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Biospecimen Collection and Handling in Clinical Trials: Integrating Nursing, Laboratory, Pharmacy, and Health Security Perspectives

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Abstract

Background: Biospecimen integrity is fundamental to the validity of clinical trial results, yet the complexity of modern protocols requires seamless multidisciplinary coordination. Pre-analytical variables introduced during collection, processing, and handling can compromise specimen quality and research outcomes. **Aim:** This narrative review synthesizes evidence-based best practices for biospecimen management in clinical trials, examining the integrated roles of nursing, laboratory personnel, pharmacy, and health security professionals in maintaining specimen integrity. **Methods:** A comprehensive literature search was conducted across PubMed, Scopus, and clinical research databases for peer-reviewed articles published between 2010 and 2024, supplemented by regulatory guidance documents and industry best practice recommendations. **Results:** Five key determinants of biospecimen quality are identified: (1) standardized collection protocols with comprehensive training; (2) timely pharmacokinetic sampling with coordination between pharmacy and nursing; (3) laboratory processing factors such as cold ischemia time; (4) proper documentation and temperature-controlled logistics; and (5) adherence to evolving regulatory standards like ICH E6(R3). The BEACH trial illustrates effective multidisciplinary integration through continuous research team availability and structured nursing education. **Conclusion:** Optimal biospecimen management requires systematic integration of multidisciplinary perspectives from protocol design through sample disposition. Institutions must invest in training infrastructure, technology-enabled tracking systems, and risk-based quality management approaches to ensure research validity and regulatory compliance.

Keywords: biospecimen integrity; clinical trial operations; multidisciplinary coordination; pre-analytical variables; chain of custody.

Introduction

The integrity of biospecimens collected during clinical trials constitutes the foundation upon which research validity rests. Biological samples—ranging from blood and tissue to urine and cerebrospinal fluid—serve as the primary material for evaluating pharmacokinetic parameters, pharmacodynamic responses, biomarker expression, and safety endpoints that determine whether investigational products progress through the development pipeline or fail to demonstrate efficacy (Botturi et al., 2020; Xie et al., 2024). Yet the path from patient to laboratory is fraught with potential sources of error, many of which originate not in the analytical phase but in the pre-analytical processes of collection, handling, processing, and storage (Ammerlaan et al., 2018).

The complexity of modern clinical trials has intensified the challenges associated with biospecimen management. Protocols now routinely require timed collections coordinated with drug administration, multiple specimen types per time point, specialized processing procedures for labile analytes, and shipment to centralized laboratories across global networks (Santillan et al., 2024). Each step introduces opportunities for deviation that can compromise specimen quality, invalidate results, and undermine the substantial investments of resources and patient

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participation that clinical trials represent (Mohs & Greig, 2017).

Addressing these challenges requires more than technical proficiency within individual disciplines. Effective biospecimen management demands seamless integration across the multiple professional groups whose responsibilities intersect at the point of sample collection and handling. Nurses prepare patients and perform collections, ensuring proper identification and timing (Bunce et al., 2020). Pharmacists coordinate sampling relative to drug administration, particularly for pharmacokinetic studies where precise timing is essential (Watson et al., 2017). Laboratory personnel process, store, and analyze specimens, maintaining quality control throughout (Tsibin et al., 2022; Santillan et al., 2024). Health security professionals ensure regulatory compliance, chain-of-custody documentation, and adherence to evolving standards such as the International Council for Harmonisation's ICH E6(R3) guidelines (Klingstrom et al., 2018). When these groups operate in silos, the risk of error multiplies; when they function as an integrated team, specimen integrity is optimized.

This narrative review examines evidence-based best practices for biospecimen collection, processing, and handling in clinical trials, with particular emphasis on the multidisciplinary coordination required to ensure specimen integrity and research validity. By synthesizing evidence across nursing, pharmacy, laboratory, and regulatory domains, this review aims to provide practical guidance for clinical research teams seeking to enhance the quality and reliability of their biospecimen operations.

