Understanding your Protocol:
Logistics, Workflows and Strategies

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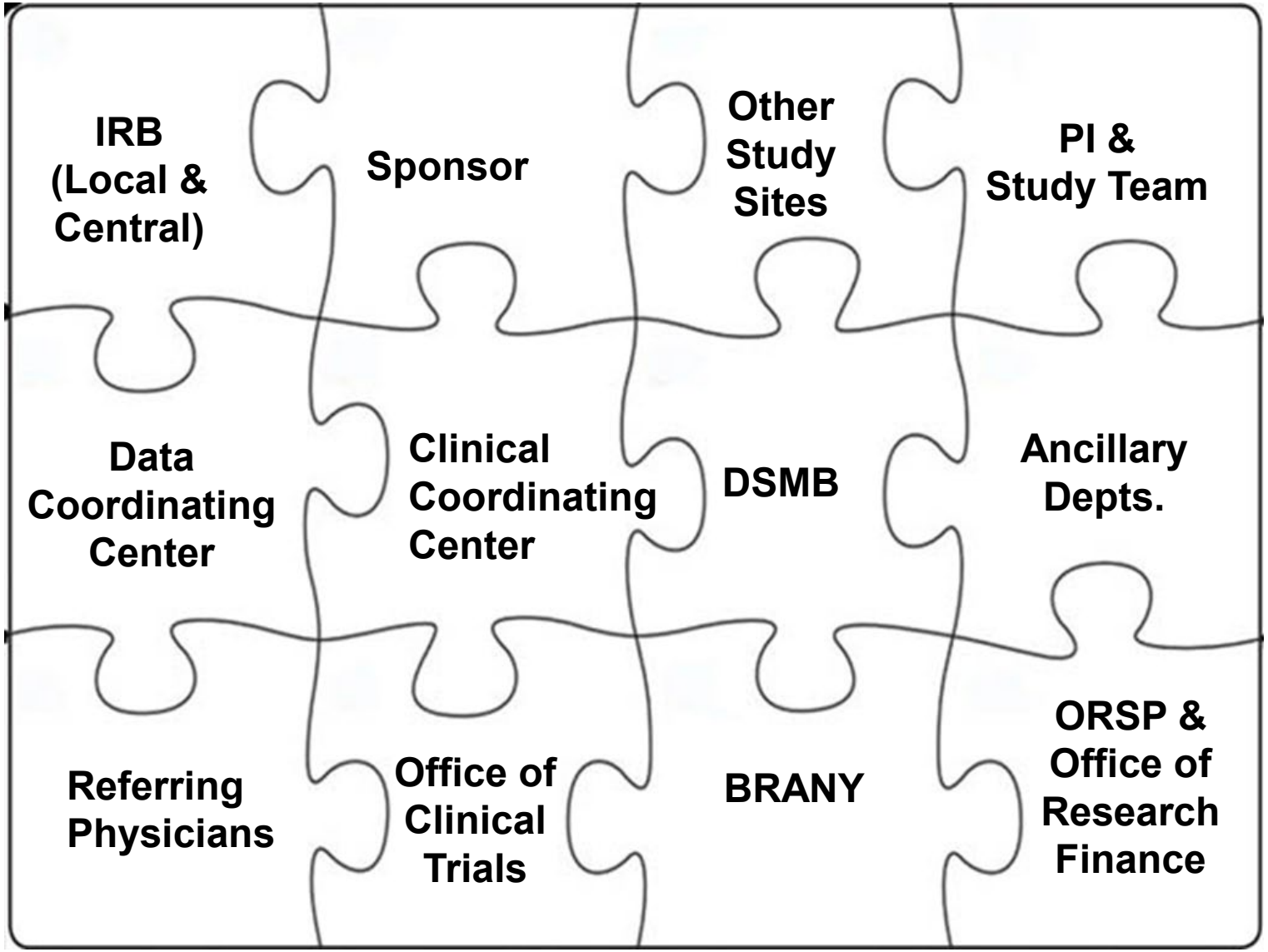
Objectives

Discuss tools and strategies for…

- Identifying key stakeholders and expectations for your research study (Sponsors, Ancillary Departments, etc)
- Understanding how safety and data oversight plans impact study process (DSMB, monitoring visits etc)
- Understanding the role of institutional systems in the research process (Epic, Velos, EDC, etc)
- Delegating roles and tasks (personnel, workflows, etc)
- Determining enrollment and visit capacity

Identify Stakeholders



Identify & Understand Milestones

Contractual Milestones [Industry or Government Funded]

Billing Implications and Expectations

What you need to know:

Where they would find the info.

