



November 2020

CLINICAL LABS

Studies Suggest Biopsy Specimen Misidentification and Contamination Errors Are Infrequent

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GAO Highlights

Highlights of [GAO-21-59](#), a report to the Ranking Member, Committee on Finance, U.S. Senate

Why GAO Did This Study

In 2017, over 1.7 million new cases of cancer were reported in the United States. For patients to receive proper diagnosis and treatment, labs must ensure that biopsy specimens are not misidentified or contaminated. Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), clinical labs that perform tests to diagnose disease must meet requirements. CMS has issued regulations to implement CLIA and is responsible for overseeing and certifying lab compliance with these regulations.

This report describes (1) what is known about the rates and causes of specimen source errors and potential solutions to address them, and (2) CMS's efforts to prevent specimen source errors.

GAO examined peer-reviewed literature published from January 2010 to April 2020 on the rates, causes, and potential solutions of specimen source errors. GAO also reviewed CMS regulations and guidance relevant to preventing specimen source errors, as well as data regarding the number of labs found deficient in meeting those requirements in 2018, the most recent complete data at the time of GAO's review. Finally, GAO interviewed or obtained written responses from CMS officials and representatives from various stakeholder groups, including medical provider organizations, state survey agencies, and lab accreditation organizations. GAO received technical comments on a draft of this report from the Department of Health and Human Services and incorporated them as appropriate.

View [GAO-21-59](#). For more information, contact Jessica Farb at (202) 512-7114 or farbj@gao.gov.

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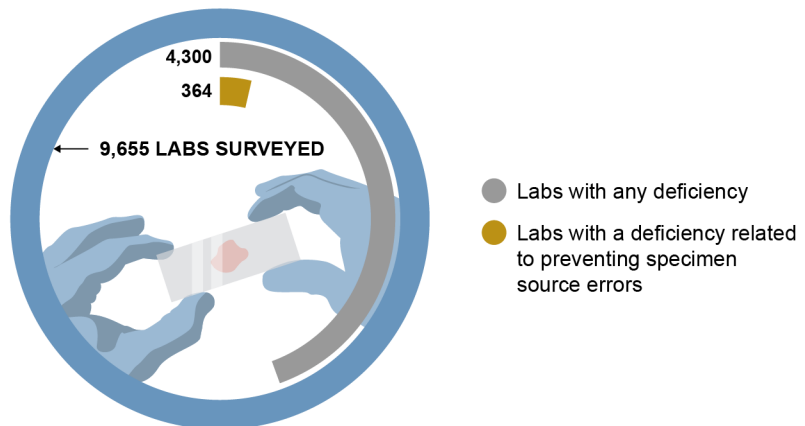
What GAO Found

Health care providers use biopsies—the removal and examination of cells or tissue—to diagnose diseases like cancer. Biopsy specimen source errors include the misidentification or contamination of one patient's biopsy with another.

Centers for Medicare & Medicaid Services (CMS) officials and stakeholders with direct knowledge about specimen source errors told GAO that such errors are infrequent. Representatives from one accreditation organization said they only cited two such errors in the last 2 years. GAO identified six studies that estimated the prevalence of specimen source errors, though these studies cannot be generalized. The highest estimated rate of specimen source errors was 2.3 percent. Studies GAO reviewed attributed specimen source errors to a variety of causes that may occur at different points in the biopsy process. For example, a lab technician may mix up specimens when manually cataloging them upon their arrival to the lab. Integrating technology—like a printed barcode system that allows for specimens to be easily identified and tracked throughout the process—and effective specimen collection and handling procedures may decrease the risk of specimen source errors, according to the literature and stakeholders.

CMS regulations require labs to establish procedures related to preventing specimen source errors. CMS ensures lab compliance with these regulations through biennial inspections conducted either by surveyors acting on behalf of CMS or by lab accreditation organizations. Surveyors also review a sample of labs inspected by each accreditation organization to ensure inspection quality or in response to a complaint. CMS data show that in 2018, 3.8 percent (364 out of 9,655) of labs inspected by surveyors were cited as deficient in at least one of the regulations relevant to specimen source errors. These types of deficiencies were not among the agency's list of the top 10 lab-related deficiencies reported in October 2018.

Lab Inspection Findings in Calendar Year 2018



Source: Centers for Medicare & Medicaid Services data. | GAO-21-59

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Abbreviations

CLIA	Clinical Laboratory Improvement Amendments of 1988
CMS	Centers for Medicare & Medicaid Services

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November 10, 2020

The Honorable Ron Wyden
Ranking Member
Committee on Finance
United States Senate

Dear Senator Wyden:

Health care providers often use biopsies—the removal and examination of cells or tissue—to diagnose and plan treatment for diseases such as prostate and other cancers. In 2017, the latest data available, over 1.7 million new cases of cancer were reported in the United States and over 200,000 of those were for prostate cancer, one of the most common forms.¹ If a patient’s biopsy specimen is inadvertently misidentified or contaminated with another patient’s specimen—a mistake known as a specimen source error—it could contribute to inaccurate diagnoses and lead to the wrong treatment. Unnecessary treatment or a failure to treat can result in patient harm or avoidable medical costs for patients and insurers, with Medicare being one of the largest insurers, covering over 58 million beneficiaries in 2018.²

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), clinical labs that perform tests on human specimens to diagnose, prevent, or treat disease, including the examination of biopsy specimens, must meet certain requirements.³ The Centers for Medicare & Medicaid Services (CMS) within the Department of Health and Human Services has issued regulations to implement CLIA and is responsible for

¹A disproportionate amount of new prostate cancer cases are among Black men; they are diagnosed almost 1.7 times more often than White men. See Centers for Disease Control and Prevention, *U.S. Cancer Statistics Data Visualizations Tool*, accessed August 18, 2020, www.cdc.gov/cancer/dataviz.

