply plans. This includes adjusting included supplies when needed to avoid shipping unnecessary supplies that will be wasted. Additionally, other study materials provided to sites must be aligned, inclusive of timely laboratory manual updates when protocol amendments are received. To tackle this issue, sponsors are encouraged to incorporate laboratory information in the updated protocol documents to ensure new and necessary information related to sample collections is received at the time a new protocol amendment is implemented.

Laboratory-focused portals have become an ongoing challenge for sites to navigate as a single study may have multiple portals associated with data entry, lab query resolution, sample logging, chain of custody, shipment generation, and kit ordering. These misaligned systems waste site resources and cause inefficiencies. Sponsors are encouraged to limit the number of portals needed for a single study and create sustainable, simple options to ensure compliance. To reduce the burden of long-term sample storage at research sites, sponsors are also encouraged to allow immediate shipping of samples, in lieu of storing at

the site, although immediate shipment may drive up costs and impact environmental sustainability. In addition to saving precious space at the site level, it is also important that sites receive confirmation about sample integrity in a timely manner. Additionally, sponsors should work with vendors to ensure increased sample stability, allowing for more flexible processing windows to increase feasibility across research sites and reducing compliance errors. The feasibility of biospecimen collections and associated processing windows must be considered when designing research protocols and their corresponding instructional documents.

Arguably most importantly, sponsors are also encouraged to consider the participant's experience when developing protocols, especially when considering the research collections needed. Sponsors should reduce and eliminate, where possible, extraneous sample collections for participants, inclusive of mid-night collections. Time is precious, and particularly important for oncology trial participants.

To address the challenges noted in the site survey and work toward a sustainable future, the BMC has outlined a multi-year strategy and partnered with key stakeholders at academic research sites, biopharmaceutical and medical device companies, and laboratory and technology vendors The BMC aims to codify and publish cross-ecosystem best practices, develop a shared biospecimen data model and interoperability guidelines, elevate regulatory awareness and harmonized interpretations, and drive adoption through community building, membership growth and measurable awareness of biospecimen management.

The issues highlighted in this survey speak to deep rooted challenges in the current clinical research biospecimen management ecosystem. Sponsors, central lab vendors and clinical research sites are all operating in a vacuum, trying to solve the same problems, and ultimately wasting precious time, resources and money. Ultimately, the solution is not to work independently, but to bring stakeholders together for a complete biospecimen reform. There is no more time or money to waste – there are patients waiting.

Acknowledgements

We'd like to thank the AACI participating sites in providing valuable feedback for this paper. Additionally, we'd like to acknowledge the members of the BMC who supported the creation of this survey and the ongoing mission of improving biospecimen management.

References:

1. J. Voyten, M.P. Holtzman, L. Pantanowitz, R. Dhir, H.S. Beasley, J. Cuda, S.E. Monaco Lessons learned from clinical trial queries on small biopsy collections: importance of rapid on-site evaluation. J. Am. Soc. Cytopathol., 9 (5) (2020 Sep-Oct), pp. 461-468, 10.1016/j.jasc.2020.04.012. Epub 2020 May 6. Review. PubMed PMID: 32499137
2. J. Voyten, J. Urban, & M. Horak. (2023, June 26-28). Descending the Apex of the Slippery Slope of Kit Management [Poster Presentation]. AACI CRI 2023 (abstract 110) Rosemont, IL, USA. https://www.aaci-cancer.org/Files/Admin/CRI/2023%2DAbstracts%2Dand%2DPosters.pdf p236-237
3. J. Voyten, A. Yant. M Horak. (2025, June 26-28). Papers & Spreadsheets & Calls, Oh My!: Where Sample Data Falls Through the Cracks AACI CRI 2025 (abstract 121) Rosemont, IL, USA. https://www.aaci-cancer.org/Files/Admin/CRI/2025/121%2DPoster%2DPapers%2Dand%2DSpreadsheets%2Dand%2DCalls%2DOh%2DMy%2DWhere%2DSample%2DData%2DFalls%2DThrough%2Dthe%2DCracks.pdf
4. J. Voyten, A. Yant, J. Urban, M. Horak, T. Cummings, Correlative complexity: Insights into correlative management at a large academic cancer center. Contemporary Clinical Trials, Volume 153, 2025, 107917, ISSN 1551-7144, https://doi.org/10.1016/j.cct.2025.107917 (https://www.sciencedirect.com/science/article/pii/S1551714425001119)
5. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. (2025, January 6). ICH harmonised guideline for good clinical practice (E6[R3]): Step 4 final guideline. https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf