TRENDS IN CLINICAL NGS QC MANAGEMENT: RESULTS FROM A PRACTITIONER SURVEY

A GENOMEWEB/SERACARE
SURVEY REPORT

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This report outlines the results of a first-of-its kind survey that sought to understand quality control management practices in clinical next-generation sequencing labs.

Conducted as a partnership between GenomeWeb and SeraCare, the survey aimed to gain insight into several key metrics, including:

- **Which QC metrics clinical genomics labs track for NGS assays;**
- **How clinical NGS labs determine QC failures;**
- **The impact of QC stops on reporting results and lab productivity;**
- **The use of tools such as reference materials and data management solutions**

The 16-question survey was sent to GenomeWeb readers who work in the clinical genomics field. Only those respondents who indicated that they perform next-generation sequencing for clinical testing (n = 270) were qualified to take the survey. Of those, 155 completed all questions.

TOP-LEVEL FINDINGS

The survey found that while clinical genomics labs have adopted many quality control habits commonly used in traditional diagnostics labs, QC best practices are still evolving for NGS testing.

In particular, the results indicate that lab harmonization is still a challenge for the field. A large percentage of respondents indicated they run non-comparable materials as controls and use custom methods to manage data.

- **Two-thirds of labs said that they use some form of "homebrew" controls or reference materials.**
- **Around a third of respondents have developed custom methods for managing QC data.**

Perhaps related to this lack of harmonization best practices, many labs are doing little to ensure performance and quality beyond rudimentary monitoring.

- **One-third of respondents indicate they only run positive controls at lot changes or never.**
- **The average clinical genomics lab is tracking only 11 QC metrics, and many are not tracking standard diagnostic lab metrics such as operator, reagent lot, or instrumentation.**

On the positive side, 45 percent of respondents indicate they are monitoring more than 10 positive control biomarkers in their sequencing assay—measuring multiple clinically relevant genes and variant types as part their QC strategy.

Overall, a majority of clinical genomics labs indicate a desire to improve QC programs and acknowledge significant time spent troubleshooting NGS assays.

- **Half of responding labs are spending between 12 to 60 days per year troubleshooting.**
- **Around 60 percent of respondents indicate they would like to troubleshoot their runs more quickly and track and trend their data over time more easily.**

SURVEY RESPONDENT DEMOGRAPHICS

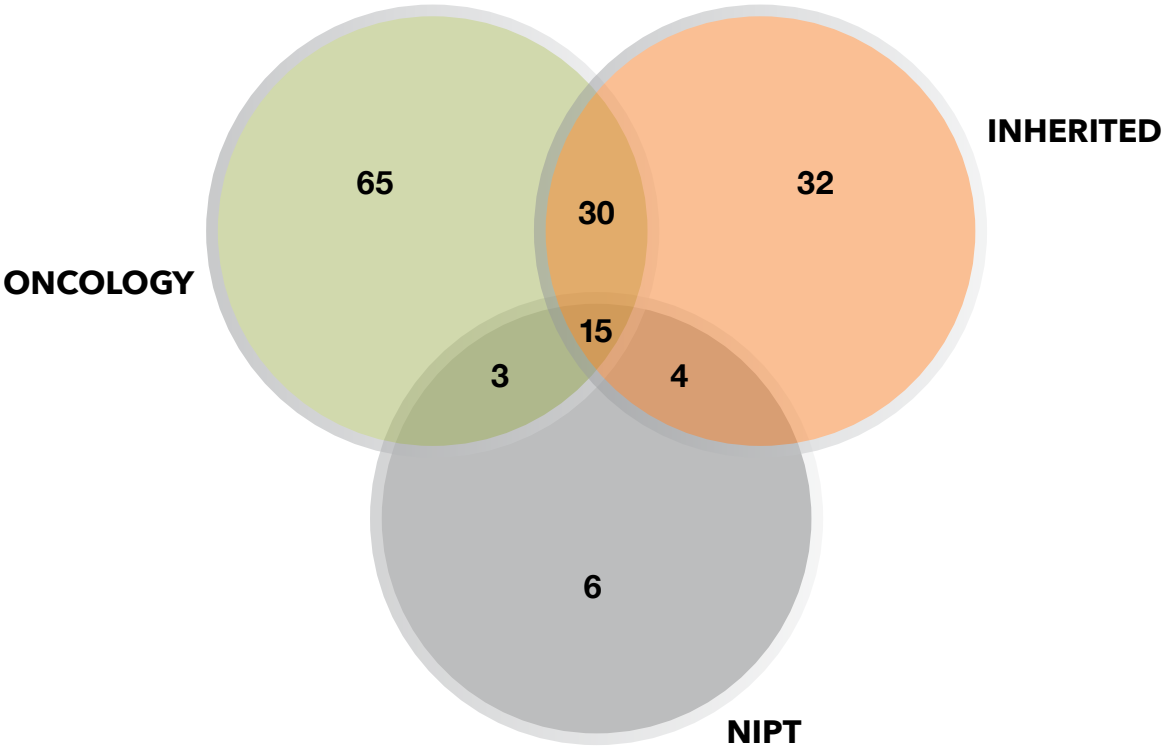
Around half of the survey respondents hold a management position in their lab. The most common title is scientist.

