

# **Current Understanding of Context of Use and Its Impact on Biomarker Assay Development and Validation**

Results from the 2020 AAPS Context of Use Survey

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Passage Bio

# Acknowledgement

- **Philip Timmerman and EBF organizers**
- **Members of AAPS Biomarkers & Precision Medicine Community Leadership Team**
- **Laruen Stevenson**

# Fit for Purpose and Context of Use

- Lee *et al.* 2006 'Fit for purpose' white paper has served as a central guidance for biomarker assay validation and biomarker data use.
- The FFP concept is sometimes mistakenly viewed as vague or less quality for some assay developer or end users.
- 'Context of Use' aims to provide a concise description of the biomarker's specified use and includes two components:
  - the BEST biomarker category
  - the biomarker's intended use

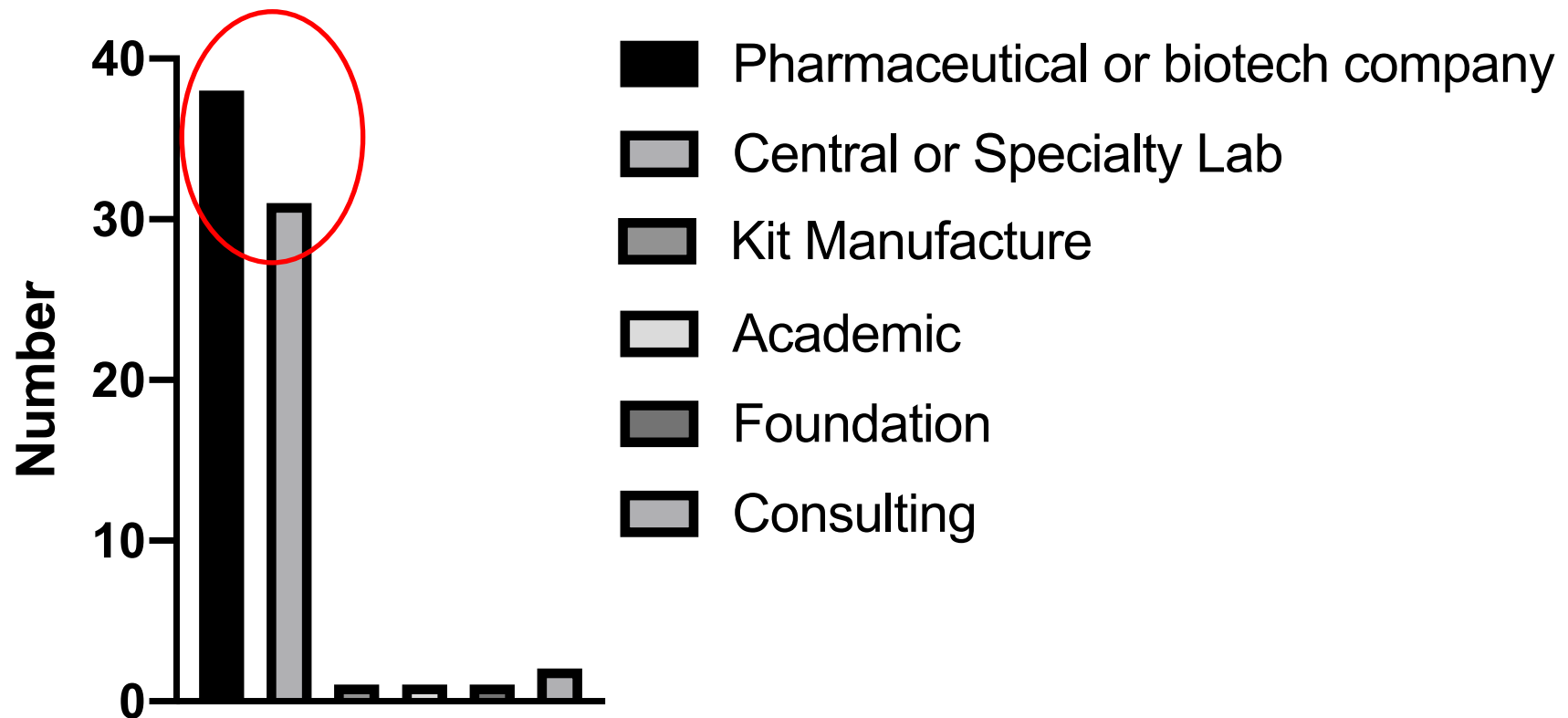
# The 2020 AAPS Context of Use (COU) Survey

