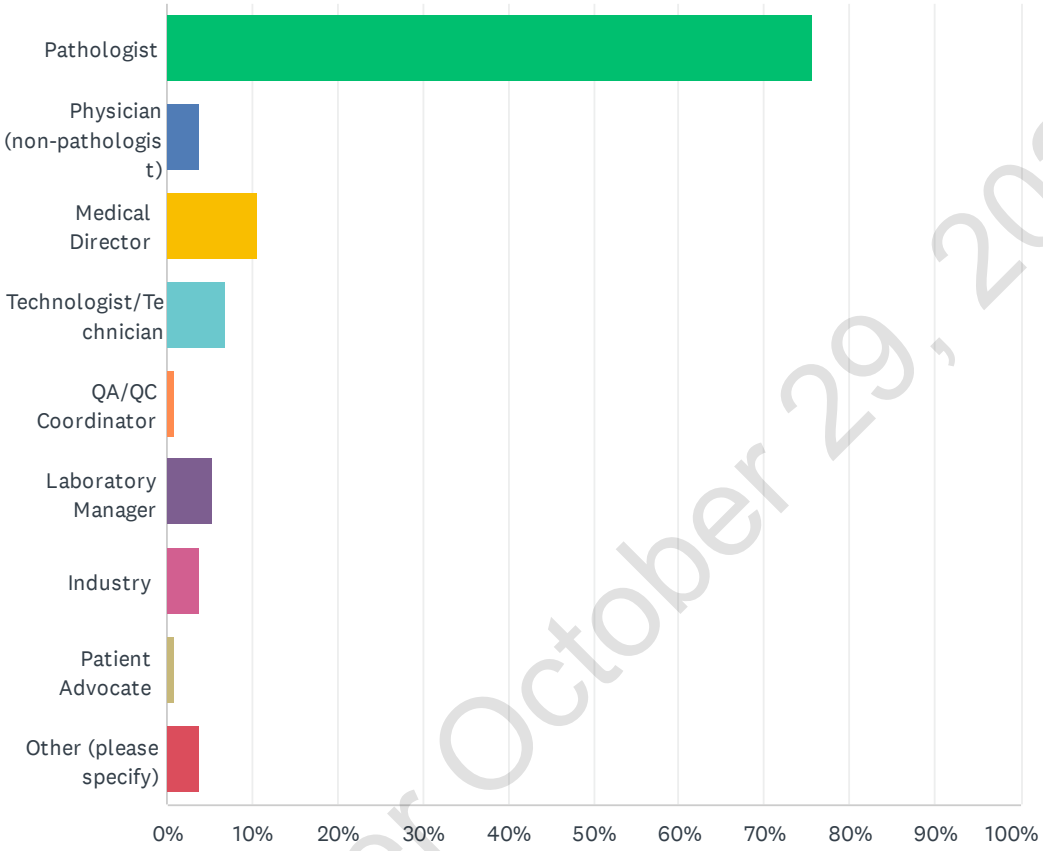
Q1 What is your occupation/role? (select all that apply)

Answered: 132 Skipped: 0



ANSWER CHOICES	RESPONSES	
Pathologist	75.76%	100
Physician (non-pathologist)	3.79%	5
Medical Director	10.61%	14
Technologist/Technician	6.82%	9
QA/QC Coordinator	0.76%	1
Laboratory Manager	5.30%	7
Industry	3.79%	5
Patient Advocate	0.76%	1
Other (please specify)	3.79%	5
Total Respondents: 132		

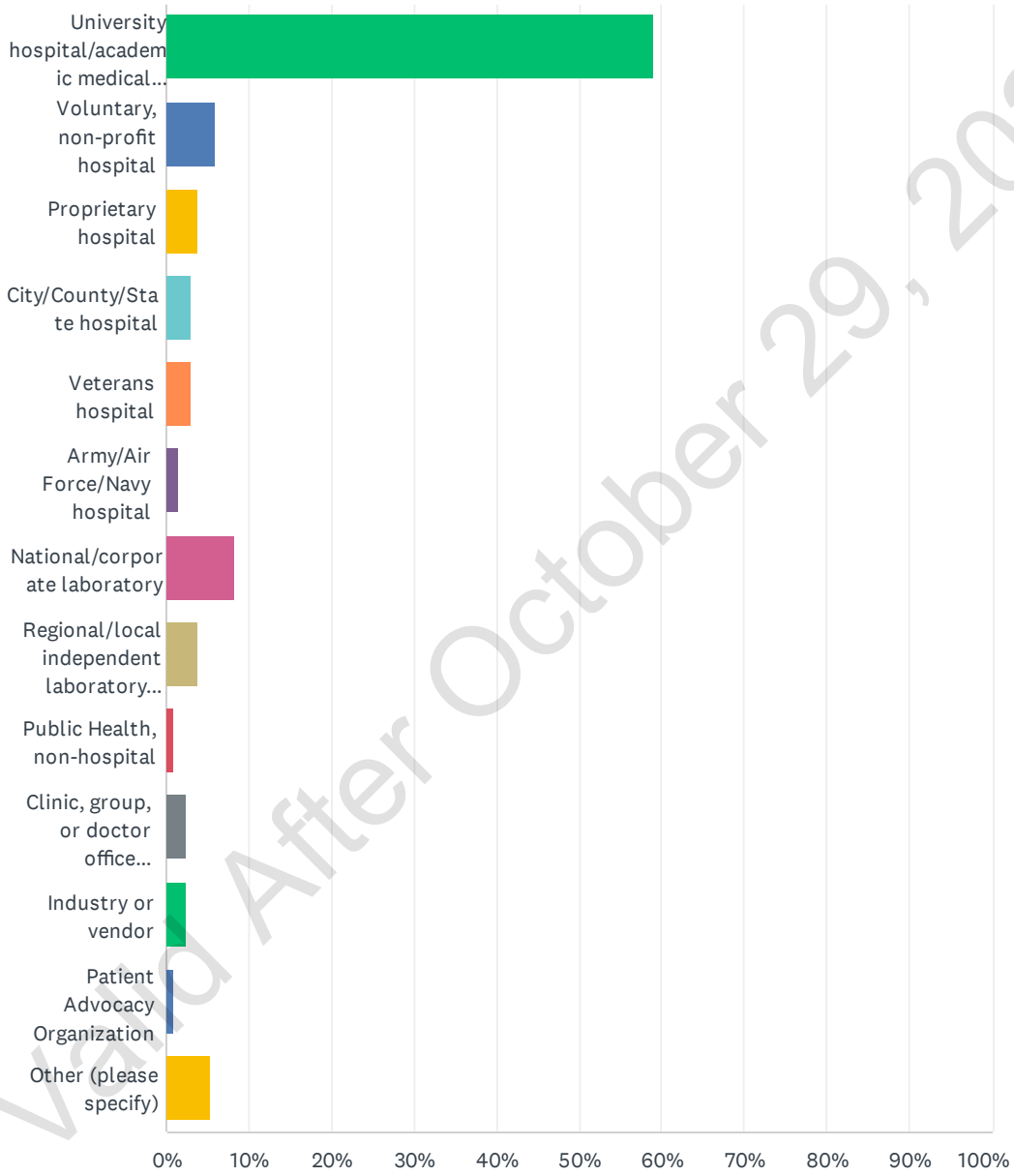
#	OTHER (PLEASE SPECIFY)	DATE
1	Medical Laboratory Scientist	10/29/2025 2:06 PM

2	clinical scientist	10/28/2025 2:44 PM
3	Clinical scientist	10/28/2025 12:03 PM
4	Retired	10/27/2025 4:47 PM
5	Scientist	10/27/2025 3:33 PM

Disclaimer
The information, data, and draft recommendations provided by the College of American Pathologists are presented for informational and public feedback purposes only.
The draft recommendations and supporting documents will be removed on November 5, 2025.
The draft recommendations along with the public comments received and completed evidence review will be reassessed by the expert panel in order to formulate the final recommendations.
These draft materials should not be stored, adapted, or redistributed in any manner.