- Contract, Payment terms, Budget

When to refer to it

Best practices for communicating

Admin. Office (OCT & BRANY) responsible for accounts receivable

Study team responsible for accounts payable

Information found in: Research Agreement/Contract, Payment Terms, Budget

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Identify & Understand Milestones

Impact of Department Infrastructure & Funding Source

Grant-Funded Research

Start

Milestone is reached

Study team alerts dept. administrator

Admin. works with Office of Research Finance

Accounts receivable

PI responsible for accounts payable

Ancillaries get paid

Industry-Funded Research

Start

Schedule of Events input to Velos or BRANY SMART

Milestone is reached

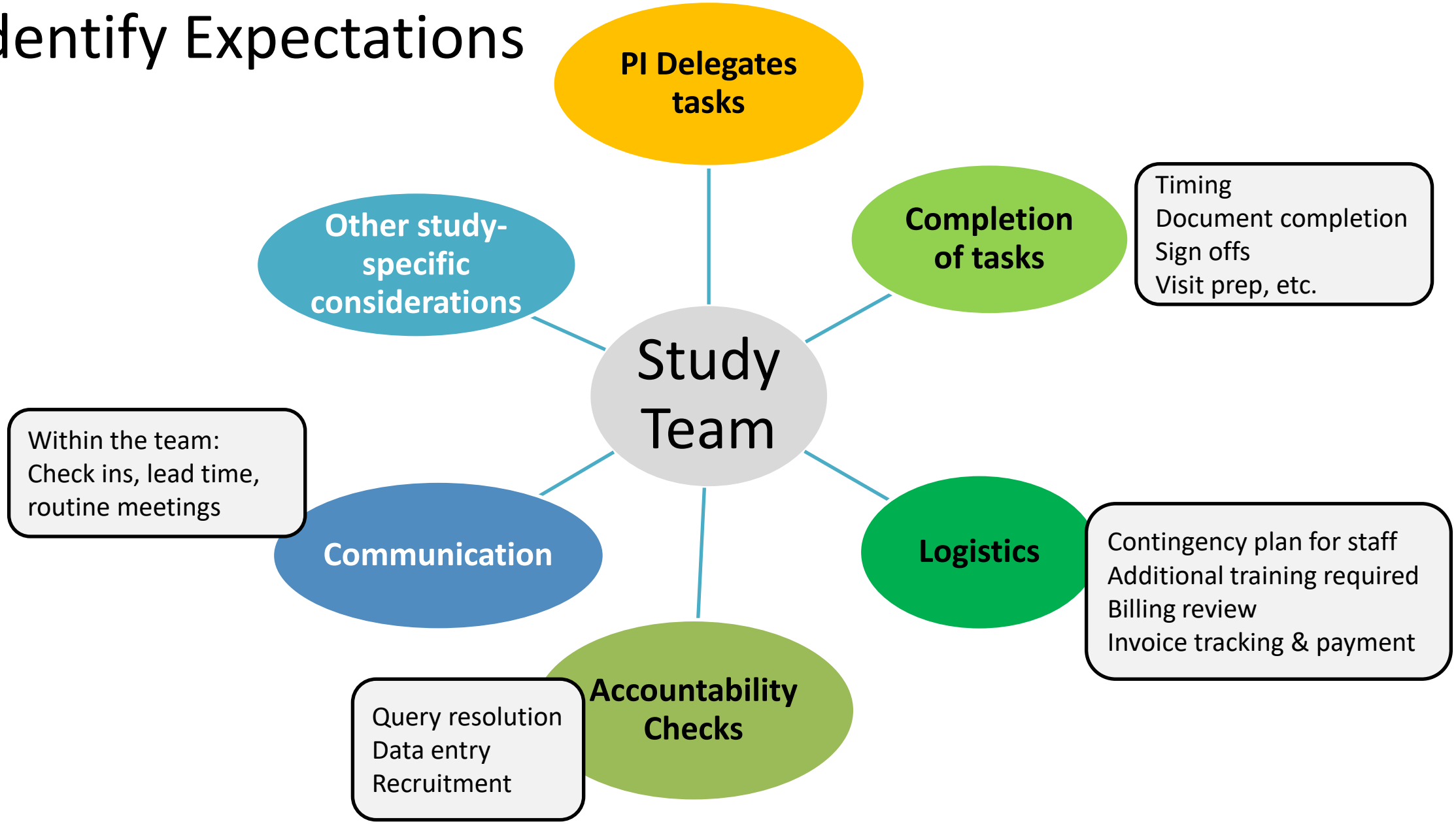
Study team enters all required data in EDC & Velos/BRANY SMART

Accounts receivable (OCT or BRANY)

PI responsible for accounts payable

Ancillaries get paid

Identify Expectations



Identify Expectations: Ancillaries & Other Collaborators

- Identify primary contact
- Know any setup requirements, how much lead time is needed
- Know how they will be notified of a needed research activity, and by who
- Know the expected turnaround time
- Know how essential document maintenance will occur, and where it is stored

Information found in: Institutional Policy & Procedures, if applicable

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Identify Milestones and Expectations

Safety and Data Oversight

IRB

- ❑ Which IRB is overseeing the study?
- ❑ What are the applicable **reporting** requirements?
- ❑ What federal, state and institutional **regulations** apply to your research?
- ❑ What is the **level of risk** of the study?

