Review of Results from MS/MS Pre-Conference Survey

APHL Newborn Screening QA/QC Subcommittee

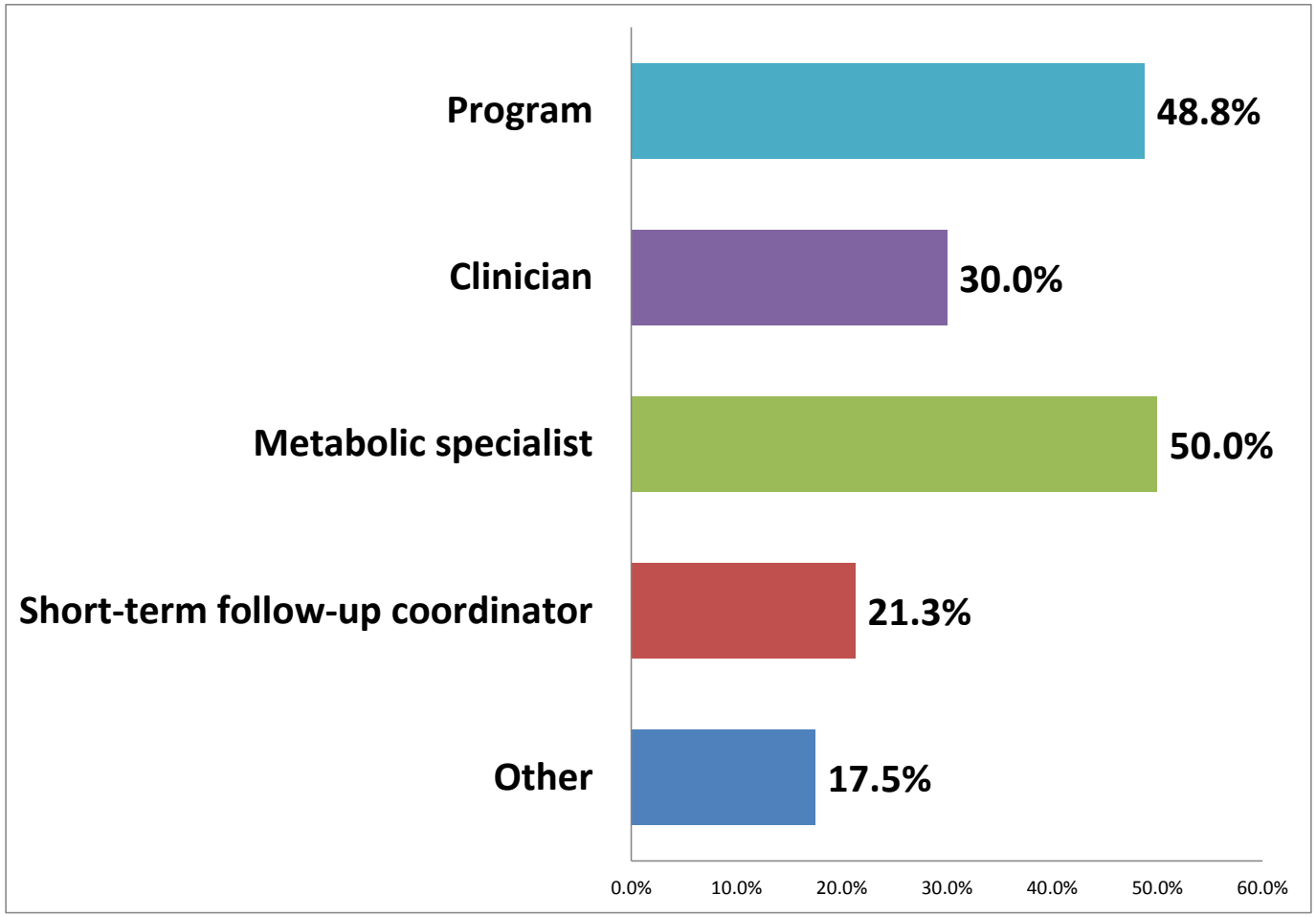
Presented by Arthur Hagar

“Missed” Cases

- Missed or Delayed Diagnosis ???