Which best describes your title? (n = 155)

SCIENTIST	37%
LAB DIRECTOR	19%
LABORATORY MANAGER	12%
OTHER (PLEASE SPECIFY)	10%
BIOINFORMATICS MANAGER	8%
QUALITY CONTROL MANAGER	6%
TECHNICIAN	5%
OPERATIONS MANAGER	2%

Nearly two-thirds of responding labs run NGS tests for oncology (113 out of 155), followed by inherited disease (81 out of 155) and non-invasive prenatal testing (28 out of 155). There were 15 responding labs who run NGS assays for all three applications.

What applications are you or will you apply NGS testing to? Please check all that apply (n = 155)

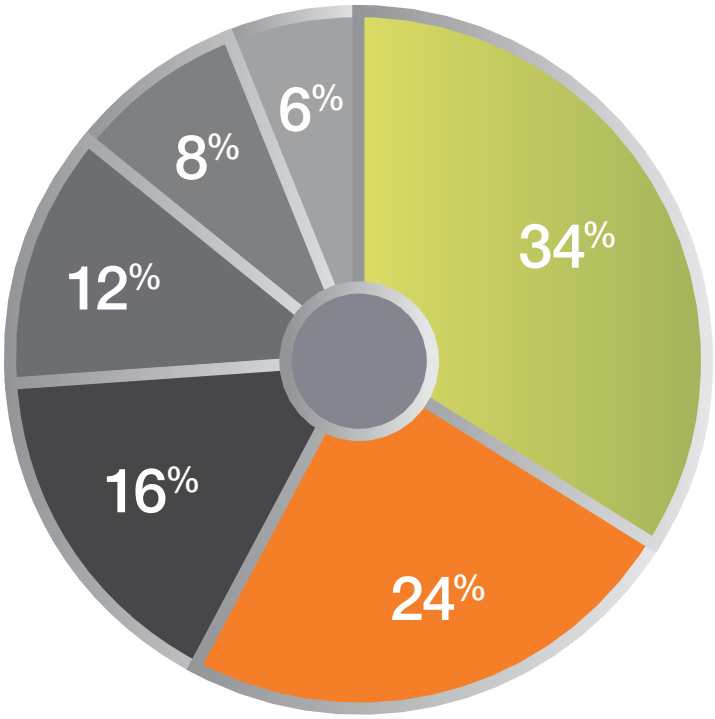


HARMONIZATION IS STILL A CHALLENGE

In particular, the results indicate that lab harmonization is still a challenge for the field. A large percentage of respondents indicated they run non-comparable materials as controls and use custom methods to manage data.

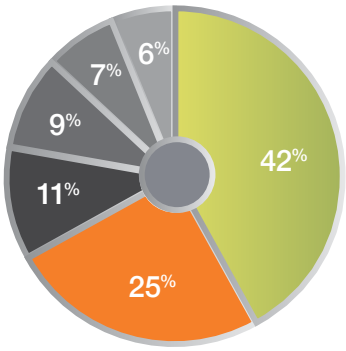
Two-thirds of labs are using some form of "homebrew" controls or reference materials, including cell lines, patient specimens, or the NIST Genome in a Bottle reference. Only 34 percent of clinical genomics labs are using commercial controls.

Which reference materials do you most use for positive run controls? (n = 155)

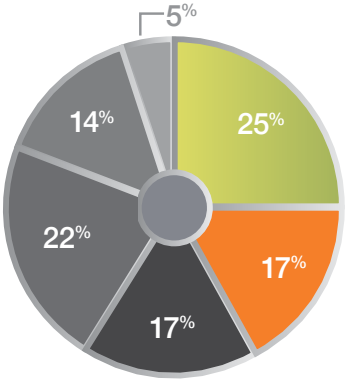


- Commercially available run controls (e.g., SeraCare, Horizon Discovery, Acrometrix)
- Cell lines
- Actual patient specimens
- (NIST) Genome in a Bottle (e.g., NA12878)
- Remnant samples from patients
- Other

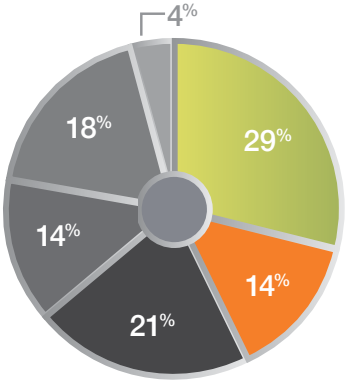
Which reference materials do you most use for positive run controls? (oncology respondents, n = 113)