DSMB

- ❑ Is there one?
- ❑ How often do they meet?
- ❑ What are the ongoing data submission requirements and deadlines?
- ❑ How will findings be shared? And by who?
- ❑ Who on the study team files and follows up on any correspondence?

Data Coordinating Center

- ❑ Is there one? Where?
- ❑ Where is data stored?
- ❑ How is data securely shared?
- ❑ Are there any blinding considerations?
- ❑ Who is responsible for compiling and sharing the data?
- ❑ At what time points is data analyzed? (interim analysis, futility, etc.)

CRO/External Monitors

- ❑ Is there one?
- ❑ Is monitoring conducted remotely or in-person?
- ❑ Have you established necessary access (to campus, to EMR)?
- ❑ How often are visits conducted?
- ❑ How are queries generated and resolved?

Protocol Sections: Adverse Events Definition & Reporting; Deviations/Unanticipated Problems; Data Collection; Data Quality Assurance; Study Monitoring; Data Safety Monitoring Plan

Example: Safety Reporting

IRB

- ❑ Which IRB is overseeing the study?
- ❑ What are the applicable **reporting** requirements?
- ❑ What federal, state and institutional **regulations** apply to your research?
- ❑ What is the **level of risk** of the study?

Einstein IRB

Multi-Center Trial
(Lead site & Sponsor: Storybook Univ.)

Greater than minimal risk

Context

Patient is hospitalized for bronchospasms within 48 hours of taking interventional medication.

Reporting Requirement:

Einstein IRB: within **5 business days** of knowledge of event
Storybook Univ.(sponsor): within **24 hours** of knowledge of event

Report Preparation:

Preparation: Review medical records, compile other relevant info.
Assessment: Review, medical assessment and sign-off

Report Submission:

Reportable Event Form (Einstein IRB/iRIS); CRF (Storybook Univ./EDC)
Principal Investigator system sign-off (both)

Report Follow Up:

Provide additional/new information, if requested
File report in regulatory binder
Further follow up with subject, as needed

Institutional and Other Systems

- Einstein IRB submission portal

- Clinical Research Management System
- Required for all human subject research at MMC-Einstein
- Interfaces with Epic & both IRB Systems (Einstein & BRANY)

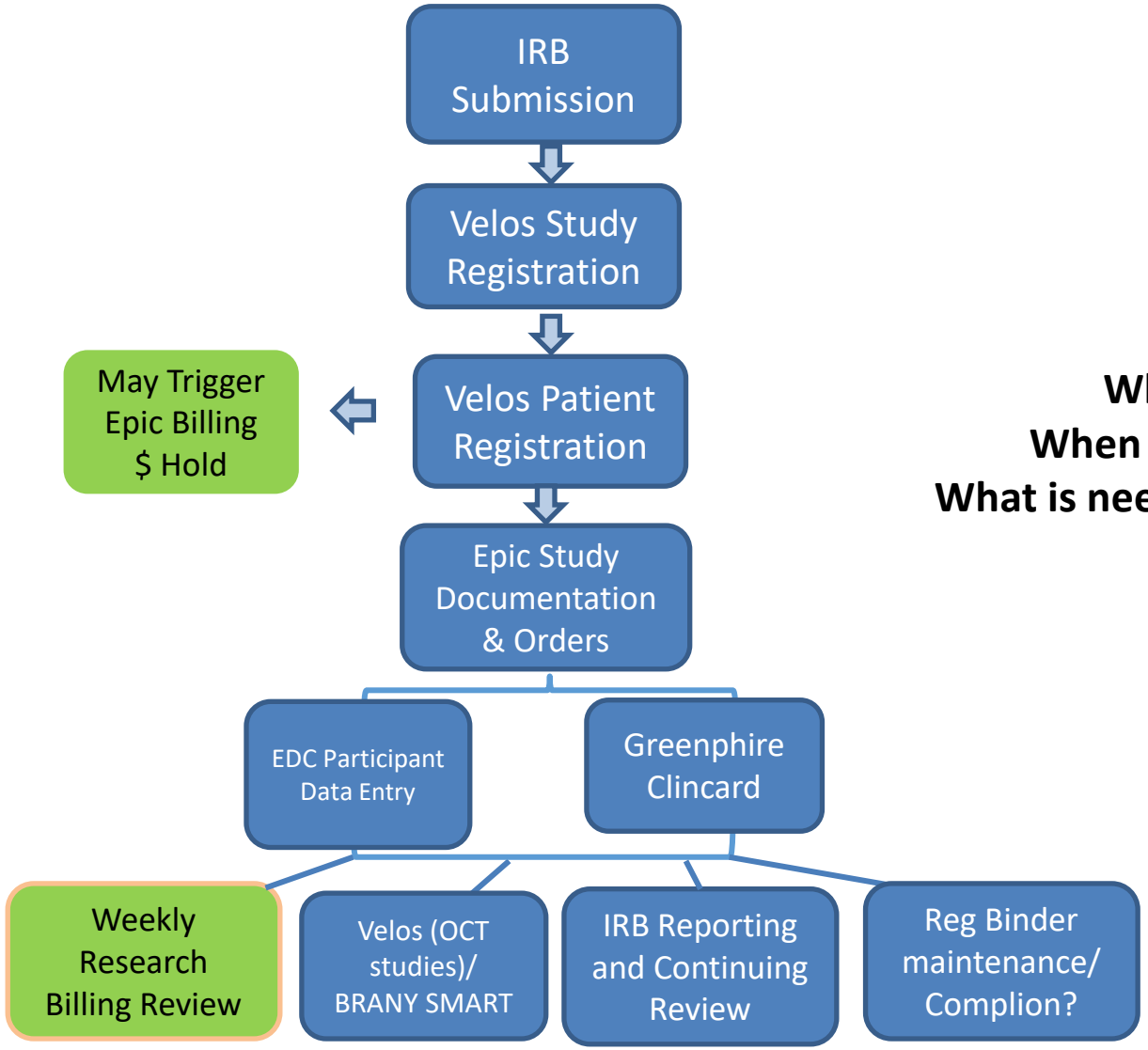
- Institutional electronic medical record system (EMR)