# of Cases	Disease
≥ 5	MSUD, TYR 1, Clb C/D, PKU
4	VLCAD, PA/MMA, BKT
3	MCAD, ASA, CUD
2	OTC, CPT II, SCAD, HCU
1	GA I, GA II, LCHAD, 2MBD, HHH

Who Determines "Missed" Cases



Reasons for “Missed” Cases

- Value of Marker Less Than the Cutoff Value
  - Occasionally “close” or borderline
  - Often mild or variant cases
- Marker Not Appropriate
  - Tyrosine instead of SUAC for TYR, Type 1
- Problem With Algorithm ???
- Infant on TPN
- Condition Not on Panel (e.g., Cbl C/D)

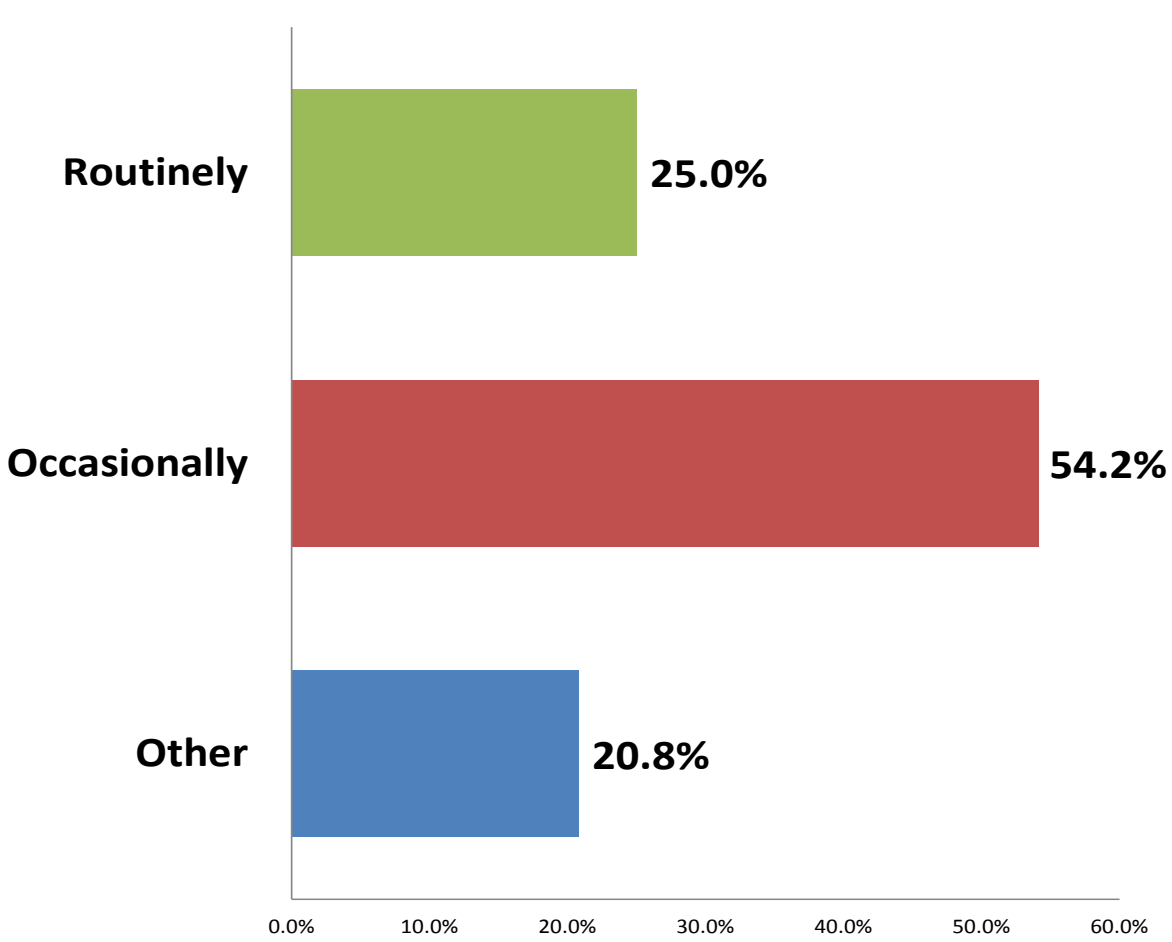
Corrective Action

- Nothing
- Change Cutoff Value(s)
  - May result in more false positives
- Change Marker
  - Tyrosine to SUAC for TYR, Type 1
- Add Marker(s) or Ratios
  - Leu/Ala for MSUD
  - C16 + C18:1 for CPT-II

Corrective Action

- Add Tiers
  - Age, weight, gestational age
- Change Protocol
  - Active follow-up of infants on TPN
- Add Second Tier Test
  - Ex: molecular tests
- Use of Region 4 Tools
  - How to implement in screening lab?

