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**IN CLINICAL RESEARCH**

# Clinical Research Unveiled: Insights from an Interim Analysis Case Study

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# Tonight's Agenda

- **Meet the Presenter:** Presenter Bio
- **Understanding the Basics:** What is an Interim Analysis?
- **Deep Dive:** Case Study Insights and Lessons Learned
- **Your Turn:** Opportunity to Ask Questions in the Q & A

# Tiffany Ashton, MAS, CCRA



With over 21 years of experience working as a highly respected professional in the clinical research community, Tiffany has served various Clinical Research roles, including the last 10 years as a consultant in the Clinical Trial Manager/Project Manager role, but also has experience as a CRC, CRA, Unblinded CRA, Lead CRA, Clinical Trial Manager, and Unblinded Clinical Trial Manager. Her firsthand industry experience is unlike others in the field. Tiffany strives to make a true and lasting impact and loves mentoring and teaching.

Tiffany is a seasoned Clinical Research Professional who has earned a BA from San Diego State University, a Masters of Advanced Studies in Clinical Research from the University of California, San Diego, an ACRP Certified Clinical Research Associate designation, and a Certificate in Clinical Trials Design and Management.

In addition, she possesses an extensive list of therapeutic experience which include: Oncology, Rare Disease, Gene Therapy, CNS, Gastroenterology, Woman's Health, and many others in Phase I through IV settings on the Study Sponsor and CRO side.

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# Understanding the Basics

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# What is an Interim Analysis (IA)?

- ✓ An Interim Analysis (IA) in Clinical Research is similar to a database lock conducted on either drug or device studies, however, an IA is a snapshot in time to help provide the study Sponsor (Merck, Pfizer, Gilead, etc.) data on how well their drug or device is performing.
- ✓ IAs usually happen at a pre-defined threshold such as the 100<sup>th</sup> patient to reach Visit 5 or 50 patients to complete the study.
- ✓ After the data is cleaned and provided to the Sponsor, the Sponsor may perform any combination of the following:
  - Proceed with the study as planned
  - Discontinue the study based on the results
  - Present emerging findings at an upcoming conference
- ✓ Not every project has an IA, but if there is one scoped in the Statement of Work (SOW), you will be prepared based off our discussion tonight.

Let's Continue to Discuss Some of the Key Players of an Interim Analysis



# Key Players in an Interim Analysis

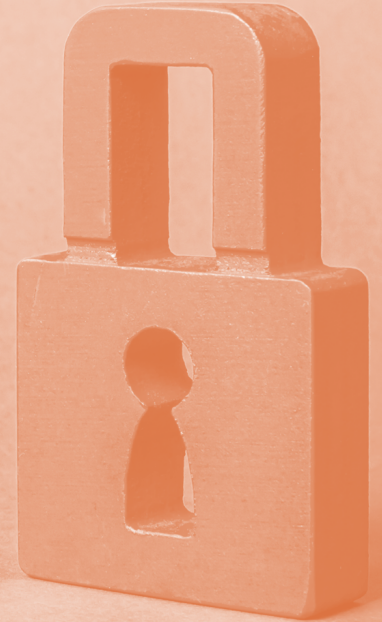
- ✓ There are several contributors to an Interim Analysis. These include contributors from: the Sponsor, Clinical Research Organization (CRO), Investigator Sites, and Study Vendors such as Central Laboratories or Imaging Centers.
- ✓ Within the CRO team, the Clinical Trial Manager (CTM) also known as the Project Manager (PM) helps drive the internal and external teams towards a successful IA.
- ✓ The CTM must work with Data Management (DM), Clinical Research Associates (CRAs), Study Vendors and Investigator Sites to inform them of the IA and the need to ensure all open queries are resolved, missing pages entered, answered queries closed, and Source Data Verification (SDV) is completed.

Let's Walk Through the Steps of Planning for an IA.



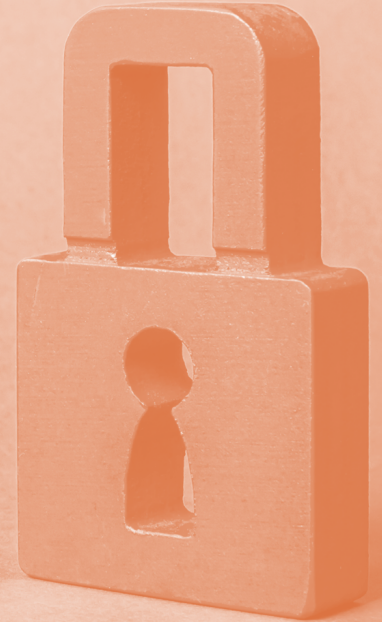
## Preparing for an Interim Analysis

- ✓ To properly prepare for an IA, the CTM must meet with the internal study team as soon as possible. This would include DM, Medical Monitoring and the CRAs. Each of these groups will have a big impact on the IA.
- ✓ The IA timelines should be reviewed (typically you have 6 weeks, but sometimes less before the data cut), and the team should work backwards and set internal deadlines. If needed, an abbreviated Gantt chart can be created for this specific study request.
  - *Example: The IA data cut will occur once the 100<sup>th</sup> person reaches Visit 5 on the trial (their half-way point on the study)*
- ✓ A CTM will need to closely track the 98<sup>th</sup>, 99<sup>th</sup> and 100<sup>th</sup> patient as any shifts to visit dates will impact the data cut.
- ✓ A CTM should ensure their sites are aware and schedule their patients towards the early side of their visit window.