- Organized by the Biomarkers & Precision Medicine Community Leadership Team
- Conducted in Jan. 2020
- 74 responders
- **Goal:**
  - What is the level of understanding of COU?
    - Q2-5
  - How does COU impact biomarker work?
    - Q 6-8
  - Which guideline our members follow for biomarker assay validation?
    - Q9

## The Survey

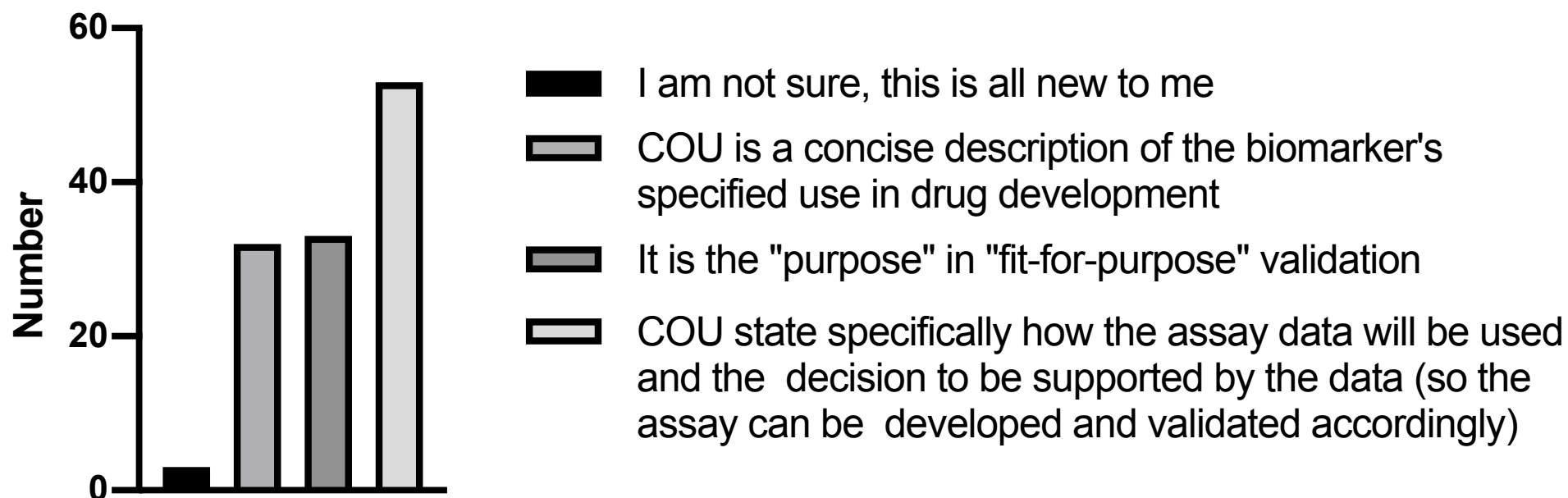
1. Where do you work?
2. What does COU for a biomarker or biomarker assay mean to you?
3. How do you define/find the COU for a biomarker assay? Who is involved in the conversation?
4. What are the essential components of COU?
5. How does COU affect assay development and validation parameters
6. How does COU affect the day-to-day practice in assay development and validation?
7. Do you agree with the following statement regarding COU?
8. Which of the following statement best describe the current practice in your organization?
9. Which guideline or document do you use for Biomarker method validation (LBA/LC-MS)

