A Window Into Clinical Next-Generation Sequencing–Based Oncology Testing Practices

Rakesh Nagarajan, MD, PhD; Angela N. Bartley, MD; Julia A. Bridge, MD; Lawrence J. Jennings, MD, PhD; Suzanne Kamel-Reid, PhD, DABMG, FACMG; Annette Kim, MD, PhD; Alexander J. Lazar, MD, PhD; Neal I. Lindeman, MD; Joel Moncur, MD, PhD; Alex J. Rai, PhD, D(ABCC); Mark J. Routbort, MD, PhD; Patricia Vasalos, BS; Jason D. Merker, MD, PhD

• Context.—Detection of acquired variants in cancer is a paradigm of precision medicine, yet little has been reported about clinical laboratory practices across a broad range of laboratories.

Objective.—To use College of American Pathologists proficiency testing survey results to report on the results from surveys on next-generation sequencing–based oncology testing practices.

Design.—College of American Pathologists proficiency testing survey results from more than 250 laboratories currently performing molecular oncology testing were used to determine laboratory trends in next-generation sequencing–based oncology testing.

Results.—These presented data provide key information about the number of laboratories that currently offer or are planning to offer next-generation sequencing–based oncology testing. Furthermore, we present data from 60 laboratories performing next-generation sequencing–based oncology testing regarding specimen requirements and assay characteristics. The findings indicate that most laboratories are performing tumor-only targeted sequencing to detect single-nucleotide variants and small insertions and deletions, using desktop sequencers and predesigned commercial kits. Despite these trends, a diversity of approaches to testing exists.

Conclusions.—This information should be useful to further inform a variety of topics, including national discussions involving clinical laboratory quality systems, regulation and oversight of next-generation sequencing–based oncology testing, and precision oncology efforts in a data-driven manner.

Arch Pathol Lab Med. 2017;141:1679–1685; doi: 10.5858/arpa.2016-0542-CP

Clinical testing for somatic or acquired variants in cancer specimens is a common modality of precision, or personalized, medicine. Detection of somatic variants in cancer specimens can be used for a wide range of clinical purposes—to assist with diagnosis, determination of prognosis, and the selection and monitoring of therapy. With the rapid adoption of next-generation sequencing (NGS) in the clinical laboratory, many laboratories are shifting from testing a single gene or limited number of genes to larger panel-based NGS testing. To evaluate current clinical laboratory practice in this area, our group surveyed several hundred laboratories that perform molecular oncology testing, by incorporation of a questionnaire into widely adopted molecular oncology proficiency testing (PT) surveys.

By embedding the survey questions into PT surveys, a laboratory quality control activity, it was possible to broadly survey laboratories likely to be performing NGS-based oncology testing, with a very high response rate. To better understand the origin of these survey data, it is helpful to provide some background about clinical laboratory PT.
Clinical Laboratory Improvement Amendments (CLIA) regulations overseen by the Centers for Medicare and Medicaid Services (CMS) require clinical laboratories to follow requirements designed to ensure the accuracy, reliability, and timeliness of patient test results. Included in these quality system laboratory regulations is the requirement that clinical laboratories verify the accuracy and precision of nonregulated clinical tests at least twice annually through external quality assessment, or proficiency testing (PT). Proficiency testing is the testing of unknown specimens sent to laboratories by a CMS-approved provider. The laboratory is required to test PT samples in the same manner as patient specimens, and upon return of results to the CMS-approved provider, the laboratory is scored on test precision or accuracy.