- Web-based payment system for research subject compensation

- Electronic Data Capture System (may incl. REDCap)
- Randomization software

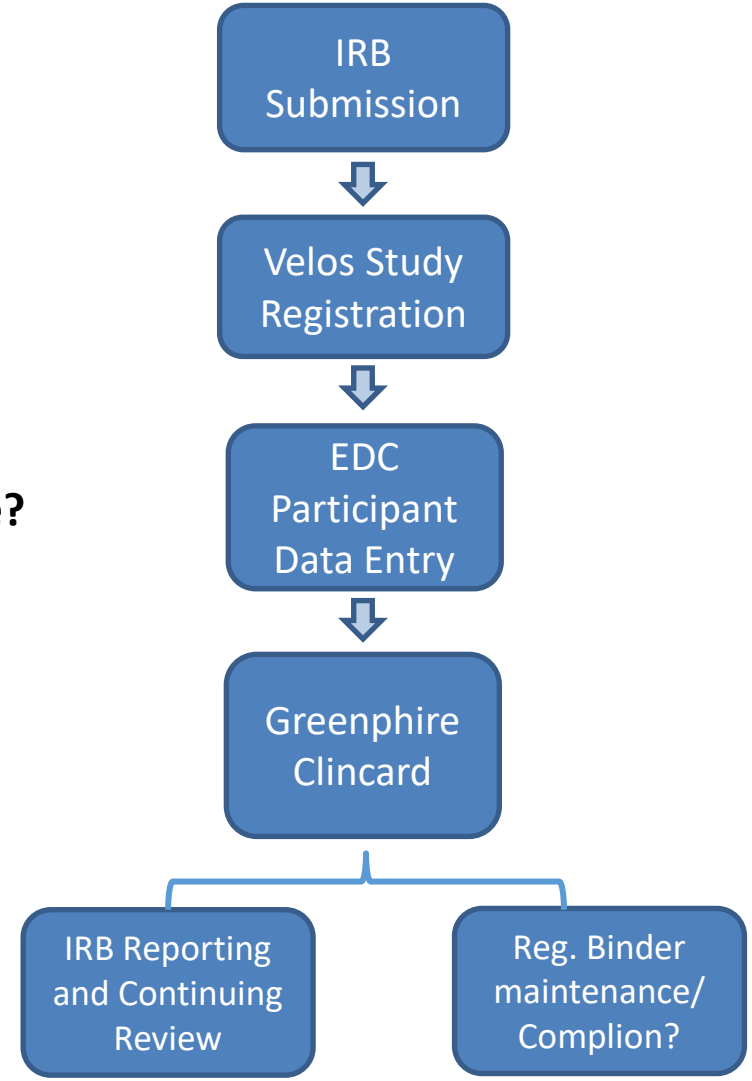
- Electronic regulatory binder platform

Interventional/IND Studies
Studies with NCT #s (registered on clinicaltrials.gov)
Studies with Epic Orders (labs, imaging, Res. Pharmacy)



Plan:
Who is updating?
When are they updating?
What is needed in order to update?

