Less is More:

The Imperative to Optimize Protocol Data Collection

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Agenda

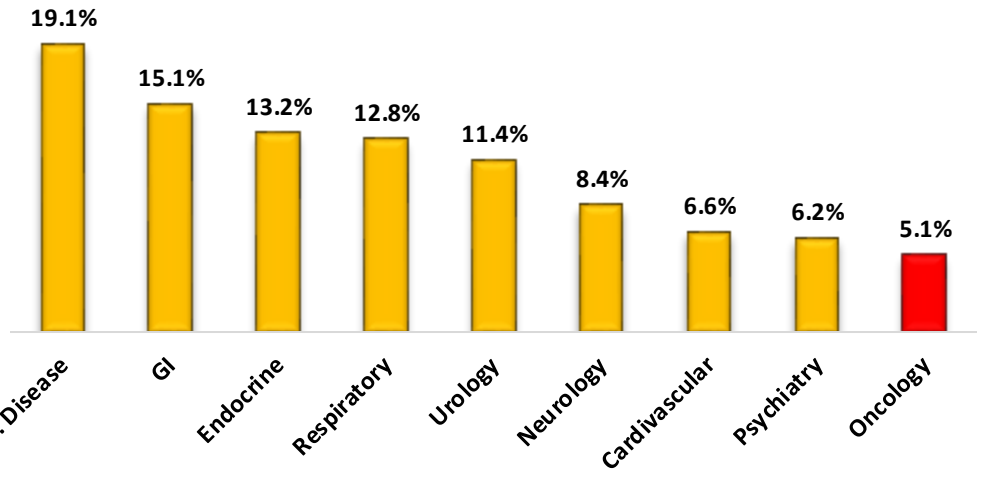
- Protocol design practices and their impact
- Tufts CSDD – TransCelerate Optimizing Clinical Data Study
  - Methods and Rationale
  - Detailed Results
- Key Takeaways and Practical Opportunities

Drug Development Risk by Phase and TA

Phase Transition Probabilities

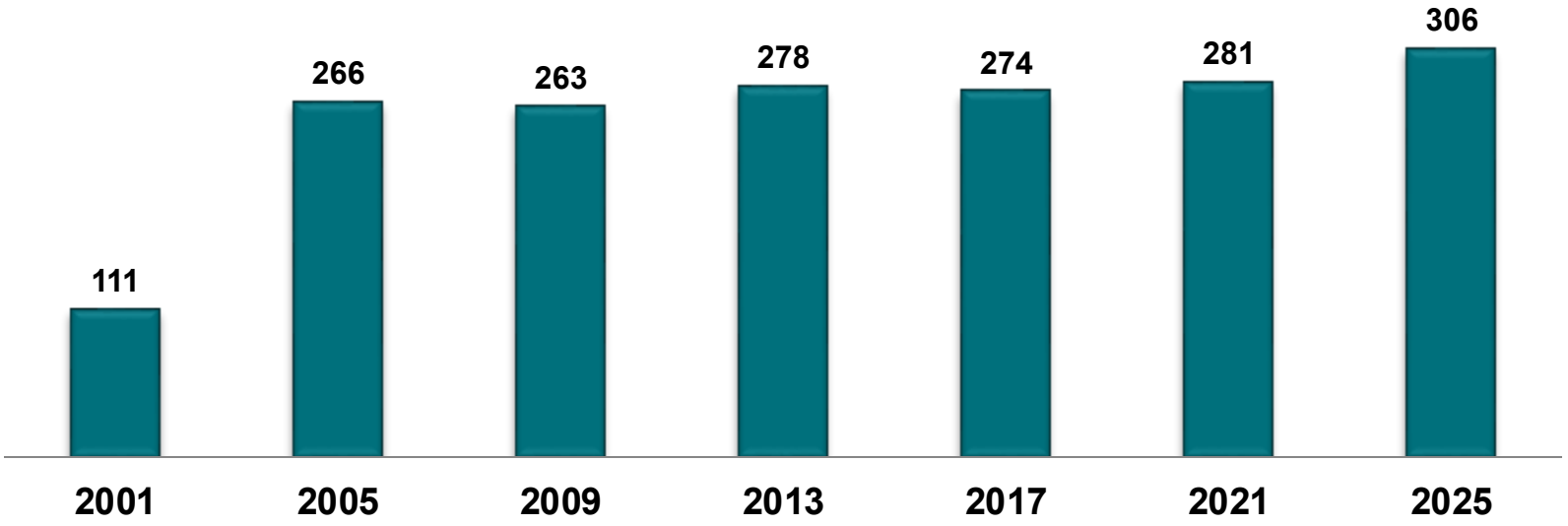
	1993 to 1998	1999 to 2004	2005 to 2013	2014 to 2021
Phase 1 to 2	67%	64%	58%	63%
Phase 2 to 3	41%	39%	34%	31%
Phase 3 to submission	63%	66%	62%	58%

