Balancing Transparency and Blind Integrity in Ongoing Clinical Trials.

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Agenda

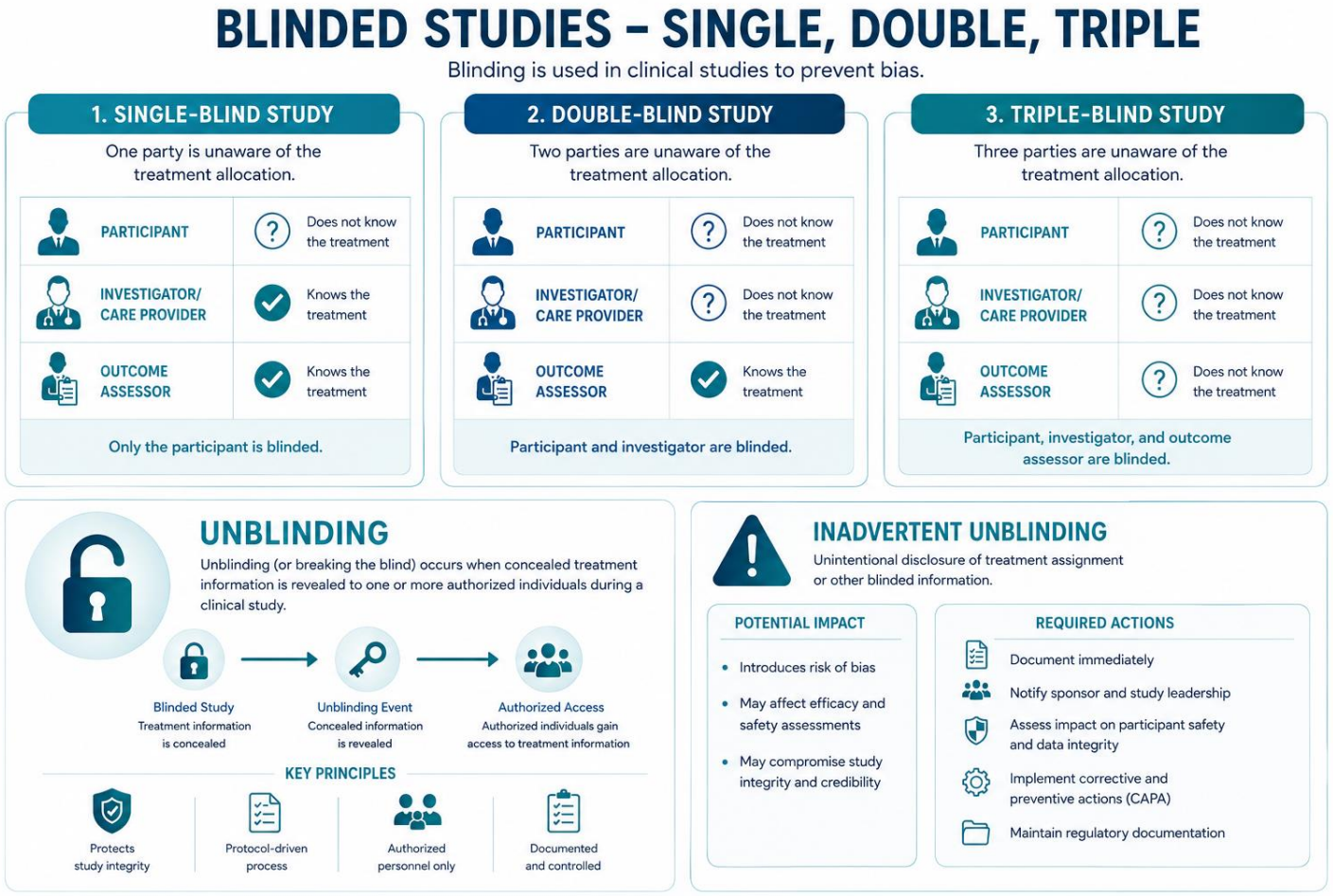
- Interim Data Disclosure
- Overview of Blinded Studies
- Consequences of Inadvertent unblinding
- Need of an Hour
- EMA Guidance on Ongoing Trials
- Finding the Right Data
- Practical Examples
- Conclusion
- Closing Message

Interim Data Disclosure

Ongoing interim trial results: Generally, not published under regulatory agencies.