Fundamental Principles of Biospecimen Quality Assurance

The Pre-Analytical Phase as the Primary Source of Variability

The quality of biospecimen-derived data depends on three sequential phases: pre-analytical, analytical, and post-analytical. Of these, the pre-analytical phase—encompassing all steps from patient preparation through specimen processing and storage prior to analysis—represents the greatest source of variability and the most vulnerable period for error (Mohs & Greig, 2017). Research indicates that most laboratory errors in clinical trials do not occur inside the laboratory but happen before samples ever arrive for testing (Di Paolo et al., 2023; Wu et al., 2018). Mislabeled tubes, mishandled specimens, and improper collection techniques during the pre-analytical phase can lead to costly delays, re-collections, and compromised data integrity (Botturi et al., 2020).

Unlike analytical procedures, which can be validated, standardized, and monitored through quality control samples, pre-analytical processes occur in diverse clinical settings, are performed by personnel with varying levels of research training, and involve biological material that cannot be recreated if compromised (Chowdhury et al., 2023). The International Society for Biological and Environmental Repositories (ISBER) has developed the Standard PREanalytical Code (SPREC) to identify and record the main pre-analytical factors that may impact specimen integrity during collection, processing, and storage (Ammerlaan et al., 2018). SPREC comprises elements for both fluid and solid samples, defining sample type, container type, periods of warm and cold ischemia, centrifugation parameters, and final storage temperature—demonstrating the complexity of variables that must be controlled.

The Concept of Biospecimen as Data

A paradigm shift in regulatory thinking treats biospecimens not merely as physical materials but as extensions of clinical trial data (Sobel et al., 2020). With the updated ICH E6(R3) guidance, sponsors are explicitly accountable for oversight of all systems, vendors, and processes that impact trial quality, data integrity, and participant safety—including biospecimen management (Lemke & Broky, 2020). The new guidance explicitly calls for clearly defined and documented roles and responsibilities across all trial activities, validated systems and tools to ensure integrity and traceability of all clinical data, and oversight of third-party vendors who handle biospecimens (Klingstrom et al., 2018).

This conceptual shift has profound implications for trial operations. It means that chain-of-custody documentation is not merely administrative paperwork but constitutes primary evidence of data quality (Santillan et al., 2024). It requires that sample tracking systems be integrated with electronic data capture and capable of producing audit-ready records (Tsibin et al., 2022). And it demands that deviations in specimen handling be treated with the same seriousness as discrepancies in case report forms, with full documentation and impact assessment (Chow et al., 2007).

Risk-Based Quality Management

The transition to ICH E6(R3) emphasizes proactive, risk-based approaches to quality management across all trial operations, including biospecimen workflows (Lemke & Broky, 2020). Rather than retrospective detection of errors, sponsors and investigators must identify potential risks to specimen integrity before they occur and implement targeted controls to mitigate those risks. This approach recognizes that not all specimens carry equal importance and that resources for quality assurance should be allocated proportionally to risk (Botturi et al., 2020).

Key elements of risk-based biospecimen management include systematic identification of high-risk activities (time-critical collections, labile analytes, complex processing requirements); implementation of controls proportional to identified risks (redundant timing alerts, enhanced training, specialized collection kits); and continuous

monitoring of risk indicators to detect emerging issues (Lemke & Broky, 2020). The goal is to build quality into biospecimen processes rather than inspecting for quality after the fact.

Standardization Through Evidence-Based Practices

Standardization of biospecimen procedures is essential for reducing variability and enabling comparison across trials and institutions. Academic medical centers are increasingly transitioning from independent laboratory and siloed projects to single software applications utilizing common ontologies, enabling access to data from multiple repositories and increasing collaboration and access to quality biospecimens annotated with clinical, molecular, and patient-associated data (Santillan et al., 2024). Central to this process is the creation of unified vocabulary across repositories, including consensus around source of truth, standardized field definitions, and shared terminology (Santillan et al., 2024).

However, standardization must be balanced with flexibility to accommodate the specific requirements of different assays and analytes (Tsibin et al., 2022). Each assay has specific specimen and processing requirements that must be well defined prior to application (Ammerlaan et al., 2018). If these upfront criteria are not understood, the risk of irreproducible results increases substantially. Therefore, evidence-based practices should serve as foundational guidelines adapted to the specific requirements of each study's endpoints and analytical methods.