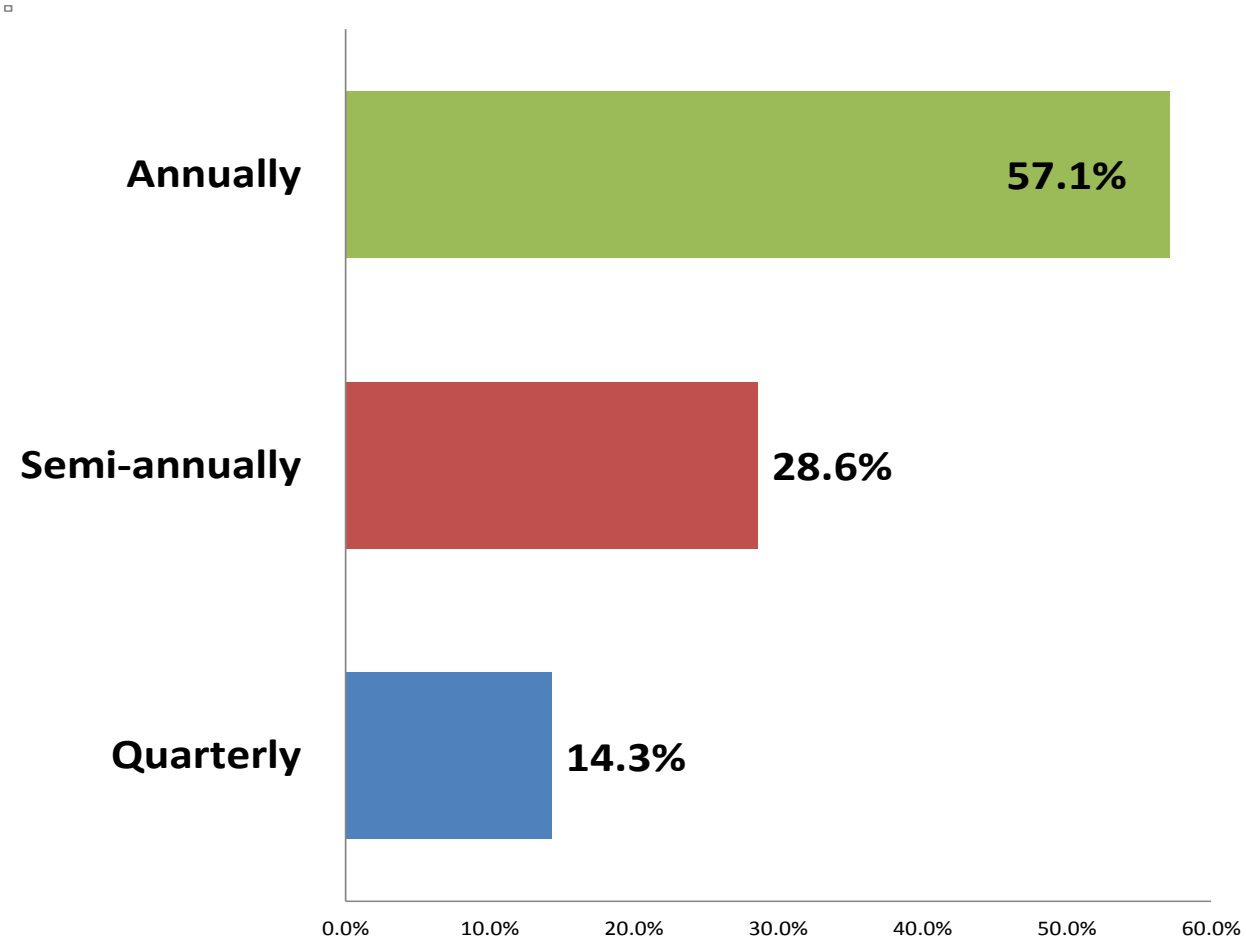
Frequency of Cutoff Review



Cutoff Review

- Routinely – 25%
- Occasionally – 54%
- Other Responses – 21%
  - False negative (missed case)
  - Increase in false positives
  - When new standards are used
  - Change in reagent kit lot
  - Request of medical director

