

# Standardization and Unification of Deficiency Language in Auditing and Monitoring

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# **BACKGROUND**

Given the ever-expanding complexity of clinical trials and the regulatory environment, the need for reproducible, consistent, and definitive terminology led the Quality Assurance unit of Clinical Research Administration at MSK to create a standardized list of detailed descriptions and gradings for observed deficiencies. This list gathers and summarizes observations from both internal MSK Auditing and Monitoring Program reviews and external agency inspections.

# 1 Unify notation and simplify communication of observations across continuum of review 2 Improve quality of CAPAs and efficacy of implementation 3 Provide roadmap-style tool for operations teams to perform gap analysis 4 Harmonize QA metrics and increase flexibility for data requests Emphasize as a practical educational resource evolving simultaneously with changing regulations

### **DEFICIENCY LANGUAGE STANDARDIZATION**

The current finalized list contains 242 unique deficiencies, each linked with the applicable institutional, federal, or ICH guideline(s); these are specified by 57 subcategories and sorted into 10 general categories:

- Regulatory Review
- ► Informed Consent
- ► Eligibility

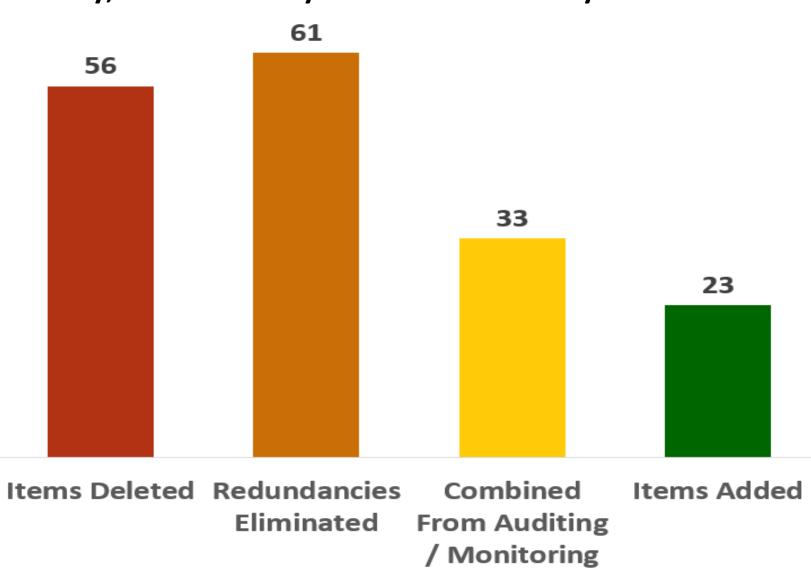
► Registration

- **▶** Evaluation
- Treatment / Intervention
- ► Toxicity / Adverse Events
- Outcome / Response
- General Data Quality
- Pharmacy Review