Q2 Which of the following best describes your practice setting? (select one)

Answered: 132 Skipped: 0



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ANSWER CHOICES	RESPONSES	
University hospital/academic medical center	59.09%	78
Voluntary, non-profit hospital	6.06%	8
Proprietary hospital	3.79%	5
City/County/State hospital	3.03%	4
Veterans hospital	3.03%	4
Army/Air Force/Navy hospital	1.52%	2
National/corporate laboratory	8.33%	11
Regional/local independent laboratory (except clinic or group practice and not owned by a national corporation(s))	3.79%	5
Public Health, non-hospital	0.76%	1
Clinic, group, or doctor office laboratory	2.27%	3
Industry or vendor	2.27%	3
Patient Advocacy Organization	0.76%	1
Other (please specify)	5.30%	7
TOTAL		132

#	OTHER (PLEASE SPECIFY)	DATE
1	Consultant and International Colaborator	10/29/2025 2:06 PM
2	retired	10/27/2025 4:31 PM
3	cap	10/23/2025 7:51 AM
4	Children's Research Hospital	10/14/2025 6:09 PM
5	reference lab	10/9/2025 7:55 AM
6	retired	10/8/2025 3:59 PM
7	Retired	10/8/2025 3:18 PM

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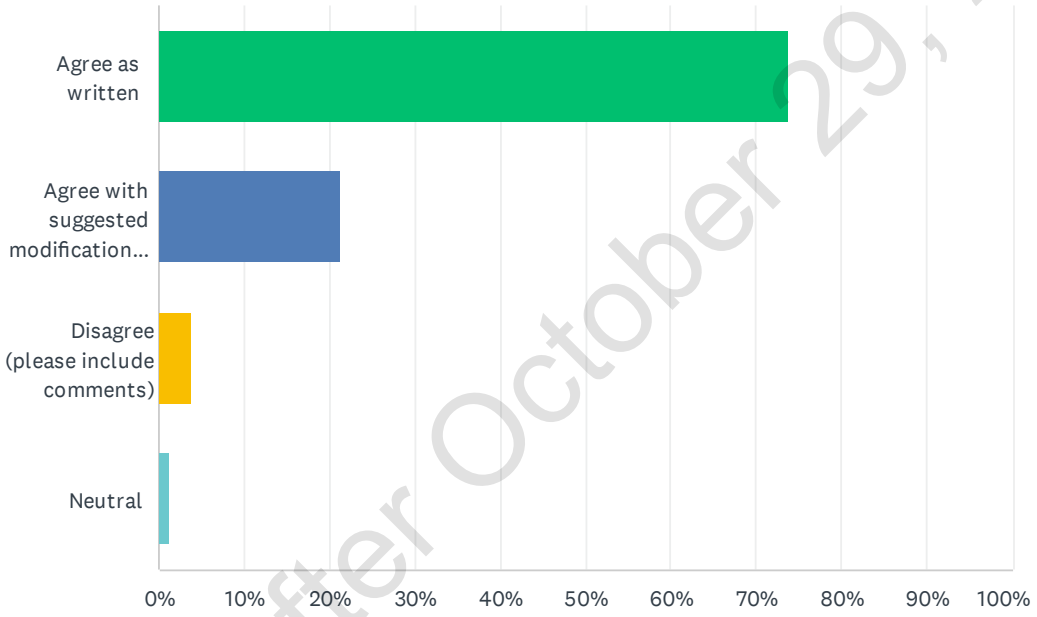
Q3 Draft Statement 1 – For adult and pediatric patients with B-cell acute lymphoblastic leukemia (B-ALL) undergoing measurable residual disease (MRD) testing for the purpose of risk stratification, laboratories should use NGS or multiparametric flow cytometry (MFC). Although NGS provides a more sensitive assessment and may be preferred for this reason, a validated MFC protocol with a lower limit of detection (LLoD) of at least 10-4 may be used.(Strong Recommendation)

Answered: 80 Skipped: 52



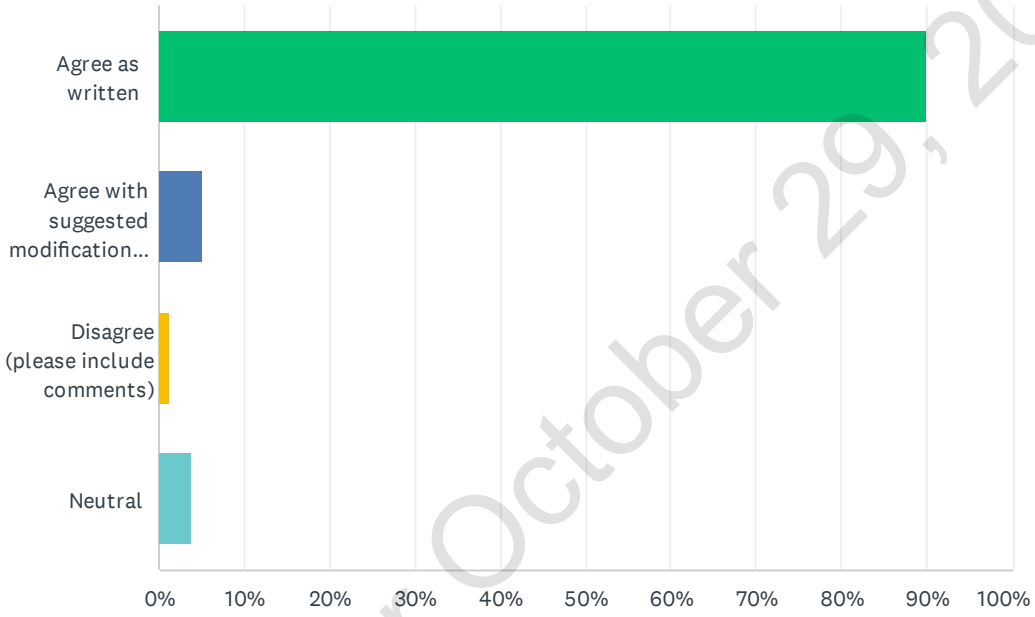
ANSWER CHOICES	RESPONSES	
Agree as written	73.75%	59
Agree with suggested modifications (please include comments)	21.25%	17
Disagree (please include comments)	3.75%	3
Neutral	1.25%	1
TOTAL		80

#	COMMENTS	DATE
1	Consider re-wording such that there isn't an implied choice to make of either molecular or flow cytometry. I think the two test modalities together best stratify patient outcomes.	10/29/2025 8:51 PM
2	Next-generation sequencing (NGS) is the best method for all timepoints, especially in post-consolidation, pretransplant, and posttransplant settings. While flow cytometry is also valuable, NGS offers greater sensitivity, providing a more reliable long-term prognosis. A complementary approach using both methods can leverage the unique advantages of each.	10/29/2025 3:00 PM
3	……., a validated MFC protocol with a lower limit of detection (LLoD) of at least 10-4 could	10/29/2025 1:18 AM