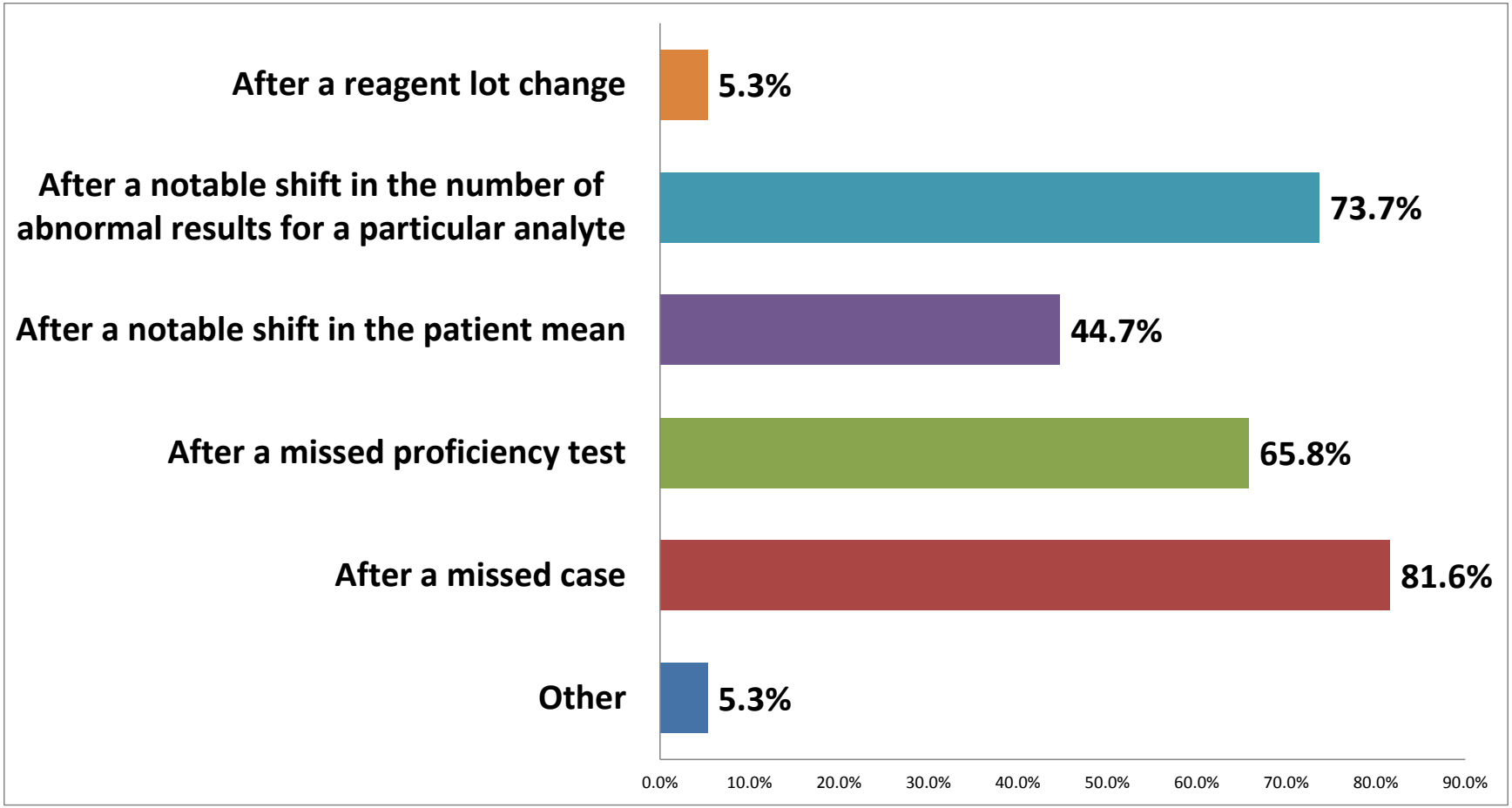
Frequency of Routine Review



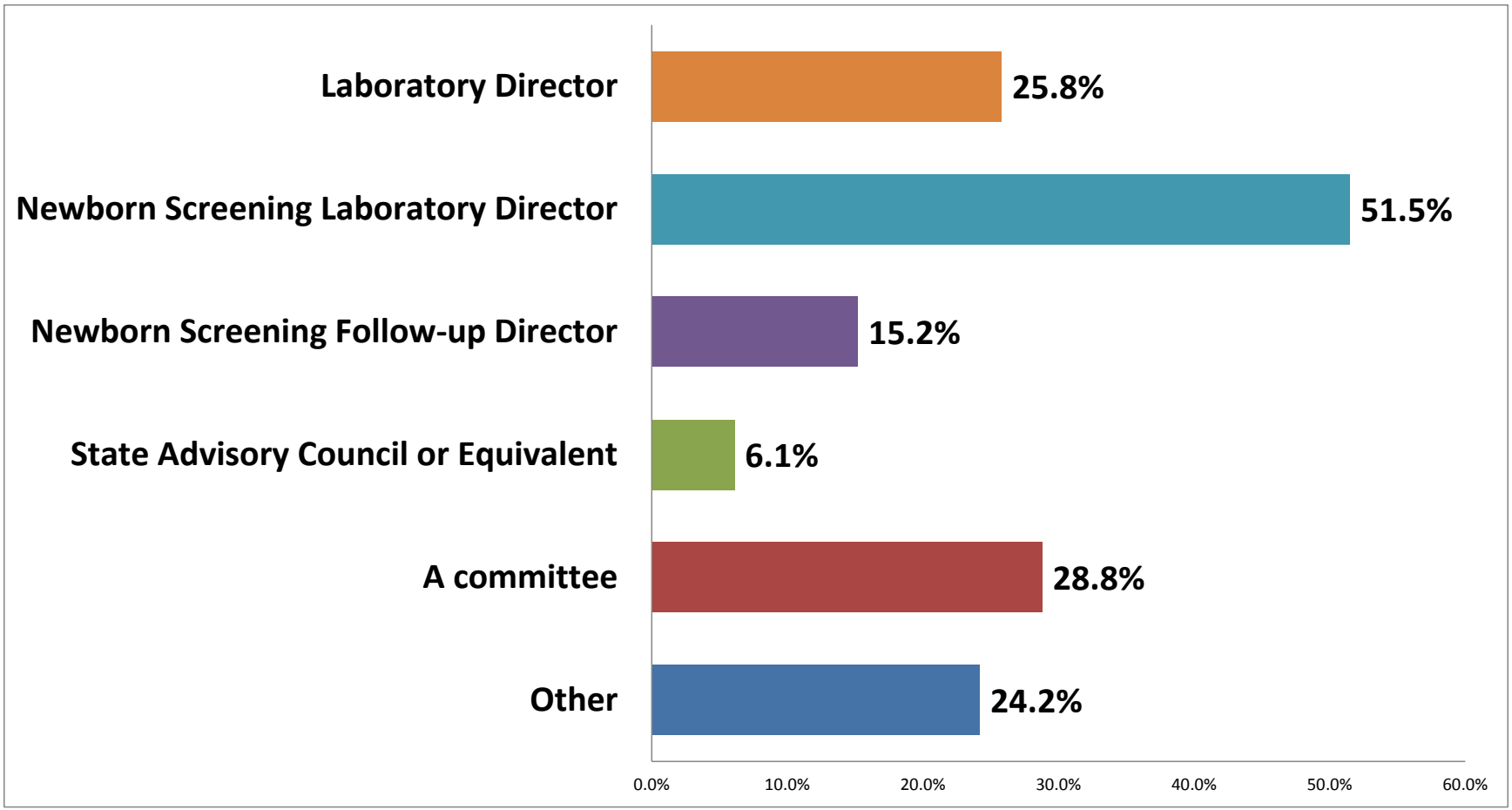
Routine Review of Cutoffs

- WHY?