Nursing Perspectives in Patient Preparation and Specimen Collection

Nurses occupy the front line of biospecimen collection in clinical trials, serving as the interface between research protocols and patient care (Bunce et al., 2020). Their responsibilities extend beyond specimen acquisition to encompass patient preparation, verification of identity and eligibility, accurate labeling, and initial processing or stabilization of samples (Di Paolo et al., 2023). In acute care settings such as intensive care units, these tasks must be performed amidst competing clinical priorities, often under significant time pressure (Wallert et al., 2018). The BEACH (Biomarker and Edema Attenuation in Intracerebral Hemorrhage) trial at Yale New Haven Hospital's Neuroscience Intensive Care Unit illustrates both the centrality of nursing to successful biospecimen collection and the strategies required to support nurses in this role (Franke et al., 2020). The trial protocol required 16 blood sample collections per patient, timed precisely around investigational product infusions occurring every 12 hours for five days. Success depended on nurses who were thoroughly educated on protocol requirements and supported by systems that facilitated compliance (Razmovski-Naumovski et al., 2020).

Effective nursing participation in biospecimen collection begins with comprehensive education extending beyond initial protocol training to ongoing reinforcement and just-in-time support (Di Paolo et al., 2023). Data from central laboratory services demonstrate that proactive site training significantly reduces error rates: standard training achieves a 10% reduction in lab errors, while targeted training for remediation yields a 42% reduction in site errors within just one month (Nallathambi et al., 2023). The BEACH study team implemented a multi-layered approach to nursing education including central site training on biospecimen collection and protocol requirements; monthly meetings with nurse educators and managers to refine workflows; ad hoc in-service sessions for unit nursing staff to review updates; and real-time training during enrollment when coordinators engaged nurses early in the process (Wallert et al., 2018). This structured approach proved essential for maintaining protocol adherence, particularly given continuous onboarding of new staff. Analysis showed that early subjects experienced increased errors when transferred to floors with untrained personnel, leading the team to prioritize designated units with trained staff (Franke et al., 2020).

Beyond formal education, nurses benefit from readily accessible reference materials at the point of care (Razmovski-Naumovski et al., 2020). The BEACH team developed several resources exemplifying best practices: the "Nursing One-Sheet" displaying the calendar of events, specific nursing tasks, contact information, and infusion safety information in a single-page format; patient room calendars visually displaying infusion schedules, vital sign measurements, blood draws, and imaging timelines; QR codes linking to the research website; and integration with electronic medical records ensuring signed consent forms were immediately accessible (Bunce et al., 2020). Central laboratory services increasingly provide comprehensive site support including on-site demonstrations, on-demand training materials, and learning management systems offering real-time visibility into training progress and weekly site- and protocol-specific training reports (Nallathambi et al., 2023). These tools recognize that even well-trained nurses cannot memorize every detail of complex protocols. By embedding essential information into clinical workflows, research teams reduce cognitive burden and increase accurate protocol execution.

Nursing responsibility for specimen quality begins with patient preparation (Wahab et al., 2022). Key elements include fasting instructions specifying not only duration but permitted items; medication guidance clearly stating which drugs to hold or continue; activity restrictions as exercise temporarily alters numerous biomarkers; and hydration status guidance as it affects hemoconcentration (Hua et al., 2023). For special populations, preparation instructions must be adapted accordingly. Pediatric patients benefit from child-friendly language and

caregiver involvement. Geriatric patients may require simplified instructions and larger print. Patients with limited health literacy or non-native language speakers need materials in accessible formats and preferred languages (Mohs & Greig, 2017).

The act of specimen collection introduces numerous variables affecting quality (Ammerlaan et al., 2018). Venipuncture technique influences hemolysis rates, with traumatic draws, prolonged tourniquet time, and small-gauge needles increasing red blood cell destruction (Xie et al., 2024). Order of draw matters because additive carryover can contaminate subsequent tubes. Tube inversion requirements must be followed precisely to ensure proper mixing without causing hemolysis (Wahab et al., 2022). For tissue biopsies, the distinction between diagnostic specimens and pharmacodynamic biopsies for research is critical (Chowdhury et al., 2023). Research biopsies require sufficient viable cells to adequately represent drug-induced changes, and collection of multiple timepoints after drug administration demands parallel processing to minimize pre-analytical variables.

