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The use of EV data and common inspection findings EMA Stakeholder Forum on EV and Signal/Data Management

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COMPLIANCE DATA IN EUDRAVIGILANCE

- Performance indicator dashboard
- Cases reported late 15/90 days reporting period
- Cases transmitted with errors without correct follow up
- Master cases and duplicate reports
- Common inspection findings

Performance indicator dashboard

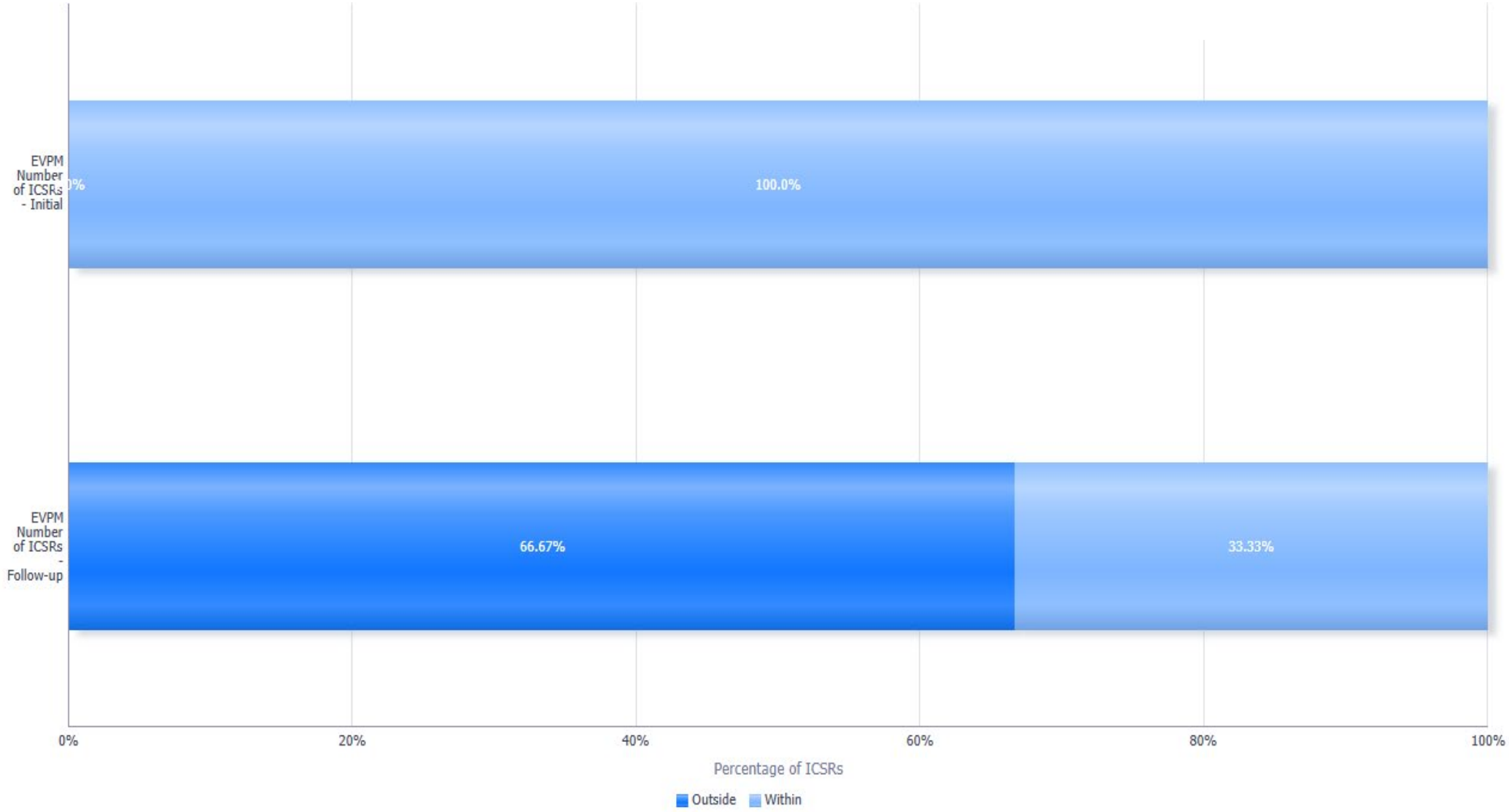
- ✓ PM and CT data
- ✓ 7/15/90 days reporting period
- ✓ Initial and follow-up cases
- ✓ Case amendments
- ✓ Nullifications