The College of American Pathologists (CAP) is a CMS-approved provider of PT materials. In an effort to develop PT for NGS-based oncology testing, our group sought to understand the breadth of NGS practices currently employed by laboratories. We subsequently included questionnaires in 2 currently offered CAP molecular oncology surveys, KRAS and a Multigene Tumor Panel (MTP) that includes KRAS, EGFR, BRAF, NRAS, and PIK3CA. This produced a unique data set with responses from more than 250 laboratories, representing a 98% response rate. These data provide key insights about the number of laboratories offering testing, specimen requirements, and assay design, characteristics, and performance. The findings do reveal common patterns, but they also demonstrate a wide variety of nuanced differences. We suggest that this information will be useful to further inform a variety of topics related to NGS-based oncology testing using a data-driven approach, including ongoing discussion regarding clinical laboratory quality management, oversight, and regulation of such testing, as well as public policy issues, such as precision oncology efforts of the US Precision Medicine Initiative.

**RESULTS**

### Overall Profile of Somatic Clinical NGS Testing

Of 278 laboratories participating in the CAP MTP or KRAS proficiency testing surveys in late 2014, 273 (98%) answered the supplemental questions (see supplemental digital content at www.archivesofpathology.org in the December table of contents) about current or planned laboratory implementation of NGS-based testing for somatic variant detection in solid tumors. Twelve laboratories participated in both surveys, yielding 261 unique laboratories answering the survey questions. Of these laboratories reporting on their current or planned practice in late 2014, 60 (23%) indicated they performed NGS-based testing for somatic variants in solid tumors, 128 (49%) intended to offer testing within 2 years (ie, by late 2016, with the last survey collected in December 2014), and 73 laboratories (28%) indicated that they did not have plans to implement testing within this timeframe (Table 1). Of the 60 laboratories that indicated they currently perform testing, 55 were from the United States, 2 from Canada, and 1 each from Belgium, Taiwan, and Greece.

The survey data indicated that approximately 119 laboratories intended to deploy NGS-based testing for somatic variants in solid tumors by the end of 2015. This estimate is consistent with the number of laboratories that are currently enrolled in the formal CAP NGS solid tumor proficiency testing survey (127 as of February 1, 2016). As of February 1, 2016, there were 230 laboratories that had NGS on their CAP activity menu, indicating that there were approximately 230 CAP-accredited laboratories performing clinical NGS-based testing. This includes laboratories that conduct germ line testing for inherited diseases, somatic testing for cancer, and NGS-based testing for microbiology, HLA, and other indications. Assuming the laboratories performing NGS on solid tumors in the current survey are among the 230 laboratories with NGS on their activity menu, NGS for solid tumors is performed in more than one-half of CAP-accredited clinical NGS laboratories, and in approximately 15% (127 of 821) of CAP-accredited laboratories that removed from further analysis. One laboratory implemented testing between filling out the 2 surveys, and we used the data from the more recent survey.

Laboratories were asked whether they currently perform or plan to perform clinical NGS-based testing for somatic variants in solid tumors in the next 2 years. Those laboratories that indicated that they currently performed clinical NGS-based testing for somatic variants in solid tumors were asked to answer additional questions about specimen and assay characteristics. If the laboratory performed more than 1 clinical NGS-based test for somatic variant detection, it was asked to answer the questions for the most commonly ordered NGS-based test it performed to analyze solid tumors.

**Table 1. Survey Results Regarding Test Performance and Workflow Process Among Somatic Clinical Next-Generation Sequencing (NGS) Laboratories**

| Perform Clinical NGS | No. (%) of Laboratories | Analysis Location | No. (%) of Laboratories |
|----------------------|-------------------------|------------------|-------------------------|
| Current              | 60 (23)                 | Internal sequencing and bioinformatics | 58 (97) |
| Next 6 mo            | 36 (14)                 | Internal sequencing and outsourced bioinformatics | 2 (3) |
| Next 7–12 mo         | 23 (9)                  | Outsourced sequencing and internal bioinformatics | 0 (0) |
| Next 1–2 y           | 69 (26)                 |                  |                         |
| Not planned in next 2 y | 73 (28)               |                  |                         |

*These data reflect the practices of clinical laboratories in late 2014 because the last survey was collected in December 2014.*

**MATERIALS AND METHODS**

**Survey Supplemental Questions**

Seventeen questions about the current or planned use of clinical NGS-based testing for the detection of somatic variants in solid tumors were embedded in the CAP MTP or KRAS proficiency testing surveys that were sent to laboratories in October or November 2014, respectively. Surveys were returned by December 2014. The MTP survey was chosen because we postulated that a significant subset of laboratories that were performing multiplex testing of several genes were using NGS; the KRAS survey was chosen because it is the largest single-gene molecular oncology survey and had minimal overlap in terms of participating laboratories with MTP.