## Question #1 - Where do you work?



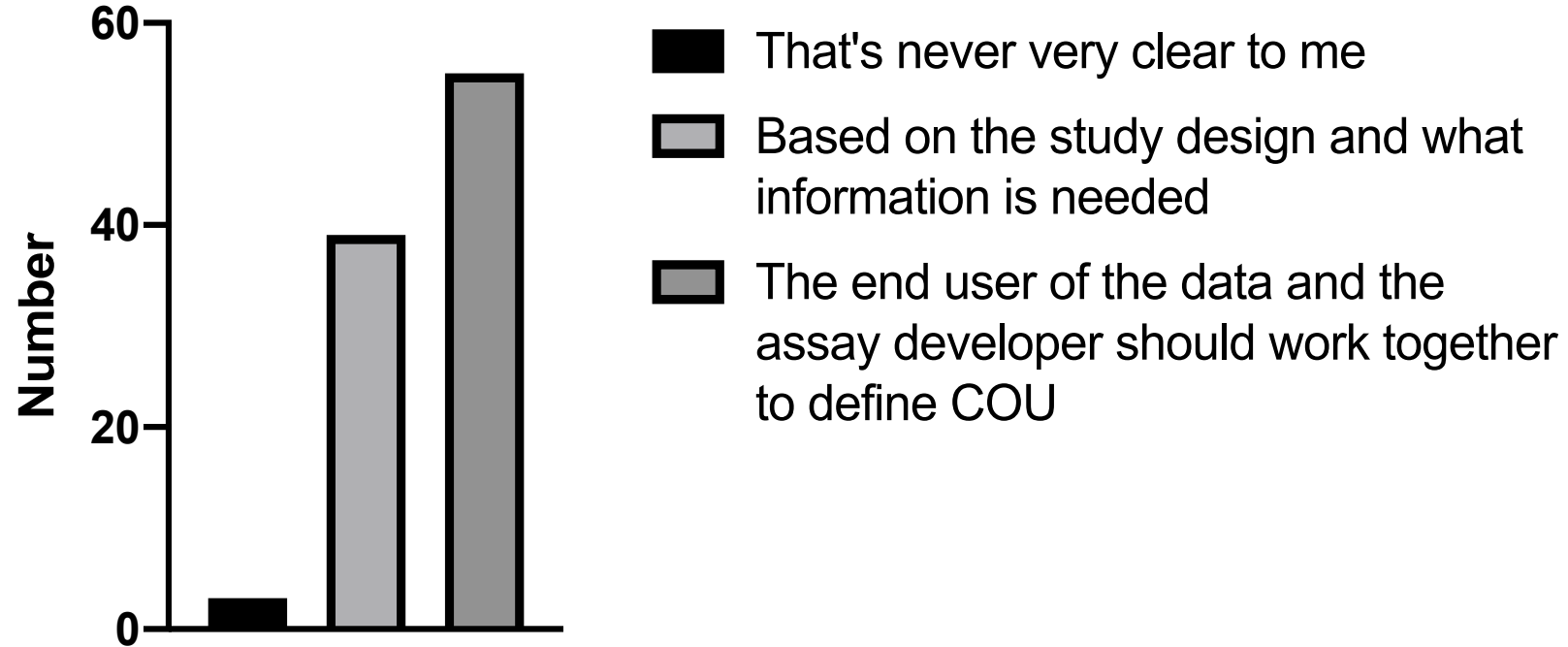
Majority participants are from pharma, biotech and CROs

## Question #2 - What does COU for a biomarker/biomarker assay mean to you?



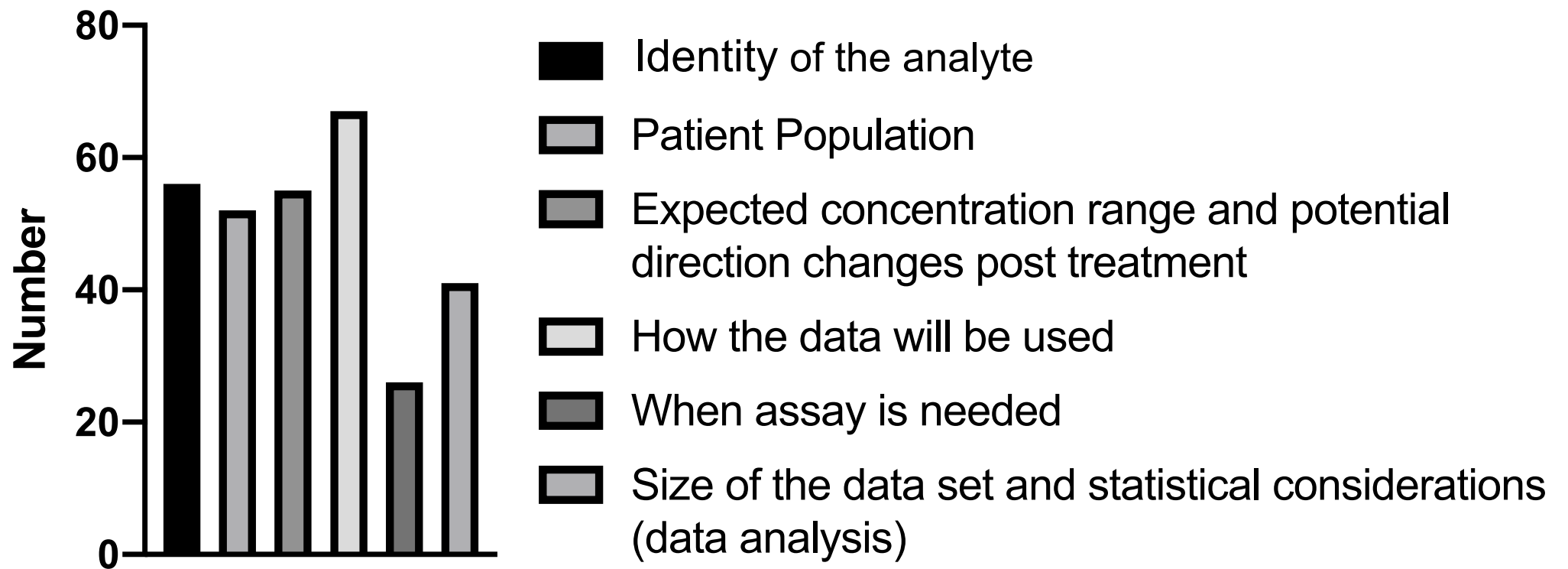
Most participants have the right concept of COU