MAH performance indicator dashboard

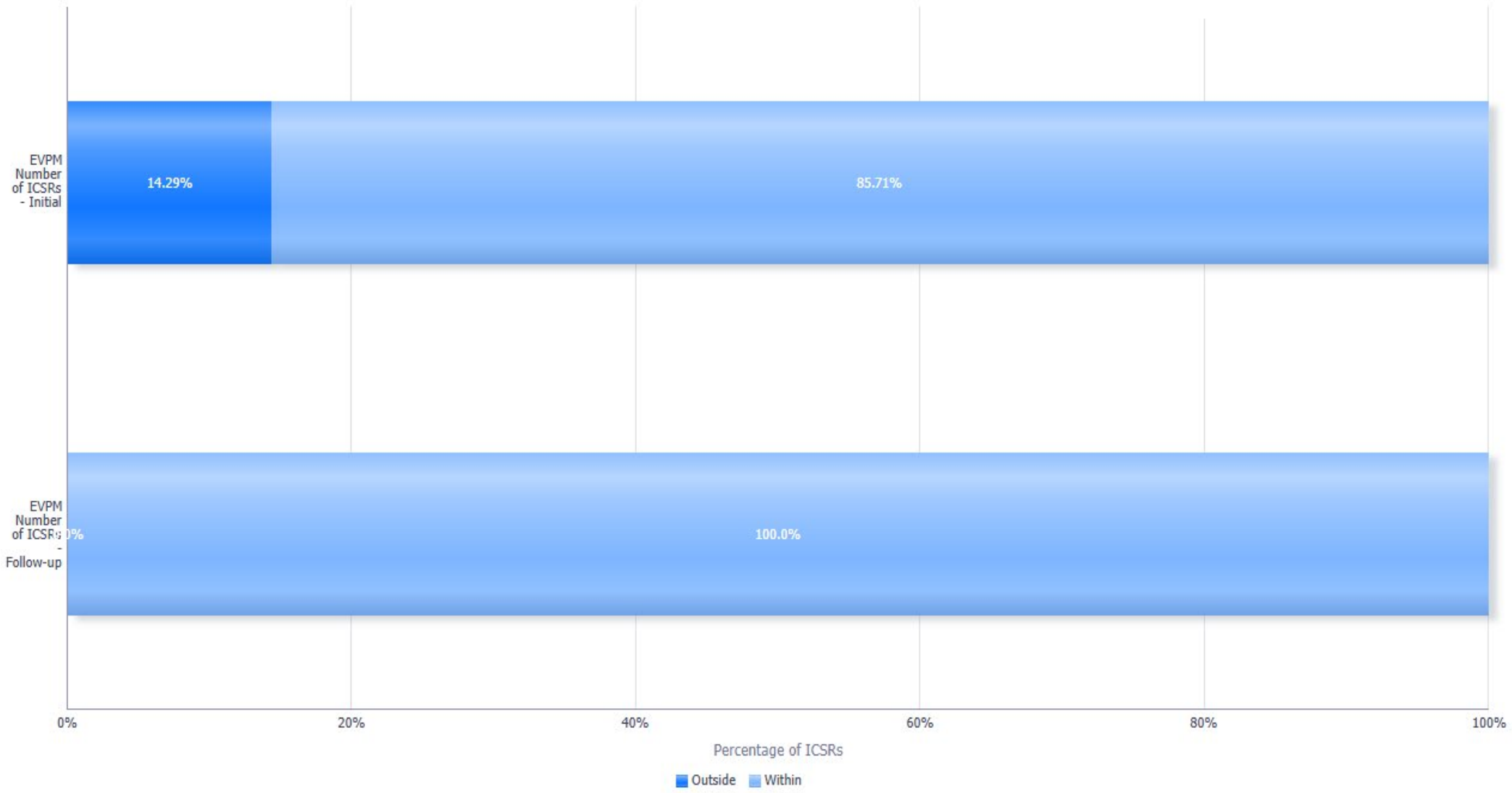
	Serious ICSRs-EVPM-Initial(15 days)		Serious ICSRs-EVPM-Follow-up(15 days)		Serious ICSRs-EVCTM-Initial(7 days)-Fatal / Life threatening		Serious ICSRs-EVCTM-Follow-up(15 days)-Fatal / Life threatening		Serious ICSRs-EVCTM-Initial(15 days)-Not Fatal / Life threatening		Serious ICSRs-EVCTM-Follow-up(15 days)-Not Fatal / Life threatening	
MAH/NCA	% compliance	Total ICSR	% compliance	Total ICSR	% compliance	Total ICSR	% compliance	Total ICSR	% compliance	Total ICSR	% compliance	Total ICSR
	97,73%	4.183	92,24%	3.275	90,91%	55	96,27%	322,00	100,00%	281,00	96,82%	1.005

