

Title: Decoding NCI-CTCAE: Smarter Lab Grading Through Metadata and Automation

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Agenda



- Introduction
- Metadata Driven Automation
- Challenges and Implementation
- Key Takeaway

Introduction

- **CTCAE is essential** for grading lab-based toxicities and identifying treatment-emergent abnormalities in oncology trials.
- **Standardized grading** ensures consistent safety reporting and supports patient protection.
- **CTCAE v5.0 adds complexity** with guidance incorporating baseline values into toxicity assessment.
- Lab toxicity grading is based on:
 - **Normal range classification:** Low, Normal, High
 - **Severity grading: Grade 1–4** (Grade 5 not applicable for labs)

“CTCAE not just a document, it provides a universal language for assessing the impact of treatments.”

Metadata Driven Automation

- A metadata-driven macro framework provides a **scalable and efficient solution** for lab toxicity grading in large clinical trials and real-world data workflows.
- By separating metadata from code, it **simplifies maintenance, reduces programming effort**, and ensures **easy adaptability** across studies and CTCAE versions.

Structure of Metadata

CTCAE5Term	LBCAT	LBTEST	LBTESTCD	LBSTRESU	ATOXGR	ATOXGRN	LowOperator	LowLimitAbsolute	LowLimitRelative
Anemia	HEMATOLOGY	Hemoglobin	HGB	g/L	Grade 1	1	GE	100	
Anemia	HEMATOLOGY	Hemoglobin	HGB	g/L	Grade 2	2	GE	80	
Anemia	HEMATOLOGY	Hemoglobin	HGB	g/L	Grade 3	3			
Hemoglobin increased	HEMATOLOGY	Hemoglobin	HGB	g/L	Grade 1	1	GT		ULN
Hemoglobin increased	HEMATOLOGY	Hemoglobin	HGB	g/L	Grade 2	2	GT		(20+ULN)
Hemoglobin increased	HEMATOLOGY	Hemoglobin	HGB	g/L	Grade 3	3	GT		(40+ULN)

CTCAE5Term	ATOXGR	ATOXGRN	HighOperator	HighLimitAbsolute	HighLimitRelative	BASEFLAG	HIGHFLAG	LOWFLAG
Anemia	Grade 1	1	LT		LLN			Y
Anemia	Grade 2	2	LT	100				Y
Anemia	Grade 3	3	LT	80				Y
Hemoglobin increased	Grade 1	1	LE		(20+ULN)		Y	
Hemoglobin increased	Grade 2	2	LE		(40+ULN)		Y	
Hemoglobin increased	Grade 3	3					Y	

Challenges

- **Rule Complexity**
- **Floating Point**
- **Clinical Context**
- **Baseline Dependence**
- **Overlapping Ranges**
- **Bi-directional Grading**



Implementation

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4
Scenario 1: Only Numeric Thresholds				
Hemoglobin increased	Increase in >0 - 2 g/dL	Increase in >2 - 4 g/dL	Increase in >4 g/dL	-
Scenario 2: Clinical Assessment & Numeric Thresholds				
Case A: Mutually Exclusive Numeric Thresholds with Clinical Assessment				
Activated partial thromboplastin time prolonged	>ULN - 1.5 x ULN	>1.5 - 2.5 x ULN	>2.5 x ULN; bleeding	-
Case B: Overlapping Numeric Thresholds				
Creatinine increased	>ULN - 1.5 x ULN	>1.5 - 3.0 x baseline; >1.5 - 3.0 x ULN	>3.0 x baseline; >3.0 - 6.0 x ULN	>6.0 x ULN
Case C: Overlapping Numeric Thresholds with Clinical Assessment				
Hyperuricemia	>ULN without physiologic consequences	-	>ULN with physiologic consequences	Life-threatening consequences