Category	Sub-Category	Deficiency		Associated Policy and/or SOP(s)	SOP Effective Date(s)
Eligibility	Eligibility	Enrolled participant does not meet eligibility criteria			
Registration	Registration	Failure to register participant		SOP# CR-401	9/8/2017
Registration	Registration	Participant not registered before intervention/interaction		SOP# CR-401	9/8/2017
Evaluation	Baseline	Specimen samples collected protocol-defined timeframe		SOP# CR-901	11/22/2017
Evaluation	During Study	Questionnaire/survey not completed	Major	SOP# CR402	1/3/2017
General Data Quality	General Data Quality	Missing or delinquent data	Major	SOP# CR-413	8/3/2018
Informed Consent	Informed Consent Document	Consent form does not contain all required signatures and/or initials	Major	SOP# IC-701	23-Jun-16
Informed Consent	Informed Consent Process	Non-English speaking participant: interpreter not used	Major	SOP# IC-704	10-May-18
Outcome / Response	Outcome / Response	Research document not certified	Lesser	SOP# CR-414	2-May-18
Outcome / Response	Outcome / Response	Tumor measurements/evaluation of status or disease not performed, not reported, or not documented per protocol		SOP# CR-423	5/14/2018
Regulatory Review	Delegation of Authority Log	Individual missing from, assigned incorrect responsibility, and/or did not sign Delegation of Authority log		SOP# CR-416	1/3/2017
Regulatory Review	Delegation of Authority Log	Missing Delegation of Authority log		SOP# CR-416	1/3/2017
Regulatory Review	Delegation of Authority Log	Original Delegation of Authority log missing from paper binder	Lesser		
Toxicity / Adverse Events	Toxicity / Adverse Events	Failure to report a Serious Adverse Event/AE of Special Interest		SOP# RR-408	4/25/2018
Toxicity / Adverse Events	Toxicity / Adverse Events	Late reporting of a Serious Adverse Event/AE of Special Interest	Major	SOP# RR-408	4/25/2018
Treatment / Intervention / Interaction	Protocol Therapy Diary	Required research document(s) not certified	Lesser	SOP# CR-414	2-May-18
Pharmacy Review	Adequate Security	Study-supplied agent is stored in an unsecured area		IP QA SOP# 0401	Pending
Pharmacy Review	Return of Study Agent	Unused/un-dispensed NCI-supplied study agents not returned, transferred or locally destroyed within 90 days when participants are in follow up and no NCI-supplied study agent is being administered		IP QA SOP# 0401	Pending
Pharmacy Review	Study Agent Storage	Temperature monitoring documentation is not completely or correctly maintained		IP QA SOP# 0401	Pending

### REVIEW AND SIMPLIFICATION OF LANGUAGE

Deficiencies/findings were collected from institutional and external (FDA, NCI, EMA, Sponsors, etc.) reports. The list created was reviewed and simplified to ensure consistency, accuracy, and uniformity without redundancy.



### REPORTING OPTIMIZATION

Results from auditing and monitoring activities are systematically entered into MSK Protocol Information Management System (PIMS) managed by MSK's Clinical Research Informatics Technology (CRIT) Unit. CR QA and CRIT worked in collaboration to increase the scope and refine the structure of electronic reports. Users are now able to generate reports selecting desired column data, as well as separate deficiencies in individual records for ease in filtering the report and generating counts. Coordination of auditing and monitoring reports allows for visualization and quantification of observations, and identification of trends.

			Audit Sur	nmary Report		
Report se	arch sele	ction:				
	Start Date		16	End Date	<b>6</b>	
Audit Sponsor			~	Overall Rating	•	
External Sponsor  Cooperative Group  Other External Sponsor  Audit Type			~	IRB/Informed Consent Content:	•	
			~	Phamacy:	•	
				Patient Care Review:		
A B	C Principal Investigate John Smith	D Overall Audit Rating Acceptable, Needs Follow-Up	participants (Details: Three subjects had no source docum chang study & RI not performed by TXC of load required in Category: Gingle Subject Type: Violation: Recurrent labels window (4-7 debys), assessment completed on 12997 (10 submitted to IPS within protocol or institutional timeframes Violation: Consent Form does not include updates or infor Type: Violation: Reconsent not obtained as required Detail Sub-Category withigh Subjects Type: Violation: No inverse SIDE IPSIC TOM; 8 of violations: 1 Code Informed Consent consent not completed for visition All 16 or Al2 Consent, an	neration in EMPI for Physical Examination; It of violations: T.Code: Cn-Sheets for all participants) Details: Three subjects each view missing compile agenatic tests during study & RIU off schedule (1) 20% of total required tests, by outside proteod unideal); If of violatione: T.Code Institutional Review is Details: SAE reports for two participants were reported outside of the IRB matrix required IRB. Sporancy Details: All part Alg I vanished information equired (IRB. Sporancy Details: All part Alg I vanished information experied unity on the concern translated into a language contemporary and the process for participant speeching foreign all Sub Category. Multiple Subjects Type: Violation: Connert Form does not del witness declaration box not conceived: If of violations: L'Code Information.	in for protocol specified diagnostic studies, lab and/or research tests (1905 of total required usity Evaluation'T esting Sub-Despons, Multiple Subjects Type: Violation Recurrent labridge form of one scheduled research blood daws, it of violations 120de Co-PSub, Evaluation'T for all participants) Details. One subject Cycle 3 Day 1 tumor assessment done outside of pleand Sub-Calegon, Multiple Subjects Type; Violation, Adverse events not reported at all to soften soon windows. It of violations: T.Code: Informed Consent Sub-Calegon, Audi-Wide I consents were not locational, 3 of violations: 120de Informed Consent Sub-Calegon, Audi-Wide I consents were not locational, 3 of violations 120de Informed Consent Sub-Calegon, Audi-Wide I consents were not locational, 3 of violations 120de Informed Consent Sub-Calegon, Audi-Wide I consents were not consent services and consent services and a service of the consent services of the services of the consent services o	