  - To decrease the number of false positives without missing cases
  - To ensure that there are no population shifts
  - To ensure comparability between instruments
  - New kit lot
  - Seasonal effects
- WHO?
- HOW?

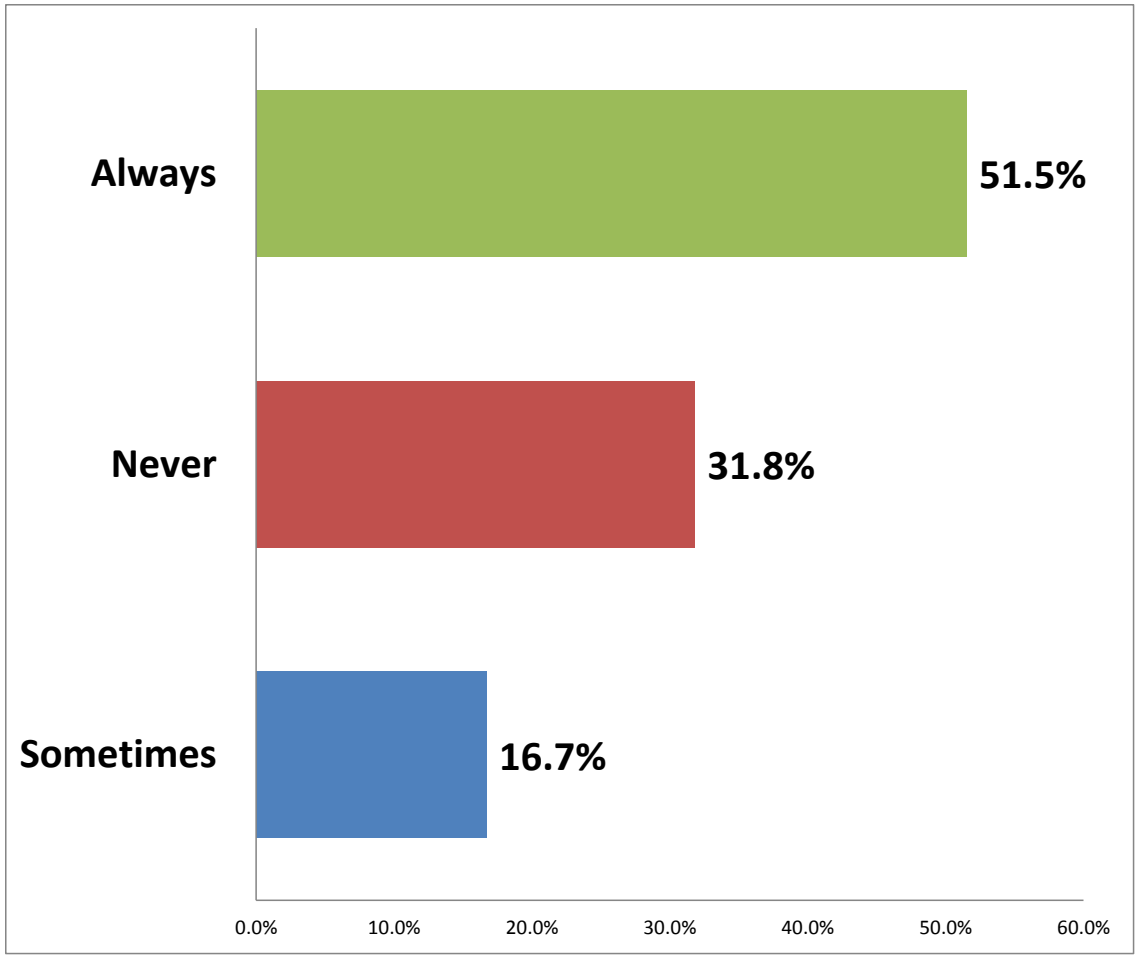
Occasional Review of Cutoffs – When?