## Preparing for an Interim Analysis

- ✓ In addition to closely monitoring patient visits, the CTM must work closely with Data Management and the CRAs on the current DM stats and upcoming monitoring visits to ensure:
  - All Missing Pages are Entered
  - All Answered Queries are Closed by the CRAs or DM
  - All Open Queries are Answered
  - All Source Data Verification (SDV) is Completed
- ✓ The CTM needs to work closely with the CRAs to understand how many visits would be needed to take care of the above.
- ✓ A CTM may even have to call the site to ask for special permission for back-to-back monitoring visits.
- ✓ Within the timelines, the CTM and DM needs to plan for at least two rounds of data cleaning for the IA (as time permits) as typically after CRA monitoring visits, additional queries are posted by DM which could require additional SDV.





# Example Data Cleaning Tracker

*\*This information was pulled from the EDC by DM and next visit dates added by CRAs.*

Site	Page pending SDV	Missing Pages	Incomplete Pages	Open Queries	CRA Answered Queries	Answered DM Queries	Pages Pending Signature	Next IMV	Next unIMV
235: Site A	62	465	47	22	17	25	3647	09-11 Dec-24	25-27 Nov-24
236: Site B	266	751	13	52	22	93	5069	14-17 Dec-24	02-03Dec-24
237: Site C	124	573	72	60	162	192	4047	11-13 Dec-24	25-26 Nov-24
238: Site D	0	0	0	1	0	0	4	3-Dec-24	Masked Team will conduct visit
239: Site E	2	160	34	9	9	10	1515	27-Nov-24	19-20 Nov-24
240: Site F	42	1277	34	12	112	45	10566	14-Nov-24	02-04 Dec-24
241: Site G	22	55	35	0	9	5	219	11-Dec-24	06-07 Nov-24
242: Site H	0	0	0	0	0	0	0	11-Dec-24	Remote: IP accountability
243: Site I	328	1770	65	6	177	49	9264	09-11 Dec-24	09-12 Dec-24
244: Site J	70	937	35	14	20	34	5988	10-12 Dec-24	03-06 Dec-24
245: Site K	69	334	8	32	8	26	2071	11-13 Dec-24	09-10 Dec-24
246: Site L	0	0	1	0	0	0	39	07 Nov 2024 - pending IP return	Masked Team will conduct visit
247: Site M	151	265	14	1	52	15	2187	16-18 Dec-24	05-06 Dec-24
248: Site N	116	343	95	95	6	29	1681	10-Dec-24	09-10 Dec-24
249: Site O	186	1030	520	18	2	29	3668	13-18 Dec-24	3-Dec-24
<b>Total</b>	<b>1438</b>	<b>7960</b>	<b>973</b>	<b>322</b>	<b>596</b>	<b>552</b>	<b>49965</b>		



# Don't Forget About Your Vendors!

- All vendor data collected for that 100<sup>th</sup> patient would need to be transferred as well.
- There may be data cleaning needed on the vendor side.
- A CTM should notify their vendors ASAP once an IA is determined as there could also be budget implications.

## Medical Monitoring

- The Medical Monitor who provides medical oversight on the trial will review the medical data for the interim analysis and will query Adverse Events and Concomitant Medications in case queries need to be issued. Their review needs to be built into the timeline as well.



# Let's Recap – Interim Analysis

1

Meet with the Internal Study Team and Vendors ASAP

2

Review Timelines

3

Inform Sites of IA and Track Patient's Visit at the Site

4

Data Cut Date

5

Have Your CRAs Schedule their MVs and Work with DM to Clear Open Issues

6

Allow For An Additional MV After Medical Monitor or DM Has Queried

7

Work With DM to Extract Data and Provide to Sponsor for Analysis and Final Decision

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**The CTM should keep the Sponsor informed during this time and be willing to help their teams as needed!**

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# Case Study Insights

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# Interim Analysis on Phase III Trial for Month 9

## Background:

- The Sponsor of a Phase III trial wanted an Interim Analysis once all 450 patients reached Month 9 on the trial in order to evaluate their primary objective and determine next steps in the study.
- All data needed to be cleaned and provided to the Sponsor as an output on the 10th January and the study team was notified on 15 October.
- The last patient reached Month 9 on 01 December.

## Challenges:

- New Clinical Trial Manager joined the team 25 November without history of the project
- Lots outstanding data at the site to be addressed.
- Holidays/Out of Office (Limited Availability) – between 23 December – 02 January; Even coordinating with the patient and their schedule
- Global Team with various holidays and time zones.



# How We Made it a Success

## Mitigations

- Sponsor and CRO CTM met daily during the data cleaning process (typically this is a task the CRO CTM manages solo with minimum Sponsor support). This ensured the study stayed on track and the CRO CTM had background information.
- Sponsor CTM sent sites tailored DM reports to help them address their outstanding data.
- CRAs planned multiple monitoring visits within window as well as took co-monitors as needed when data was too large for 1 CRA.
- Sites with early holiday closures were prioritized for data cleaning.
- For issues with data that arose, the team decided to triage those issues that would have an impact on the data cut delivery vs. those that could be dealt with later.



# Lessons Learned

- Never underestimate the data cleaning process:
  - Data should be cleaned throughout the trial. The CTM should provide oversight on data metrics (open queries, pending SDV, missing pages, etc.) to ensure there will not be an issue in case of an Interim Analysis.
  - CRAs should be held accountable for their assigned sites and be given targets that they can work towards throughout the study and the flexibility to visit their sites more often up front if data cleaning is failing behind.
- We had to build a risk management plan based off the given information at that timepoint and adapt as needed.
- You have to work as a team and be ready to pivot. Communication is key. As a CTM, you have to be ready to jump in wherever. You will be held accountable if the IA is not successful.

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# Open Discussion

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