	be used.	
4	Aim for 10-4 (0.01%) minimum; optimize for 10-5 (0.001%) when possible.	10/28/2025 11:55 PM
5	this LLoD can't be achieved by all laboratories	10/28/2025 3:20 PM
6	Currently, with more modern cytometers, there is a need for a minimum sensitivity of 10-5.	10/28/2025 4:30 AM
7	B-ALL MRD frequently involves CSF, obviously not practical for NGS, and MFC problematic due to low number of events and non-specific events.	10/27/2025 7:14 PM
8	The NGS LOD needed should be specified, not just say it is more sensitive. If sufficient nucleic acid template is not used in NGS (1ug = approx 100,000 to 150,000 cells) then a more sensitive assessment 10-5 may not be obtainable.	10/27/2025 5:04 PM
9	Provide a unit of measurement for LLoD.	10/27/2025 2:56 PM
10	Please also include language addressing the subjective nature of flow cytometry data interpretation and potential for interlaboratory variability using flow cytometry, whereas NGS data analysis is software driven and relatively non-subjective in comparison.	10/26/2025 8:23 PM
11	"a validated MFC protocol with a lower limit of detection (LLoD) of at least 10-4 may be used as it details the immunophenotype of the disease to aid in targeted therapy decisions.	10/24/2025 2:23 PM
12	Why is there emphasis on a "validated MFC protocol" and not a "validated" NGS protocol?? Same goes to the LLoD... it sounds like it only applies to MFC. I think the wording needs to be changed.	10/20/2025 3:49 PM
13	Please clearly define whether the LLoD comparison is based on the same analyte or converted benchmark. MFC and NGS target different analytes. The different target analytes and relevance of comparison between the limit of detection (LLoD) of at least 10-4 for tumor cells by MFC vs. the LLoD 1~10 ppm for ctDNA by NGS could be confusing if not misleading.	10/17/2025 3:28 PM
14	Agree but if the sample sometimes is not representative then this might make it challenging to call in negative based if it especially with difficultly of getting a good specimen in pediatric patients	10/16/2025 2:14 PM
15	Flow cytometry validated upto 0.001% or below would be of greatew value than NGS, to account for phenotypic shifts induced by targeted therapy. NGS targets may not be available in all cases for MRD.	10/16/2025 1:34 PM
16	For MFC MRD, LLOD of at least 10-5 may be used. At this one log excess (buffer zone) LLOD, the desired 10-4 can be assessed with confidence.	10/16/2025 12:56 AM
17	It is ideal to recommend that B-MRD MFC panel be validated till 0.001%. Also issue is that NGS target may not have been done at diagnosis and in era of targeted therapy MFC is a must at MRD time point to assess CD19, CD22 expression, CD123 expression and NGS assay may be additional	10/15/2025 8:08 AM
18	The assumption that NGS provides a more sensitive assessment may not always be true since flow cytometry methods can achieve LLoD equivalent to or below that of less sensitive NGS assays.	10/9/2025 2:17 PM
19	Emphasis on “or”. The vast majority of oncologists, especially pediatric, order both; therefore, a stronger emphasis on either one may help avoid excessive use.	10/8/2025 5:16 PM
20	I don't think that there is conclusive evidence that NGS is as specific as MRD detected by flow, but I have not followed this literature closely. I know that COG has had a trial studying this recently.	10/8/2025 4:07 PM
21	I believe the most sensitive test is more useful particularly that the test seems more amenable to standardization and widespread use	10/8/2025 3:38 PM
22	I would be a little more specific with the NGS technique and mention the need for sequencing at the time of diagnosis for subsequent NGS MRD detection (the original leukemic immunophenotype is preferred but not required for flow cytometry MRD detection).	10/8/2025 3:13 PM
23	Please include necessary sensitivity for NGS	10/8/2025 3:11 PM

Q4 Draft Statement 2 – For a comprehensive assessment of MRD in adults with Philadelphia positive (Ph+) B-ALL, laboratories should interpret real-time quantitative PCR (RT-qPCR) for BCR::ABL1 fusion transcripts in conjunction with additional data (eg, NGS, MFC).(Conditional Recommendation)

Answered: 79 Skipped: 53



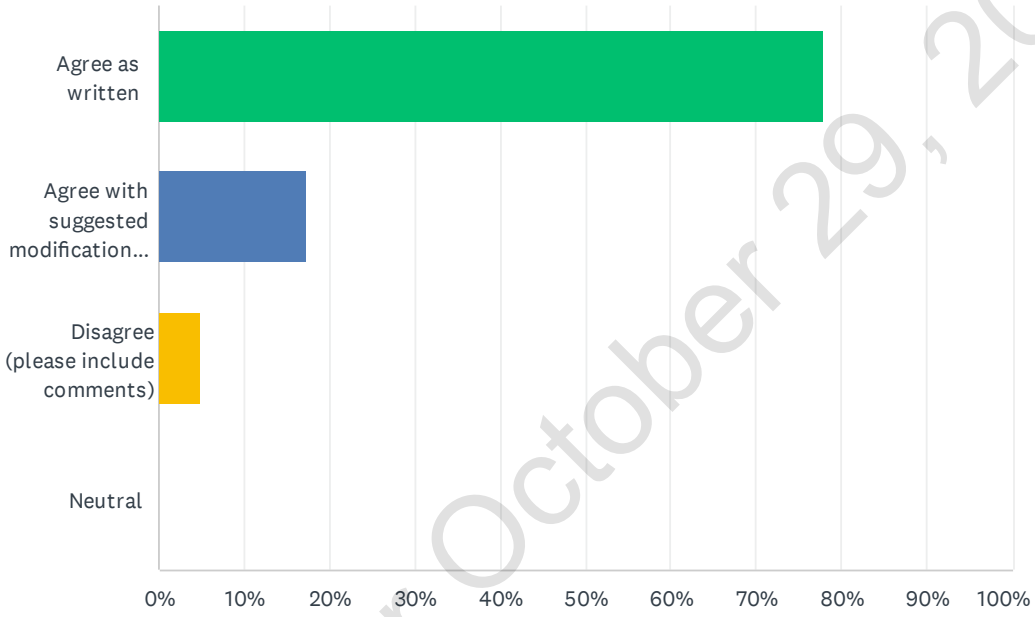
ANSWER CHOICES	RESPONSES	
Agree as written	89.87%	71
Agree with suggested modifications (please include comments)	5.06%	4
Disagree (please include comments)	1.27%	1
Neutral	3.80%	3
TOTAL		79

#	COMMENTS	DATE
1	while RT-qPCR for BCR::ABL1 is a common and useful method for monitoring Philadelphia-positive (Ph+) B-ALL, combining it with other methods like Next-Generation Sequencing (NGS) and Multiparameter Flow Cytometry (MFC) provides a more complete picture. Combining techniques accounts for potential limitations, such as the possibility of multilineage involvement in some patients, which could lead to misleading results with BCR::ABL1 qPCR alone	10/29/2025 3:00 PM
2	Adding something to this statement to emphasize the low specificity of RT PCR Bcr-abl	10/29/2025 1:18 AM
3	Quantitative analysis of BCR-ABL fusion transcripts is the preferred method and is more sensitive than NGS or MFC.	10/27/2025 10:37 AM
4	HGNC recommends usage of italics for symbols denoting genes, mRNAs, and alleles to	10/23/2025 12:07 PM

	differentiate them from proteins.	
5	Unclear what LOD should be followed. Also testing should be directed towards both p210 and p190 isoforms unless the prior is known.	10/18/2025 11:08 AM
6	BCR::ABL in italics	10/18/2025 2:57 AM
7	It would be great if additional clarification/note is provided for "additional data" again due to different target analytes.	10/17/2025 3:28 PM
8	This statement is not clear. Does the statement mean we should always perform RT-qPCR and another study?	10/9/2025 2:17 PM
9	relatively uncommon disease so generation of more data is highly desirable even though NGS based IGH/TCR may be more sensitive even in this disease subset	10/8/2025 3:38 PM

Q5 Draft Statement 3 – For patients with B-ALL undergoing assessment for MRD, laboratories should use bone marrow (BM) aspirates rather than peripheral blood specimens in most circumstances.Note: Peripheral blood may be an acceptable alternative when use of BM aspirate is not feasible. (Strong Recommendation)

Answered: 81 Skipped: 51



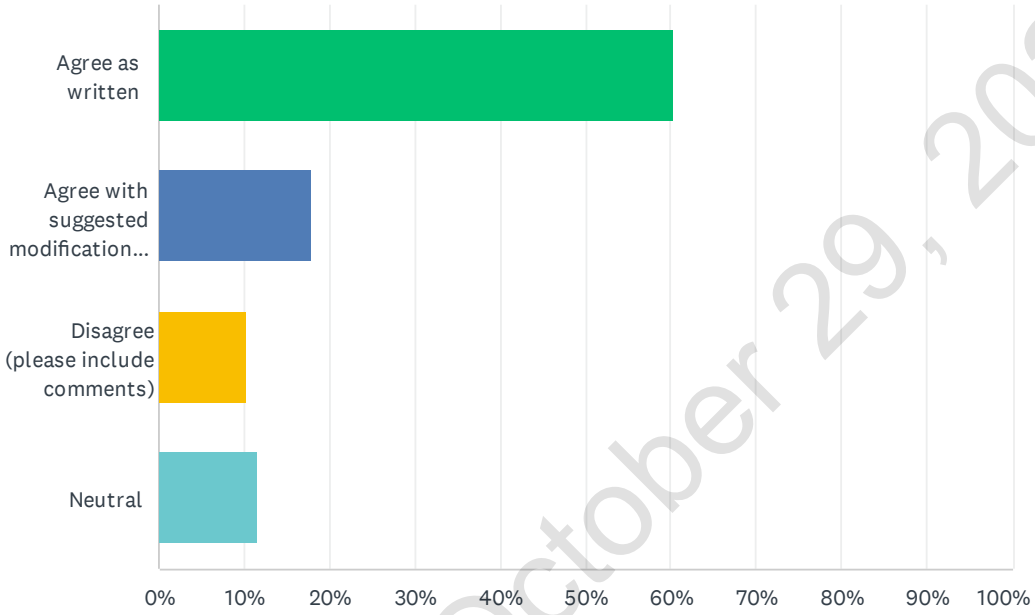
ANSWER CHOICES	RESPONSES	
Agree as written	77.78%	63
Agree with suggested modifications (please include comments)	17.28%	14
Disagree (please include comments)	4.94%	4
Neutral	0.00%	0
TOTAL		81