Non Serious ICSRs-EVPM-Initial(90 days)		Non Serious ICSRs-EVPM-Follow-up(90 days)		EVPM	EVCTM	EVPM	EVCTM	EVPM	EVCTM
% compliance	Total ICSR	% compliance	Total ICSR	Number of intial ICSR with follow-up	Number of intial ICSR with follow-up	Number of amendment ICSR	Number of amendment ICSR	Number of nullification ICSR	Number of nullification ICSR
99,83%	596	96,53%	259	1068	251	357	31	110	7

ICSRs reported within/outside 7/15 days



ICSRs reported within/outside 7/15 days



Non compliance line listing

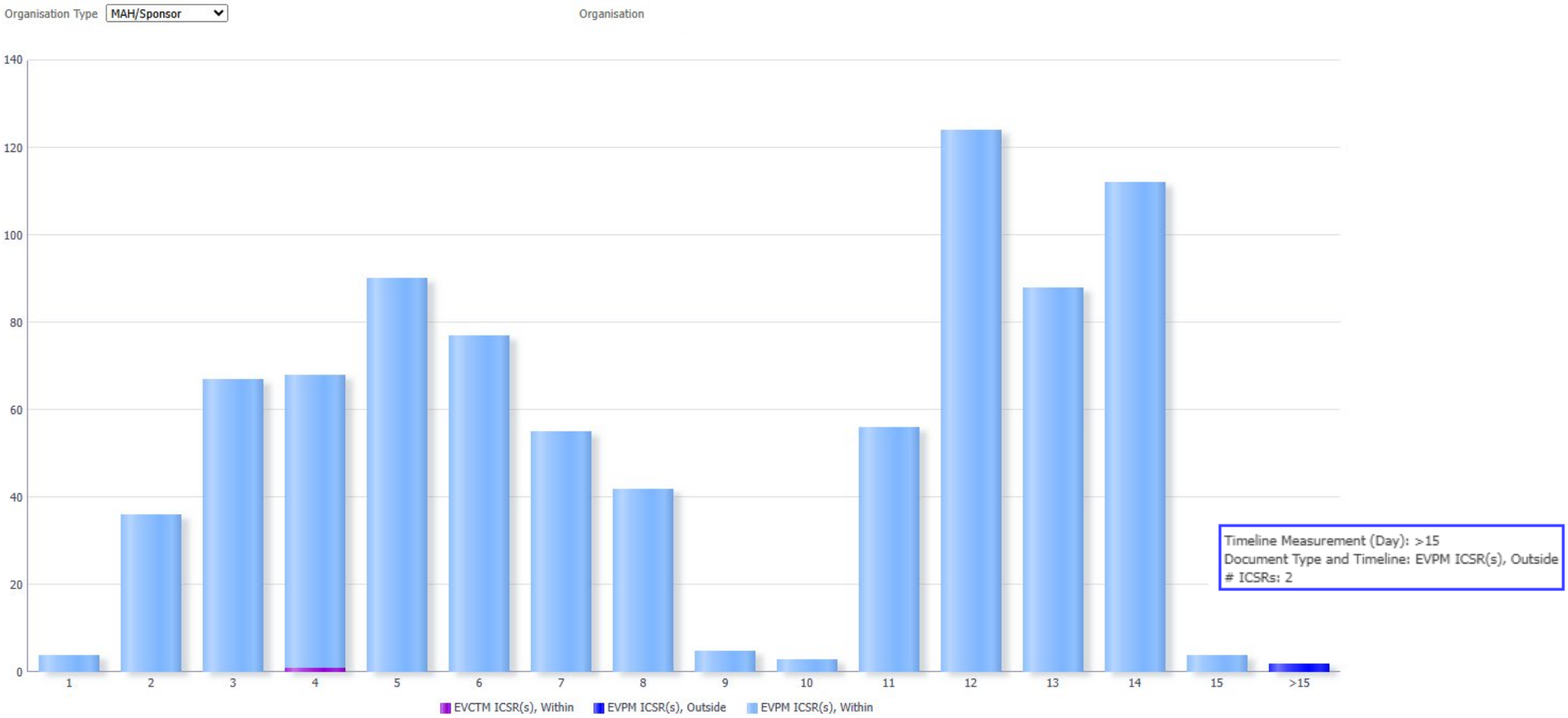
Request information regarding the late cases