- **Health Canada's PRCI initiative**- Interim analysis of ongoing studies will not be considered for release
- **EMA Policy 0070-** Interim results and reports could be published.
  - **Version 1.3-** No formal framework for handling ongoing blinded studies, interim results were generally handled case-by-case

Overview of Blinded Studies



- Blinded studies- Single, Double, Triple
- Unblinding- concealed treatment information is revealed to one or more individuals.
- Inadvertent unblinding

Consequences of Inadvertent unblinding

- Introduction of bias
- Reduced study integrity
- Statistical challenges
- Altered safety reporting
- Regulatory concerns
- Potential trial termination

Need of an hour

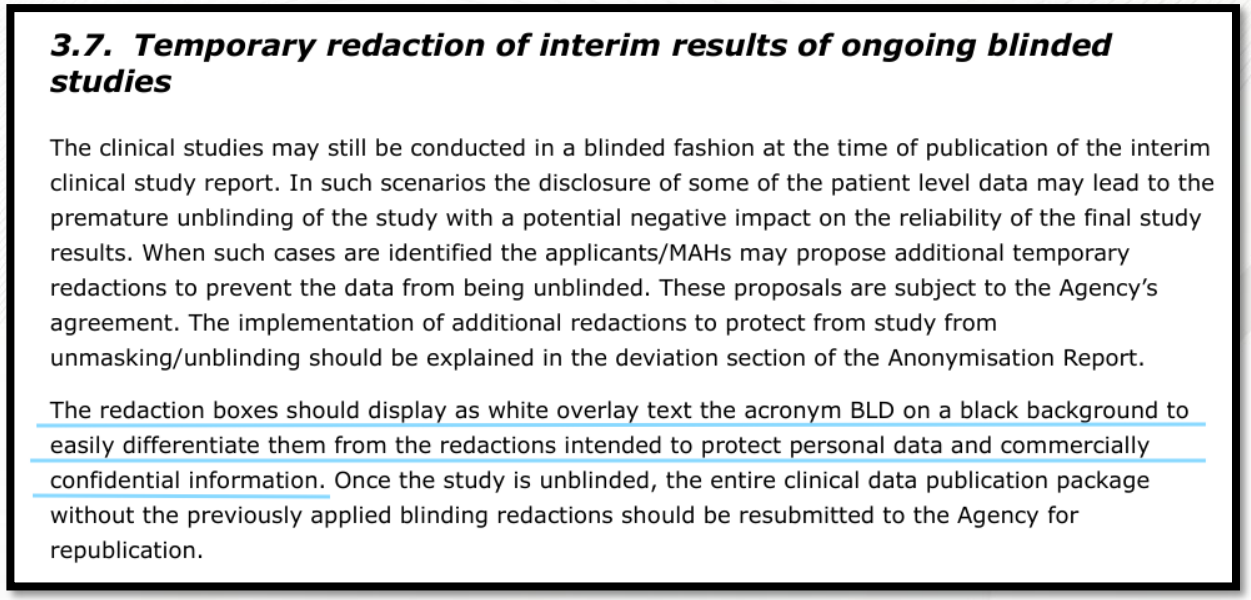
Publishing interim data from ongoing blinded studies, therefore, requires

- careful redaction and masking
- to protect the blind, prevent bias
- to maintain the validity of study outcomes.

EMA Guidance on Ongoing Trials

Version 1.5 Update: Released in May 2025, External Guidance on Policy 0070 (v1.5) formally introduced temporary structured blinded (BLD) redactions so interim results of ongoing blinded studies stay protected until full unblinding occurs

- Interim reports may be published while studies remain blinded.
- Patient-level data may risk inadvertent unblinding.
- Temporary **BLD** redactions may be applied to protect the blind and must be justified and documented.
- Remove **BLD** redactions once the study is unblinded.
- **Benefit**- Provides clear guidance and reduces ambiguity.