#	COMMENTS	DATE
1	Avoid peripheral blood due to poor sensitivity and discordance.	10/28/2025 11:55 PM
2	Peripheral blood Not acceptable.	10/28/2025 3:42 PM
3	In the event that the MRD is positive, peripheral blood may serve as an alternative to BM aspirate. Nevertheless, a BM sample should be evaluated in the event of a negative MRD result, as the likelihood of a false negative MRD result is significant.	10/28/2025 3:20 PM
4	"In most circumstances" is not defined. Either define them or remove the phrase as it is vague.	10/27/2025 5:04 PM
5	Peripheral blood is acceptable because doing bone marrow aspirates just to look for MRD is not justifiable. MFC on blood is good for routine monitoring	10/27/2025 10:37 AM

6	Blast counts in peripheral blood are often lower than marrow. Furthermore, language needs to emphasize and address that a dedicated first pull of marrow is required for B-ALL MRD testing. Similar to CML BCR::ABL PCR serial monitoring, intermixing marrow and peripheral blood is poor practice and guidelines should create a guardrail in which such practice is not to be condoned.	10/26/2025 8:23 PM
7	at serial timepoints, switching between BM and PB seems inadvisable e.g. for RT-qPCR monitoring of BCR-ABL1	10/23/2025 12:07 PM
8	The laboratory will use whatever the clinician sends them - it's not up to the lab to choose. Not sure this statement is needed.	10/20/2025 3:49 PM
9	A disclaimer should be included when performing MRD in peripheral blood to the effect that sensitivity in this matrix is often limited and a false negative can not be excluded at the typical LOD of a bone marrow MRD evaluation.	10/18/2025 11:08 AM
10	if peripheral blood, should the most sensitive technique be used ?	10/16/2025 6:08 PM
11	'High-sensitivity' peripheral blood B-ALL MRD can be used as a triage tool (performed first). If Positive, then a bone marrow B-ALL MRD can be avoided, as there will be a minimium of one log excess MRD in the bone marrow. Bone marrow MRD is to be done in patients who are peripheral blood MRD negative. PMID: 27889709	10/16/2025 12:56 AM
12	Bone marrow is preferred when available. However, if it is not readily available, it makes more sense to try peripheral blood first.	10/9/2025 2:17 PM
13	Peripheral blood is not an acceptable alternative. It lacks sufficient sensitivity. I fear that using such a statement would give the hemeoncs carte blanche to skip bone marrows, particularly in peds.	10/8/2025 4:07 PM
14	For NGS peripheral blood is an acceptable alternative. For flow cytometry bone marrow is preferable.	10/8/2025 4:03 PM
15	This statement is a little bit vague - which circumstances are acceptable or not? Although this guideline is specifically for adults, many clinicians are aware that pediatric guidelines suggest peripheral blood MRD at day 7-8, and newer data are coming out to indicate sensitive testing on blood may yield similar information.	10/8/2025 3:40 PM
16	In the initial stages of therapy including initial induction and consolidation and may be early in the course of maintenance, Bone marrow is preferable. for long-term follow up peripheral blood may be used	10/8/2025 3:38 PM
17	clarify assessment for MRD vs. surveillance in patients with remission	10/8/2025 3:13 PM

Q6 Draft Statement 4 – For patients with B-ALL in remission undergoing surveillance, laboratories may use peripheral blood samples.(Conditional Recommendation)

Answered: 78 Skipped: 54



ANSWER CHOICES	RESPONSES	
Agree as written	60.26%	47
Agree with suggested modifications (please include comments)	17.95%	14
Disagree (please include comments)	10.26%	8
Neutral	11.54%	9
TOTAL		78

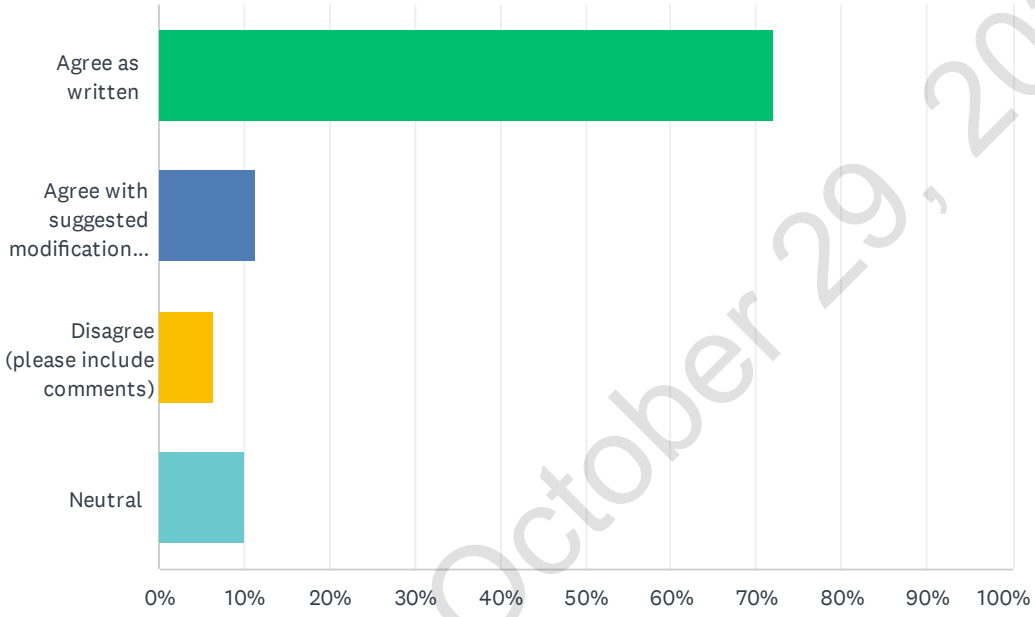
#	COMMENTS	DATE
1	The best assessment for B-ALL MRD is examination of bone marrow (see Draft Statement 3). Not sure that this statement adds much beyond Draft Statement 3, but it does imply that PB assessment of MRD is acceptable (and not inferior to bone marrow). I would prefer this statement be better refined (or perhaps even deleted), as the content seems appropriately covered by Statement 3.	10/29/2025 8:51 PM
2	For B-cell acute lymphoblastic leukemia (B-ALL) patients undergoing measurable residual disease (MRD) assessment, laboratories should use bone marrow (BM) aspirates rather than peripheral blood (PB) specimens in most circumstances. This is a strong recommendation based on key differences between B-ALL and T-cell ALL (T-ALL): Discordant MRD levels: In B-ALL, the level of MRD in the bone marrow is often significantly higher—sometimes by one or more orders of magnitude—than in the peripheral blood. This poor correlation means a negative or low result from a less-sensitive peripheral blood test could be inaccurate. In contrast, MRD levels in T-ALL correlate well between the two sample types. Low sensitivity of PB: Studies comparing matched BM and PB samples in B-ALL have demonstrated that peripheral blood has a low sensitivity relative to bone marrow for detecting MRD via standard methods like flow	10/29/2025 3:00 PM