There were 12 laboratories currently performing clinical NGS-based oncology testing that reported results for both surveys. The results of 11 were identical, and the duplicate surveys were
Abbreviation: FFPE, formalin-fixed, paraffin-embedded.

Table 2. Survey Results Regarding Specimen Details

| Specimen Approach | No. (%) of Laboratories | Specimen Types | No. of Laboratories | Genomic DNA Input Requirement, ng | No. (%) of Laboratories |
|--------------------|-------------------------|----------------|---------------------|----------------------------------|------------------------|
| Tumor-only         | 57 (95)                 | FFPE tissues   | 59                  | 0–100                            | 44 (73)                |
| Tumor-normal       | 3 (5)                   | FFPE cell blocks| 41                  | 101–200                          | 7 (12)                 |
|                    |                         | Fine-needle aspirates | 22                  | 201–500                          | 7 (12)                 |
|                    |                         | Fresh/frozen tissues | 18                  | 501–1000                         | 1 (2)                  |
|                    |                         | Blood          | 5                   | 1001–2000                        | 1 (2)                  |
|                    |                         | Bone marrow    | 4                   | >2000                            | 0                     |
|                    |                         | Othera         | 2                   |                                   |                        |

Abbreviation: FFPE, formalin-fixed, paraffin-embedded.

*a Other included formalin vial (1 laboratory) and touch prep (1 laboratory).

perform any type of molecular testing, as defined by those laboratories that are inspected with the molecular pathology checklist. Such molecular oncology testing is still performed in a small number, less than 2% (127 of 7964), of total CAP-accredited laboratories.

Outsourcing of aspects of the sequencing or bioinformatics analysis was rare for laboratories performing NGS-based testing for somatic variant detection in solid tumors. Consistent with the fact that all 60 laboratories were accepted by all 60 laboratories, which is consistent with current clinical specimen workflows in pathology practice. With regard to the number of platform type(s) used by participant laboratories, most of the respondents (n = 47) are using only a single platform for somatic variant detection for this test. Fewer laboratories are using 2 (n = 11) or 3 (n = 2) platforms. Laboratories may be using more than 1 platform in order to rapidly verify mutations from large panels during validation, in order to

![Figure 1.](http://www.meridian.allenpress.com/doi/pdf/10.5858/arpa.2016-0542-CP) Number and percentage of platforms (Ion PGM and Ion Proton, Thermo-Fisher Scientific, Waltham, Massachusetts; and MiSeq, HiSeq 2500, NextSeq 500, and MiSeqDx, Illumina, San Diego, California) used by laboratories performing clinical next-generation sequencing (NGS)-based testing for somatic variants in solid tumors.
run different assay types on different platforms (e.g., hotspot assays on Ion Torrent [ThermoFisher Scientific, Waltham, Massachusetts] or MiSeq [Illumina, San Diego, California] versus larger targeted sequencing, exome or genome on Proton [ThermoFisher Scientific] or HiSeq [Illumina]), or because of the differences in input DNA requirements for different platforms.

Of the 47 laboratories that use a single instrument, most are using the Ion PGM system (ThermoFisher Scientific; n = 29; 62%) or the Illumina MiSeq (Illumina; n = 16; 34%), consistent with the fact that most laboratories are performing either hotspot or targeted sequencing assays. These instruments have a smaller desktop footprint with a lower price, and are generally easier to operate than the higher-throughput NGS instruments; therefore, they may be more accessible to many clinical laboratories wishing to perform NGS testing.