Overall Probability of Achieving Regulatory Approval



Source: Tufts CSDD

Complaints Filed with the FDA for Non-Compliance



Source: FDA

Scientific and Executional Customization

Phase III Pivotal Trials (Means per Protocol)	2013-2015	2023-2025
Total Endpoints	14	18
Total Eligibility Criteria	31	35
Total Procedures	187	301
Total Countries	9	13
Total Investigative Sites	65	106
Total Patients Randomized	597	737
Total Data Volume	1.8 million	5.9 million

Source: Tufts CSDD

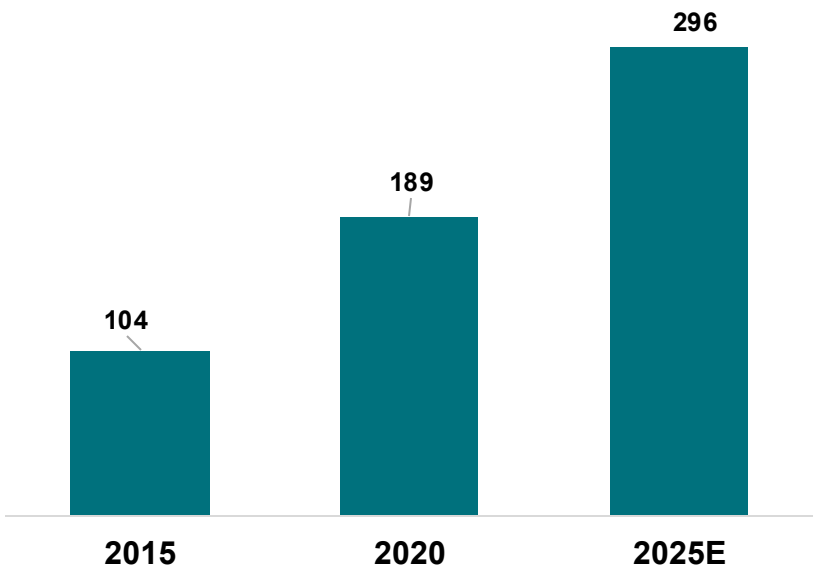
Impact on Enrollment, Cycle Time and Quality

Phase III Pivotal Trials	Overall Change Between Means 2015 – 2025
Initiation Duration (approval to FPFV)	27.2%
Enrollment Duration (FPFV – LPLV)	36.9%
Closeout Duration (LPLV to DBL)	16.3%
Total Protocol Deviations	184.6%
Total Substantial Amendments	52.2%
Drop-Out Rates	105.1%

Source: Tufts CSDD

Deviations and Amendments per Protocol

Mean Deviations per Pivotal Trial



Source: Tufts CSDD

Substantial Amendments per Pivotal Trial

	2013-2015 (N=836)		2018-2021 (N=952)	
	Percent with at least 1 amendment	Mean Number per protocol	Percent with at least 1 amendment	Mean Number per protocol
Phase I	52%	1.8	67%	3.1
Phase II	77%	2.2	89%	3.3
Phase III	66%	2.3	82%	3.5

Source: Tufts CSDD 2015 and 2022 Studies

The Realities of Participation Burden

"I had so many study visits that took up so much time – waiting to meet with the study nurse or the doctor, waiting to collect my meds from the pharmacy, having a procedure. It was unbelievable and I often wanted to simply quit."

"I lived so far away that every visit required that I take time off from work and make up for this time using my vacation and sick days"

"Navigating the hospital itself was such a pain… tests and blood work required so much time getting there and having to sit around in the waiting room, sometimes breaking up my study visit.'