## Question #3 - How do you define/find the COU for a biomarker assay? Who is involved in the conversation?



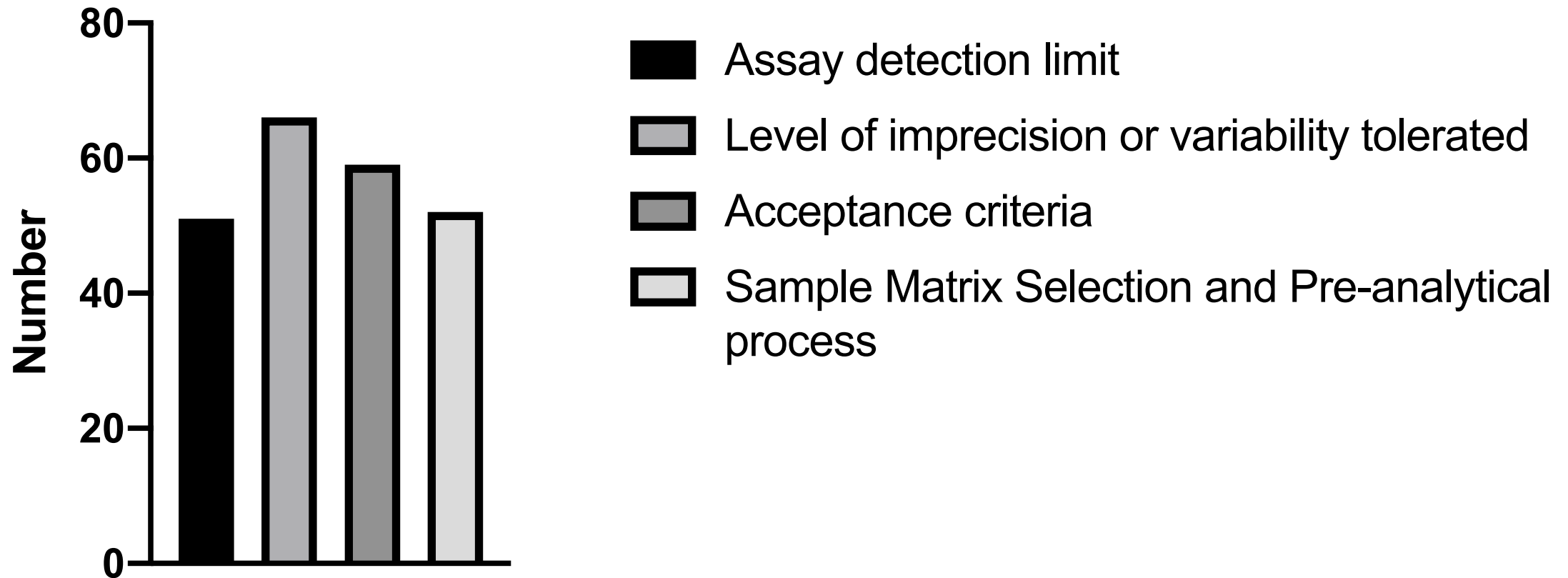
Most participants understand how COU is defined