²Medicare is a federal health insurance program for people age 65 and older, certain individuals with disabilities, and individuals diagnosed with end-stage renal disease.

³For example, CLIA requires that labs be tested for proficiency in certain procedures and examinations they perform. See Pub. L. No. 100-578, § 2, 102 Stat. 2903 (codified as amended at 42 U.S.C. § 263a).

overseeing and certifying lab compliance with these regulations, including for labs that participate in Medicare and Medicaid.⁴

You asked us to review specimen source errors and CMS actions to prevent them. In this report, we describe:

1. what is known about the rates and causes of specimen source errors in prostate and other biopsies, and potential solutions to address them; and
2. CMS's efforts to prevent specimen source errors.

To describe what is known about the rates and causes of specimen source errors in prostate and other biopsies, and potential solutions to address them, we reviewed relevant peer-reviewed literature published from January 2010 to April 2020.⁵ Of the 218 potentially relevant study citations we identified, we reviewed 61 full studies and identified four additional studies cited within them. Of these 65 studies, 49 contained results that directly informed our objective, and six estimated rates of misidentification or contamination that met our criteria for inclusion; however, these six studies cannot be generalized to a population because they did not randomly select biopsy specimens to test for these errors.⁶

To describe CMS efforts to prevent specimen source errors, we reviewed agency regulations and guidance related to labs. In addition, we obtained data from CMS about the number of labs found to be out of compliance with any one of six selected regulations—that is, cited as deficient—related to preventing specimen source errors in 2018, the most recent complete year of data available at the time of our review. We selected the six deficiencies most likely to indicate an issue with preventing specimen

⁴See 42 C.F.R. pt. 493, Laboratory Requirements (§§ 493.1 et seq.) (2019). All subsequent citations in this report to specific regulations contained in 42 C.F.R. pt. 493 are to the 2019 annual edition.

⁵We identified relevant peer-reviewed literature using keywords searches in ProQuest, EBSCO, Dialog, and Scopus.

⁶To meet our criteria for inclusion, the study needed to estimate the rate of specimen source errors or summarize multiple studies that did so, and it needed to use sufficiently rigorous methods to select a sample, identify errors, and calculate the error rate.

source errors.⁷ CMS officials confirmed that the deficiencies we selected were the ones most related to issues with preventing specimen source errors.

For both objectives, we interviewed or obtained written responses from CMS officials and other stakeholders, including two medical provider organizations, the four accreditation organizations that are certified by CMS to oversee pathology testing, the CLIA Advisory Committee, officials from two selected state agencies that oversee labs, and a company that performs DNA tests to confirm the identity of specimens.⁸

Because Medicare is one of the largest insurers, we also obtained Medicare claims data to determine the number of Medicare beneficiaries who had biopsy specimens examined in 2018—the most complete year of data available at the time of our review—and the amount of Medicare spending on the preparation and examination of biopsy specimens under the physician fee schedule. We determined which Healthcare Common Procedural Coding System codes to include through a review of CMS documents and information obtained from medical provider organizations.⁹ We assessed the reliability of the data we used by comparing our analysis to other published data and determined the data were sufficiently reliable for our purposes.

⁷CMS data identifies deficiencies by regulation and an associated identification code. We requested data on deficiencies related to the following regulations: 42 C.F.R. §§ 493.1232, 493.1234, 493.1239, 493.1242(a), 493.1242(d), and 493.1249. These regulations are associated with the following identification codes: D5203, D5207, D5291, D5311, D5317, and D5391.

⁸These organizations included the Accreditation Association for Hospitals and Health Systems/Healthcare Facilities Accreditation Program, the American Association for Laboratory Accreditation, the American Clinical Laboratory Association, the American Urological Association, the College of American Pathologists, the Joint Commission, and Strand Diagnostics. The College of American Pathologists is one of the four accrediting organizations, and it is a medical provider organization. The CLIA Advisory Committee provides advice and guidance to the Department of Health and Human Services regarding clinical laboratory quality and includes members with a variety of experiences related to labs. We obtained written responses from state survey agencies in Connecticut and Ohio. To select these agencies, we identified the states with the median number of labs in each of four census regions and then selected from among those states based on population and geography. We also contacted a third state agency, which was unable to provide a response due to their responsibilities related to the Coronavirus Disease 2019 pandemic.

⁹These organizations include the American Medical Billing Association, American Urological Association, and College of American Pathologists.