Average read lengths reported by respondents were minimally 100 bp and maximally 300 bp (Figure 2), and most laboratories (50 of 58; 86%) generated sequence reads between 100 and 150 bp. For those using Illumina MiSeq, the median read length was 150 bp, and for the Ion PGM it was 125 bp. The read length is thus roughly comparable for the 2 common platforms. Laboratories likely chose read lengths between 100 and 150 bp because of the smaller DNA fragment size purified from formalin-fixed, paraffin-embedded tissues. Finally, for laboratories with single instruments, all Illumina users are performing paired-end sequencing, and all PGM users are performing single-end sequencing.

Regarding assay methodology, most of the 58 laboratories that specified selection method use the Ion AmpliSeq Cancer Hotspot Panel v2 (ThermoFisher Scientific), the Illumina TruSeq Amplicon Cancer Panel, or the Illumina TruSight Tumor Sequencing Panel (39 of 58; 67%; Table 3). Furthermore, an amplicon-based preparation (53 of 58; 91%) is used by the vast majority of respondents, whereas a smaller cohort uses capture-based approaches. This is consistent with the more frequent use of the smaller-sequence output systems. Of those using a custom enrichment approach, multiple vendor products were used, with no one technology being adopted broadly (Table 3).

### Bioinformatics Software Use

Regarding analysis software used for alignment, data preprocessing, and somatic variant calling, slightly more than half of the 57 laboratories that reported on their bioinformatics approaches (n = 31; 54%) are using commercial software associated with their sequencers (Ion Reporter and MiSeq Reporter), and just under half (n = 24; 42%) are using custom approaches, whereas 2 laboratories reported using other commercial software. Of those laboratories using custom approaches, 14 laboratories still use at least 1 component (i.e., aligner or variant caller) provided by instrument vendors, whereas the remainder use different open source or commercially available aligners and variant callers, with no one set of tools being predominantly used.

### Assay Performance and Scope of Reporting

Of the 60 laboratories that reported performing clinical testing for the detection of somatic variants in solid tumors, 59 laboratories indicated which categories of variants were detected by their assay (Table 4). Laboratories primarily focused on the detection of single-nucleotide variants (SNVs) and small insertions and deletions (<50 bp).

---

**Table 3. Survey Results Regarding Selection Method**

| Selection Method                          | No. (%) of Laboratories | Custom Enrichment Approach                  | No. (%) of Laboratories |
|-------------------------------------------|-------------------------|--------------------------------------------|-------------------------|
| Ion AmpliSeq Cancer Hotspot Panel v2      | 28 (47)                 | Ion AmpliSeq Custom DNA Panel              | 5 (8)                   |
| Custom Enrichmenta                       | 17 (29)                 | Illumina TruSeq Custom Amplicon            | 4 (7)                   |
| Illumina TruSeq Amplicon Cancer Panel     | 6 (10)                  | Agilent Custom SureSelect                   | 4 (7)                   |
| Illumina TruSight Tumor Sequencing Panel  | 5 (8)                   | Fluidigm Access Array                       | 3 (5)                   |
| Ion AmpliSeq Cancer Panel v1             | 1 (2)                   | Nimblegen                                    | 1 (2)                   |
| Ion AmpliSeq Comprehensive Cancer Panel   | 1 (2)                   | Anchored multiplex PCR                      | 1 (2)                   |
| Other—unspecified                         | 1 (2)                   |                                            |                         |

Abbreviation: PCR, polymerase chain reaction.

a One laboratory reported using 2 separate custom enrichment approaches (Ion AmpliSeq [ThermoFisher Scientific] and the Illumina TruSeq Custom Amplicon).
Approximately 15% of laboratories report intermediate-sized insertions and deletions (50 bp to 1 kb), copy number variants (>1 kb), or other structural variants.