Observational Studies



General Considerations

Request existing procedural documents [Sponsor, collaborators, ancillaries]

Thoroughly read those documents, ask questions, understand the process detailed

Develop local workflow, referencing existing docs, embed study team and institutional specifics

Common Terminology:

Manual of Procedures (MOP)
Standard Operating Procedures (SOP)
Workflows

- ✓ Level of detail should be proportional to study
- ✓ Don't "reinvent the wheel"
- ✓ Workflow will serve as a tool for communication and building in accountability
- ✓ Be sure all regulatory requirements are baked into your process- safeguard from risk of noncompliance

Prepare and Plan: Recruitment & Enrollment

Consider	*Action Plan*
Enrollment Target	• Understand any contractual obligations
Recruitment Milestones	• Identify recruitment timeline (Are there specific windows) • Set periodic goals ("x" pts/week, month, etc.) based on enrollment target and visit capacity (new pts & follow-up visits)
Recruitment Strategies	• Develop a recruitment strategy & resources (account for staff availability) • Develop all patient-facing materials in prep for IRB review & approval
Participant Retention	• Plan for following up with participants • Create visit reminders, email templates, phone scripts, handouts, etc.

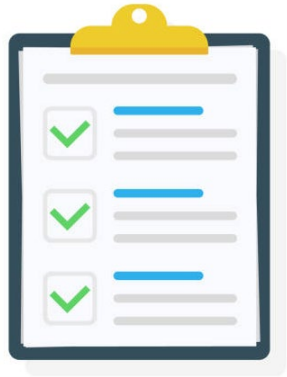
Protocol Sections: Recruitment, Enrollment, and Retention

Prepare and Plan: Study Procedures

Consider	*Action Plan*
Study Roles & Responsibilities	• Clearly define roles/responsibilities [Delegation of Authority Log] • Ensure necessary training for all responsibilities • Establish contingency plans for back-ups, if needed
Consent Process	• Identify how and where subjects will be consented • Identify who is conducting consent and how is it being documented
Space & Location	• Identify how/where procedures will take place • Make necessary preparations (who orders labs, reserve space, etc.)
Documentation	• Understand and define how documentation will occur • Identify documentation source for all activities

Protocol Section: Study Procedures, Study Schedule, Informed Consent Process

Prepare and Plan: Data Collection



Consider	*Action Plan*
Data Generation	• Understand how data is generated (Retrospective/prospective?)
Data Source	• Identify what is official source for all required data (EMR? Paper? Both?) • Ensure user access
Data Collection Tools	• Identify data collection tools and prepare in advance (Questionnaires? Participant Diaries?)
Frequency	• Identify timing needs – consider visit windows and time sensitive values • Plan for follow-up phone interviews (set reminders)

Protocol Section: Data Collection; Data Quality Assurance

Prepare and Plan:
Data Entry & Management

Consider	*Action Plan*
Database/EDC	• Identify what database is being used, who and who is providing/managing? • Identify who is doing data entry and ensure proper training & user access
Frequency	• Understand data entry TAT requirements (e.g. 48 hrs after visit?) • Schedule blocks of data entry time
Data query resolution	• Identify who communicates queries • Understand requirement for correcting/updating the EDC record
Monitoring visits	• Identify the space/time requirements • Plan for follow-up on findings/report to sponsor
DSMB Meeting/ Data lock	• Plan for “crunch” time before upcoming DSMB meeting dates

Protocol Section: Study Records; Access to Source; Study Monitoring; Data Safety Monitoring Plan

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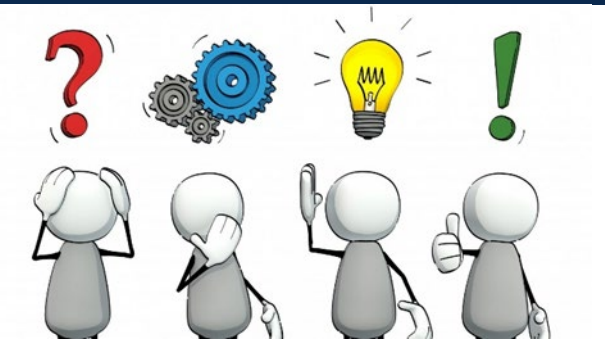
Prepare and Plan:
Sample Collection & Packaging/Shipping