We conducted this performance audit from December 2019 to October 2020 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

To diagnose diseases such as cancer, providers collect, prepare, and examine a biopsy specimen. (See fig. 1.) While the treating physician may collect the biopsy specimen, the preparation and examination of the specimen is performed by other technicians and physicians. The preparation of the biopsy specimen involves a complex series of steps; a lab technician may conduct over 20 distinct steps before a specimen is sent to a pathologist for examination. A pathologist is a specialty physician trained to examine and interpret specimens. Specimen source errors may occur at any stage of the process.

Figure 1: Simplified Illustration of the Biopsy Process



Source: GAO. | GAO-21-59

Note: The figure represents the simplified stages of the typical biopsy process. An individual patient's biopsy may undergo additional steps or otherwise deviate from the typical process. For example, the collection of tissue may result in a single specimen or multiple specimens, depending on the type of biopsy or other circumstances specific to an individual.

CMS data show that in 2018, over 8 million Medicare beneficiaries had at least one biopsy specimen examination paid for under the physician fee schedule, including approximately 128,000 who had a prostate biopsy. For these beneficiaries, Medicare paid \$889.9 million to labs and pathologists for the preparation and examination of biopsy specimens

under the physician fee schedule, including \$34.7 million specifically for prostate biopsies.¹⁰

CLIA Certification and Surveys

To perform moderate- to high-complexity tests, including examining prostate and other biopsy specimens, labs must obtain either a Certificate of Compliance or a Certificate of Accreditation from CMS.¹¹ Nationwide, 33,674 (13 percent) of clinical labs had one of these certificates in 2018. The requirements for these certificates are enumerated in CMS's CLIA regulations. After the initial certification, these labs are subject to biennial inspections referred to as surveys, which involve the on-site review and observation of lab records and procedures.¹² The lab decides the type of certificate to obtain, which then determines who conducts the surveys:

- **Certificate of Compliance.** A state survey agency or other entity, acting on behalf of CMS, verifies that the lab meets all applicable CMS regulations. CMS provides guidance to the state survey agencies and other surveyors on conducting the surveys, and CMS Operations Branch staff review the agencies' work on an annual basis to ensure quality.¹³ CMS data show that in 2018, 17,807 labs had a Certificate of Compliance, and surveyors acting on behalf of CMS conducted surveys of 9,273 of these labs in that same year.
- **Certificate of Accreditation.** An accreditation organization approved by CMS verifies that the lab meets the organization's requirements.¹⁴ In addition, state survey agencies conduct validation surveys of a

¹⁰Biopsies performed in a hospital may be partly paid for under other Medicare payment systems than the physician fee schedule.

¹¹Labs in New York and Washington may be certified through those states' programs rather than through CMS, based in part on a determination by CMS that their state requirements meet or exceed certain federal requirements. CMS exempts labs meeting the requirements of those states. See 42 C.F.R. § 493.551(a). In 2018, there were 9,412 labs in exempt states. Labs that only perform lower complexity tests, such as pregnancy tests and fecal occult blood tests, may apply for a Certificate of Waiver. In 2018, there were 187,403 labs with a Certificate of Waiver.

¹²Inspections are to be conducted on a biennial basis or with such other frequency as CMS determines necessary. 42 C.F.R. § 493.1777(b).

¹³CMS Operations Branches are regional offices.

¹⁴As with exempt state lab requirements, CMS reviews accreditation organization requirements to ensure that they meet or exceed the broad requirements referred to as condition-level regulations in CMS's CLIA-related regulations. See 42 C.F.R. § 493.551(a). CMS considers labs that meet an approved accreditation organization's requirements compliant with CMS condition-level regulations.

sample of these labs on behalf of CMS to help ensure that accreditation organizations are identifying lab deficiencies appropriately. A state survey agency may also survey an accredited lab if it receives a complaint about the lab. CMS data show that in 2018, 15,867 labs had a Certificate of Accreditation, and surveyors acting on behalf of CMS conducted 382 validation and complaint-related surveys of these labs in that same year.

A state survey agency or other surveyor might identify deficiencies during a survey of a Certificate of Compliance lab or a Certificate of Accreditation lab. These deficiencies are classified as either condition or standard level based on the related regulation.¹⁵ CMS guidance instructs surveyors to cite a condition-level deficiency when significant noncompliance could adversely affect patient care. When citing a condition-level deficiency, surveyors may also identify at least one standard-level deficiency that contributed to the issue.

Stakeholders and Studies Indicate Specimen Source Errors Occur Relatively Infrequently and Identified Several Solutions to Address Them

Specimen Source Errors Occur Relatively Infrequently in Prostate and Other Biopsy Specimens

A majority of agency officials and stakeholders we interviewed indicated that specimen source errors occur infrequently in prostate and other biopsy specimens. Specifically, CMS officials and six of 10 stakeholders—including three of four accrediting organizations overseeing labs that review biopsy specimens—told us that specimen

¹⁵According to CMS officials, a standard-level deficiency is a minor deficiency that does not rise to the severity of a condition-level deficiency, but it is still a requirement. A condition-level deficiency is a serious or major deficiency. Condition-level regulations generally consist of one or more standard-level regulations.

source errors are not common.¹⁶ For example, representatives from one accreditation organization said they had only cited specimen source error issues twice in the past 2 years. Representatives from another accreditation organization said that in past surveys they cited significantly fewer labs for specimen source errors compared to more common issues, such as failing to verify lab instruments are correctly calibrated at appropriate intervals. In addition, one medical provider we interviewed noted that their lab reviews thousands of biopsy specimens each year with only two or three instances of specimen misidentification.