When asked to report the lower limit of detection (LLOD) in terms of somatic allele percentage, more than 90% of laboratories report an LLOD between 5% and 10% for SNVs and small insertions and deletions (Table 5). These data reflect laboratory self-reported claims and are not directly tested using blinded PT samples with low somatic allele percentage. Furthermore, more than 80% of laboratories reported achieving an average coverage of more than 500× (Table 6) and require a minimum coverage of 51 reads or more (Table 7). The survey did not directly query whether laboratories incorporate library complexity when evaluating depth of coverage. However, given that more than 90% of laboratories use amplification-based methods (see Sequencing Platform and Assay Methodology section above), most laboratories are unable to directly measure this quality metric. The minority of laboratories using hybridization-based capture methods have the ability to directly measure library complexity. This enables determination of independent coverage depth, which is a more accurate quality metric for following assay performance.

**Variant Confirmation**

About half of the 58 laboratories that reported on their variant confirmation procedures of laboratories are not performing variant confirmation (n = 28; 48%), whereas the others are confirming results (n = 30; 52%). For those laboratories that are performing variant confirmation, they are divided into those using Sanger (n = 26), targeted mutation testing (n = 11), pyrosequencing (n = 8), or other technologies (n = 5). Note that some laboratories use more than 1 confirmation approach, thus accounting for a higher number than unique laboratories performing confirmatory testing. Laboratories may be confirming results during their validation phase only, and subsequently only confirming variants that fall below their verification threshold of analytical sensitivity and specificity, using an orthogonal technology. For example, they may only confirm recurrent variants that fall below an allelic frequency of 5% to 10% using alternate methodologies, such as the Amplification Refractory Mutation System.

**DISCUSSION**

In this manuscript, we report on the survey results from 261 clinical laboratories performing molecular oncology testing and their current or planned future practices with respect to NGS-based testing for somatic variants in solid tumors. This represents a 98% response rate, illustrating the utility of using ongoing proficiency testing programs to better understand current clinical laboratory practices. Sixty laboratories that already performed clinical NGS-based oncology testing reported on specimen requirements, as well as assay design, characteristics, and performance. Two major themes emerged from the survey results. First, most laboratories are performing targeted sequencing of tumor-only specimens to detect SNVs and small insertions and deletions, with a reported 5% to 10% LLOD based on analytical sensitivity and not blinded PT sample-based performance data. Second, the testing is primarily performed using amplicon-based, predesigned commercial kits using desktop sequencers. Despite these trends, a significant minority of laboratories are using different approaches to perform clinical testing, reflecting the diversity of clinical needs to report variant types in different genes.

The survey data indicated that 119 laboratories were planning to offer clinical NGS-based testing for somatic variants in solid tumors by the end of 2015. Follow-up indicates that 127 laboratories were enrolled for NGS-based oncology PT by the beginning of 2016. Assuming that most laboratories enrolled in the PT are performing clinical testing, which we posit is a reasonable assumption given

---

**Table 4. Categories of Somatic Variants Detected**

| Variant Category | No. (%) of Laboratories |
|------------------|-------------------------|
| Single-nucleotide variants | 59 (100) |
| Small insertions and deletions (≤50 bp) | 57 (97) |
| Intermediate-sized insertions and deletions (50 bp to 1 kb) | 9 (15) |
| Copy number variants (>1 kb) | 9 (15) |
| Other structural variants (e.g., translocations) | 8 (14) |
| Other—loss of heterozygosity | 1 (2) |

* The percentage is calculated based on the number of laboratories that reported which categories of variants were detected by their assay.