## Question #4 - What are the essential components of COU?

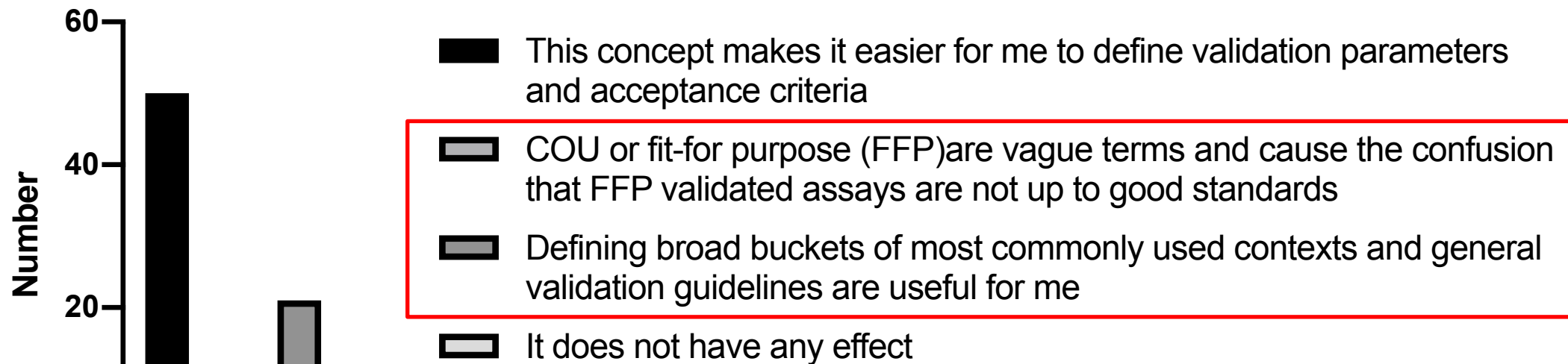




## Question #5 - How does COU affect assay development and validation?

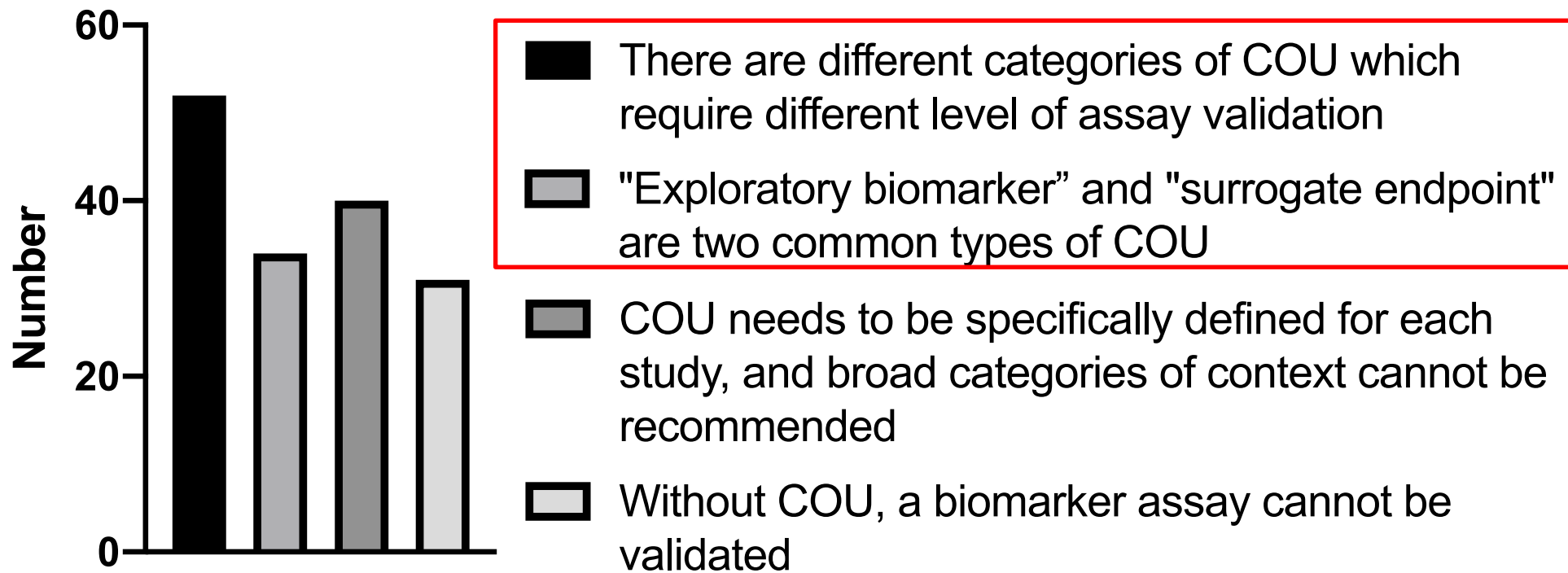


## Question #6 How does COU affect the