The literature we reviewed also indicates that specimen source errors are relatively infrequent, though these studies cannot be generalized. Of the 49 studies we reviewed that directly informed our objectives, six studies estimated rates of specimen misidentification, contamination, or both. Some studies reviewed lab records of errors to estimate a specimen source error rate, while others used records of specimens that had been sent for independent DNA testing to verify their identity.¹⁷ Each of the six studies arrived at different estimates of the frequency of specimen source errors. The highest estimated rate of errors was 2.3 percent. The six studies we identified are described below:

- One study reviewed lab records at a university lab system over approximately 5 years (521,661 specimen slides in total, of various biopsy types, 2005 to 2010) and found 65 instances of specimen contamination, or 0.01 percent.¹⁸ The study also reviewed 1,000 additional slides as they went through the biopsy process, and it found 12 instances of specimen contamination, or 1.20 percent.
- Another study reviewed records of 12,947 prostate biopsy specimens collected over approximately 2 years (2009 to 2011) that were sent for

¹⁶Of the remaining four stakeholders, three had limited or no data to determine overall frequency. The fourth stakeholder did not characterize specimen source errors as infrequent but noted that specimen source errors occur approximately 1.5 to 2.0 percent of the time, according to their own research regarding prostate, breast, and bladder biopsies using a DNA testing kit they manufacture to verify specimen identity.

¹⁷DNA testing may involve, for example, a provider taking a cheek swab from a patient during the collection of the biopsy specimen that could later be compared to the DNA of the biopsy specimen at the time of diagnosis to confirm identity.

¹⁸L. J. Layfield et al., "Extraneous Tissue: A Potential Source for Diagnostic Error in Surgical Pathology," *American Journal of Clinical Pathology*, vol. 136, no. 5 (2011): pp. 767–772.

DNA testing.¹⁹ Based on these data, the study found specimen misidentification occurred in 0.26 percent of prostate biopsies and specimen contamination in 0.67 percent.

- One study reviewed records of 2,134 prostate biopsy specimens from a single urology practice that were sent for DNA testing over a 3-year period (2014 to 2016).²⁰ The study identified 49 instances of specimen contamination, or 2.3 percent, though none resulted in a change in treatment plan.
- In one study based on a prostate cancer risk reduction clinical trial, 6,458 prostate biopsy specimens were sent for DNA testing in the second year of the trial after researchers discovered three instances of biopsy misidentification.²¹ They found 26 instances of specimen misidentification, or 0.40 percent. After implementing quality improvements such as re-training staff, 4,777 specimens were sent for testing in the fourth year, and they found one instance of specimen misidentification, or 0.02 percent. In addition, the study found a specimen contamination rate of 1.50 percent across both years.
- One study at a large teaching hospital lab analyzed whether adopting a barcode-enabled lab information system would lower rates of misidentification errors.²² The study reviewed records of biopsy specimens processed during a 16-month period (2012 to 2013).²³ Of the 76,958 specimens examined in total, researchers found 794 instances of misidentification, or 1.03 percent. After implementing the

¹⁹J. D. Pfeifer and J. Liu, "Rate of Occult Specimen Provenance Complications in Routine Clinical Practice," *American Journal of Clinical Pathology*, vol. 139, no. 1 (2013): pp. 93–100. This study used data provided by a commercial DNA test manufacturer.

²⁰L. Wojno et al., "Specimen Provenance Testing Identifies Contamination That Affects Molecular Prognostic Assay Results in Prostate Cancer Biopsy Specimens," *Urology*, vol. 115 (2018): pp. 87–91. Some of the authors were affiliated with a commercial DNA test manufacturer.

²¹Patients were recruited for the clinical trial in 2003 and 2004 and remained in the study for 4 years. M. Marberger, et al., "Biopsy Misidentification Identified by DNA Profiling in a Large Multicenter Trial," *Journal of Clinical Oncology*, vol. 29, no. 13 (2011): pp. 1744–1749.

²²Y. K. Heher et al., "Achieving High Reliability in Histology: An Improvement Series to Reduce Errors," *American Journal of Clinical Pathology*, vol. 146, no. 5 (2016): pp. 554–560.

²³In this study, "specimens" refers to cases of specimens, meaning the container in which an individual patient's tissue and paperwork arrive at the lab. Lab technicians may subsequently divide the encased specimen(s) among glass slides for preparation and examination.

barcode labeling system, they reviewed 37,880 more records of cases over 8 months (2013 to 2014) and found 107 errors, or 0.28 percent.