"I had to keep a daily diary on a device that they gave me that was so slow and unreliable. It didn't always save my responses and the battery life was terrible."

Source: CISCRP, 2025

Participant Burden Trends

How burdensome was your participation? *Percent report 'Somewhat' or 'Very'*	2021 (n = 3654)	2025 (n = 5505)
Traveling to the study clinic	29%	44%
Diagnostic tests (e.g., x-rays, MRIs)	21%	42%
The length of the study visits	21%	40%
Lab work (e.g., blood tests, urine)	17%	38%
Taking the study medicine	15%	37%
Completing questionnaires or diaries	18%	32%

Source: CISCRP Global Patient Perceptions Survey

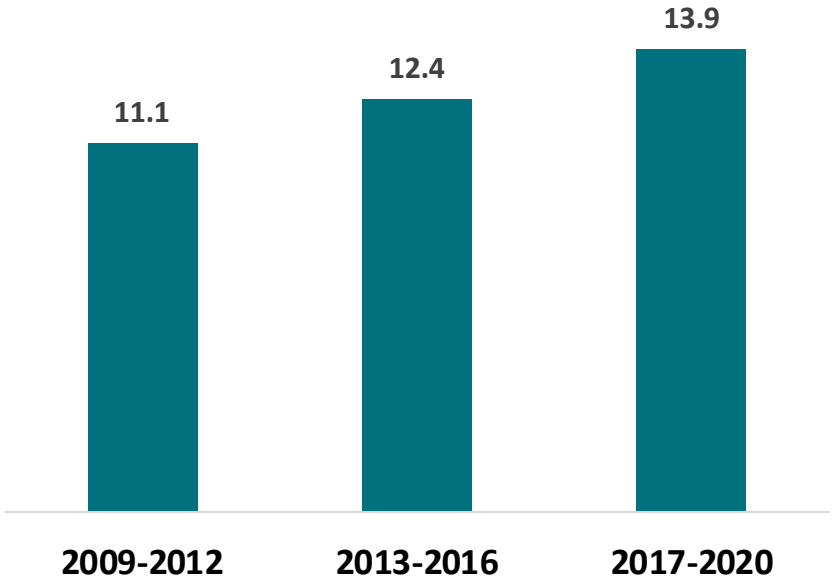
Premature Termination

	Due to Patient Choice
2007-2010	20.8%
2011-2014	40.4%
2015-2018	48.1%
2019-2023	64.3%

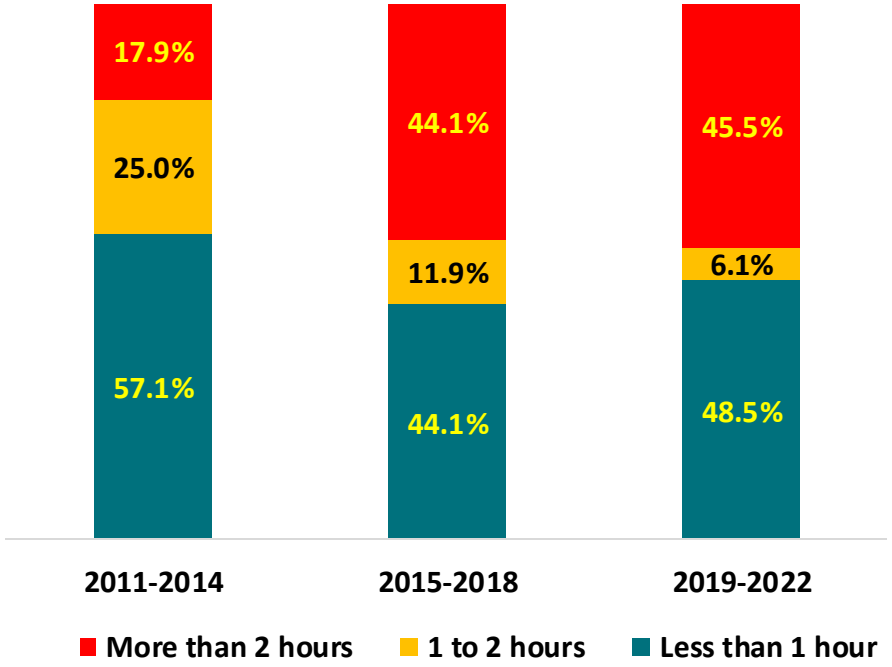
Source: Tufts CSDD, 2024

Participant Burden Trends *(continued)*

Mean Procedures per Patient Visit
(Phase II & III protocols, All TAs)