	cytometry. Historical validation: The prognostic value of MRD testing in B-ALL has been historically validated using bone marrow samples. Therefore, BM is considered the gold standard for reliable results. Exceptions and special considerations While BM is generally the preferred sample, there are specific scenarios where peripheral blood can be used: Early-stage assessment: For a convenient, non-invasive option to assess the kinetics of leukemia cell clearance early in treatment, such as on day 8 post-induction, PB may be used. Surveillance: After MRD negativity has been confirmed with a bone marrow sample, ongoing surveillance may be performed using peripheral blood with a highly sensitive assay, such as next-generation sequencing (NGS). This offers a less-invasive alternative for long-term monitoring. High-sensitivity testing: When a bone marrow aspirate is not feasible, PB can be an alternative if a highly sensitive method like NGS is used. Suspected extramedullary relapse: In some cases of relapse following treatment, particularly chimeric antigen receptor T-cell (CAR-T) therapy, a patient can have a negative BM aspirate but positive PB MRD or other imaging evidence of disease. In these rare instances, PB can provide valuable diagnostic information. Highly concordant cases: For adult patients with ALL receiving cellular therapies, some studies have shown a strong concordance between NGS-based MRD results in paired PB and BM samples. This suggests that PB monitoring could be an adequate, less-invasive alternative in this specific clinical context. Best practices for bone marrow sampling To minimize potential inaccuracies, such as hemodilution from peripheral blood contamination, laboratories should use the "first pull" of the bone marrow aspirate. This initial sample, typically under 5 mL, provides the highest concentration of leukemic cells for analysis. This is for informational purposes only. For medical advice or diagnosis, consult a professional. AI responses may include mistakes. Learn more When is peripheral blood MRD assessment preferred over bone marrow in B-ALL? What other factors influence MRD test choice in B-ALL besides sample type? What are the sensitivity limits of NGS for MRD detection in peripheral blood?	
3	In most cases of MRD When BM positive the PB is negative so there is a high risk of false negative	10/28/2025 3:42 PM
4	LSCs reside in the bone marrow and if they are not expelled in the peripheral blood until it reach a specific threshold. However, Peripheral blood can be used in two conditions 1. increase the number of events that are acquired. 2. Conduct the test at close intervals. NOT APPLICABLE to high risk patients.	10/28/2025 3:20 PM
5	It depends on the number of events purchased. A minimum of 10-4	10/28/2025 4:30 AM
6	PB has limited usefulness and mostly not representative.	10/27/2025 7:14 PM
7	see above comment.	10/26/2025 8:23 PM
8	depends on when in remission. If still during the chemotherapy, they should still use bone marrow. If after chemotherapy is complete, screening PB may be useful.	10/24/2025 2:23 PM
9	It would give our clinical colleagues additional flexibility if "may use peripheral blood or bone marrow samples" was explicitly stated.	10/21/2025 12:31 PM
10	"May" but discouraged given the limited sensitivity. We don't want clinical folks thinking the sensitivity between BM and PB is the same and to conflate the results.	10/18/2025 11:08 AM
11	Not sure what this means - what time points? for suspected relapse, yes PB would work just fine, but this statement sounds like PB could replace bone marrow which is not true. or suggests that regular testing might be done for surveillance??	10/17/2025 4:55 PM
12	but if one is at a decision state, should not the most sensitive assay be used on peripheral blood ?	10/16/2025 6:08 PM
13	MRD parameters including sensitivity and LOD/LOQ on peripheral blood need to be established and validated independently.	10/16/2025 1:34 PM
14	high-sensitivity peripheral blood MRD (LLoD at least 10-5)	10/16/2025 12:56 AM
15	I am unsure - if peripheral blood is sensitive enough for evaluation during remission undergoing surveillance. At certain time points - BM should be a must but in between PB may be suggested	10/15/2025 8:08 AM
16	For patients with B-ALL in remission undergoing MRD surveillance, laboratories should ideally use bone marrow samples; however, peripheral blood samples may be used if bone marrow sampling is not feasible	10/10/2025 5:00 AM

17	Surveillance during remission?	10/9/2025 2:17 PM
18	Only if a high sensitivity is used.	10/8/2025 6:46 PM
19	Discrepancies between bone marrow and peripheral blood are common at diagnosis and during follow-up. The gold standard for assessing MRD, irrespective of technique or remission status should remain bone marrow aspirate testing.	10/8/2025 5:16 PM
20	Not sure there is sufficient evidence to support this.	10/8/2025 4:07 PM
21	For what purposes? Is this for MRD or not? Flow or molecular or both?	10/8/2025 3:40 PM
22	As for the above question, In the initial stages of therapy including initial induction and consolidation and may be early in the course of maintenance, Bone marrow is preferable. for long-term follow up peripheral blood may be used	10/8/2025 3:38 PM

Q7 Draft Statement 5 – For patients with B-ALL undergoing MRD assessment from peripheral blood at end of induction or later, laboratories should use high-sensitivity methods (LLoD at least 10-5).(Strong Recommendation)

Answered: 79 Skipped: 53



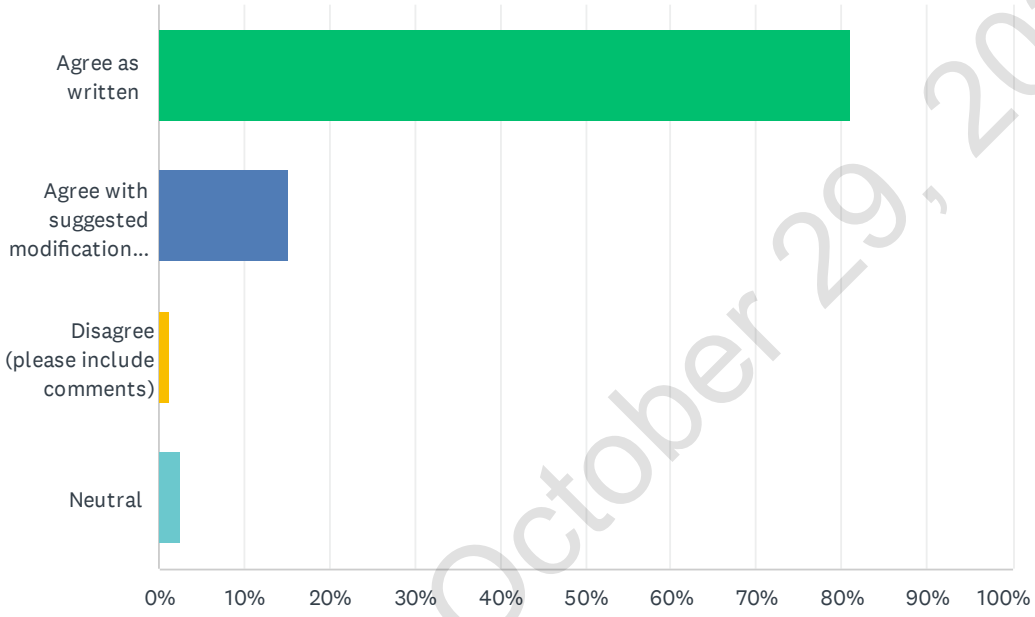
ANSWER CHOICES	RESPONSES	
Agree as written	72.15%	57
Agree with suggested modifications (please include comments)	11.39%	9
Disagree (please include comments)	6.33%	5
Neutral	10.13%	8
TOTAL		79

#	COMMENTS	DATE
1	This sensitivity (0.001% or 1:100,000 cells) is not widely used by labs performing B-ALL MRD flow cytometry COG Day+29 protocol.	10/29/2025 8:51 PM
2	significance of MRD results varies depending on when the test is performed. High sensitivity is especially important for later time points, such as post-induction and during surveillance.	10/29/2025 3:00 PM
3	Agree only with higher sensitivity. But still BM is a must	10/28/2025 3:42 PM
4	Why is 10-4 acceptable in statement 1, but 10-5 is required here?	10/27/2025 5:04 PM
5	Although 10-5 LLOD is preferable, there are no prospective studies to definitively say what level of MRD offers the best prognostic signifcance	10/27/2025 10:37 AM
6	marrow is preferable (dedicated first pull).	10/26/2025 8:23 PM
7	Agree that if they do peripheral blood, they should use high-sensitivity methods, but they really	10/24/2025 2:23 PM

	should be doing bone marrows while they are still in their chemotherapy regimen.	
8	why limit to PB? seems BM also qualifies	10/23/2025 12:07 PM
9	While a good recommendation it is potentially non-feasible as many labs struggle to achieve 10^-4. Additionally, this should include a statement for how to handle low cellularity specimens if this recommendation remains.	10/21/2025 12:31 PM
10	PB shouldn't necessarily be used at end of induction - bone marrow is the standard	10/17/2025 4:55 PM
11	Could there be clarification around "high-sensitivity methods (LLoD at least 10-5)." - will anyone of PCR, NGS, advanced MFC, ddPCR, et al. all be eligible? or only one of the three PCR, NGS, MFC?	10/17/2025 3:28 PM
12	I would still feel that BM is better than blood. A better quality BM sample with less events is more sensitive than a PB sample where one aquires more events and shows higher sensitivity on paper	10/15/2025 8:08 AM
13	Contradicts Statement 1 which requires 10^-4.	10/9/2025 2:17 PM
14	Ideally, the MRD method chosen for peripheral blood testing will have been previously shown to detect the patient's tumor cells with high sensitivity.	10/8/2025 5:30 PM
15	Same concerns as mentioned under statement 4 above.	10/8/2025 5:16 PM
16	Disagree with the use of peripheral blood for MRD testing. Insufficient correlation with bone marrow aspirate.	10/8/2025 4:07 PM