Organisation Type	MAH/Sponsor	Organisation		EV Document Type
		Type of Transmission	EVPM Number of ICSRs - Initial	EVPM Number of ICSRs - Follow-up
Expedited Reporting Time (in Days)	EV Local Report Number	EV World Wide Unique Case Identifier		
21			1	
23				1
24			1	
29			1	
48				1

Non-serious cases

Organisation Type	MAH/Sponsor	Organisation		
		Transmission Type	EVPM Number of ICSRs - Initial	EVPM Number of ICSRs - Follow-up
Expedited Reporting Time (Days)	EV Local Report Number	EV World Wide Unique Case Identifier		
115				1
217			1	
			1	
239			1	
242			1	

ICSRs reported for a selected drug substance



Non compliance data

- ✓ Check compliance rate and the number of cases affected
- ✓ Break down to smaller periods, e.g. monthly or quarterly
- ✓ Compare with PSMF Annex F data
- ✓ Document request: assessment and action taken for late cases, deviations/CAPAs raised?
- ✓ Summary slides for the inspection

Case transmissions with errors without correct follow up

- ✓ Get line listing of cases for the selected MAH and period
- ✓ Request documented evidence of corrections for the respective case and ACKs/xml files

Acknowledgement codes

- ✓ ACK.A.4 Transmission acknowledgement code
- ✓ Information on the submitted batch
  - AA – *Application Acknowledgement Accept* (message successfully processed, no further action)
  - AE – *Application Acknowledgment Error* (error detected, error response has additional detail, some ICSR message(s) need further action)
  - AR – *Application Acknowledgment Reject* (parsing error, no data extracted, **re-send the entire transaction**)

Acknowledgement codes

- ✓ ACK.B.r.6 Acknowledgement code for the ICSR message
- ✓ Information on the loading of the ICSR message
  - ➢ CA – Commit Accept (the ICSR message successfully loaded)
  - ➢ CR – Commit Reject (the ICSR message contains fatal error that prevents the ICSR from being loaded)

  ➡ re-submission required

Acknowledgement codes

- ✓ ACK.B.r.7 Error / Warning message or comment
- ✓ Description of the error(s) detected in the ICH ICSR message
- ✓ Non fatal warning message when ACK.B.r.6 is “CA”