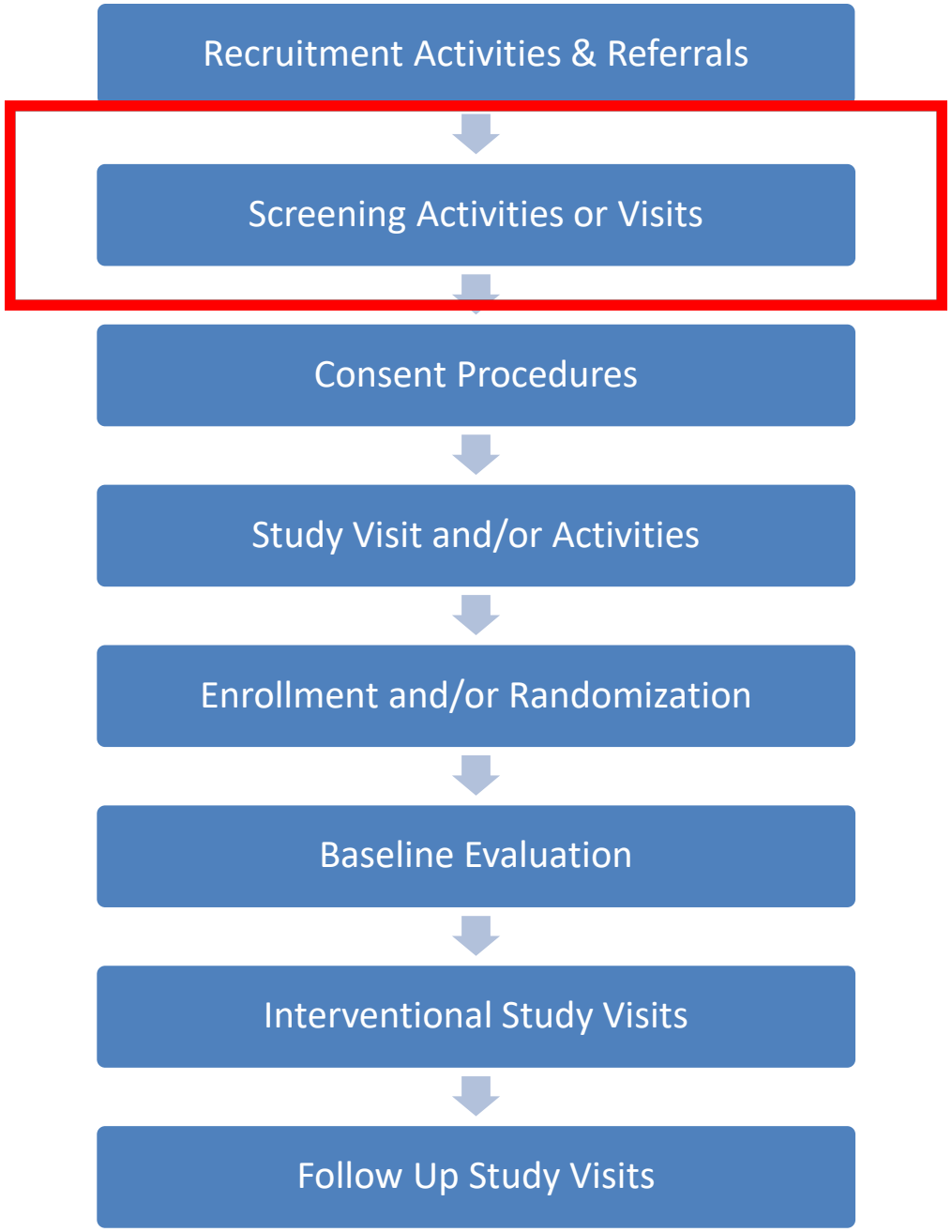
Consider	*Action Plan*
Collection	• Identify who will collect samples, where they will be collected & at what time points. • Work with Pathology, CRC, as applicable
Processing and/or Storage	• Understand how/whether sample must be processed prior to storage or shipping • Coordinate with Pathology/BIOR/BARC if applicable
Kits & Materials	• Identify whether sponsor provides sample collection/shipment kits • Plan for requesting kits in time for study visits
Shipping	• Identify who will package and ship specimens to central labs • Ensure IATA compliant training for personnel
Transport & Tracking	• Plan for transport to BARC or BIOR • Create a tracking log (include study IDs, collection date, tracking #’s, etc.)

Overall “Workflow” Development



- *Also known as: Manuals of Procedures, Manual of Operations, Standard Operating Procedures*
- **Level of detail** should match complexity of study
- Should include:
  - **Study-specific** task breakdown: full “lifecycle” (Recruitment → Off Study)
  - **Institutional** requirements
  - **Funder** and/or **sponsor** requirements (if applicable)
- Be aware of applicable **policies and regulations** (local & federal)
- **Embed plan** for study documentation and regulatory maintenance

Sample high-level workflow



Workflow Development: Core Elements

Activity	Represents a single step of the process
Action	Preparatory steps & how the activity is accomplished (including *who*, *how* and *when*)
Transition	Movement from one activity to the next, or "*trigger*"
Sub-process *(If applicable)*	Defines a set of activities that may be called for based on outcome of prior steps (ex: for ancillary services, once triggered)