3.7. Temporary redaction of interim results of ongoing blinded studies

The clinical studies may still be conducted in a blinded fashion at the time of publication of the interim clinical study report. In such scenarios the disclosure of some of the patient level data may lead to the premature unblinding of the study with a potential negative impact on the reliability of the final study results. When such cases are identified the applicants/MAHs may propose additional temporary redactions to prevent the data from being unblinded. These proposals are subject to the Agency's agreement. The implementation of additional redactions to protect from study from unmasking/unblinding should be explained in the deviation section of the Anonymisation Report.

The redaction boxes should display as white overlay text the acronym BLD on a black background to easily differentiate them from the redactions intended to protect personal data and commercially confidential information. Once the study is unblinded, the entire clinical data publication package without the previously applied blinding redactions should be resubmitted to the Agency for republication.

Finding the Right Data

Narratives

CSR body and synopsis: Text, Mini-narratives, Listings, Summary tables, Figures

Module 2: Summary tables, Mini narratives, Text

TLF

Data Identifier

- ❑ Treatment group identifier
- ❑ Randomization codes/ Kit number
- ❑ Dose levels or titration schedules
- ❑ Biomarker/Pharmacokinetic data

Practical Examples

Example 1-Narrative

- Subject 111-1111
- Subject 111-1111, a 23-year-old, Asian male from Japan with Type 2 diabetes was randomized to the [redacted] on 23 December 2018. The subject experienced a serious adverse event of diarrhoea.

- Subject 111-4444
- Subject 111-4444, a 30-year-old, White female from Germany with Type 2 diabetes was randomized to [redacted] on 30 November 2018. The subject experienced serious adverse event of herpes zoster.

Summary Data Strategies

- Small subgroup sizes increase the risk of re-identification and inadvertent unblinding, necessitating additional data masking or redaction i.e. in case of

❑ Low or null frequency Demography

❑ Null frequency in treatment group for AE category

❑ Other tables with low or null frequency

- Balancing Act: Maximize data transparency while safeguarding study blinding and integrity.

Example 2-Demography

Summary of Baseline Characteristics- Approach 1

Attribute	BLD [redacted]		
Age (years), mean (SD)	14.68 (1.72)	14.94 (1.61)	14.56 (1.78)
Female, n (%)	47 (53.4)	39 (46.4)	41 (48.2)
Male, n (%)	41 (46.6)	45 (53.6)	44 (51.8)
Race			
American Indian or Alaska native, n (%)	1 (1.1)	1 (1.2)	0
Asian, n (%)	26 (29.5)	23 (27.4)	23 (27.1)
Black or African American, n (%)	6 (6.8)	5 (6.0)	9 (9.4)
White, n (%)	52 (58.0)	52 (61.9)	52 (61.2)
Multiple, n (%)	3 (3.4)	3 (3.6)	1 (1.2)

Example 2-Demography

Summary of Baseline Characteristics- Approach 2

Attribute	PBO N=88	Drug XYZ 4mg N=84	Drug XYZ 6mg N=85
Age (years), mean (SD)	14.68 (1.72)	14.94 (1.61)	14.56 (1.78)
Female, n (%)	47 (53.4)	39 (46.4)	41 (48.2)
Male, n (%)	41 (46.6)	45 (53.6)	44 (51.8)
Race			
American Indian or Alaska native, n (%)	BLD		
Asian, n (%)			
Black or African American, n (%)			
White, n (%)			
Multiple, n (%)			