➡ Recommendation for the MAH to review warning ACKs

with focus on relevant warnings to enhance ICSR quality

Master cases and duplicate reports

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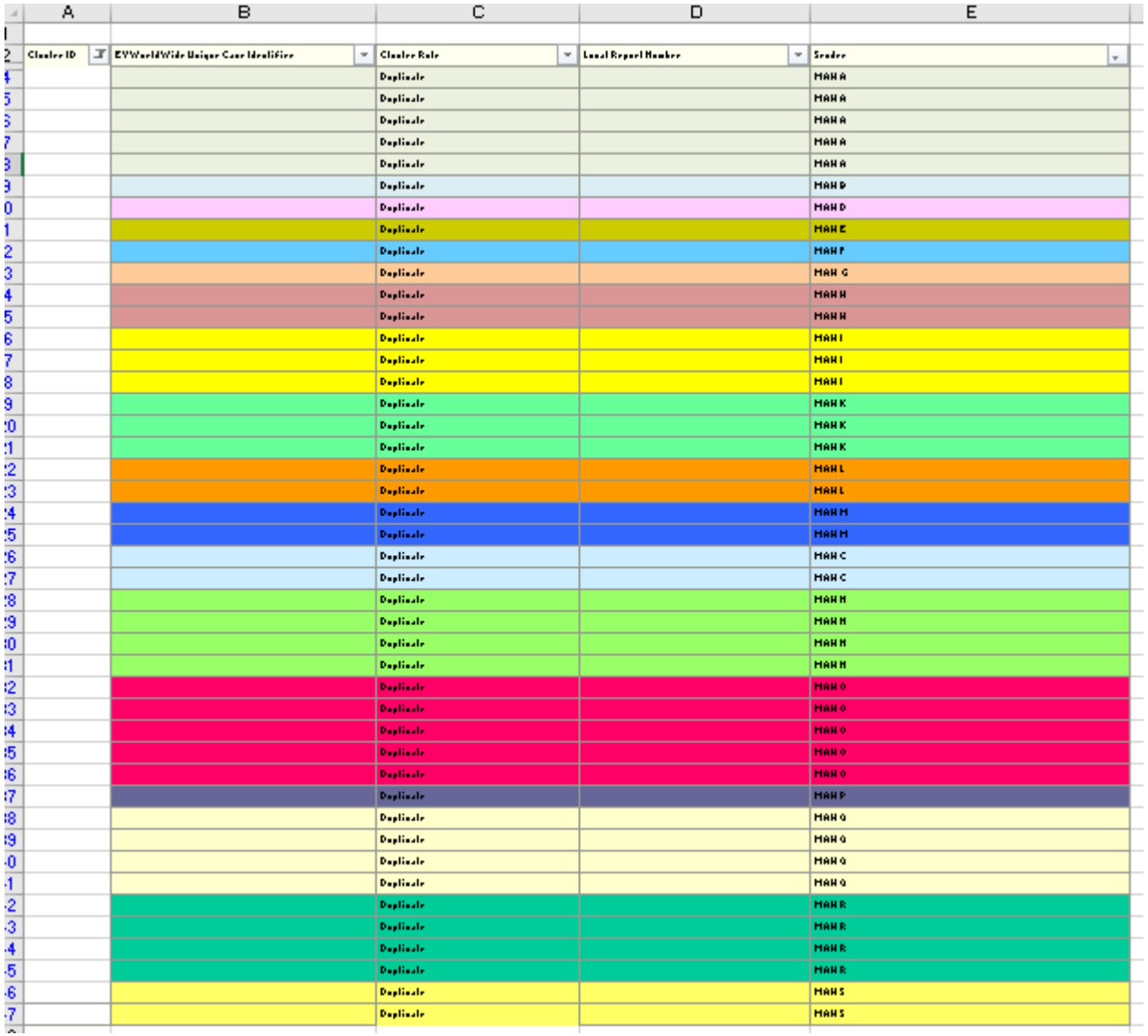
Cluster ID	EV World Wide Unique Case Identifier	Cluster Role	Local Report Number	Sender
		Master		EUDRAVIGILANCE WEB TRADER
		Duplicate		MAH A
		Duplicate		MAH A
		Duplicate		MAH A
		Duplicate		MAH A
		Duplicate		MAH A
		Duplicate		MAH B
		Duplicate		MAH D
		Duplicate		MAH E
		Duplicate		MAH F
		Duplicate		MAH G

Each colour represents a separate MAH

Master cases and duplicate reports

- ✓ Select cases from the MAH to be inspected
- ✓ Ask for the duplicate check procedure and documentation
- ✓ Check selected cases in the safety data base of the MAH
- ✓ Date case received, duplicate check, reported to EV?
- ✓ Which elements are looked at for duplicate check?
- ✓ How can several duplicates from the same MAH be found in EV?