Which reference materials do you most use for positive run controls? (inherited disease respondents, n = 81)

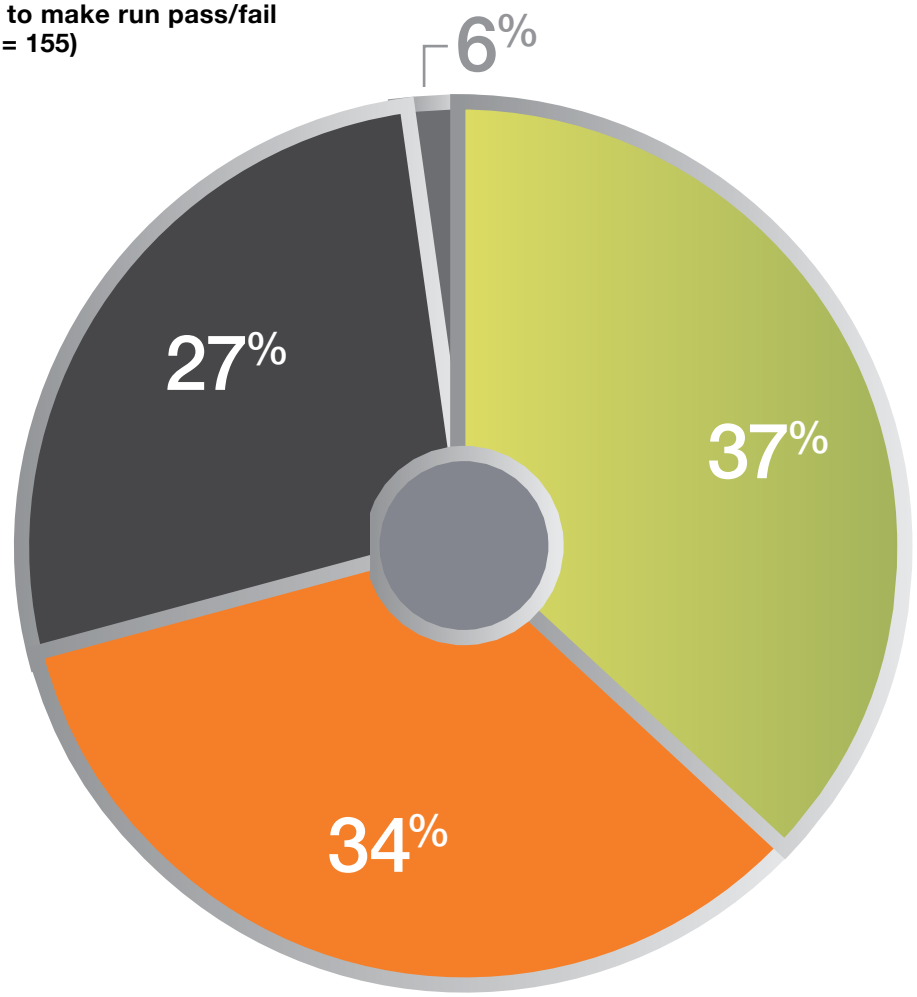


Which reference materials do you most use for positive run controls? (NIPT respondents, n = 28)



Labs are also taking a do-it-yourself approach to managing QC data, with 37 percent of respondents using custom methods for managing QC data and another 34 percent using Excel.

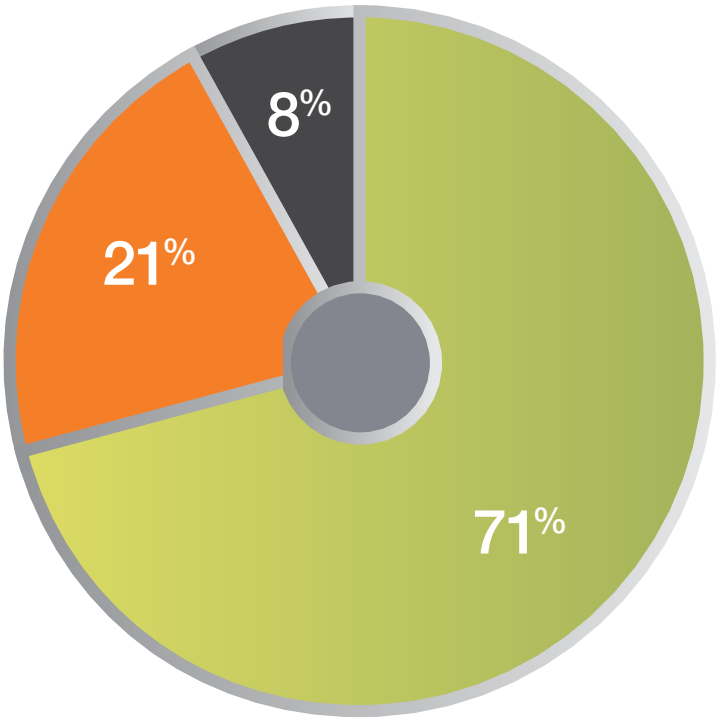
How are you currently managing QC data used to make run pass/fail decisions? (n = 155)



RUDIMENTARY MONITORING PRACTICES

Around 30 percent of responding labs said they use positive run controls only on new lots or not at all, while 71 percent of responding labs run a positive control every few runs.