Example 2-Demography

Summary of Baseline Characteristics- Approach 3

Attribute	PBO N=88	Drug XYZ 4mg N=84	Drug XYZ 6mg N=85
Age (years), mean (SD)	14.68 (1.72)	14.94 (1.61)	14.56 (1.78)
Female, n (%)	47 (53.4)	39 (46.4)	41 (48.2)
Male, n (%)	41 (46.6)	45 (53.6)	44 (51.8)
Race			
American Indian or Alaska native, n (%)	BLD		
Asian, n (%)			
Black or African American, n (%)	6 (6.8)	5 (6.0)	9 (9.4)
White, n (%)	52 (58.0)	52 (61.9)	52 (61.2)
Multiple, n (%)	3 (3.4)	3 (3.6)	1 (1.2)

Example 3-Adverse Event

CSR synopsis and body- Maintain consistency within documents

Overview of Adverse events

A numerically higher proportion of participants in the Drug XYZ treatment groups reported TEAEs compared to the placebo group. Most AEs were of mild or moderate severity. A similar proportion of participants in the Drug XYZ treatment groups reported severe AEs compared to the placebo group. A similar proportion of participants in the Drug XYZ 6 mg group reported SAEs compared to the placebo group. No SAEs were reported in the Drug XYZ 4 mg group. A similar proportion of participants permanently discontinued study intervention due to AEs in the Drug XYZ 6mg and placebo group

CSR synopsis and body- Overview of Adverse events

Attribute	PBO N=88, n(%)	Drug XYZ 4mg N=84, n(%)	Drug XYZ 6mg N=85, n(%)
TEAEs	47 (53.4)	50 (60.2)	60 (70.6)
Mild	27 (30.7)	37 (44.6)	43 (50.6)
Moderate	18 (20.5)	12 (14.5)	15 (17.6)
Severe	2 (2.3)	1 (1.2)	2 (2.4)
SAE	3 (3.4)	0	2 (2.4)
AE leading to permanent discontinuation of study drug	2 (2.3)	0	1 (1.2)
AE leading temporary interruption of study drug	9 (10.2)	5 (6.0)	8 (9.4)
AE leading discontinuation from study	1 (1.1)	0	1 (1.2)

Example 3-Adverse Event

CSR synopsis and body- Maintain consistency within documents

Overview of Adverse events

A numerically higher proportion of participants in the Drug XYZ treatment groups reported TEAEs compared to the placebo group. Most AEs were of mild or moderate severity. A similar proportion of participants in the Drug XYZ treatment groups reported severe AEs compared to the placebo group. A similar proportion of participants in the BLD group reported SAEs compared to the BLD No SAEs were reported in the BLD group. A similar proportion of participants permanently discontinued study intervention due to AEs in the BLD

Attribute	PBO N=88, n(%)	Drug XYZ 4mg N=84, n(%)	Drug XYZ 6mg N=85, n(%)
TEAEs	47 (53.4)	50 (60.2)	60 (70.6)
Mild	27 (30.7)	37 (44.6)	43 (50.6)
Moderate	18 (20.5)	12 (14.5)	15 (17.6)
Severe	2 (2.3)	1 (1.2)	2 (2.4)
SAE	BLD		
AE leading to permanent discontinuation of study drug			
AE leading temporary interruption of study drug	9 (10.2)	5 (6.0)	8 (9.4)
AE leading discontinuation from study	BLD		

Example 4-Adverse Event

CSR synopsis and body, Module 2.5, Narrative -Cross-document consistency

CSR synopsis and body- Overview of Adverse events

Attribute	PBO N=88, n(%)	Drug XYZ 4mg N=84, n(%)	Drug XYZ 6mg N=85, n(%)
TEAEs	47 (53.4)	50 (60.2)	60 (70.6)
Mild	27 (30.7)	37 (44.6)	43 (50.6)
Moderate	18 (20.5)	12 (14.5)	15 (17.6)
Severe	2 (2.3)	1 (1.2)	2 (2.4)
SAE	3 (3.4)	0	2 (2.4)
AE leading to permanent discontinuation of study drug	2 (2.3)	0	1 (1.2)
AE leading temporary interruption of study drug	9 (10.2)	5 (6.0)	8 (9.4)
AE leading discontinuation from study	1 (1.1)	0	1 (1.2)