Following collection, many specimens require immediate processing or stabilization at the point of care: maintaining specific temperatures, protecting light-sensitive analytes, separating serum or plasma within defined time windows, or adding preservatives (Tsibin et al., 2022). Rapid preservation at the point of care is essential for labile biomarkers (Ammerlaan et al., 2018). Nurses must be equipped with clear instructions and necessary supplies (Nallathambi et al., 2023). Collection kits designed specifically for each study and visit, containing all required tubes, labels, and processing materials, reduce error risk (Wahab et al., 2022). When processing requires equipment unavailable at the bedside, clear protocols for transport to the laboratory must specify acceptable time intervals and temperature conditions (Wilson et al., 2019).

Pharmacy Integration in Timing, Drug Administration, and Pharmacokinetic Sampling

Pharmacy involvement in biospecimen management centers on the temporal relationship between drug administration and sample collection (Watson et al., 2017). For pharmacokinetic studies, precise timing of blood draws relative to dosing is not merely protocol compliance but a fundamental determinant of whether concentration-time data can be accurately interpreted (Mohs & Greig, 2017). Pharmacists are uniquely positioned to coordinate this interface, ensuring investigational product preparation and administration synchronize with collection schedules (Chow et al., 2007). In the BEACH trial, patients received ten infusions every twelve hours for five days, with 16 blood sample collections timed around these administrations (Bunce et al., 2020). This schedule required constant communication between investigational pharmacy and clinical team to ensure infusion start times were documented accurately and collection windows calculated correctly.

Pharmacokinetic parameters—maximum concentration (Cmax), time to maximum concentration (Tmax), area under the curve (AUC), half-life, and clearance—are derived from concentration measurements at specific timepoints post-administration (Booth et al., 2019). Deviations from scheduled collection times can substantially alter calculated parameters, potentially leading to incorrect conclusions about drug exposure, bioavailability, or bioequivalence (Wu et al., 2018). Standard operating procedures for handling deviations in PK sampling time define deviations as any sampling time outside permitted windows (commonly ±2 to ±5 minutes depending on time point) (Watson et al., 2017). Minor deviations within protocol-specified range are recorded without requiring corrective action; major deviations outside windows or missed samples must be documented and evaluated for impact on data integrity (Chow et al., 2007). The precision required varies by drug and sampling strategy. For drugs with rapid absorption and distribution phases, even minutes of deviation significantly impact concentration measurements (Mohs & Greig, 2017).

Effective communication between pharmacy and nursing is essential for time-sensitive collections (Razmovski-Naumovski et al., 2020). The BEACH study's 24/7 research team availability exemplifies one approach: study coordinators present for all protocol steps, including test article infusion and biospecimen collection, serving as dedicated links between pharmacy, nursing, and clinical team (Franke et al., 2020). Technology supports coordination through automated alerts and integrated scheduling systems (Tsibin et al., 2022). Electronic medical record integration displaying infusion schedules, collection times, and pending tasks ensures all team members share the same information (Franke et al., 2020). However, technology alone is insufficient without clear responsibility assignment. Protocols must specify who calculates collection times from actual administration time, who documents deviations, and how communication failures escalate (Szapacs et al., 2023).

Comprehensive deviation documentation is essential for regulatory compliance and data interpretation (Chow et al., 2007). PK sampling deviation logs record subject identification scheduled and actual times, deviation magnitude, type (early, late, or missed), and remarks (Szapacs et al., 2023). For major deviations, corrective and preventive action (CAPA) forms document deviation description, root cause, corrective actions taken, and preventive measures implemented to reduce recurrence (Booth et al., 2019). Quality assurance personnel review sampling deviations monthly, implementing retraining, checklist improvements, or automated alarms to reduce reoccurrence (Watson et al., 2017). This systematic approach to deviation management

transforms errors into learning opportunities, continuously improving site performance.

Accurate documentation of drug administration is essential for interpreting biospecimen results (Chow et al., 2007). This includes not only administration time but also details affecting drug concentrations: infusion rate, injection site, fed or fasting state, and any deviations from planned administration (Xie et al., 2024). This documentation must link to biospecimen records to support reconstruction of temporal relationships. If a sample is collected 30 minutes after documented administration but actual administration occurred 15 minutes late, the sample effectively represents a 45-minute post-dose collection (Chow et al., 2007).