Master cases and duplicate reports



	A	B	C	D	E
1					
2	Cluster ID	EVWorldWide Unique Case Identifier	Cluster Role	Local Report Number	Sender
4			Duplicate		MAH A
5			Duplicate		MAH A
6			Duplicate		MAH A
7			Duplicate		MAH A
8			Duplicate		MAH A
9			Duplicate		MAH B
10			Duplicate		MAH D
11			Duplicate		MAH E
12			Duplicate		MAH F
13			Duplicate		MAH G
14			Duplicate		MAH H
15			Duplicate		MAH H
16			Duplicate		MAH I
17			Duplicate		MAH I
18			Duplicate		MAH I
19			Duplicate		MAH K
20			Duplicate		MAH K
21			Duplicate		MAH K
22			Duplicate		MAH L
23			Duplicate		MAH L
24			Duplicate		MAH M
25			Duplicate		MAH M
26			Duplicate		MAH C
27			Duplicate		MAH C
28			Duplicate		MAH N
29			Duplicate		MAH N
30			Duplicate		MAH N
31			Duplicate		MAH N
32			Duplicate		MAH O
33			Duplicate		MAH O
34			Duplicate		MAH O
35			Duplicate		MAH O
36			Duplicate		MAH O
37			Duplicate		MAH P
38			Duplicate		MAH Q
39			Duplicate		MAH Q
40			Duplicate		MAH Q
41			Duplicate		MAH Q
42			Duplicate		MAH R
43			Duplicate		MAH R
44			Duplicate		MAH R
45			Duplicate		MAH R
46			Duplicate		MAH S
47			Duplicate		MAH S

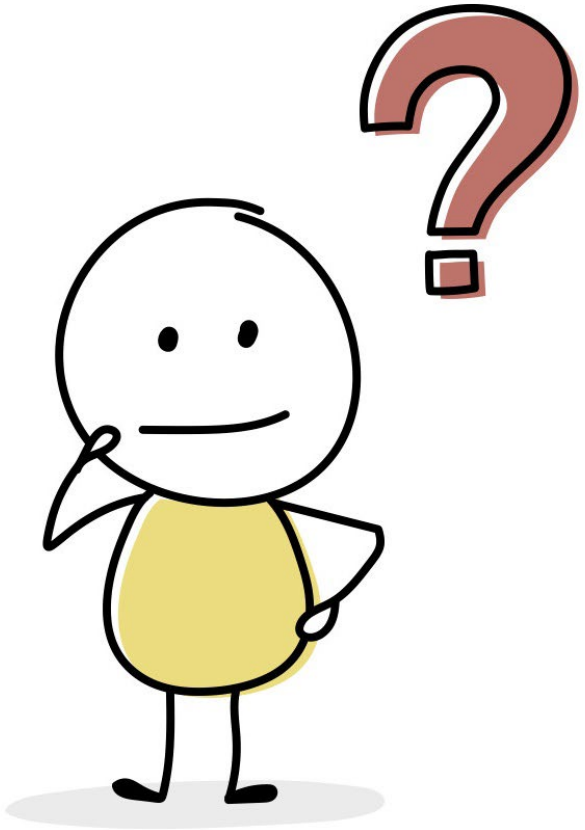
- 43 duplicates detected for one master case
- Several MAHs with 4 or 5 duplicates
- Duplicates significantly increase the size of EV data and impair analysis time

Common findings related to ICSR quality

- ✓ Inconsistencies between narrative and structured fields
- ✓ Not all information in narrative entered into structured fields, e.g. tests, patient's medical history etc.
- ✓ Incorrect coding of reported events, e.g. associated symptoms of a diagnose were entered as reaction
- ✓ Maternal exposure, missed dose, product issue, therapy cessation without associated event entered as reaction
- ✓ Events occurring at different time points were captured in one case
- ✓ Appropriate nullflavor not used for patient initials, batch number etc.

Common findings related to ICSR reporting

- ✓ Overreporting of invalid reports without an identifiable patient, no reported event, or suspected drug as placebo
- ✓ Overreporting of cases with outcome death, insufficient follow-up, no medical assessment and coding to a fitting LLT
- ✓ Overreporting of special situation cases
- ✓ Incorrect seriousness assessment
- ✓ Incorrect/missing causality assessment
- ✓ Incorrect handling of follow-up information, new case versus case amendment



THANK YOU VERY MUCH

FOR YOUR ATTENTION

ANY QUESTIONS ?

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