Harmonizing Cerebrospinal Fluid Analysis for Multiple Sclerosis Investigation: An Update from the hCAMI Subcommittee of the Canadian Society of Clinical Chemists (CSCC)

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INTRODUCTION

- Cerebrospinal fluid (CSF) oligoclonal banding (OCB) analysis, specifically ≥2 CSF-specific OCBs, can substitute for dissemination in time criteria of multiple sclerosis (MS) diagnosis [1]
- Associated tests (e.g., CSF immunoglobulin G (IgG), CSF albumin) and calculated indices (e.g., albumin quotient, IgG index) can support clinical interpretation
- There is significant variability in processes and reporting practices across Canadian clinical laboratories[2]
- To address this issue, the Harmonized CSF Analysis for MS Investigation (hCAMI) subcommittee (clinical chemists and neurologist) of the CSCC Reference Interval Harmonization Working Group was formed

OBJECTIVE

Establish recommendations for laboratory processes and reporting of CSF OCB and associated tests supporting MS diagnosis.

METHODS

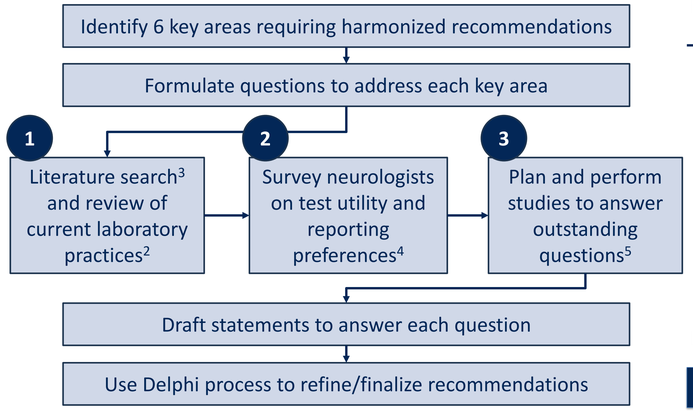

Figure 1. hCAMI Subcommittee Workflow

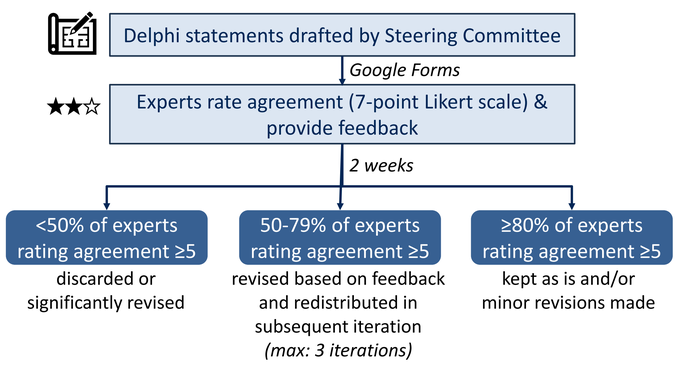

Figure 2. Modified Delphi Process. Town Hall held between Iterations 1 and 2 to provide evidence for statements that did not reach consensus.

RESULTS

Table 1. Characteristics of each Delphi Iteration

	Delphi Iteration		
	Iteration 1, n (%)	Iteration 2, n (%)	Iteration 3, n (%)
Time Interval	Feb 20 – Mar 6, 2025	Mar 27 – Apr 10, 2025	April 12 – 22, 2025
Number of Statements	25	4 (+4 informally)	2
Total Responses	36	28	30
Responses Rate	36/51 (70.6%)	28/50 (56.0%)	30/50 (60.0%)
hCAMI Committee Member			
Yes	15 (41.7%)	14 (50.0%)	16 (53.3%)
No	21 (58.3%)	14 (50.0%)	14 (46.7%)