Laboratory Perspectives in Processing, Storage, and Quality Control

The interval between specimen collection and laboratory arrival represents a period of vulnerability (Wilson et al., 2019). Time, temperature, light exposure, and physical handling influence specimen quality, with relative importance varying by analyte and assay method (Ammerlaan et al., 2018). Laboratories must establish clear acceptance criteria and communicate requirements to collection sites through detailed laboratory manuals (Cassim et al., 2022). Central laboratory services are designed to support operational and scientific needs of complex, multi-site studies through standardized processes, regulatory rigor, and end-to-end traceability (Simons & Capraro, 2020). From initial custom kit design through global distribution with strict temperature control and chain-of-custody oversight, to meticulous sample processing and integrated data management, every step is engineered for accuracy and traceability (Sanguino et al., 2014).

Processing transforms collected specimens into forms suitable for analysis or long-term storage (Hua et al., 2023). Common steps include centrifugation, aliquoting, and addition of preservatives or stabilizers. Each step introduces variables requiring control (Wilson et al., 2019). Centrifugation parameters—speed, time, temperature, and brake settings—affect quality of separated plasma or serum (Chowdhury et al., 2023). Inadequate centrifugation leaves cellular elements in supernatant; excessive force causes hemolysis or releases intracellular contents (Mohs & Greig, 2017). The SPREC standard captures centrifugation details including speed and temperature, enabling documentation of these critical variables (Ammerlaan et al., 2018).

Aliquoting creates multiple portions for different assays or future use, but each transfer introduces opportunities for contamination, mislabeling, or analyte degradation (Tsibin et al., 2022). Standard operating procedures must specify aliquot volumes, container types, and labeling requirements (Santillan et al., 2024). Preservation methods vary by analyte and intended use (Ammerlaan et al., 2018). Formalin fixation preserves tissue morphology but cross-links proteins and fragments nucleic acids. Flash freezing preserves labile proteins and nucleic acids but requires specialized equipment and cold chain maintenance (Cassim et al., 2022). The choice must be guided by planned analytical assays, not convenience.

Once processed, specimens may be stored for weeks, months, or years before analysis (Santillan et al., 2024). Storage conditions must maintain analyte stability throughout this period. Common storage methods include refrigeration, ultra-cryopreservation (-80°C), and liquid nitrogen (Wilson et al., 2019). When stability data is lacking, the precautionary principle applies (Eklund et al., 2020). For DNA-based analyses, sample dehydration enabling long-term room temperature storage at reduced costs without compromising results represents an emerging trend (Snapes et al., 2023).

Temperature monitoring systems with continuous recording and alarm capabilities are essential (Simons & Capraro, 2020). Biorepository capabilities include all temperature conditions: ambient, refrigerated, frozen, ultra-low, and liquid nitrogen storage, utilizing environmental monitoring systems with 24/7 on-call surveillance (Sanguino et al., 2014). Freeze-thaw cycles represent a particular threat (Eklund et al., 2020). Each cycle can degrade labile analytes, alter protein conformation, and cause analyte precipitation. Protocols should minimize freeze-thaw by aliquoting specimens into single-use portions whenever possible (Tsibin et al., 2022).

Laboratory quality control encompasses both pre-analytical and analytical components (Cassim et al., 2022). Pre-analytical quality control focuses on verifying incoming specimens meet acceptance criteria, processing follows standard operating procedures, and storage conditions remain within specified ranges (Santillan et al., 2024). Specimen acceptance criteria include visual inspection for hemolysis, lipemia, or clotting; verification of proper tube type and volume; confirmation of labeling accuracy; and documentation of collection and transport times (Wu et al., 2018).

Specimens not meeting acceptance criteria should be rejected or flagged, with impact assessed and documented (Simons & Capraro, 2020). Central laboratory services utilize Laboratory Information Management Systems (LIMS) to track and record sample shipments, conditions, and location within biorepository and analytical services, enabling seamless transfer for internal or external analysis and providing comprehensive, regulatory-compliant chain-of-custody documentation (Tsibin et al., 2022).