- One study reviewed lab records at a university lab system for an 18-month period to identify rates of misidentification that occurred in the lab.²⁴ During this period, out of 29,479 various types of specimens, there were 55 with a misidentified patient name, or a rate of 0.19 percent.²⁵

These studies may under- or overestimate the rate of specimen source errors depending on the study design. For example, institutions that are motivated to participate in quality assurance studies may have lower rates of error (e.g., due to better error-prevention measures) or higher rates of error (e.g., due to better error-detection protocols) than institutions that do not choose to participate. In addition, studies that relied on reviews of past records may underestimate the error rate if some specimen source errors made it through the biopsy process without being detected and reported by quality assurance procedures. Alternatively, studies that used DNA testing may under- or overestimate the error rate. Some providers sent specimens for testing only when the diagnosis was positive for cancer or when they already suspected an error had occurred.

Among the types of biopsy specimens, three of the 49 studies we reviewed suggested prostate biopsy specimens may be more susceptible to errors.²⁶ Prostate biopsy specimens may be prepared and examined in designated urology labs where technicians and pathologists exclusively process the same type of specimen, which these studies suggest may increase the likelihood that they inadvertently switch patients' specimens or fail to identify contamination.²⁷ In addition, one medical provider we interviewed noted that the similarity of prostate biopsy specimens across

²⁴L. J. Layfield and G. M. Anderson, "Specimen Labeling Errors in Surgical Pathology: An 18-month Experience," *American Journal of Clinical Pathology*, vol. 134, no. 3 (2010): pp. 466–470. Errors identified and corrected during the collection phase of the biopsy process were not included, and the authors did not report the date of their study.

²⁵In this study, "specimens" refers to cases of specimens. Lab technicians may subsequently divide the encased specimen(s) among glass slides for preparation and examination.

²⁶The majority of the studies did not address which types of biopsy were most susceptible to error. Other types of biopsies that studies suggested may be more susceptible to specimen source errors include breast, skin, and gastrointestinal biopsies.

²⁷D. J. Demetrick, "Molecular Auditing: An Evaluation of Unsuspected Tissue Specimen Misidentification," *Archives of Pathology & Laboratory Medicine*, vol. 142, no. 11 (2018): pp.1407–1414 and Wojno, et al., "Specimen Provenance Testing," pp. 87–91.

patients may make it more difficult to determine if a prostate specimen has been misidentified with or contaminated with another; prostate biopsy specimens typically involve multiple small tissue samples of equal size, number, and color, whereas other types of biopsy specimens—for example, a breast biopsy specimen—typically involve one tissue sample that is unique in size and color.

Among the infrequent specimen source errors that do occur, some of the studies we reviewed and stakeholders we interviewed indicated that labs often catch and correct such errors before diagnosis through their quality assurance processes, and the errors may not always significantly affect patient treatment. For example, one study that reviewed past records of 774,373 specimens across 136 independent and hospital labs found that labs corrected misidentification errors over 96 percent of the time before returning the pathologist's report to the ordering provider.²⁸ According to literature we reviewed and stakeholders we interviewed, labs typically have quality assurance protocols for receiving and cataloging a specimen to detect any misidentification errors that may have occurred during collection.²⁹ In some cases, the pathologist can identify contaminated specimens by routine examination because the contaminating tissue does not resemble the tissue being analyzed.³⁰

In addition, one study reviewing lab records for 29,479 specimen cases found that of the 75 misidentification errors they identified, 62 (or 83 percent) would not have had a significant effect on patient care if they had not been caught.³¹ According to three studies specific to prostate biopsies, although specimen misidentification may result in an incorrect diagnosis, it may not affect the treatment plan because prostate cancer is

²⁸R. E. Nakhleh et al., "Mislabeling of Cases, Specimens, Blocks, and Slides: A College of American Pathologists Study of 136 Institutions," *Archives of Pathology & Laboratory Medicine*, vol. 135, no. 8 (2011): pp. 969–974.

²⁹Nakhleh et al., "Mislabeling of Cases, Specimens, Blocks, and Slides," pp. 969–974; Layfield and Anderson, "Specimen Labeling Errors," pp. 466–470; H. Martin, S. Metcalfe, and R. Whichello, "Specimen Labeling Errors: A Retrospective Study," *Online Journal of Nursing Informatics*, vol. 19, no. 2 (2015).

³⁰S. Harada and C. D. Gocke, "Specimen Identity Testing Using Deoxyribonucleic Acid Analysis in Clinical and Surgical Pathology Setting," *Pathology Case Reviews*, vol. 15, no. 4 (2010): pp. 116–120 and Layfield, et al., "Extraneous Tissue," pp. 767–772.

³¹Layfield and Anderson, "Specimen Labeling Errors," pp. 466–70.

slow to develop.³² Many men with a positive biopsy result choose to “watch and wait” instead of starting active treatment.

Specimen Source Errors Are Due to a Variety of Causes and Several Solutions Are Available to Address Them

Literature we reviewed and stakeholders we interviewed described various potential causes of specimen source errors and solutions to lower rates of errors. Most specimen source errors occur in the collection and preparation phases of the biopsy process. Below are several examples of these potential causes and solutions, which were identified both in the literature we reviewed and by stakeholders we interviewed.