day-to-day practice in assay development and validation?



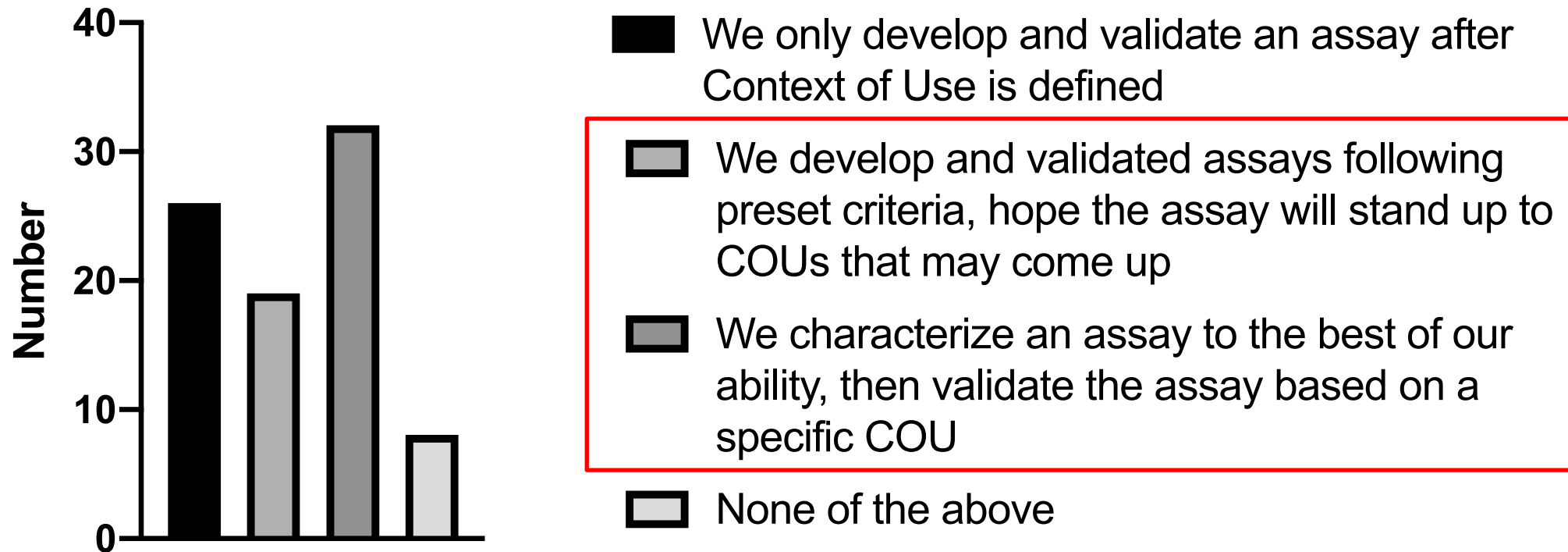
*For day-to-day practice, significant numbers of participants still feel that COU is not often well defined and causes a lot of confusion within the study team*