Laboratory-Nursing-Pharmacy Communication

Effective laboratory involvement requires robust bidirectional communication (Wilson et al., 2019). Laboratory manuals serve as primary communication tools, providing detailed guidance on collection tube types, required volumes, handling after

collection, processing requirements, labeling, and shipping instructions (Eklund et al., 2020). Feedback loops from laboratory to collection sites are equally important (Koukourikos et al., 2021). When quality issues are detected—hemolyzed specimens, incorrect tube types, delayed processing—this information should be communicated promptly to responsible parties for corrective action (Mohs & Greig, 2017). Aggregate quality data identifies training needs or systemic issues requiring process improvement (Cornish et al., 2021).

Health Security and Regulatory Compliance

Biospecimen management operates within a complex regulatory framework sharing common principles of quality, integrity, and participant protection (Klingstrom et al., 2018). Recent developments, particularly ICH E6(R3), have heightened expectations for sponsor oversight and risk-based quality management across the specimen lifecycle (Lemke & Broky, 2020). Section 3.10 states: "The sponsor should implement an appropriate system to manage quality throughout all stages of the trial process," including tools and procedures for trial conduct, particularly those used for data collection and management—a category in which sample metadata squarely fits (Sobel et al., 2020). Section 3.16.1 requires that "data acquisition tools are fit for purpose and designed to capture the information required by the protocol. They should be validated and ready for use prior to their required use in the trial" (Klingstrom et al., 2018). The implication is clear: if biospecimen processes—or supporting tools and vendors—are not fit for purpose, validated, or fully documented, sponsors face non-compliance risk (Lemke & Broky, 2020).

Chain of custody refers to chronological documentation tracking specimen possession, transfer, handling, and disposition from collection through analysis or destruction (Santillan et al., 2024). Complete chain of custody requires unique specimen identification, documented transfers with date, time, and responsible parties, and recorded condition at each step (Wilson et al., 2019). Technology solutions strengthen chain of custody through barcoded labeling, electronic tracking systems, and integration with LIMS (Santillan et al., 2024). RFID chips enhance traceability and efficiency (Snapes et al., 2023). Label materials must be compatible with transport and storage conditions, remaining readable after storage at -196°C in liquid nitrogen (Eklund et al., 2020). Robust electronic systems compliant with 21 CFR Part 11 are essential, providing secure access for sample owners, real-time inventory tracking, and detailed location and status data facilitating retrieval and reporting (Santillan et al., 2024).

Temperature control throughout the specimen lifecycle is essential for preserving analyte integrity (Simons & Capraro, 2020). Cold chain management begins at collection, with specimens placed immediately into appropriate temperature conditions (Eklund et al., 2020). Temperature-monitored shipping containers with data loggers provide continuous recording during transport. Upon laboratory arrival, temperature must be verified before specimens are accepted (Tsibin et al., 2022). For specimen transport, experienced carriers complying with international standards are critical (Wahab et al., 2022). Packaging must ensure temperature control and include monitoring to detect excursions, maintaining required conditions for validated minimum duration (Wilson et al., 2019).

Transport of biological samples must adhere to IATA, MOTs, ADR, and other dangerous goods regulations, with Category A (UN2814/UN2900) or Category B (UN3373) materials requiring specific packaging (Snapes et al., 2023). Storage facilities must be secure using badges, codes, or facial recognition, with access limited to authorized personnel (Santillan et al., 2024). Equipment should be clean, clearly identified, and monitored 24/7, with contingency plans for malfunctions (Tsibin et al., 2022).

The ultimate test of biospecimen management systems is performance during regulatory inspection or sponsor audit (Lemke & Broky, 2020). Inspectors expect complete documentation of all specimen-related activities; evidence processes followed approved protocols; documentation of deviations and impact assessment; and demonstration of adequate personnel training (Chow et al., 2007). Audit readiness requires organized, accessible, searchable documentation (Santillan et al., 2024). Electronic systems with centralized data repositories facilitate rapid response to information requests (Wilson et al., 2019). Proactive risk assessment identifies potential compliance gaps before inspection findings (Lemke & Broky, 2020). Many sponsors operate with partial compliance—implementing quality measures for some steps but not achieving end-to-end control (Klingstrom et al., 2018).