Potential Causes of Specimen Source Errors

- **Manual data entry.** Recording patient or specimen information by hand during collection, or manually cataloging and labeling specimens upon receipt at the lab, could increase the possibility of misidentification error.³³
- **Failure to verify patient identification.** If a nurse does not verbally verify with the patient that the name and date of birth on the specimen label is correct, or if technicians at the lab do not continually verify that the two pieces of identification on the specimen slide match the accompanying paperwork, it increases the likelihood of specimen misidentification.³⁴
- **Contamination through shared chemicals or tools.** Specimen contamination can occur in a lab when small pieces of tissue become

³²J. D. Pfeifer et al., “Development of a Decision-Analytic Model for the Application of STR-Based Provenance Testing of Transrectal Prostate Biopsy Specimens,” *Value in Health*, vol. 15 (2012): pp. 860–867; Marberger et al., “Biopsy Misidentification,” pp. 1744–1749; and D. G. Bostwick, C. E. Day, and I. Meiers, “Optimizing Prostate Specimen Handling for Diagnosis and Prognosis,” *Methods in Molecular Biology*, vol. 1180 (2014): pp. 337–352.

³³For example, see E. J. Dunn and P. J. Moga, “Patient Misidentification in Laboratory Medicine: A Qualitative Analysis of 227 Root Cause Analysis Reports in the Veterans Health Administration,” *Archives of Pathology & Laboratory Medicine*, vol. 134, no. 2 (2010): pp. 244–255; S. Miller, “Eliminate Mislabeled Specimens, Even in the Emergency Department,” *Clinical Leadership & Management Review*, vol. 26, no. 4 (2012): pp. 18–20; and Heher et al., “Achieving High Reliability in Histology,” pp. 554–560.

³⁴For example, see Dunn and Moga, “Patient Misidentification,” pp. 244–255; A. M. Saathoff, R. MacDonald, and E. Krenzischek, “Effectiveness of Specimen Collection Technology in the Reduction of Collection Turnaround Time and Mislabeled Specimens in Emergency, Medical-Surgical, Critical Care, and Maternal Child Health Departments,” *Computers, Informatics, Nursing*, vol. 36, no. 3 (2018): pp. 133–139; and M. A. Zervakis Brent, “OR Specimen Labeling,” *AORN Journal*, vol. 103, no. 2 (2016): pp. 164–176.

Potential Solutions to Specimen Source Errors

detached and “float” onto other specimens via shared chemicals or tools.³⁵

- **Inadequate staff training.** Without adequate training, nurses may incorrectly label or contaminate specimens, and lab assistants may be more likely to improperly clean tools, which could increase the possibility of misidentification and contamination errors.³⁶
- **Integrated technology.** Barcode labeling systems can replace handwritten and pre-printed labels and be integrated with automated lab cataloging systems that print barcode labels for glass slides.³⁷ Thus, specimens could be easily identified and tracked throughout the biopsy process.
- **Specimen labeling in the presence of the patient.** Printing specimen labels in real-time and in the presence of the patient and labeling specimen containers at the time of the biopsy procedure allows the patient to verbally verify their identifying information.³⁸ This may decrease misidentification errors.
- **Effective specimen handling procedures.** Implementing procedures—such as processing specimens one by one in the lab, rather than grouping similar specimens together, and dyeing specimens different colors for different patients—may decrease the

³⁵For example, see Harada and Gocke, “Specimen Identity Testing,” pp. 116–120; and Layfield et al., “Extraneous Tissue,” pp. 767–772.

³⁶For example, see Martin, Metcalfe, and Whichello, “Specimen Labeling Errors”; Layfield and Anderson, “Specimen Labeling Errors,” pp. 466–470; and V. M. Steelman et al., “Surgical Specimen Management: A Descriptive Study of 648 Adverse Events and Near Misses,” *Archives of Pathology & Laboratory Medicine*, vol. 140, no. 12 (2016): pp. 1390–1396.

³⁷For example, see Dunn and Moga, “Patient Misidentification,” pp. 244–255; Heher et al., “Achieving High Reliability in Histology,” pp. 554–560; and Nakhleh et al., “Mislabeling of Cases,” pp. 969–974.

³⁸For example, see Marberger et al., “Biopsy Misidentification,” pp. 1744–1749; Miller, “Eliminate Mislabeled Specimens,” pp. 18–20; and Saathoff et al., “Effectiveness of Specimen Collection Technology,” pp. 133–139.

likelihood technicians will misidentify specimens or not notice specimen contamination.³⁹

- **Quality assurance checks.** Quality assurance checks at key points in the biopsy process—like requiring technicians to verify biopsy specimens are accompanied by the correct paperwork when a specimen arrives at the lab—may help reduce errors.⁴⁰ In addition, auditing random, routine specimens or requiring a second pathologist to review and sign the pathology report for positive cancer diagnoses may decrease misdiagnoses due to specimen source errors.⁴¹
- **Staff training.** Training and re-training staff on specimen collection procedures may decrease the possibility for misidentification error and, when errors do occur, make it more likely they will be identified and corrected. Educating lab technicians in properly cleaning chemical baths and lab tools could decrease contamination error.⁴²
- **DNA testing.** DNA testing can be used to verify specimen identity and integrity, particularly when there is no visual or process-related indication that an error has occurred, though literature also noted the testing process is vulnerable to the same specimen source errors as the biopsy process.⁴³

³⁹For example, see T. Van der Kwast et al., “Guidelines on Processing and Reporting of Prostate Biopsies: the 2013 Update of the Pathology Committee of the European Randomized Study of Screening for Prostate Cancer (ERSPC),” *Virchows Archiv: An International Journal of Pathology*, vol. 463 (2013): pp. 367–377; and Layfield and Anderson, “Specimen Labeling Errors,” pp. 466–470.