## Question #7 - Do you agree with the following statement regarding COU?



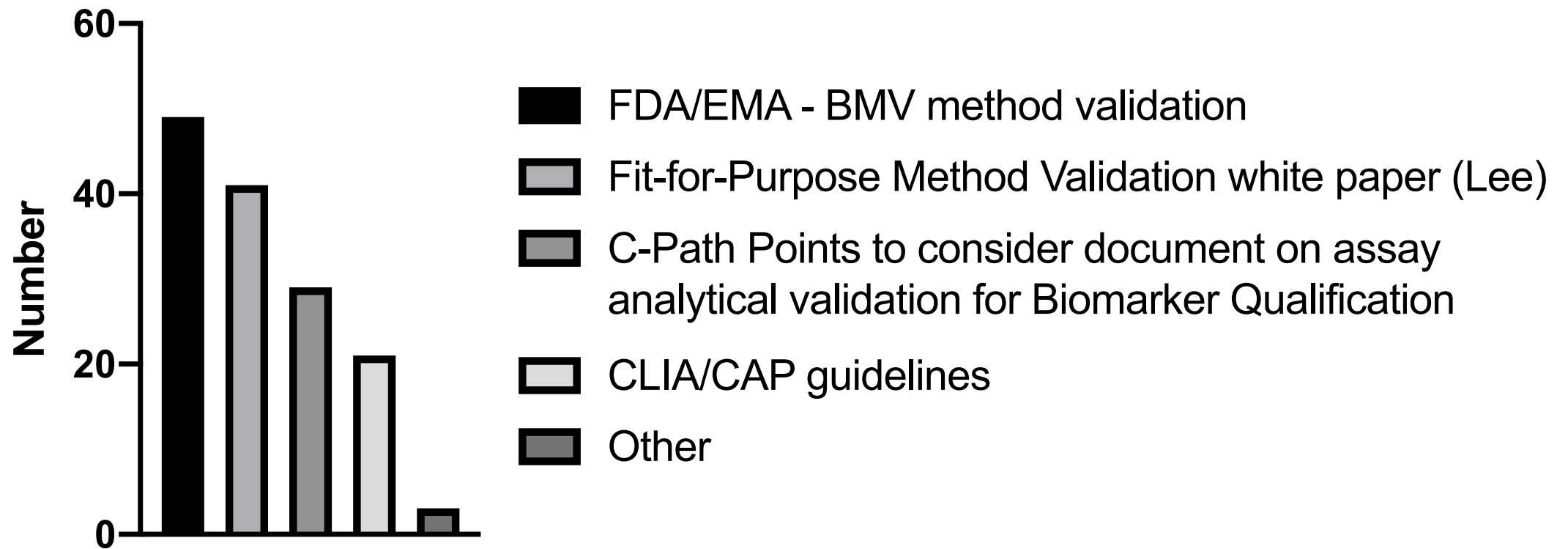
*Many participants think there are categories of COUs and corresponding levels of validation requirement*

## Question #8 - Which of the following statement best describes the current practice in your organization?



*Varied practice cross different organizations; COU is not always applied.*

## Question #9 - Which guidance document do you use for biomarker method validation (LBA/LC-MS)?



*Varied views on which guidance document to follow  
Shall there be a guidance document for biomarker assays?*

# *Thoughtful comments and insights...*

- **What are the essential components of COU?**
  - ...biomarker category and risk level of data use, comparability of results (within a single study, across various studies, between various labs), number of expected samples, frequency of measurements (online, interim analysis, at the end of the study)...
  - ...whether the data will be used for patient management...
  - ...expected differences between patient population and healthy individuals...
- **How does COU affect assay development and validation?**
  - ...choice of technical platform to be used...
  - ...sample preparation and storage...
  - ...what regulation does the lab need to follow (CLIA, FDA, non-regulated)...
- **Which of the following statement best describes the current practice in your organization?**
  - ...being a CRO, we always discuss this with Sponsors, but if we don't get a firm answer we use default criteria or assumptions, at least for the first study...
- **Which guideline or document do you use for Biomarker method validation (LBA/LC-MS)?**
  - ...GSP (Good Scientific Practice) in developing and validating analytical methods...
  - ...Internal guidelines/SOPs...
  - ...Guidelines used are based on use of data (e.g., data going to physician must be performed under CLIA, but that could permit a BMV style validation if the data is also to be used to support a label claim)...
  - ...New M10 draft guidance...



# What does the survey show and what next?

- Most participants have conceptual understanding of COU; and appreciate its central role in guiding biomarker assay development and validation.
- Implementing the FFP/COU principle in day-to-day practice is still lagging.
  - COU is not clearly defined or communicated
  - There is desire to have simple categories of COU and levels of validation
- Continuing discussion/debate: which guidance document to follow for biomarker assay validation? Should there be a guidance document?

## AAPS Effort on COU Discussion

### OSD 1: Jan 2020

- What is context of use?
- How to define/find COU?
- Key components of COU (what should be included in COU)?

### OSD 2: March 2020

- Context of Use Survey and Perspectives on Key Questions

### OSD 3: May 2020

- Biological Variability and Minimum Required Precision

**Coming soon: Nov 9-10, 2020, PharmSci360**

- **Context of Use Workshop**