How often do you use positive run controls? (all respondents, n = 155)



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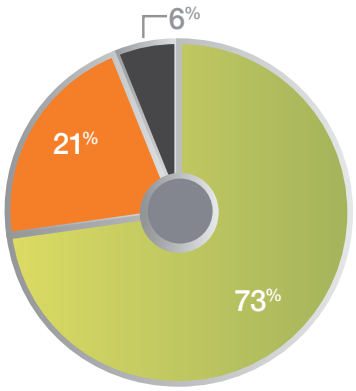

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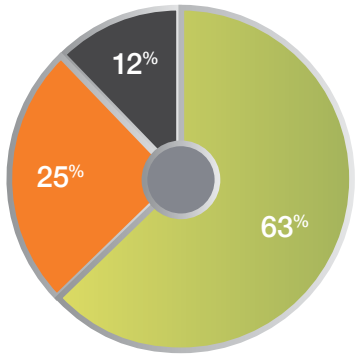
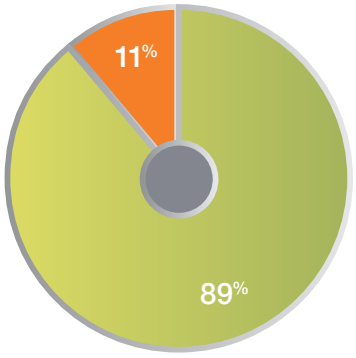


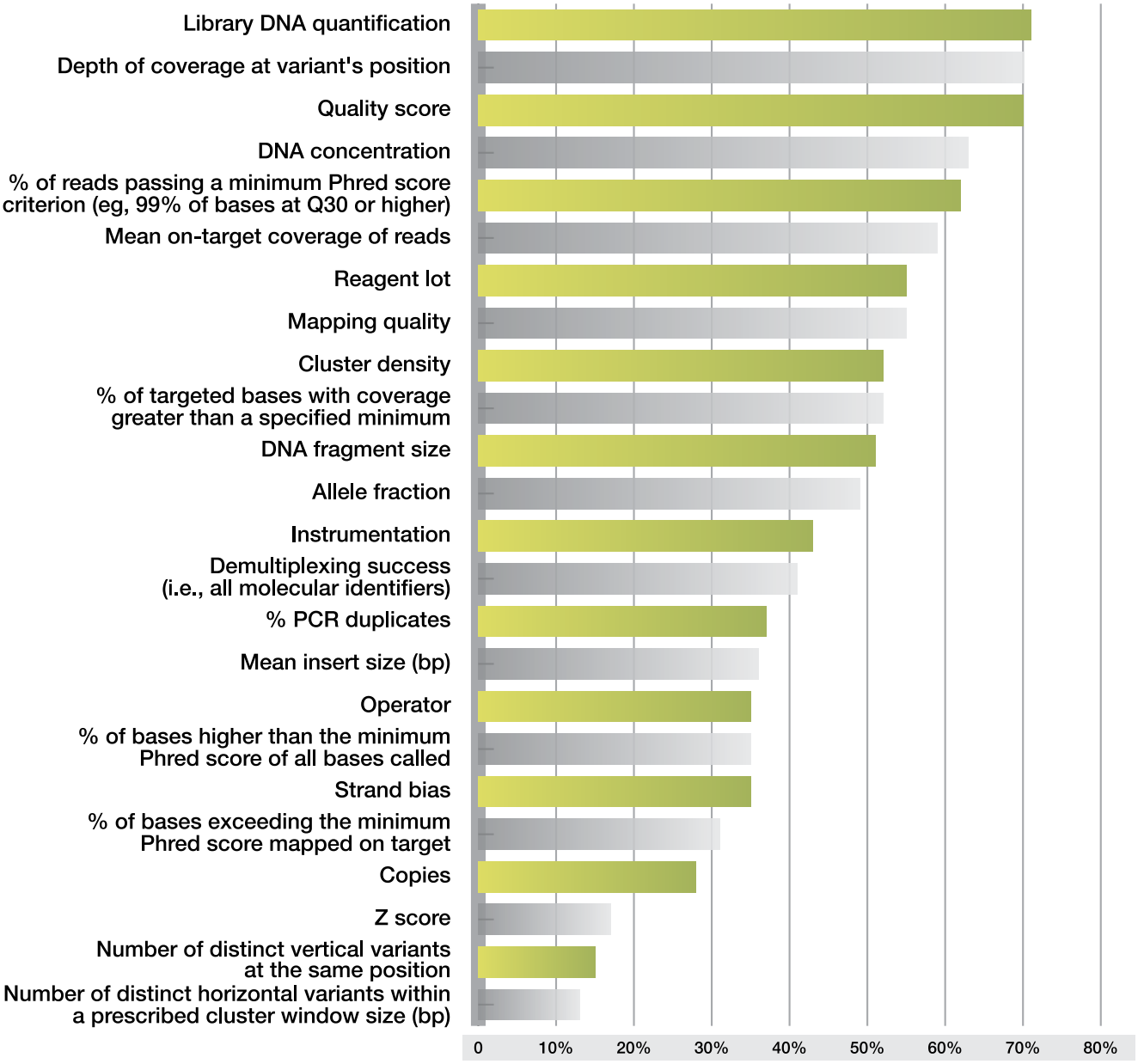
How often do you use positive run controls? (NIPT respondents, n = 28)