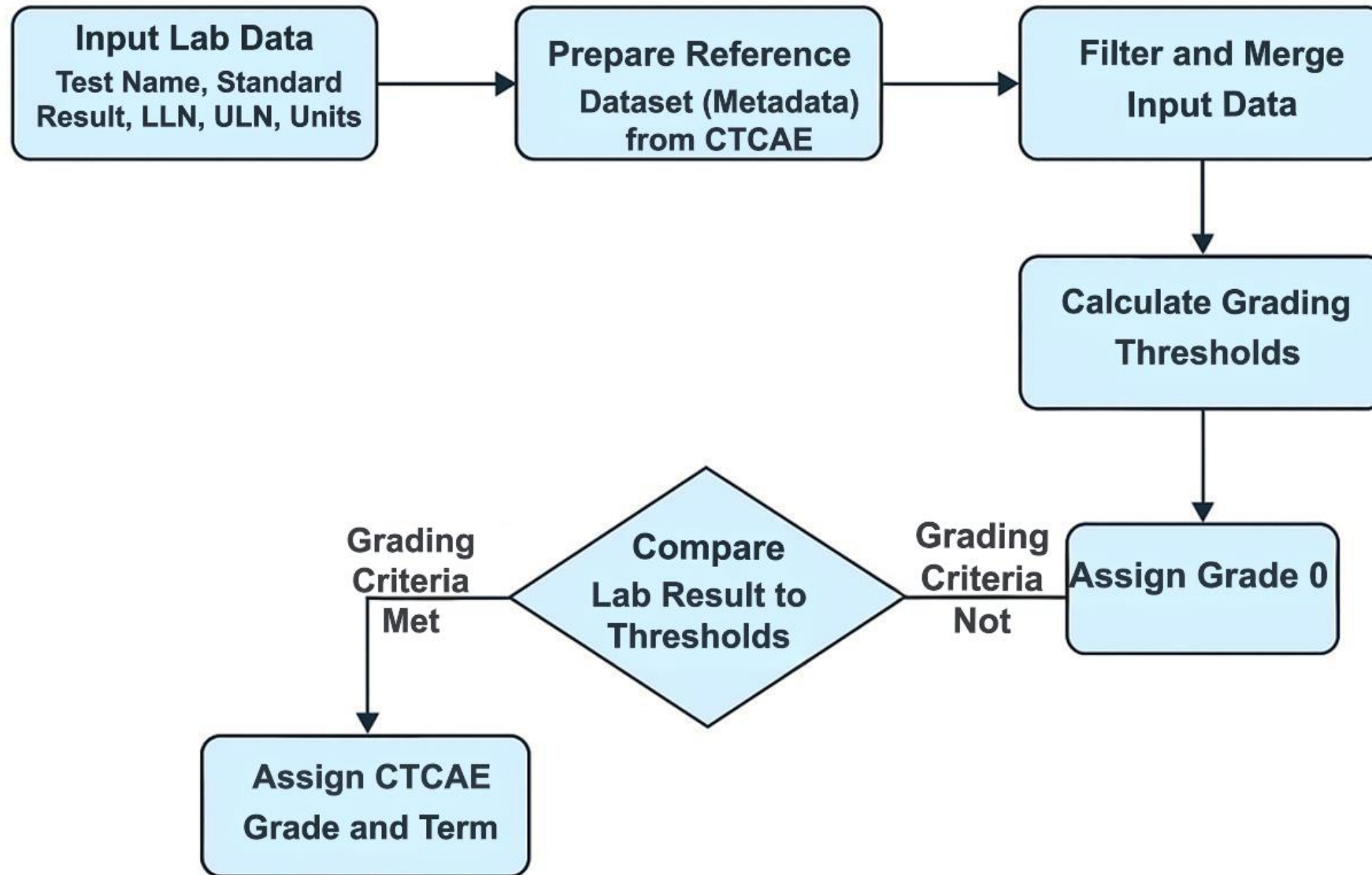
Implementation (Contd.)