- Module 2.5 - Overview of Adverse events from Placebo controlled set

Attribute	PBO N=88, n(%)	Drug XYZ 4mg N=84, n(%)	Drug XYZ 6mg N=85, n(%)
SAE	3 (3.4)	0	2 (2.4)
TEAEs	47 (53.4)	50 (60.2)	60 (70.6)
Mild	27 (30.7)	37 (44.6)	43 (50.6)
Moderate	18 (20.5)	12 (14.5)	15 (17.6)
Severe	2 (2.3)	1 (1.2)	2 (2.4)
Permanent DC from study drug due to AE	2 (2.3)	0	1 (1.2)
Temporary interruption from study drug due to AE	9 (10.2)	5 (6.0)	8 (9.4)
DC from study due to AE	1 (1.1)	0	1 (1.2)

- TOC of patient narratives

Sr no.	Subject ID	Event categories	Treatment group	Sr no.	Subject ID	Event categories	Treatment group
1	111-1111	SAE	Placebo	6	111-6666	AEDC	Placebo
2	111-2222	SAE	Placebo	7	111-7777	AEDC	Drug XYZ 6mg
3	111-3333	SAE	Placebo	8	111-8888	AESI	Placebo
4	111-4444	SAE	Drug XYZ 6mg	9	111-9999	AESI	Drug XYZ 6 mg
5	111-5555	SAE	Drug XYZ 6mg	10	111-0000	AESI	Drug XYZ 6 mg

Example 4-Adverse Event

CSR synopsis and body, Module 2.5, Narrative -Cross-document consistency

- CSR synopsis and body- Overview of Adverse events

Attribute	PBO N=88, n(%)	Drug XYZ 4mg N=84, n(%)	Drug XYZ 6mg N=85, n(%)
TEAEs	47 (53.4)	50 (60.2)	60 (70.6)
Mild	27 (30.7)	37 (44.6)	43 (50.6)
Moderate	18 (20.5)	12 (14.5)	15 (17.6)
Severe	2 (2.3)	1 (1.2)	2 (2.4)
SAE	BLD		
AE leading to permanent discontinuation of study drug			
AE leading temporary interruption of study drug	9 (10.2)	5 (6.0)	8 (9.4)
AE leading discontinuation from study	BLD		

- Module 2.5 - Overview of Adverse events from Placebo controlled set

Attribute	PBO N=88, n(%)	Drug XYZ 4mg N=84, n(%)	Drug XYZ 6mg N=85, n(%)
SAE	BLD		
TEAEs	47 (53.4)	50 (60.2)	60 (70.6)
Mild	27 (30.7)	37 (44.6)	43 (50.6)
Moderate	18 (20.5)	12 (14.5)	15 (17.6)
Severe	2 (2.3)	1 (1.2)	2 (2.4)
Permanent DC from study drug due to AE	BLD		
Temporary interruption from study drug due to AE	9 (10.2)	5 (6.0)	8 (9.4)
DC from study due to AE	BLD		

- TOC of patient narratives

Sr no.	Subject ID	Event categories	Treatment group	Sr no.	Subject ID	Event categories	Treatment group
1	111-1111	SAE	BLD	6	111-6666	AEDC	BLD
2	111-2222	SAE		7	111-7777	AEDC	
3	111-3333	SAE		8	111-8888	AESI	
4	111-4444	SAE		9	111-9999	AESI	
5	111-5555	SAE		10	111-0000	AESI	

Other Tables

- Other summary tables e.g. Protocol Deviation, Lab parameter, Concomitant Medication, Medical History, PK data
- Shift table
- TLFs

Conclusion

Blinded Data (BLD) redaction should protect trial integrity without compromising transparency.

The key principles are:

- Enable Transparency for ongoing trial
- Protect trial integrity
- Maintain Consistency
- Avoid Over-Redaction
- Be Precise and Targeted
- Preserve Data Utility

Closing Message

Effective BLD redaction is far more than a masking exercise. It requires deep expertise in regulatory clinical documents and the ability to connect and interpret information across multiple sources to ensure trial integrity.

Thank You

Questions & Discussion

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