This habit varies across the application areas of oncology, inherited disease, and noninvasive prenatal testing. For example, 89 percent of NIPT labs said they use a positive control every few runs (compared to 73 percent for oncology labs and 63 percent for inherited disease labs), while 12 percent of inherited disease labs said they never run a control (compared to 6 percent for oncology labs and zero NIPT labs).

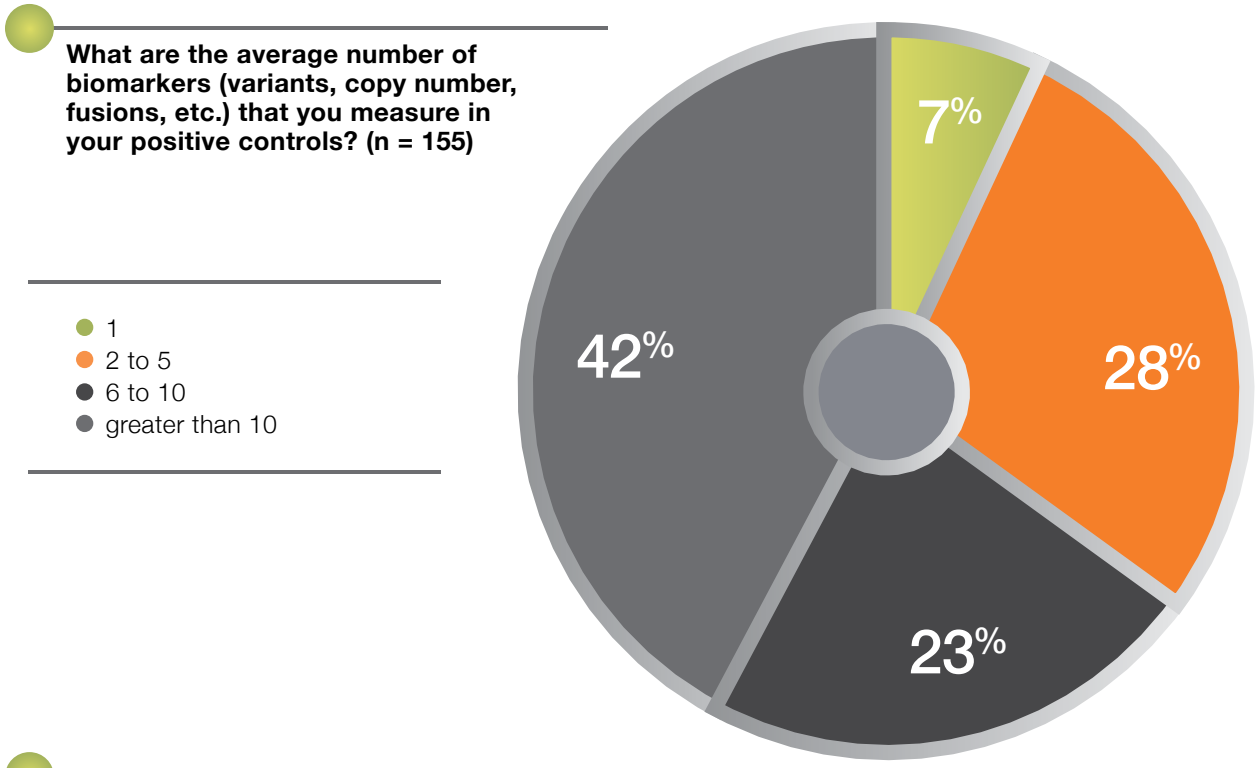
On average, responding labs are only tracking 11 common QC metrics, out of 24 listed in the survey. Only 9 out of 155 responding labs (6 percent) are tracking 20 or more of these metrics, while 29 labs (19 percent) are tracking five or fewer.

What type of metrics do you track for NGS testing? Check all that apply.