Example: Manual of Procedure Snapshot

Screening Patients → Activity

Action

- Coordinator will:
  - Identify potential participant on report or database, verifies eligibility criteria (pre-screen) Call/email patient to gauge interest.
  - Schedule in-person screening with PI (or MD) Reserve space (insert specific CRC scheduling steps, if needed) Email patient with visit confirmation, directions, estimated duration of visit, procedures to be done, and ICF
  - Call patient 48 hrs. before visit to confirm
  - Email PI (or investigators) with name, contact info, visit requirements, etc.
  - Prepare folder with necessary case report forms, up to date ICF etc.
  - Greet patient in lobby
- Investigator will:
  - Obtain informed consent per institutional requirements, complete all visit procedures
  - Notify team if patient is eligible, agreeable and ready to enroll

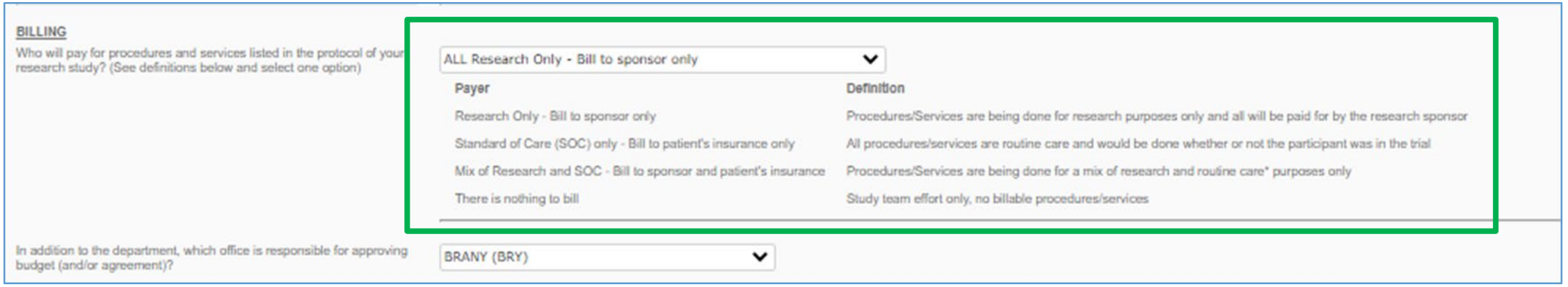
Sub-process

- Coordinator will:
  - Enter screening data in EDC within 24 hrs.
  - Randomize patient in EDC within 48 hrs.

Transition

Billing Review and Clearing Charges

Velos Study Billing Type/Status



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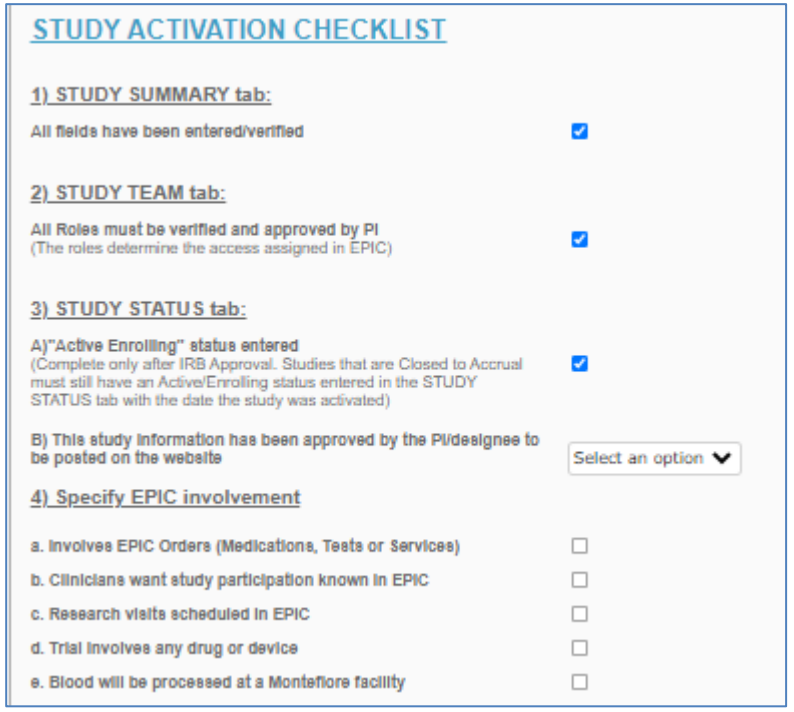
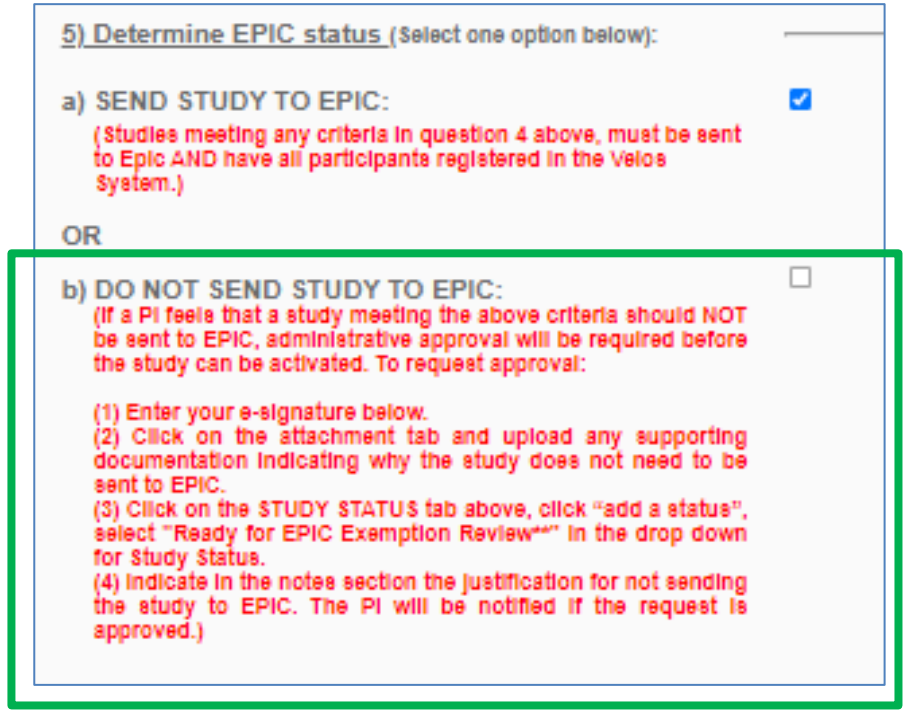
Billing Review and Clearing Changes