Benchmark Proportion of Protocols By Average Visit Duration



Source: Tufts CSDD

Tufts CSDD – TransCelerate
ODC Study Methods and Rationale

- The data collection instrument was workshopped throughout Spring 2024; A data warm-up exercise was conducted between June and July 2024.
- 14 Companies collected and provided their own data between July and November 2024.
- Tufts CSDD conducted data quality checks to ensure accuracy, validity and completeness and conducted a comprehensive QC process. Database locked and analysis initiated at the end of January 2025
- 105 Total protocols
  - 41% phase II; 59% phase III
  - 63% small molecules
  - 26% oncology, 16% endocrinology, 13% immunology, 11% infectious diseases, 9% neurology

Rationale

- Improve patient and site experience by reducing burden and simplifying protocol design
- Reduce complexity of data collection
- Enhance trial execution through better design decisions
- Maintain and improve research integrity and quality

Procedure Types by Endpoint Category

CORE

- Procedures supporting primary and/or secondary objectives
- Procedures supporting primary, *key* secondary and safety endpoints

NON-CORE

- Procedures supporting tertiary and exploratory and supplementary secondary endpoints
- Safety, efficacy or other procedures that are not included as an endpoint or objective

REQUIRED (Regulatory Compliance)

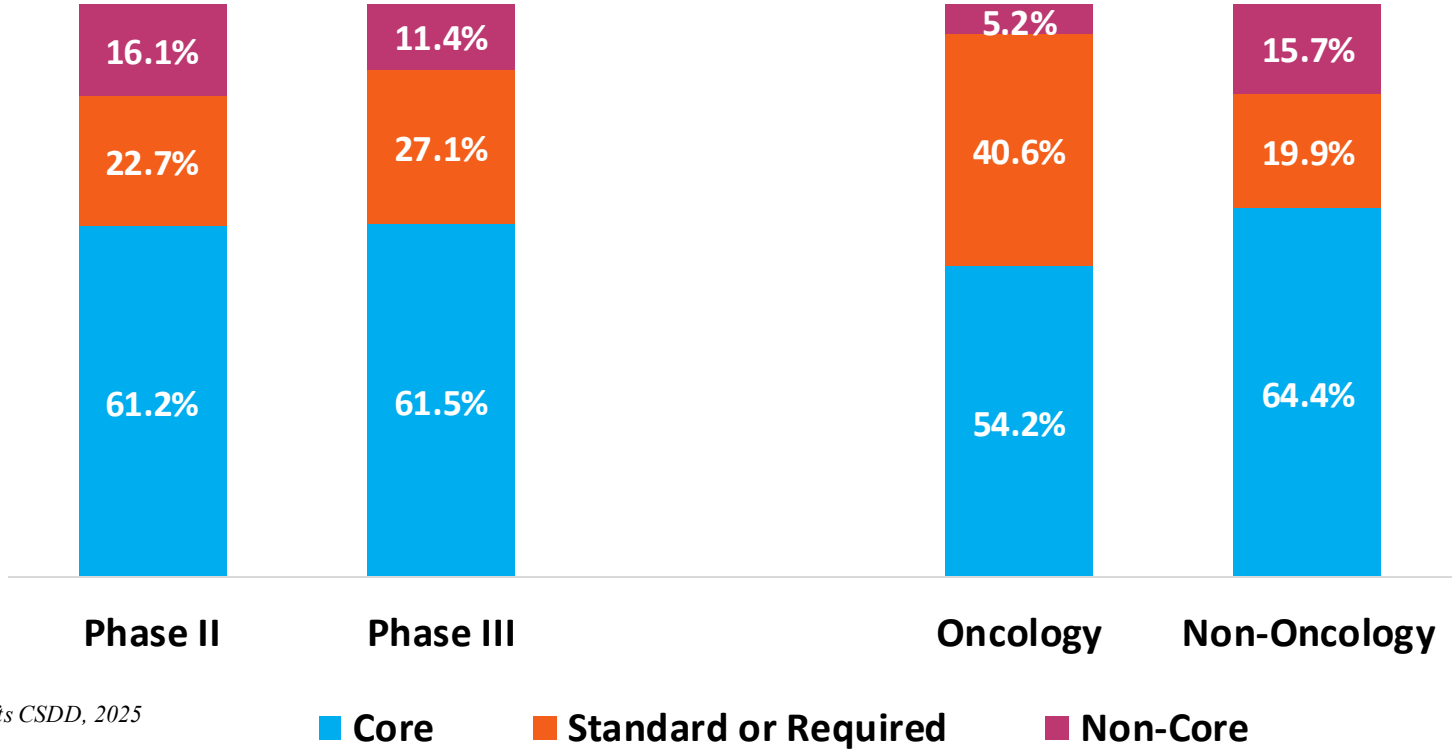
- Screening requirements
- Informed Consent
- Drug dispensing (compliance)