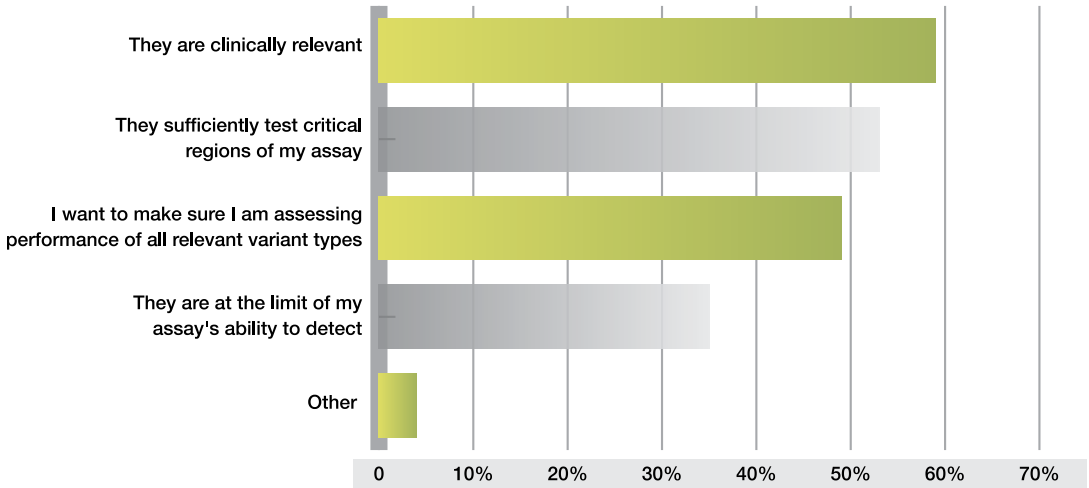


Despite the low frequency of run controls and minimal tracking of QC metrics in clinical genomics labs, 42 percent of respondents indicate they use positive controls to look at more than 10 biomarkers covering critical areas of their assay and representing clinically relevant biomarkers.

What are the average number of biomarkers (variants, copy number, fusions, etc.) that you measure in your positive controls? (n = 155)



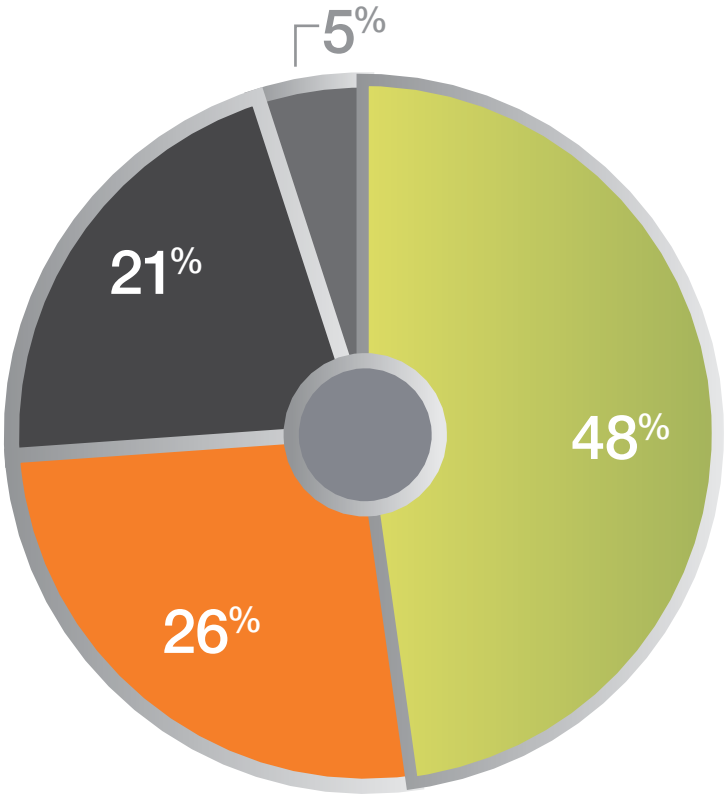
What are the reasons you chose the biomarkers you did? Please check all that apply. (n = 155)



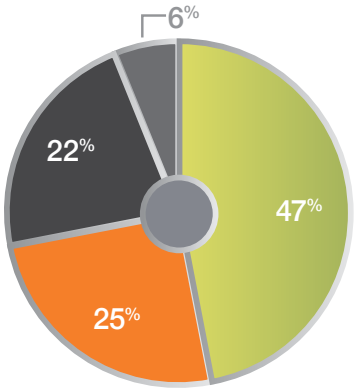
LOSS OF PRODUCTIVITY

More than half of responding labs experience QC stops daily, weekly, or monthly that typically take more than one day to resolve.