Studies Sent to Epic vs Not Sent to Epic





Follow instructions in Red in order verify Study does not need to be in Epic

Ensure you understand how your study is listed in Velos as this will have implications in Epic!

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Billing Review and Clearing Charges

For Studies sent to Epic and are mixed SOC/Res billable:

- Patient status = Initial Consent Signed
- All charges for patients associated to research study will be “held” in Epic (including any non study-related charges) for duration of patient’s association to research study.
- All research patient charges must be reviewed in Epic at minimum on a **weekly basis**
- Once patient has completed the research study- they must be marked “completed/off-study” in Velos- this will trigger Epic to stop holding charges

- ❑ **Clarify with your PI – who is doing this?**
- ❑ **Familiarize yourself with the Billing and Epic details of the study in the Velos Study Summary**

Common Problems that Hinder Success

- Inadequate training
  - Protocol, applicable regulations (local and federal), SOPs, investigational product management, reviewing IRB requirements, etc.
  - *Misunderstanding leads to mistakes!*
- Inadequate documentation
  - If you didn't document it, it didn't happen! Records are retained for years after the study is completed- don't leave any gaps that can lead to bigger questions!
- Ineffective/unclear communication
  - Over-communicating/under-communicating
  - "Closed loop" communication
- Limited resources means importance of planning ahead!

General Troubleshooting

Contact Type	Email
Key Study Team	PIs, Co-Investigators, Study Coordinators, Regulatory Coordinator, Research Assistants, etc.
Central Study Stakeholders	Sponsor, Clinical Research Organization, Data Coordinating Center, DSMB, Clinical Coordinating Center
Ancillary Collaborators	Pharmacy, Pathology, Radiology, Clinical Research Center, Biorepository, etc.
IRB	Einstein IRB: IRB@einsteinmed.org BRANY IRB: esummers@brany.com
Institutional Systems	Epic IT: Jason Hussey jhussey@montefiore.org Velos Helpdesk: veloshelp@montefiore.org Einstein iRIS Support: iris-support@einsteinmed.org
Research Compliance	ClinicalResearch@montefiore.org

Keep these contacts accessible and in a central location!

Coordinator as “Navigator”

- Success relies heavily on CRC’s ability to effectively **manage day-to-day study tasks**
  - Problem-solving, taking initiative, effective time management, collaboration, and prioritization of tasks.
  - Build in turnaround time!

– **Effective Communication**: Be concise and clear

  - What do stakeholders need to know?
  - Determine frequency and nature of team meetings
  - Create scripts/templates; practice interpreting study jargon

- **Seeing the “bigger picture”:** orient yourself on where you, and the patient, are in the overall study process

Research Studies as a “Service”

Participation in Research is an *Experience* for Patients

- Support their needs wherever possible
- Listen to their feedback and use it for improvement
- Be knowledgeable about your research, but be honest about what you don’t know
- Practice empathy

Resources

- DOM Coordinator Training & User Access Checklist
- Epic/Velos Checklists & Tip Sheets
  - Study Management and Activation
  - Patient Status Flow
  - Checklist – Patient Enrollment
  - Placing and Linking Orders to a Study
  - New Research Study Review Workflow
  - Research Billing Review Criteria Set-up
- NIH Guidelines for Developing a Manual of Procedures
- Einstein Policies:
  - Principal Investigator Requirements
  - Principal Investigator Responsibilities

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