STANDARD

- Routine procedures including gathering data on baseline health, concomitant medications, demographics, adverse event and adverse drug reactions

Source: Tufts CSDD

Distribution of Datapoints Collected per Participant



Source: Tufts CSDD, 2025

Procedural Datapoints that are Non-Core

Combined Phase II - III Clinical Trials	Mean Percentage of Total Data Collected by Procedure that is Non-Core
Patient Diaries	37.5%
Questionnaires	37.1%
Invasive Procedures	25.9%
Lab & Blood	16.0%
Imaging	14.9%
Non-Invasive Procedures	10.0%
Routine Procedures	4.5%
Medication Dispensing	0.0%
Other	12.1%

Source: Tufts CSDD, 2025

Non-Core Procedural Contribution to Participant and Site Burden

	Phase II	Phase III
PARTICIPANT BURDEN		
Non-Core Procedures	19.8%	16.7%
SITE BURDEN		
Non-Core Procedures	18.1%	16.6%

Smith et al. Enhancing the measure of participation burden in protocol design to incorporate logistics, lifestyle and demographic characteristics. TIRS. 2021; 55(6): 1239-1249

Florez et al. Quantifying site burden to optimize protocol performance. TIRS. 2024; 58(2): 347-356

Source: Tufts CSDD, 2025

Reasons for Conducting Non-Core Procedures

Reason	Phase II	Phase III		Oncology	Non-Oncology
Safety	19.7%	21.4%		10.9%	23.5%
Future Use	23.7%	18.8%		23.4%	19.8%
Exploratory	21.9%	15.9%		43.1%	11.3%
Quality of Life/Symptom Evaluation/PRO	5.3%	13.3%		2.9%	12.5%
Efficacy	5.7%	10.8%		10.2%	8.7%
Market Differentiation	9.6%	5.8%		2.9%	8.3%
Support Reimbursement	4.8%	5.1%		1.5%	5.9%
Regulatory Request	0.4%	3.1%		1.5%	2.4%
PK/PD	2.2%	1.2%		1.5%	1.6%
Screening	0.9%	0.0%		0.0%	0.4%
Other	5.7%	4.6%		2.2%	5.7%

Source: Tufts CSDD, 2025

Data Included in the Clinical Study Report

Endpoint Classification	Main Body		Appendix			Total
	Discussed	Referenced	Discussed	Referenced	Included but not Discussed or Referenced	
Core	58.9%	16.7%	2.3%	12.8%	1.2%	92%
Standard/Required	45.0%	14.8%	0.8%	11.7%	4.7%	77%
Non-Core	46.5%	15.3%	1.5%	8.0%	2.9%	74%

Top Reasons Non-Core Procedure Data was Not Included (*percent reported*):