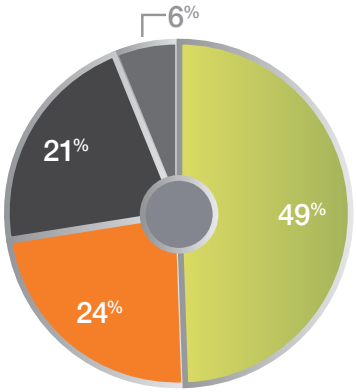
How frequently, on average, do you experience QC stops? (n = 155)



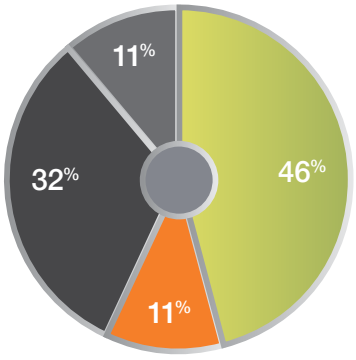
How frequently, on average, do you experience QC stops? (oncology respondents, n = 113)



How frequently, on average, do you experience QC stops? (inherited disease respondents, n = 81)



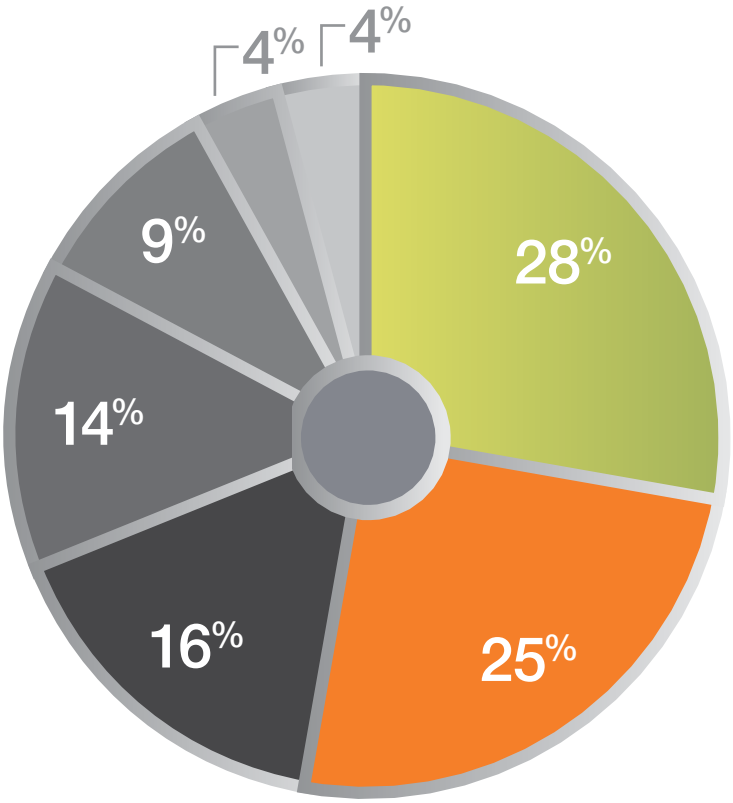
How frequently, on average, do you experience QC stops? (NIPT respondents, n = 28)



NIPT labs are more likely to experience QC stops on a daily or weekly basis than oncology or inherited disease labs.

The primary reason for a QC stop is the control not passing, but other factors such as library prep quality, instrument malfunction, and operator error also play key roles.

Which of the following most often contributes to QC stops? (n = 155)



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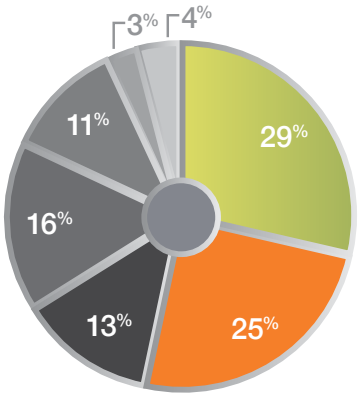
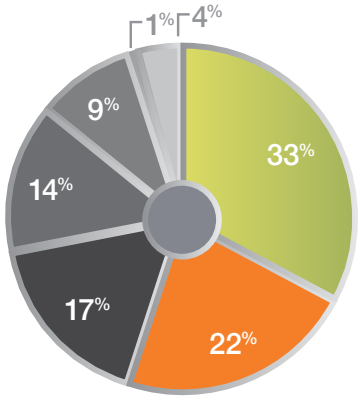


Which of the following most often contributes to QC stops? (inherited disease respondents, n = 81)