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			Α	В	C		D	E		F		i
Audit Retrospecti	ive Deviations Report	1	IRB#	Dept/Service	Investig	gator	Start Date	Major Deviations - Categor		ations - General Description	Major Deviat Four subjects not re-consented to one or more	
		2						Informed Consent		sent not obtained as required	one of these subjects	
Report search selection:								Informed Consent		t dated by participant and/or consenting ites entered by a third party, or incorrect	RD filed for incorrect year date	entered on original consent.
IRB #:	MRN #:	3					<u>-</u>		Failure to report or	date(s) entered delayed reporting of an adverse event that	S Committee of the SAF(s) and	
Investigator	Audit#:	4	08-123	Medicine/Sarcoma	John Smit	ith, MD	5/1/2018	Toxicity/Adverse Event		an expedited Adverse Event (AE) report or reporting to the Group	One subjects experienced an SAE(s) not requi	
Investigator:	Audit Date - To:	5						On-Study Evaluation/Testing	Existing source do	cumentation for diagnostic, lab, research nto the EMR (>10% of total required tests for all participants)	Two subjects not have RECIST response	nse assessment forms in the EMR.
Audit Report Date:	Audit Due Date:	6						Treatment/ Intervention/ Interaction	n wrong questionns	r QOL questionnaires or administering the ire in a study where they represent the I intervention (> 10% of the time)	One subject not administered the protocol	QOL questionnaire at multiple timepoin
Dept/Service: Administration	Audit Sponsor: Institutional	7						Informed Consent		not documented in the patients progress erapeutic and/or study with MSK-held IND/IDE)	A(8) Reconsent discussion not d	
Anesthesiology/ Critical Care	Departmental	8						Informed Consent	Consent of an	cilliary studies not executed properly	Optional studies section on the English long not left blank for Non English-speaking pa	
Blood Bank/ Hem Lab Service	External	9						Toxicity/Adverse Event	Adverse event	s cannot be substantiated via source documentation	Original SAE report submission not found for	
CRA/Correlative Sciences Program		10						Treatment/ Intervention/ Interaction		le alterations or delays unjustified as per	Three subjects did not self-administer	azemetostat on numerous occasions.
Audit Type: Routine Re-Audit	External Sponsor: Cooperative Group FDA	11	11-899	Medicine/GU Onc	Sally Davis, I	MD. PhD	6/18/2018	Treatment/ Intervention/ Interaction	Treatment doses	idelines (chemo, RT, QOL forms) incorrectly or not fully documented (e.g. ition name, date, time, duration, missing RN signature)	Three subjects had pill diaries missing indic subjects did not sign off	
Random Selection Special Request	NCI OHRP	12			000,0000,			Treatment/ Intervention/ Interaction	treatment given o nursing drug admini	ned documentation for dose modifications, r other form of protocol intervention (e.g. stration sheets, patient calendars, diaries	One subject's Cycle 2 nill dia	y was not found in the EMR.
NCI#:	Cooperative Group: ACRIN ACOSOG 13 CALGB 14							On-Study Evaluation/Testing	(>10% of total required tests for all participants)  Recurrent lab/diagnostic tests during study & F/U not		per protocol.  One subject did not have one pre-dose PK collected, as well as the post-treatment	