⁴⁰For example, see D. G. Bostwick, “Radiofrequency Identification Specimen Tracking in Anatomical Pathology: Pilot Study of 1067 Consecutive Prostate Biopsies,” *Annals of Diagnostic Pathology*, vol. 17 (2013): pp. 391–402; and Nakhleh et al., “Mislabeling of Cases,” pp. 969–974.

⁴¹For example, see Demetrick, “Molecular Auditing,” pp. 1407–1414 and M. B. Hall et al., “Sinonasal Malignancy: What to Do with an Unexpected Pathology Result?” *American Journal of Otolaryngology*, vol. 37 (2016): pp. 473–476.

⁴²For example, see Layfield et al., “Extraneous Tissue,” pp. 767–772 and Martin, Metcalfe, and Whichello, “Specimen Labeling Errors.”

⁴³For example, see Pfeifer and Liu, “Rate of Occult Specimen Provenance Complications,” pp. 93–100 and Wojno et al., “Specimen Provenance Testing,” pp. 87–91. Some of the studies we identified that discussed this potential solution used data provided by a commercial DNA test manufacturer or were authored by individuals otherwise affiliated with the same manufacturer.

CMS Regulates Labs to Prevent Specimen Source Errors and Uses Surveys to Ensure Compliance

CMS Has Multiple Regulations Related to Preventing Specimen Source Errors in Labs

Out of more than 100 regulations that Certificate of Compliance labs must meet, there are six standard-level regulations most related to preventing specimen source errors.⁴⁴ (See table 1.) One of these regulations requires labs to establish and follow procedures to ensure the proper identification and integrity of specimens.⁴⁵ Specifically, CMS interpretive guidance for this regulation directs surveyors to assess whether the lab has policies to prevent mislabeling and avoid mixing up specimens when patients have similar names or birthdates.⁴⁶ Five other regulations also relate to preventing specimen source errors. However, they encompass a greater range of lab activities and require labs to establish and follow procedures for communication, the handling of specimens, and quality assurance, among other things.

⁴⁴We present the six regulations that CMS and we deemed the most relevant; other regulations, such as those related to the management of lab staff, may also contribute to preventing specimen source errors. See 42 C.F.R. §493.1451. According to CMS officials, a standard-level deficiency is a minor deficiency that does not rise to the severity of a condition-level deficiency, but it is still a requirement. A condition-level deficiency is a serious or major deficiency. Condition-level regulations generally consist of one or more standard-level regulations.

⁴⁵42 C.F.R. § 493.1232.

⁴⁶Centers for Medicare & Medicaid Services, *Survey Procedures and Interpretive Guidelines for Laboratories and Laboratory Services, State Operations Manual Appendix C* (Baltimore, Md.: Feb. 3, 2017).

Table 1: Centers for Medicare & Medicaid Services (CMS) Regulations Related to Preventing Specimen Source Errors

Regulation^a	Description
42 C.F.R. § 493.1232 Specimen Identification and Integrity	A lab must establish and follow procedures to ensure proper identification and integrity of a specimen from the time the lab obtains the specimen through when the results of the test are reported.
42 C.F.R. § 493.1234 Communications	A lab must have a system to address problems in communication between the lab and the person who orders or receives test results.
42 C.F.R. § 493.1239 General Laboratory Systems Quality Assessment	A lab must establish and follow procedures to monitor, assess, and correct problems in general lab requirements, including problems with the proper identification and integrity of specimens.
42 C.F.R. § 493.1242(a) Specimen Submission, Handling, and Referral	A lab must establish and follow procedures for handling a specimen, including labelling to properly identify specimens with patient names or unique patient identifiers.
42 C.F.R. § 493.1242(d) Specimen Submission, Handling, and Referral	A lab must make written instructions available to everyone that sends specimens to the lab, including instructions about how to handle specimens.
42 C.F.R. § 493.1249 Preanalytic Systems Quality Assessment	A lab must establish and follow procedures for an ongoing mechanism to monitor and correct problems with laboratory quality requirements, including proper specimen identification and integrity.

Source: GAO analysis of CMS regulations. | GAO-21-59

^aThis column includes only standard-level regulations because of their specificity; condition-level regulations generally incorporate by reference one or more standard-level regulations. These standard-level regulations may also include requirements that do not directly pertain to preventing specimen source errors, such as requiring labs to preserve specimens properly.