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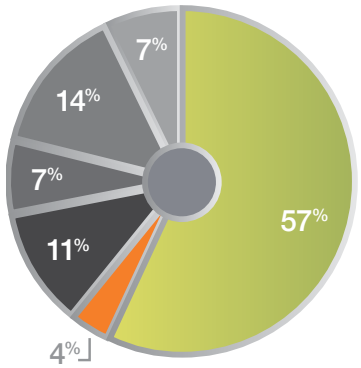
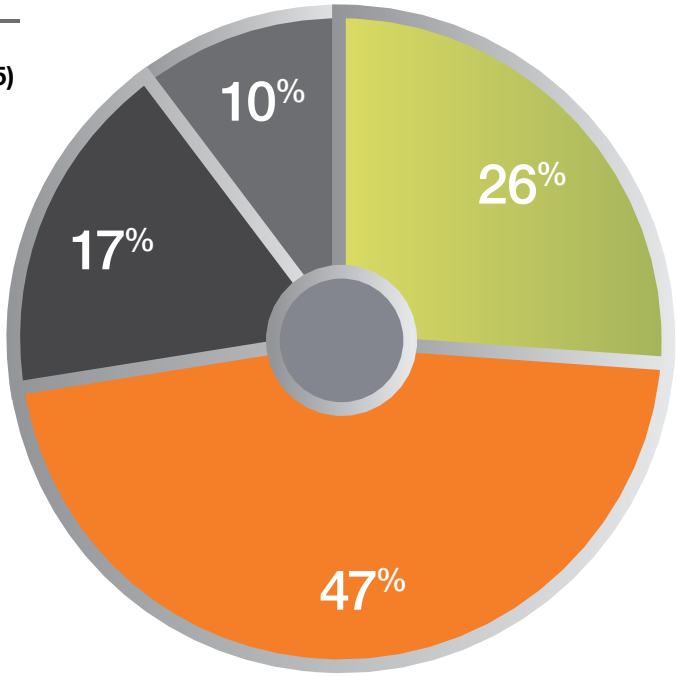


The reasons for QC stops don't vary much for labs running oncology or inherited disease assays, but labs running NIPT assays are much more likely to report that the root cause of a QC stop is because the QC control did not pass.

Nearly three-quarters of labs said that their average time to resolution after a QC stop is more than a day, with 10 percent saying it can take more than five days to resolve a QC issue.

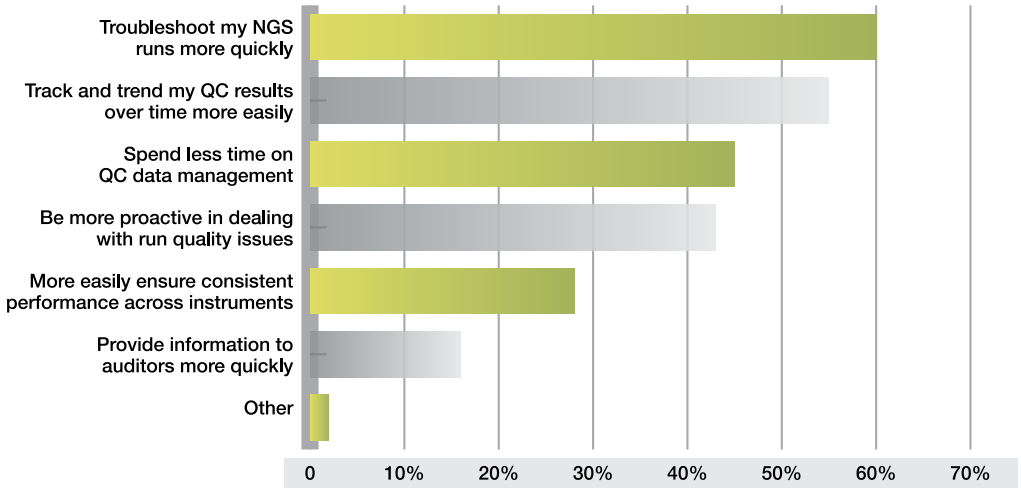
With half the responding labs experiencing QC stops at least monthly, this means these labs are spending between 12 to 60 days per year troubleshooting.

What is your average time to resolution when you experience a QC stop? (n = 155)



Labs are seeking better and more efficient solutions to QC management. Around 60 percent of respondents indicate they would like to troubleshoot their runs more quickly and track and trend their data over time more easily.

Please select up to three of the following outcomes that would have the most positive impact on your QC management program (n = 155)



CONCLUSIONS AND NEXT STEPS

The survey results indicate that QC best practices are still a work in progress for the clinical genomics community. Lab harmonization is still a challenge for the field, with the majority of labs using non-comparable materials as controls and custom methods to manage data. Many labs are not tracking standard diagnostic lab metrics, such as operator, reagent lot, or instrumentation.

The result of this is lost time and productivity: More than half of responding labs experience QC stops at least once per month that typically take several days to resolve. One quarter of responding labs said they lose more than three days for each QC stop.

These findings raise questions about the impact of clinical genomics QC practices on patient care, reimbursement, and the rate of adoption of NGS within the broader diagnostics market. While these issues were beyond the scope of the survey, they were discussed during a live webinar where a panel of industry experts shared their thoughts about the results and discuss next steps for the field.