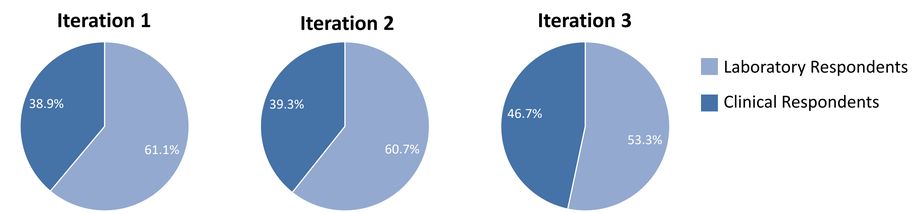

Figure 3. Subject Experts' Profession across all Iterations

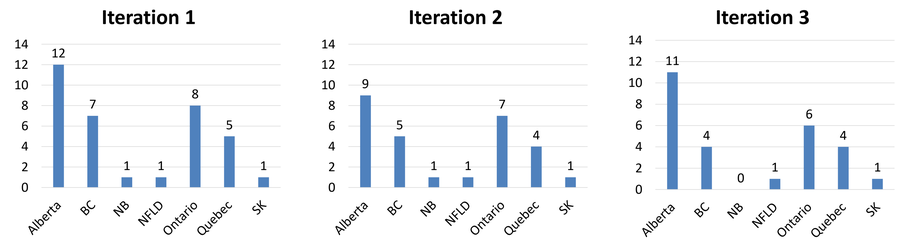

Figure 4. Subject Experts' Province of Practice across all Iterations

CONCLUSION

- 24/25 Delphi Statements met consensus by Iteration 3 of the Delphi Process and will be formally recommended by the hCAMI subcommittee
- Recommendations to harmonize laboratory reporting will promote alignment of CSF OCB reporting practices with the latest evidence, ultimately enhancing diagnostic accuracy and patient care

Table 2. Results of the Delphi Process. *Green text: acceptable/met consensus; Red text: not acceptable/did not meet consensus*

Delphi Statement	Iteration	Responses (n) ≥10 acceptable	% Agreement ≥ 5 Overall (Lab/Clinical) Consensus criteria: ≥80%
Section 1: Quality assurance practices			
#1. QC material	1	35	89 (86/92)
#2. QC documentation	1	36	86 (96/71)
	2 (Informal)	28	93 (88/100)
#3. Competency assessment	1	36	97 (96/100)
#4. External quality assurance	1	36	97 (100/93)
#5. Unclear cases	1	35	63 (55/77)
	2	28	75 (71/82)
	3	30	100 (100/100)
Section 2: Plasma acceptability and time interval requirements for paired CSF and blood			
#6. Plasma acceptability	1	35	97 (96/100)
#7. Paired specimen timing for CSF OCB	1	35	60 (52/71)
	2	28	96 (94/100)
#8. Paired specimen unavailable	1	36	83 (86/79)
	2 (Informal)	26	92 (94/90)
#9. Paired specimen unavailable & no CSF bands	1	36	92 (96/86)
#10. Paired specimen unavailable & 1 CSF band	1	36	94 (96/93)
#11. Paired specimen unavailable & 2+ CSF bands	1	35	94 (96/92)
#12. Paired specimen timing for associated tests	1	34	82 (70/100)
	2 (Informal)	27	89 (82/100)
Section 3: If and how to report CSF-specific band counts			
#13. Reporting CSF-specific band counts	1	36	75 (64/93)
	2	28	75 (77/73)
	3	36	79 (80/79)
#14. Reporting CSF-specific band counts as categories	1	36	83 (96/64)
	2 (Informal)	26	77 (73/82)
#15. Reporting CSF-specific band counts using listed categories	1	35	74 (68/85)
	2	27	85 (75/100)
Section 4: Interpretation and follow-up for mirror patterns (i.e., inflammatory response, monoclonal gammopathy)			
#16. Mirror pattern	1	36	100 (100/100)
#17. Mirror pattern - monoclonal protein	1	36	89 (82/100)
#18. Mirror pattern - inflammatory response and/or monoclonal protein	1	36	89 (82/100)
Section 5: Interpretation of matched bands with differing intensity between CSF and serum			
#19. Matched bands of differing intensity.	1	34	91 (91/92)
Section 6: Panel components and reference intervals/decision limits			
#20. Panel components	1	34	97 (95/100)
#21. Decimal places & units	1	33	94 (90/100)
#22. Reference intervals	1	32	81 (80/83)
#23. Band count abnormal flagging	1	35	86 (86/85)
#24. Reference to MS clinical guidelines	1	35	89 (91/85)
#25. Albumin quotient interpretation	1	35	83 (81/86)

REFERENCES

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