Multidisciplinary Coordination: Case Study and Best Practices

The BEACH Trial: A Model of Integration

The BEACH trial at Yale New Haven Hospital provides an instructive case study in multidisciplinary biospecimen management, requiring coordination across neurology, neurocritical care, nursing, investigational pharmacy, and multiple laboratories for pharmacokinetic sampling, biomarker analysis, and imaging correlates (Bunce et al., 2020; Table 1).

Several features exemplify best practices: 24/7 research team availability ensuring dedicated coordinator accessibility; structured nursing education including initial training, ongoing in-service sessions, and just-in-time support; communication tools embedded in clinical workflows; pharmacy coordination facilitated by study coordinator presence during all protocol steps; and continuous quality

monitoring through deviation tracking identifying problems early (Bunce et al., 2020).

Essential Elements of Multidisciplinary Programs

Synthesizing evidence, several essential elements emerge: integrated protocol development engaging all disciplines during design (Snapes et al., 2023); clear role definition specifying responsibility for each step (Watson et al., 2017); shared information systems providing all team members access to same real-time information (Santillan et al., 2024); regular communication forums bringing disciplines together to review quality metrics (Bai et al., 2022); cross-training helping each discipline understand others' requirements (Razmovski-Naumovski et al., 2020); and escalation pathways specifying issue resolution across disciplinary boundaries (Xie et al., 2024).

Technology-Enabled Coordination

Technology supports multidisciplinary coordination through centralized inventory management tracking kit availability and expiration dates (Snapes et al., 2023); barcoded labeling systems ensuring specimen identification across sites and laboratories (Santillan et al., 2024); integrated scheduling tools displaying collection timelines for all team members (Franke et al., 2020); and electronic data capture linking biospecimen results to clinical data (Wilson et al., 2019). However, technology must be implemented with attention to workflow integration and user experience (Bunce et al., 2020). Tools adding burden without reducing complexity will be resisted. Successful implementations involve end users in design and testing, provide adequate training, and continuously refine based on feedback (Ménard & Trant, 2020). Table 2 illustrates the evidence-based best practices by biospecimen lifecycle phase.

Table 1: Summary of Multidisciplinary Roles in Biospecimen Management

Discipline	Primary Responsibilities	Key Integration Points
Nursing	Patient preparation, specimen collection, point-of-care processing, documentation (Bunce et al., 2020; Ménard & Trant, 2020)	Coordination with pharmacy for timed collections; communication with laboratory about special handling; integration with research team for protocol adherence
Pharmacy	Investigational product preparation, administration timing, documentation of dosing (Watson et al., 2017; Xie et al., 2024)	Coordination with nursing for infusion schedules; communication with laboratory about pharmacokinetic sampling; deviation documentation and CAPA implementation
Laboratory	Specimen processing, storage, analysis, quality control (Wilson et al., 2019; Santillan et al., 2024; Eklund et al., 2020)	Receipt verification from collection sites; communication with nursing about collection requirements; integration with data management for results reporting
Health Security/Regulatory	Compliance oversight, chain-of-custody documentation, inspection readiness (Klingstrom et al., 2018, 2025b; Santillan et al., 2024)	Audit trail verification; temperature monitoring and cold chain management; integration with quality assurance for deviation trending
Research Coordination	Overall protocol management, communication facilitation, training (Bunce et al., 2020; Ménard & Trant, 2020)	Central coordination across all disciplines; 24/7 availability for troubleshooting; integration of data from all sources

Table 2: Evidence-Based Best Practices by Biospecimen Lifecycle Phase

Lifecycle Phase	Best Practices	Key Evidence Sources
Protocol Design	Engage all disciplines; define specimen requirements based on analyte stability; establish acceptable deviation windows	Snapes et al. (2023); Eklund et al. (2020); Klingstrom et al. (2018)
Site Preparation	Develop comprehensive laboratory manuals; provide collection kits with all supplies; implement training with initial and ongoing components	Ménard & Trant (2020); Bunce et al. (2020); Wilson et al. (2019)
Patient Preparation	Provide clear, accessible instructions; verify understanding; accommodate special population needs	Snapes et al. (2023); Eklund et al. (2020); Xie et al. (2024)
Collection	Use barcoded labels; document collection time accurately; follow tube-specific requirements	Santillan et al. (2024); Xie et al. (2024); Eklund et al. (2020)