Q8 Draft Statement 6 – For flow cytometry-based MRD testing in patients with B-ALL, laboratories should collect sufficient numbers of intact cells after excluding debris to achieve reported sensitivity.(Good Practice Statement)

Answered: 79 Skipped: 53



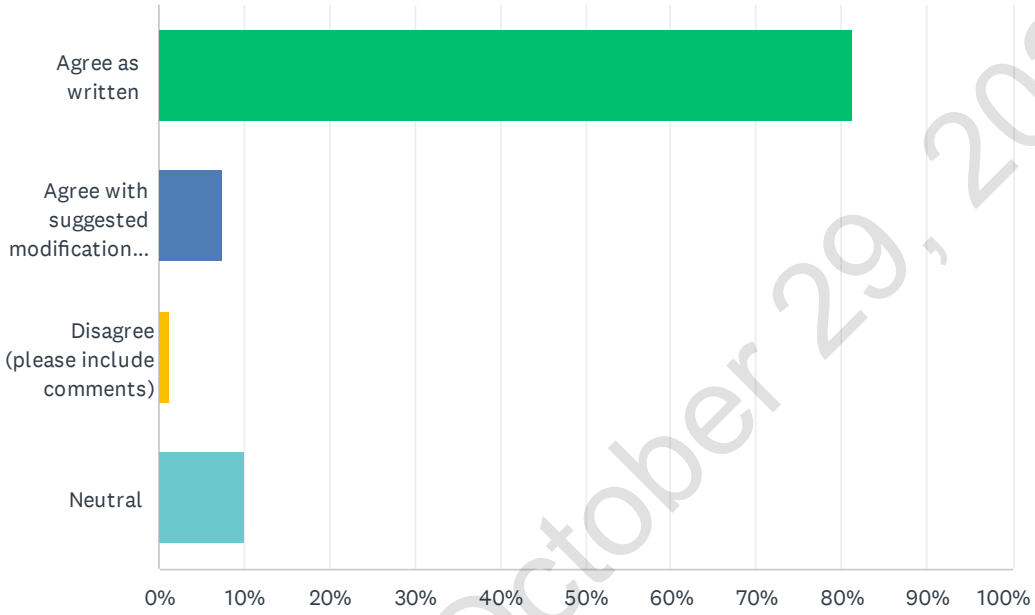
ANSWER CHOICES	RESPONSES	
Agree as written	81.01%	64
Agree with suggested modifications (please include comments)	15.19%	12
Disagree (please include comments)	1.27%	1
Neutral	2.53%	2
TOTAL		79

#	COMMENTS	DATE
1	High-sensitivity methods are highly dependent on Lower limits of detection and enough events collected . If the bone appears hemodilute or clotted, the lab should consider setting up two sers os the panel's tubes, pool them together, mis well in order to collect enough events.	10/29/2025 3:00 PM
2	Add recommendation of what is the "sufficient numbers"	10/29/2025 1:18 AM
3	Minimum: 1 million viable nucleated cells per tube. Optimal: 2-5 million cells for enhanced sensitivity.	10/28/2025 11:55 PM
4	Should be "Strong Recommendation".	10/27/2025 7:14 PM
5	You may get a higher % of abnormal if you include events falling in debris.	10/27/2025 12:27 PM
6	The statistical confidence to adequately power and establish a true lower limit of quantitation is often lost on practitioners. Please explicitly state required leukocyte cell counts (e.g. 1 x 10^6	10/26/2025 8:23 PM

	cell equivalents) to adequately inform an MRD analysis in which a negative is truly reflective of negative (at the level of 1 x 10^-4 or 1x10^-5, or even 1x10^-6. Adaptive clonoseq assay is marketed as 10^-6, although the assay input is often insufficient to truly inform an LOD at that level with high statistical confidence. As a result, many LDTs will be perceived as inferior. The guideline comments need to address this to ensure the playing field is level in the industry and patient care is optimized.	
7	And should report that number And should report the denominator	10/21/2025 11:56 AM
8	Would enrichment step be acceptable to gain higher numbers of cells including tumor cells?	10/17/2025 3:28 PM
9	bone marrow morphologic adequacy should be an adjunct to the study	10/16/2025 6:08 PM
10	To be refined as "viable singlet gated events" (where viability is grossly determined by forward and side scatter properties)	10/16/2025 12:56 AM
11	Use the first pull, and the specimen must be sent in a timely manner	10/14/2025 1:48 PM
12	Exact number and percentage of total and abnormal events should be mentioned	10/12/2025 12:52 AM
13	Would include a statement regarding the minimum number. COG requires 500,000.	10/8/2025 4:07 PM
14	At least 1000000 cells/events	10/8/2025 4:03 PM
15	This should go without saying - I would rather see this statement indicate that reporting should indicate the sensitivity that was achieved for the specific sample.	10/8/2025 3:40 PM

Q9 Draft Statement 7 – For molecular-based MRD testing in patients with B-ALL, laboratories should analyze sufficient genomic equivalents of nucleic acid to achieve reported sensitivity.(Good Practice Statement)

Answered: 80 Skipped: 52

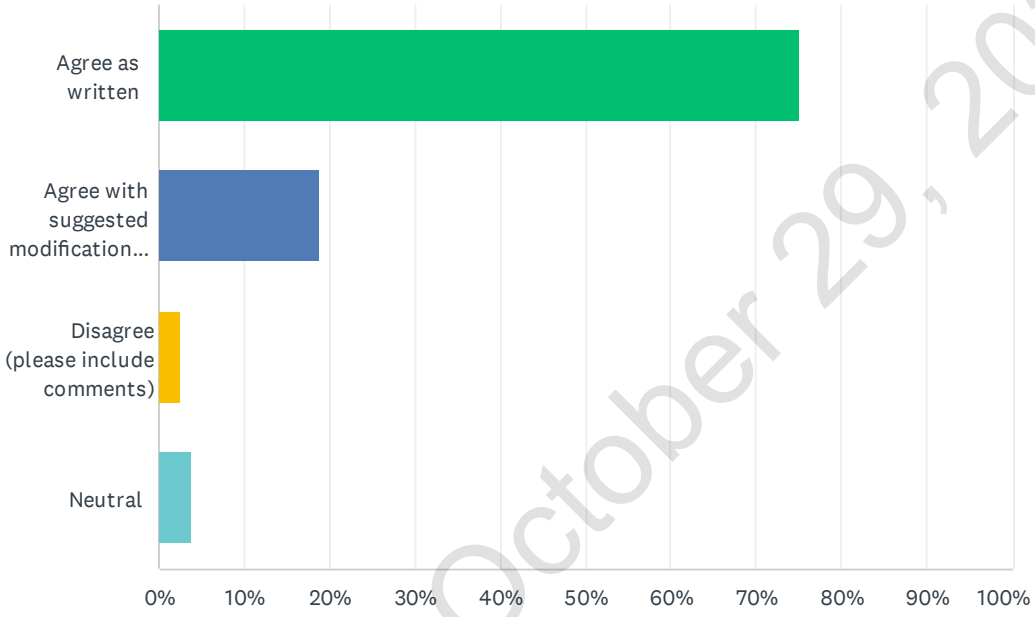


ANSWER CHOICES	RESPONSES	
Agree as written	81.25%	65
Agree with suggested modifications (please include comments)	7.50%	6
Disagree (please include comments)	1.25%	1
Neutral	10.00%	8
TOTAL		80

#	COMMENTS	DATE
1	For molecular-based MRD testing in patients with B-ALL, laboratories should analyze sufficient genomic equivalents of nucleic acid to achieve reported sensitivity.	10/29/2025 3:00 PM
2	Must analyze at least 1000,000 genome eq. i.e 6600ng DNA	10/27/2025 10:37 AM
3	Please include suggestions for number of micrograms of leukocyte derived DNA equivalents from Buffy coat fractions. This should not be vague or ambiguous.	10/26/2025 8:23 PM
4	Number needed to be mentioned	10/12/2025 12:52 AM
5	Suggest including a specific number.	10/8/2025 4:07 PM
6	Similar to Draft Statement 6 - this is better indicated in the actual report.	10/8/2025 3:40 PM
7	Give examples	10/8/2025 2:15 PM