**Table 5. Reported Lower Limit of Detection for Single-Nucleotide Variants and Small Insertions and Deletions (<50 bp)**

| No. (%) of Laboratories |
|-------------------------|
| Single-nucleotide variants, % (n = 59) |
| 2 | 2 (3) |
| 3 | 2 (3) |
| 4 | 1 (2) |
| 5 | 40 (68) |
| 6 | 1 (2) |
| 7 | 1 (2) |
| 10 | 12 (20) |
| Small insertions and deletions, % (n = 57) |
| 1 | 1 (2) |
| 2 | 1 (2) |
| 5 | 30 (53) |
| 6 | 2 (4) |
| 10 | 20 (35) |
| 15 | 2 (4) |
| 20 | 1 (2) |

* The percentage is calculated based on the number of laboratories that reported the lower limit of detection for that variant type.

**Table 6. Average Number of Reads Covering Targeted Bases**

| No. (%) of Laboratories |
|-------------------------|
| 0-50× | 0 |
| 51-150× | 0 |
| 151-250× | 3 (5) |
| 251-350× | 2 (3) |
| 351-500× | 2 (3) |
| 501-750× | 3 (5) |
| 751-1000× | 8 (14) |
| 1001-1500× | 10 (17) |
| 1501-2500× | 15 (25) |
| >2500× | 14 (24) |
| Metric not established | 2 (3) |

* The percentage is calculated based on the number of laboratories that reported the average number of reads covering targeted bases or reported that they did not use this metric.
that PT is a quality management activity required, under CLIA, to offer clinical testing, the survey predictions were consistent with observed clinical practice. This supports the extensibility of at least this aspect of the survey results; however, the survey results do have several limitations. First, the survey data are 2 years old. Given the dynamic nature of this field, it may be questioned how long data reported here represent current clinical practice. We note that many of the major themes reported here are still observed in current CAP PT survey results. That is, most laboratories are performing targeted sequencing of tumor-only specimens to detect SNVs and small insertions and deletions, with a reported 5% to 10% LLOD, and the testing is primarily performed using amplicon-based, predesigned commercial kits using desktop sequencers. Second, performance data are self-reported, and we do not yet have performance data about actual detection rate for low-level variants. The third limitation is that the survey data were derived from laboratories that were enrolled in CAP proficiency testing for molecular oncology indications, and subsequently did not capture laboratory practices from laboratories that (1) were not performing molecular oncology testing at that time (eg, laboratories for which NGS-based testing is their first clinical molecular oncology assay), (2) verify test accuracy at least twice annually using a mechanism other than CAP proficiency testing, or (3) did not participate in 1 of the 2 molecular oncology PT surveys that contained the questionnaires. Fourth, more than 90% of the laboratories that reported on their NGS oncology practices were from the United States. Although it is not clear how the above 4 factors would potentially bias the results, we cannot rule this out.

To our knowledge, this manuscript is the broadest and most detailed survey to date about the range of laboratory practices used for NGS-based oncology testing. Prior survey data of National Comprehensive Cancer Network member institutions and their member affiliate sites primarily focused on how molecular profiling/diagnostic testing was being used at these sites; however, this manuscript did touch on how such testing was performed. This included whether such testing was performed in-house or outsourced, organizations used for outsourced testing, platforms used in conjunction with NGS, the number of genes included in in-house testing, as well as whether samples were from new biopsies, archived tissue, primary tumors, or metastatic sites. The only significant overlap with the current data relates to their finding that the most frequently used in-house NGS panel included 50 genes or less. We also observed that most surveyed clinical laboratories used panels with 50 genes or less.