CTCAE Term	Grade 1	Grade 2	Grade 3	Grade 4
Case D: Character Lab Results				
Proteinuria	1+ proteinuria; urinary protein ≥ULN - <1.0 g/24 hrs	Adult: 2+ and 3+ proteinuria; urinary protein 1.0 - <3.5 g/24 hrs; Pediatric: Urine P/C (Protein/Creatinine) ratio 0.5 - 1.9	Adult: Urinary protein ≥3.5 g/24 hrs; 4+ proteinuria; Pediatric: Urine P/C (Protein/Creatinine) ratio >1.9	-
Scenario 3: Dependent on Baseline Status				
Blood bilirubin increased	>ULN - 1.5 x ULN if baseline was normal; > 1.0 - 1.5 x baseline if baseline was abnormal	>1.5 - 3.0 x ULN if baseline was normal; >1.5 - 3.0 x baseline if baseline was abnormal	>3.0 - 10.0 x ULN if baseline was normal; >3.0 - 10.0 x baseline if baseline was abnormal	>10.0 x ULN if baseline was normal; >10.0 x baseline if baseline was abnormal

```
graph LR; A[Start of condition] --> B[Start condition without LLN  
Numeric value is less than 1]; B --> C[Start condition when ULN/LLN  
needs to be consider]; C --> D[End condition without LLN  
Numeric value is greater than 1]; D --> E[End condition when ULN/LLN  
needs to be consider]; E --> F[Test related to High  
toxicity grade]; E --> G[Test related to Low  
toxicity grade];
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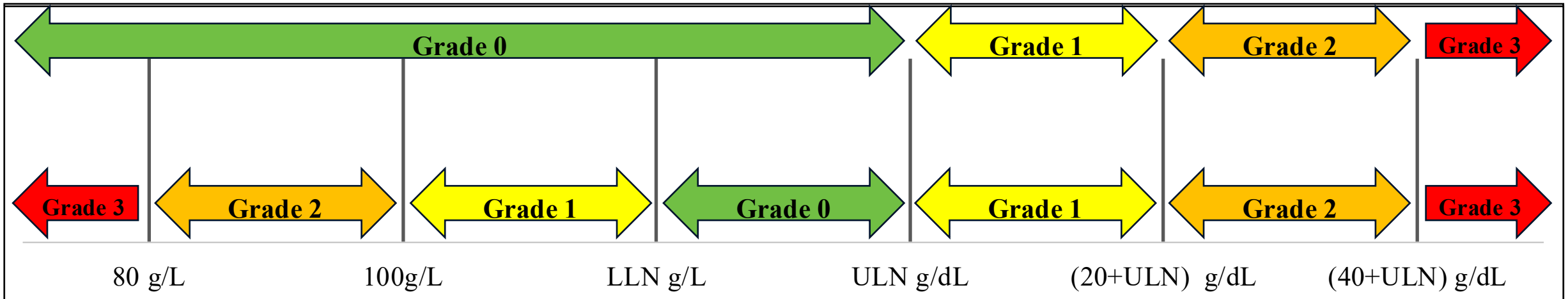
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SAS Macro Framework



Consolidated Output with CTCAE v5.0 Grades

USUBJID	PARAMCD	PARAM	AVISITN	AVAL	ABLFL	ANRLO	ANRHI	ATOXDIR	ATOXGR	ATOXGRL	ATOXDSC	ATOXGRH	ATOXDSCH
002	HGB	Hemoglobin (g/L)	10	114		110	161		Grade 0	Grade 0	Anemia	Grade 0	Hemoglobin increased
002	HGB	Hemoglobin (g/L)	20	117	Y	110	161		Grade 0	Grade 0	Anemia	Grade 0	Hemoglobin increased
002	HGB	Hemoglobin (g/L)	50	115		110	161		Grade 0	Grade 0	Anemia	Grade 0	Hemoglobin increased
002	HGB	Hemoglobin (g/L)	100	115		110	161		Grade 0	Grade 0	Anemia	Grade 0	Hemoglobin increased
002	HGB	Hemoglobin (g/L)	130	121		110	161		Grade 0	Grade 0	Anemia	Grade 0	Hemoglobin increased
002	HGB	Hemoglobin (g/L)	180	108		110	161	L	Grade 1	Grade 1	Anemia	Grade 0	Hemoglobin increased
002	HGB	Hemoglobin (g/L)	240	104		110	161	L	Grade 1	Grade 1	Anemia	Grade 0	Hemoglobin increased
002	HGB	Hemoglobin (g/L)	300	102		110	161	L	Grade 1	Grade 1	Anemia	Grade 0	Hemoglobin increased
002	HGB	Hemoglobin (g/L)	360	108		110	161	L	Grade 1	Grade 1	Anemia	Grade 0	Hemoglobin increased
005	HGB	Hemoglobin (g/L)	10	161		130	175		Grade 0	Grade 0	Anemia	Grade 0	Hemoglobin increased
005	HGB	Hemoglobin (g/L)	20	160	Y	130	175		Grade 0	Grade 0	Anemia	Grade 0	Hemoglobin increased
005	HGB	Hemoglobin (g/L)	50	.		.	.						
005	HGB	Hemoglobin (g/L)	100	158		130	175		Grade 0	Grade 0	Anemia	Grade 0	Hemoglobin increased
005	HGB	Hemoglobin (g/L)	180	177		130	175	H	Grade 1	Grade 0	Anemia	Grade 1	Hemoglobin increased



Key Takeaways

- **Grading rules vary by assessment** - Numeric thresholds are most common
- **Multiple criteria** - Apply worst-case scenario
- **Lab toxicity grades need clinical review** - Cannot rely solely on data
- **Ensure transparency & traceability** - Document assumptions, imputations, and key decisions
- **Future-proof with metadata-driven approach** - Develop reusable, modular code for quick upgrades



Thank You

We look forward to staying in touch

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