Q10 Draft Statement 8 – For flow cytometry-based MRD testing of bone marrow aspirate from patients with B-ALL, laboratories should assess hemodilution.Note: First pull is strongly preferred. (Good Practice Statement)

Answered: 80 Skipped: 52



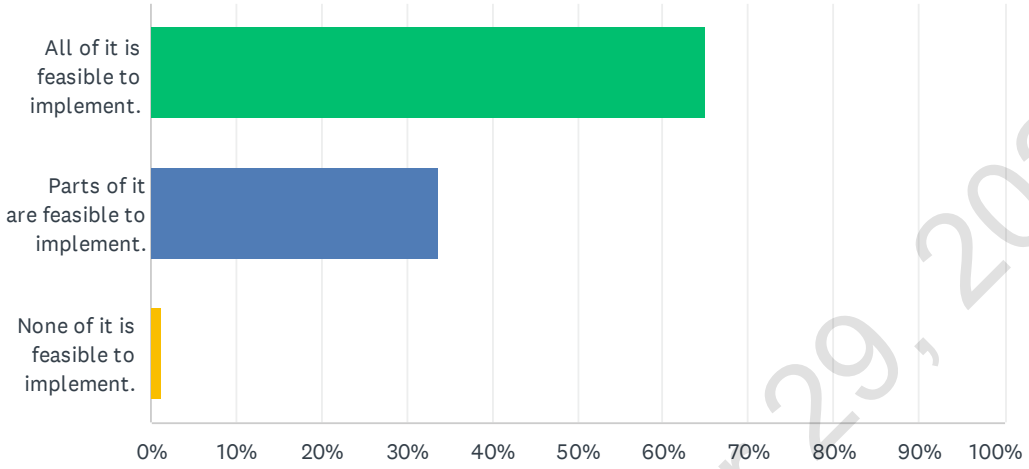
ANSWER CHOICES	RESPONSES	
Agree as written	75.00%	60
Agree with suggested modifications (please include comments)	18.75%	15
Disagree (please include comments)	2.50%	2
Neutral	3.75%	3
TOTAL		80

#	COMMENTS	DATE
1	High-sensitivity methods are highly dependent on Lower limits of detection and enough events collected . If the bone appears hemodilute or clotted, the lab should consider setting up two sers os the panel’s tubes, pool them together, mis well in order to collect enough events.	10/29/2025 3:00 PM
2	Avoid hemodilution-ensure marrow integrity. Process within 24-48 hours of collection. Use viability dyes and proper gating to exclude debris and other non-viable cells.	10/28/2025 11:55 PM
3	Unlike other statements, this one is too vague and does not apply in settings where morphology is not strongly coupled with flow cytometry at an operational level. Either clarify or consider adding in the text.	10/27/2025 2:56 PM
4	First pull is mandatory. if there is assessment for hemodilution, what recommendations are made (PCs? gran maturation? mast cells?). MRD tubes would potentially need to be modified or additional testing performed to further assess	10/27/2025 12:27 PM

5	Also emphasize that laboratories should include a disclaimer statement in the reports indicating that hemodilute sample analysis may under-represent the MRD status and must be interpreted with caution. Also, please include more explicit language addressing how hemodilution should be addressed.	10/26/2025 8:23 PM
6	please suggest some ways to assess for hemodilution (based upon morphology, based upon flow, etc).	10/24/2025 2:23 PM
7	Perhaps include some suggested ways of doing so including morphologic assessment, CD16 etc.	10/21/2025 12:31 PM
8	I think more clarification on how to assess hemodilution is needed.	10/20/2025 3:49 PM
9	and comment on the limitations on sensitivity given hemodilution.	10/18/2025 11:08 AM
10	replace should with must. But then what criteria are to be used especially if timing is off and testing is at a marrow suppression state rather than recovered	10/16/2025 6:08 PM
11	Should define what the parameters (and their cut-offs) are to determine hemodilution.	10/16/2025 12:56 AM
12	This is true also for molecular based MRD testing, first pull being strongly preferred. This should be stated.	10/14/2025 1:20 PM
13	How exactly to assess hemodilution should be mentioned to make practice standardized	10/12/2025 12:52 AM
14	Include a statement on preferred method, as there is no widely accepted method to my knowledge. Best way is to compare bone marrow aspirate smear with blood, in my opinion.	10/8/2025 4:07 PM
15	"…should assess for and comment on hemodilution with limitations and need to correlate with other high-sensitivity methods."	10/8/2025 3:44 PM
16	This can be extremely challenging depending on the panel chosen and the method preferred for assessment of hemodilution. May labs have adopted the COG protocol for B-ALL assessment, and I don't believe there is an easy way to assess hemodilution using that panel. The first pull being strongly preferred should definitely stay though.	10/8/2025 3:40 PM
17	Are there suggested method(s) for assessing hemodilution?	10/8/2025 3:13 PM

Q11 How feasible is it to implement this guideline?

Answered: 77 Skipped: 55

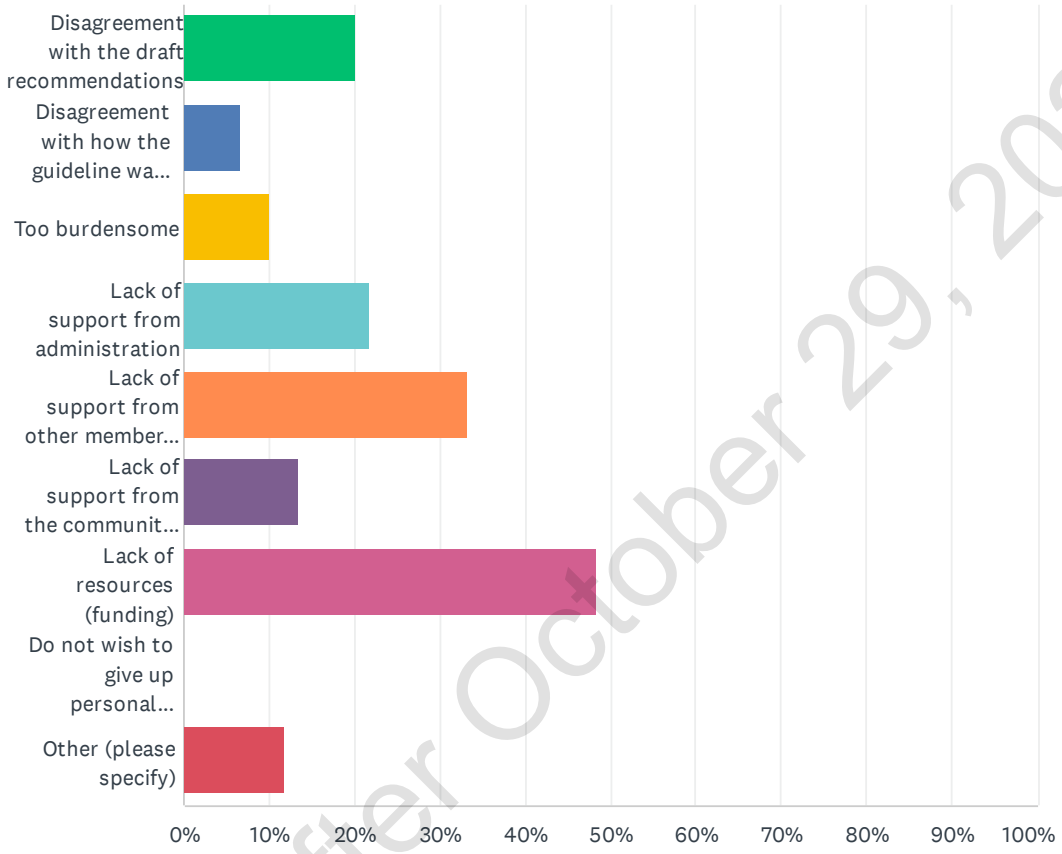


ANSWER CHOICES	RESPONSES	
All of it is feasible to implement.	64.94%	50
Parts of it are feasible to implement.	33.77%	26
None of it is feasible to implement.	1.30%	1
TOTAL		77