Given that NGS is an emerging testing methodology with significant diversity with respect to the sequencing methodology, library preparation, bioinformatics analysis, and assay claims (eg, what types of variants the assay detects and what the LLOD is for each type of variant), it will be important to evaluate the performance of these various approaches. In the Next-Generation Sequencing Solid Tumor Survey (NGSST-A-2016), 111 laboratories were provided blinded specimens containing 10 recurrent somatic SNVs in AKT1, ALK, BRAF, EGFR, FBXW7, IDH1, KIT, KRAS, NRAS, and PIK3CA, with a variant allele fraction between 15% and 50%. Laboratories demonstrated an overall accuracy of 98.3% (995 of 1010; J.D.M., unpublished data, 2017). Further evaluation of laboratory performance when challenged with lower allele fractions (ie, between 5% and 15%) and with insertions and deletions is ongoing, and these data are ultimately required to broadly understand laboratory performance of NGS-based testing for somatic variants in solid tumors. This is especially important in light of the fact that the current survey asked laboratories to report LLOD, average number of reads covering targeted bases, and minimum number of reads required for each targeted base, and that the association of these 3 responses was unclear. Namely, it was unclear if the LLOD was based on the reported minimum number of reads, reported average number of reads, or some other factor. This ambiguity is likely caused by the challenge in reporting a single LLOD for an NGS assay covering tens of thousands of bases, given the variability in depth of coverage and other factors affecting variant calling across these targeted regions. Future proficiency testing surveys and associated questions will help clarify this ambiguity. It is also critical for laboratories to ensure that their assays are challenged with variants at or near the reported LLOD during the validation of their assays. This can be accomplished by mixing studies or by the use of commercially available materials with low-level variants.

We suggest that these data will help inform several national discussions involving clinical laboratory quality systems, regulation, and oversight of NGS-based oncology testing, as well as precision oncology efforts of the US Precision Medicine Initiative and the former vice president’s Cancer Moonshot Initiative.

References
1. Bombard Y, Bach PB, Offit K. Translating genomics in cancer care. J Natl Compr Canc Netw. 2013;11(11):1343–1353.
2. MacConaill LE, Garcia E, Shvidansk P, et al. Prospective enterprise-level molecular genotyping of a cohort of cancer patients. J Mol Diagn. 2014;16(6):660–672.
3. Chen K, Meric-Bernstam F, Zhao H, et al. Clinical actionability enhanced through deep targeted sequencing of solid tumors. Clin Chem. 2015;61(3):544–553.
4. Cottrell CE, Al-Kateh H, Bredemeyer AJ, et al. Validation of a next-generation sequencing assay for clinical molecular oncology. J Mol Diagn. 2014;16(1):89–105.
5. Medicare, Medicaid and CLIA programs; revision of the laboratory regulations for the Medicare, Medicaid, and Clinical Laboratories Improvement Act of 1967 programs—HCFAs: final rule with comment period. Fed Regist. 1990;55(106):9538–9610.
6. Regulations for implementing the Clinical Laboratory Improvement Amendments of 1988: a summary. MMWR Recommm Rep. 1992;41(RR-9):1–17.
7. CLIA program; approval of the College of American Pathologists—HCFAs: notice. Fed Regist. 1995;60(27):7774–7780.
8. Uliwatck ED, Mansfield E, Shuren J. The FDA and genetic testing. N Engl J Med. 2015;372(23):2273–2274.
9. Evans BJ, Burke W, Jarvik GP. The FDA and genomic tests-getting regulation right. N Engl J Med. 2015;372(23):2258–2264.
10. Jaffe S. Planning for US Precision Medicine Initiative underway. Lancet. 2015;385(9986):2448–2449.
11. Kurzrock R, Colevas AD, Olszanski A, et al. NCCN Oncology Research Program’s Investigator Steering Committee and NCCN Best Practices Committee molecular profiling surveys. J Natl Compr Canc Netw. 2015;13(11):1337–1346.
12. National Academies of Sciences, Engineering, and Medicine; Graig LA, Phillips JK, Moses HL, eds. Biomarker Tests for Molecularly Targeted Therapies: Key to Unlocking Precision Medicine. Washington, DC: The National Academies Press; 2016.
13. Investing in the National Cancer Moonshot [fact sheet]. The White House Office of the Press Secretary Web site. https://www.whitehouse.gov/the-press-office/2016/02/01/fact-sheet-investing-national-cancer-moonshot. Accessed April 5, 2017.