- **Exploratory (28%)**
- **Future Use (27.7%)**
- **Safety (13.8%)**

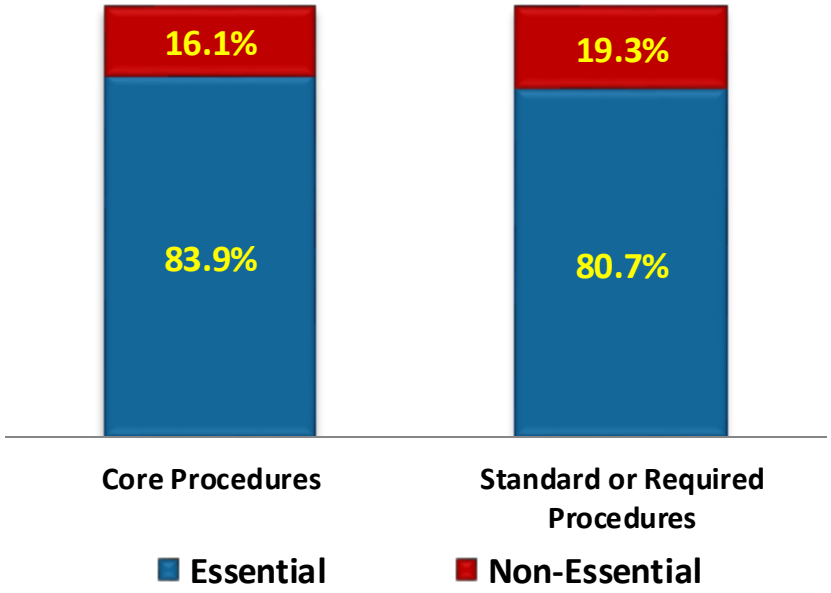
Source: Tufts CSDD, 2025

Introducing : ‘Non-Essential Procedures’

Procedures determined by the clinical team or protocol authors as being conducted more times than necessary to demonstrate a clinical outcome, fulfill a regulatory requirement or support standard/routine procedures

Mean percent of datapoints collected per participant by Endpoint Category

(Phase II/III combined)



Source: Tufts CSDD, 2025

Datapoint Contribution from Non-Core and Non-Essential Procedures

(Phase II/III Clinical Trials)	Datapoints per Participant from Non-Core Procedures	Datapoints per Participant from Non-Essential Core, Standard/Required Procedures	Total
Questionnaires	37.1%	18.3%	55.4%
Patient Diaries	37.5%	3.5%	41.0%
Invasive Procedures	25.9%	7.1%	33.0%
Lab & Blood	16.0%	13.4%	29.4%
Imaging	14.9%	6.1%	21.0%
Non-Invasive Procedures	10.0%	17.1%	27.1%
Routine Procedures	4.5%	11.9%	16.4%
Medication Dispensing	0.0%	3.1%	3.1%
Other	12.1%	1.9%	14.0%

Source: Tufts CSDD, 2025

Contribution of Non-Core and All Non-Essential Procedures to Participant and Site Burden

		Phase II	Phase III
PARTICIPANT BURDEN			
Non-Core Procedures		19.8%	16.7%
Non-Essential Core, Standard or Required Procedures		5.9%	12.7%
	TOTAL	25.7%	29.4%
SITE BURDEN			
Non-Core Procedures		18.1%	16.6%
Non-Essential Core, Standard or Required Procedures		7.0%	12.9%
	TOTAL	25.1%	29.5%

Source: Tufts CSDD, 2025

Key Takeaways

Getz et al. Insights Informing Strategies for Optimizing the Collection of Clinical Trial Data. TIRS 2025

- **More than one-third of all data collected comes from non-core and non-essential procedures and they contribute 25-30% of total participant and site burden**
- **Participant questionnaires and diaries collect a disproportionately high amount of non-core and non-essential data; Safety and Exploratory/Future Use purposes are the top reasons non-core data is collected.**
- **The majority (74%) of non-core data – much of it exploratory and/or intended for future use – appears in the Clinical Study Report**
- **Our study findings provide empirical evidence and insights encouraging protocol design discussion and a shift in mindset towards more intentional and fit-for-purpose data collection strategies**
- **These study results inform the development of tools and frameworks to support optimizing data collection**

Applying Optimization Insights

- Protocol authoring tools
  - Spirit, Metrics Champion Consortium, TransCelerate Common Protocol Template
  - Protocol digitization and AI-enablement
- Patient burden assessment
- Patient panels providing input into draft protocol designs
- TransCelerate's new 'CDP Framework'
  - Endpoint selection tied to label claims
  - Endpoint alignment with clinical phase
  - Match TPP target population with design feasibility/convenience
  - Remove high burden, low protocol relevance/value procedures
  - Participant and site input – early and often
  - Continuous measurement and refinement

Thank You!

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