#	COMMENTS ABOUT THE FEASIBILITY OF IMPLEMENTING THE GUIDELINE:	DATE
1	The recommendation for 0.001% sensitivity will be challenging to implement with current instrumentation and data storage capabilities in our laboratory. It is a good idea, though! Also, I don't think I would defer bone marrow evaluation for MRD assessments in lieu of peripheral blood assessments, so I would likely not recommend our clinicians adopt that.	10/29/2025 8:56 PM
2	Time is sometimes an issue because flow validation and implementation usually is time consuming especially when you have more than one flow cytometer.	10/29/2025 3:06 PM
3	These are common practices in flow cytometry	10/29/2025 12:01 AM
4	sensitivity higher than 0.01%-0.001%	10/28/2025 3:22 PM
5	depending on what is chosen for hemodilution assessment, additional tubes would need to be incorporated	10/27/2025 12:30 PM
6	Practically speaking, how would NGS be better implemented for incremental gains when MFC is already in the clinical workflow? It might be rare for same people doing both MFC and NGS. People doing MFC will have very little support in adopting NGS despite its certain benefits over MFC such as abundant ctNDA. Will this recommendation help improving practice?	10/17/2025 3:34 PM
7	molecuar may prove costly but if aspirate is replaced by peripheral blood, then it could be cost neutral	10/16/2025 6:09 PM
8	Some labs may only be soing flow cytometry and don't have NGD or PCR	10/12/2025 12:53 AM
9	NGS-based testing will not be feasible in our laboratory, but the other types of proposed testing are feasible	10/8/2025 5:45 PM

Q12 What barriers might impede adoption of the final guideline? (Choose all that apply.)

Answered: 60 Skipped: 72



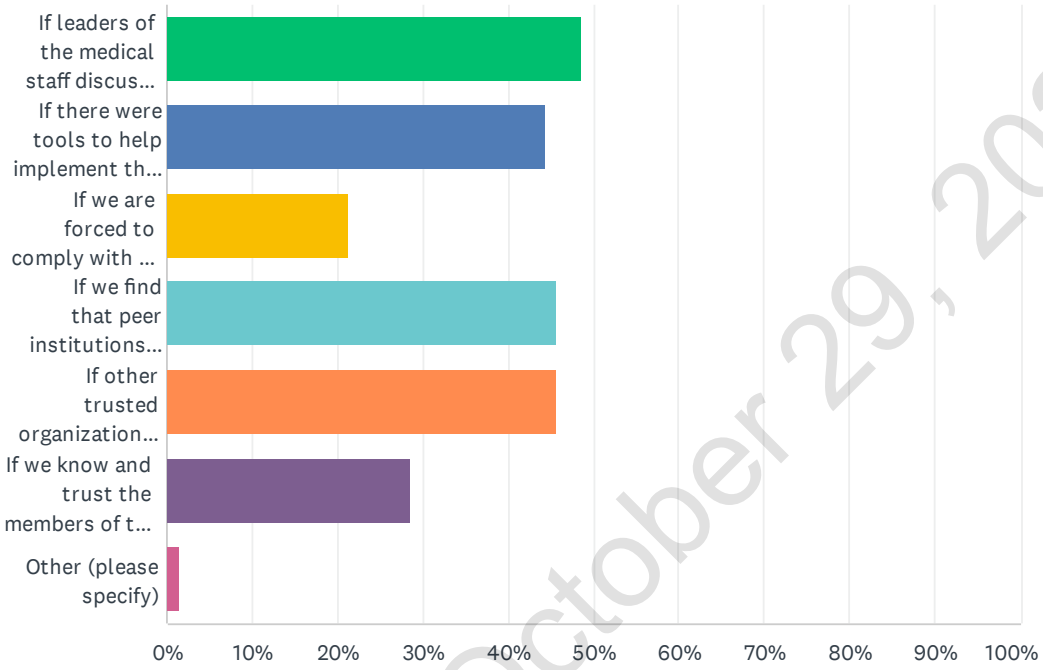
ANSWER CHOICES	RESPONSES	
Disagreement with the draft recommendations	20.00%	12
Disagreement with how the guideline was developed	6.67%	4
Too burdensome	10.00%	6
Lack of support from administration	21.67%	13
Lack of support from other members of the medical team	33.33%	20
Lack of support from the community (others outside your institution e.g., patients, industry)	13.33%	8
Lack of resources (funding)	48.33%	29
Do not wish to give up personal autonomy to follow the guideline	0.00%	0
Other (please specify)	11.67%	7
Total Respondents: 60		

#	OTHER (PLEASE SPECIFY)	DATE

1	Lack of laboratory resources to implement	10/29/2025 8:56 PM
2	NGS by itself or MRD from Adaptive Biotech (ClonoSeq)?	10/27/2025 7:20 PM
3	potential money loss if additional tubes need to be run for hemodilution.	10/27/2025 12:30 PM
4	Lack of Histopathology equipment	10/27/2025 9:40 AM
5	NGS MRD remains expensive and without a formal CPT code (81261). A CPT code crosswalked to the reimbursement level recently established in early 2025 should be established by the AMA, with lobbying by CAP and other regulatory bodies. Achieving statistical confidence may sometimes even require preparation of multiple libraries, rendering the assay cost upside-down with respect to the only closest available code for IGH clonality detection	10/26/2025 8:28 PM
6	None.	10/9/2025 12:38 PM
7	None	10/8/2025 2:11 PM

Q13 What facilitators might assist in your adoption of the final guideline? (Please select your top 3 facilitators.)

Answered: 70 Skipped: 62



ANSWER CHOICES	RESPONSES	
If leaders of the medical staff discussed adoption/adaption of the guideline for our practice setting	48.57%	34
If there were tools to help implement the guideline	44.29%	31
If we are forced to comply with the guideline by administration or an accreditation body	21.43%	15
If we find that peer institutions/practices adopt the guideline	45.71%	32
If other trusted organizations endorse the guideline	45.71%	32
If we know and trust the members of the panel members and/or organizations who developed the guideline	28.57%	20
Other (please specify)	1.43%	1
Total Respondents: 70		

#	OTHER (PLEASE SPECIFY)	DATE
1	hematologists should be brought on board.	10/18/2025 11:08 AM

Q14 Please provide any general comments or concerns:

Answered: 10 Skipped: 122

#	RESPONSES	DATE
1	Having a standardized approach to doing things across the board is really very important, and being patient with the results produced.	10/29/2025 12:01 AM
2	We currently offer NGS based clonality to detect MRD in B-ALL. We quantitate the malignant clone after we have established the clonal sequence in a diagnostic specimen. It is critical that we analyze the diagnostic specimen, without which it is impossible to establish the clonal sequence and then do MRD in followup specimens. This is a problem when patients are transferred from another facility and we don't have access to the diagnostic specimen. So, the guideline MUST specify that we first establish the clonal seq from a diagnostic specimen - blood or bone marrow, before doing MRD analysis in follow up specimens Also, our assay cannot detect partial D-J rearrangements. So, if a B-ALL has only a D-J rearrangement without a V segment, our IGH assay will be falsely negative. In such cases we send the specimen out for MRD analysis. So, the guideline MUST specify that if IGH NGS clonality is negative in a B-ALL with an assay that has primers that bind V and J segments, analysis must be performed for partial D-J rearrangements and then MRD should be done with the assay that can detect partial D-J rearrangements of IGH	10/27/2025 10:47 AM
3	Great ideas however, pathology practitioners in resource limited regions can hardly participate	10/27/2025 9:40 AM
4	None of the comments addressed utilization of RNA versus DNA for NGS MRD in B-ALL. Please advise. My personal opinion has been that DNA is a more accurate reflection of genomic / cellular equivalents; whereas RNA transcripts : B-ALL cells in sample may be discordant if residual disease is physiologically or transcriptionally over-active, for example.	10/26/2025 8:28 PM
5	Advocate for LDTs since FDA kits may not be suited for the degree of QA recommended	10/23/2025 12:11 PM
6	Useful common sense recommendations based on years of experience. Congratulations.	10/18/2025 3:00 AM
7	Practical implementation examples in various healthcare settings would provide stronger evidences and frameworks for final guideline recommendation. Despite of that, clear, thorough and unbiased comparison (converted to same analyte(s) or using same reference materials/standards) would be of great help.	10/17/2025 3:34 PM
8	Good Initiative, In Low middle income countries, the availability of assay and costs decides the choice for clinician	10/15/2025 8:10 AM
9	Bone marrow biopsy is painful and time consuming. While it is the best test to date, I hope we will have a better and validated way to access MRD in the future.	10/14/2025 1:49 PM
10	Nice job	10/8/2025 2:11 PM