Final Decision to Change Cutoffs



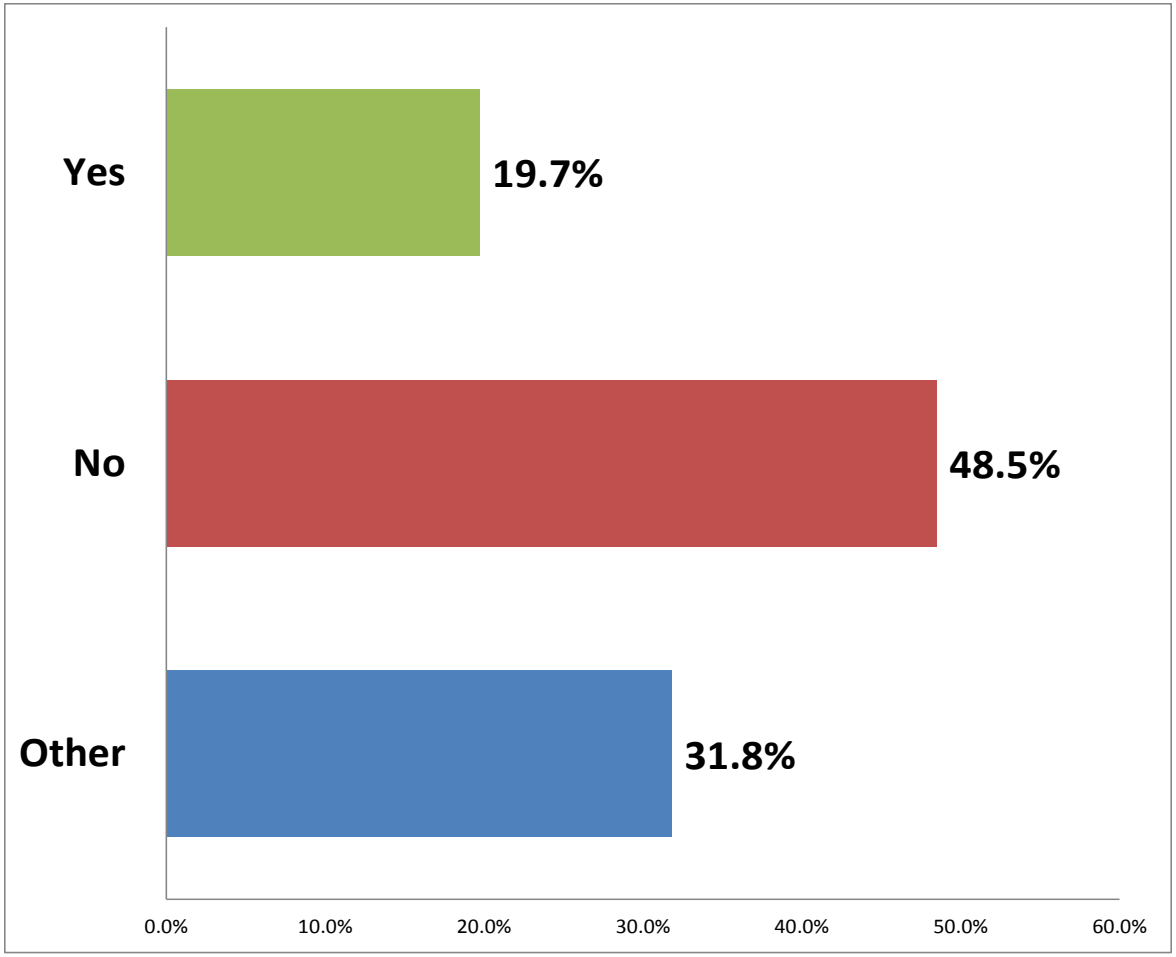
Are Clients Notified



Question 11

- Rather than updating your cutoffs, do you take any other type of corrective action when you encounter a scenario that may require a cutoff change?

Question 11 Responses



Question 11 – Other Responses

- Review interpretation algorithm
- Add secondary marker(s) and ratios
- Review possible effect of age, GA, season
- If due to reagent lot change, may wait out
- Check instruments
  - Review maintenance records
  - Consult vendor engineer
  - Perform instrument comparison

Question 12

- If applicable, what type of corrective action do you take when you encounter a scenario that may require a cutoff change?

Corrective Actions in Situations that May Require a Change in Cutoffs

- Review of six months of data
  - normals, abnormals, missed cases
- Statistical analysis and study
- Correlate change in number of call outs and confirmed cases
- Full investigation
  - Shifts in means of controls or patients
  - Retest old specimens (confirmed cases & borderline results) and PT samples

Acknowledgements

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Breakout Group Topics

Missed Case/Delayed Diagnosis

- Is it a missed case or delayed diagnosis?
  - What is the difference between the two?
  - Are there different implications?
- How are missed cases identified?
  - How do they come to the lab's attention?