Point-of-Care Processing	Process within time limits; maintain temperature requirements; protect light-sensitive analytes	Wilson et al. (2019); Eklund et al. (2020); Snapes et al. (2023)
Transport	Maintain chain-of-custody; use temperature-monitored shipping; verify receipt at destination	Wilson et al. (2019); Snapes et al. (2023); Santillan et al. (2024)
Laboratory Processing	Follow validated SOPs; document all steps; implement quality control for reagents and equipment	Wilson et al. (2019); Santillan et al. (2024); Eklund et al. (2020)
Storage	Maintain continuous temperature monitoring; minimize freeze-thaw cycles; track inventory	Wilson et al. (2019); Santillan et al. (2024); Eklund et al. (2020)
Deviation Management	Document all deviations; categorize as minor/major; implement CAPA for major deviations	Watson et al. (2017); Xie et al. (2024); Lemke & Broky (2020)
Data Integration	Link results to clinical data with audit trail; ensure traceability from collection through reporting	Wilson et al. (2019); Santillan et al. (2024); Klingstrom et al. (2018)

Challenges and Future Directions

Despite advances, several challenges persist (Wahab et al., 2022). Site-level variability remains significant, with thousands of clinical sites operating under diverse conditions with varying research infrastructure (Hill Jr & Finster, 2016). Inventory management presents particular challenges; sites running hundreds of trials simultaneously manage collection kits from multiple sponsors, each with unique requirements and expiration dates (Snapes et al., 2023). The science of biospecimen stability continues evolving, with new analytes and assay methods requiring updated understanding of pre-analytical variables (Eklund et al., 2020). What constitutes evidence-based practice today may be superseded by new findings tomorrow, requiring continuous updating of protocols and training (Xie et al., 2024).

Several technological developments offer promise (Theissinger et al., 2023). Centralized biospecimen management platforms integrating inventory tracking, chain-of-custody documentation, and data integration across sites and laboratories provide end-to-end visibility (Santillan et al., 2024). RFID chips enhance traceability and efficiency (Botturi et al., 2020). Automation and robotic solutions significantly improve efficiency, reducing human errors depending on balance between installation costs and productivity gains (Santillan et al., 2024). Decentralized trial models expand collection locations, with home health nurses, local laboratories, and patient self-collection becoming more common (Wahab et al., 2022). Remote trial locations influence sample types and preservation methods (e.g., dried blood spot) (Snapes et al., 2023). These models increase participant convenience but introduce new challenges for standardization and oversight (Giavarina & Lippi, 2017).

The multidisciplinary nature of biospecimen management requires workforce development strategies extending beyond traditional disciplinary silos (Razmovski-Naumovski et al., 2020). Nursing curricula should include research protocols and biospecimen integrity (LaRocco et al., 2016). Pharmacy training should address pharmacokinetic sampling requirements and coordination with collection schedules (Chow et al., 2007). Laboratory programs should emphasize pre-analytical variables and their impact on analytical results (Wilson et al., 2019). Comprehensive training in biospecimen operations across all lifecycle phases is essential for research coordinators (Franke et al., 2020). The BEACH study's model of postgraduate clinical research associates rotating through all trial operations provides a template for developing next-generation research professionals (Bunce et al., 2020).

Conclusion

Biospecimen integrity is crucial for valid clinical trial results, challenging due to complex protocols and diverse disciplines involved. This review discusses best practices throughout the biospecimen lifecycle, highlighting several key themes. Firstly, pre-analytical variables are major sources of error; thus, every step from patient preparation to specimen processing requires systematic attention. Second, clear communication and defined roles across various disciplines are essential for effective management, as exemplified by the BEACH trial's success through education and real-time communication. Third, evolving regulatory expectations emphasize risk-based quality management and comprehensive oversight, warning against partial compliance which jeopardizes data integrity. Fourth, while technology can aid in management, it cannot substitute for well-trained personnel and established processes. Looking forward, addressing challenges in variability and workforce development, alongside harmonization efforts and emerging technologies, will further enhance biospecimen quality. Ultimately, the focus must be on producing reliable, reproducible research to advance knowledge and improve patient care, honoring patient trust in clinical trials.

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