

Checklists now made to fit for next-gen sequencing labs

Valerie Neff Newitt

October 2022—As the diagnostic uses for next-generation sequencing have grown, so too has the length of the NGS section of the CAP molecular pathology accreditation program checklist. Now, with the release of the new checklist edition this month, NGS laboratories will find the NGS section in their customized checklists leaner, more relevant, and easier to read.

For laboratories and inspectors using the 2022 checklist edition (and subsequent editions), the NGS section of the checklist will now be tailored to the type or types of testing an NGS laboratory performs. This means more pertinent notes accompanying each NGS requirement and greater clarity and efficiency.

“The real driver behind this has been the growing diversity of [NGS] applications and the complexity that creates, and the need to truly customize,” says Karl Voelkerding, MD, an advisor to and past chair of the CAP Genomic Medicine Committee and an author of the original NGS section of the checklist, published in 2012.

“Every subsequent year since that first publication, we updated, edited, revised, and it was the notes where we addressed the elements specific to inherited disease, molecular oncology, infectious disease, and histocompatibility testing,” he continues. In time it became increasingly clear that the notes were becoming “quite extensive,” he says, “and there will be additional areas going forward.” The changes in the new 2022 edition are the first reflection of the work that’s been done to address that.



Dr.
Voelkerding

“The goal was to get into the hands of the laboratory directors the critical and most pertinent areas of the NGS checklist requirements, in a way that reduces their need to read lengthy notes to find the areas most relevant to their efforts,” Dr. Voelkerding says.

The NGS section of the checklist has also been updated to reflect changes in the field, says Amer Mahmoud, MD, member of the CAP Checklists Committee and clinical associate professor of pathology at the University of New Mexico and CLIA medical director, TriCore Reference Laboratories. For example, “A common question asked in the past was, ‘When I do my wet bench validation, do I need to include every tumor in which this mutation shows? Do I need to include all mutation types?’ When we updated the checklist, we spelled out to labs that it’s not a requirement to test every tumor unless the medical director decides that a certain tumor is of particular significance in validation.

“So, depending on the application, the updated checklist contains more information that will give better guidance and dispel confusion,” he says.

“Crisp and clear” was the aim, Dr. Mahmoud says, and one of the ways it was achieved was with the language. “We used the word ‘must’ whenever something is required and avoided using more subjective terms like ‘should’ wherever we could.”

When a written policy or procedure is needed to demonstrate compliance with a requirement, about which he says

there has been confusion in the past, there will be an icon to indicate such. This new icon, a stylized document page, appears throughout all CAP checklists beginning with the new edition, “and molecular is no exception,” he says. (See “Need a written policy or procedure? Look for icon,” <https://bit.ly/CAP-icon>.)

Customizing the checklist to each laboratory section performing NGS relies on the laboratory reporting its test information accurately to the CAP. “An up-to-date activity menu is essential,” says Daniel Rhoads, MD, vice chair of the CAP Microbiology Committee and section head of microbiology at the Cleveland Clinic. If the laboratory does not accurately describe the testing it is performing, he says, “then the CAP might not include checklist requirements in the customized checklist that should be included because the CAP doesn’t know the laboratory is doing a certain type of testing.”

To achieve the customization, members of the Checklists Committee worked with members of the Microbiology, Molecular Oncology, Histocompatibility and Identity Testing, and CAP/ACMG Biochemical and Molecular Genetics committees and other experts. Their task was to ensure the requirements contain the right content for each NGS application. “I feel the microbiologists are a bit unique in their applications of NGS,” Dr. Rhoads says. “And I hope pathologists and laboratories that are doing NGS for infectious disease testing feel some benefit knowing the customized checklist was crafted with them in mind.”

A new requirement was added specific to infectious disease testing by NGS: MOL.35880 Microbial Nucleic Acid Contamination. For clinical metagenomic assays, the requirement says, the lab must evaluate the potential impact of microbial nucleic acid contamination from environmental and reagent sources and implement mitigation processes.



Dr. Gandhi

Some requirements are common to all areas of NGS testing, and it was the committee members, working in subgroups, who scrutinized the checklist notes to determine what was common and what wasn’t, says Manish Gandhi, MD, Checklists Committee member and vice chair of the Histocompatibility and Identity Testing Committee and professor of laboratory medicine and pathology, Mayo Clinic. “When content is not relevant, an inspector might incorrectly interpret a requirement and tell a lab it should be doing something it’s not doing, which puts the lab in jeopardy of noncompliance. The new customization gives much more clarity,” Dr. Gandhi says. The subgroups also drafted new application-specific requirements and notes to ensure each NGS application was addressed appropriately. For HLA testing, MOL.35855 Discrepancy Resolution—NGS HLA Typing is a new requirement that calls for the lab to follow a written procedure to resolve typing discrepancies within and between labs.

Customization also means shorter notes. “We received feedback about the checklist notes being long, and it was because of the generic nature of these requirements that tackled everything within the notes. We knew something had to be done,” Dr. Gandhi says.

Now that it has, Dr. Voelkerding stresses the importance of the link with the activity menu. “I can imagine undergoing a year or two of transition to fine-tune this,” he says.

“If now a lab receives just that which is pertinent to inherited diseases, if that is what it’s doing, and then it takes on molecular oncology, it is critical, prudent, for the lab to immediately reach out to the CAP and say, ‘We’re adding this new area and the checklist requirements you sent to us for our last inspection don’t cover this area.’” Laboratories need to be aware of that, he says, so they receive the most current set of checklist requirements

relevant to their testing. “Even as they’re onboarding and developing a new area, they would be well served to have the pertinent checklist notes section.”

Dr. Mahmoud, too, emphasizes the importance of the activity menu being correct and up to date. “When everything was lumped together in one big, redundant, less efficient set of requirements, there was more tolerance, if you will, to mistakes made by a lab when it picked its activity menu. Regardless of the tests you picked, you probably would have ended up with the same requirements because it was so big and overreaching.

“However, the new checklist is going to be less tolerant when you make errors defining your activity menu because of the customization,” he continues. “So if you have questions and are not sure what test you need to pick, call the CAP for clarification.”

The customization of the checklists will not end with the 2022 checklist edition. The plan is to produce a standalone NGS checklist consisting of generic requirements that apply to all NGS and sections tailored to each type, possibly for 2023.



Dr. Mahmoud

Despite the multiple layers of review and feedback provided before the 2022 edition was released, Dr. Mahmoud says it’s possible that further tweaking will be needed and that the checklist remains an evolving document. “So feedback is always welcome.” The CAP doesn’t release a checklist until it’s fully vetted and user-friendly, he notes, but “if you point out something that doesn’t make sense or to which you object, the CAP is responsive, and at an impressive speed.”

Dr. Voelkerding says this of the customization in the 2022 edition: “For a decade we worked with generation one and continued to refine it. Now, this is second generation, first version.”□

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