  - What is your mechanism for picking them up?
- Are conditions not on your panel counted?
  - What are the implications of either choice?

Barriers to Changing Markers

- Compile a list of barriers
  - Categorize as administrative or technical

- Discuss possible solutions/approaches

Barriers to Method Selection

- Is an FDA-cleared/approved kit required?
- What are the barriers to using a laboratory-developed test (LDT)?
- Is implementation of second-tier tests feasible?
  - What are the advantages and disadvantages?
- Discuss possible solutions/approaches

Cutoff Reviews

- How often are cutoffs reviewed?
  - How often should they be reviewed?
- Who does the review?
  - Who should be involved in the review?
- What data are used when reviewing cutoffs?

- Discuss possible solutions/approaches

Use of Ratios and Enhanced Interpretation Schemes

- Are ratios included in the laboratory report?
- How would you report an enhanced interpretation scheme?
- What are the barriers to using ratios or enhanced interpretation schemes?
  - Ex: use of ratios or an enhanced interpretation scheme with a FDA-approved kit?
- Discuss possible solutions/approaches

Quality Assurance: Corrective and Preventative Action Procedures

- What are the common QA failures in the lab?
- What are the common triggers of CAPA Procedures?
- Review examples of CAPA investigations.

- Discuss possible solutions/approaches