								On-Study Evaluation/Testing				
							<u>-</u>	On-Study Evaluation/Testing	performed (>10% Missing source	of total required tests for all participants) documentation for protocol specified	scan at the	
	Joos	4.0						On-Study Evaluation/Testing		lab and/or research tests (>10% of total	No documentation of Pre dose PK collect Tazemetostat	ion and ECG done before Cycle 3 Day idministration.
Report Formatting:			Α	В	С	D	E	F	G	Н	J	K
Available Fields: Selected Fields: Name	Sort Order: Name Sort	. 1	Protocol #	Start Date	End Date	Report Date	Overall Rating	IRB/Regulatory Binder Review	Informed Consent Procedures	Participant Case Review	Major Deficiencies	Lesser Deficiencies
Audit Category Audit Dates From Audit Dates To	○ Audit Number Asc ∨	2	08-123	5/1/2018	5/30/2018	7/16/2018	Unacceptable	Unacceptable	Acceptable, Needs Follow-Up	Acceptable, Needs Follow- Up	Regulatory (1), Eligibility (3), Evaluation (2), Treatment (3), Outcome (3), General Data Quality (4)	Informed Consent (2), Eligib (5)
Audit Type  CAP Date		3	11-899	5/29/2018	6/20/2018	6/20/2018	Acceptable, Needs Follow-Up	, NR	Acceptable, Needs Follow-Up	Acceptable, Needs Follow- Up	Informed Consent (4), Eligibility (1) Evaluation (5), Treatment (7), Outcome (1), Toxicity/Adverse Event (5), General Data Quality (2)	Eligibility (1), Outcome
CAP Required  Database #/Registry #/Name		4	12-346	4/11/2018	4/23/2018	5/1/2018	Acceptable, Needs	, NR	Acceptable, Needs Follow-Up	Acceptable, Needs Follow- Up	Informed Consent (1), Evaluation (3)	General Data Quality (
			12 107	8/9/2018	9/21/2018	9/27/2018	Acceptable, Needs	Acceptable, Needs	Acceptable, Needs	Acceptable, Needs Follow-	Regulatory (1), Informed Consent	Regulatory (1), Informe
Dept/Service >> Description of Deficiencies <<	Up	5	13-187	0/3/2018	3/21/2018	3/2//2018	Follow-Up	Follow-Up	Follow-Up	Up	(1), Eligibility (1), Evaluation (1)	Consent (1)
Description of Deficiencies <<	Up Dn		14-199	4/23/2018	5/18/2018	8/20/2018	Unacceptable	Unacceptable	Unacceptable	Unacceptable	Regulatory (3), Informed Consent (9), Eligibility (3), Evaluation (1), Treatment (4), Outcome (1),	Treatment (1), General D Quality (2)
IRB/Informed Consent Rating		6									Toxicity/Adverse Event (2)	

# **OUTCOME AND FUTURE DIRECTIONS**

By using a common language for auditing and monitoring activities, communications between operational and quality assurance teams are enriched; implementation of CAPAs have been expedited and recommended standard actions created; corresponding policies may be easily referenced to guide re-training and generate targeted educational materials; and metrics have been harmonized to provide a complete, real-time picture of institutional compliance. Over time, we anticipate additions to account for changing regulations and best practices; these changes will affect future projects such as a planned CAPA response library.

# ACKNOWLEDGMENTS

We thank all the staff from the CRQA Auditing and Monitoring teams for their thoughtful contributions, with special thanks to Dawn Caron and Michael Ayerov of the CRIT team for their significant efforts.

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