Although labs with a Certificate of Accreditation are not specifically required to meet standard-level regulations, including those listed in table 1, the labs' accreditation via a CMS-approved organization indicates they would meet condition-level requirements if inspected.⁴⁷ The standard-

⁴⁷CMS reviews accreditation organization requirements to ensure that they meet or exceed the broad requirements referred to as condition-level regulations in CMS's CLIA-related regulations. See 42 C.F.R. § 493.551(a). CMS considers labs that meet an approved accreditation organization's requirements compliant with CMS condition-level regulations.

level regulations we identified above fall under two condition-level regulations—General Lab Systems and Preactalytic Systems.⁴⁸

Additionally, labs with a Certificate of Accreditation must meet the requirements related to preventing specimen source errors of their respective accreditation organizations. All four accreditation organizations that are approved for pathology testing have requirements to help prevent specimen source errors. Moreover, according to their representatives, two of the accreditation organizations took additional steps to ensure preventing specimen source errors is a priority. Specifically, one accreditation organization includes the proper labeling of pathology specimens as a quality measure, and another includes proper identification of specimens as part of a patient safety goal.

When Certificate of Compliance or Accreditation labs do not comply with the regulations, CMS may take enforcement action. Generally, CMS enforcement actions are usually taken in response to noncompliance with condition-level regulations, such as noncompliance with the General Lab Systems regulation. Enforcement actions may include suspending part of or all Medicare payments, suspending or revoking a lab's certificate, imposing civil money penalties, or requiring labs to take specific actions to come into compliance.

Surveys to Ensure Compliance Identified About 4 Percent of Labs Surveyed Had Deficiencies Related to Specimen Source Errors in 2018

CMS requires at least biennial surveys of labs to ensure compliance with its CLIA-related regulations. For Certificate of Compliance labs, these surveys include examining whether they are complying with the six standard-level regulations we identified as related to preventing specimen source errors. For Certificate of Accreditation labs, the relevant accreditation organization verifies that the lab meets the organization's requirements, but surveyors acting on behalf of CMS who are conducting validation or complaint-related surveys might identify deficiencies related to these standard-level regulations.

⁴⁸The condition-level regulation General Lab Systems (42 C.F.R. §493.1230) requires labs to meet regulations 42 C.F.R. §§493.1231 - 493.1236 and 493.1239, which include requirements related to protecting patient confidentiality, complaint investigations, and assessment of personnel, as well as those we identified as relevant to preventing specimen source errors. The condition-level regulation Preactalytic Systems (42 C.F.R. §493.1240) requires labs to meet regulations 42 C.F.R. §§493.1241, 493.1242, and 493.1249, which include requirements related to steps taken prior to the actual testing of a patient specimen.

Our analysis of CMS data shows that in 2018, 3.8 percent (364 out of 9,655) of Certificate of Compliance and Certificate of Accreditation labs surveyed by surveyors acting on behalf of CMS had standard-level deficiencies related to preventing specimen source errors.⁴⁹ In comparison, 44.5 percent (4,300 out of 9,655) of labs surveyed by these surveyors had a deficiency related to any CLIA regulation. CMS officials noted that in cases where issues related to preventing specimen source errors are part of a systemic issue, surveyors may report the systemic issue without listing one of the related standard-level deficiencies. For example, officials at one state survey agency said that they identify whichever deficiencies will lead a lab to take the correct actions to address the problem. Therefore, these deficiencies may not capture all issues related to preventing specimen source errors.

Certificate of Compliance Labs

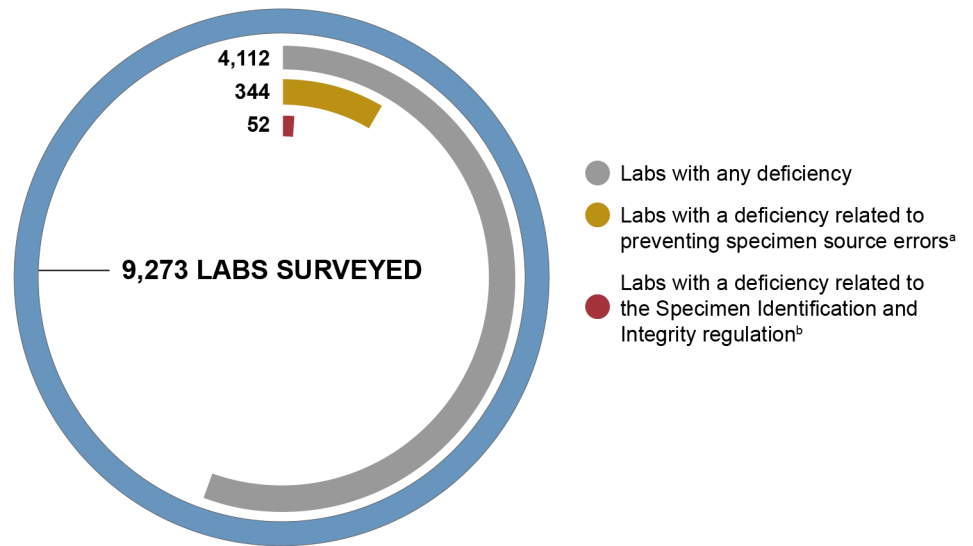
CMS data show that CMS identified 3.7 percent (344 out of 9,273) of Certificate of Compliance labs as having standard-level deficiencies related to preventing specimen source errors in 2018. (See fig. 2.) More specifically, 0.56 percent (52 out of 9,273) were found to be deficient in meeting the regulation related to specimen identification and integrity, which requires labs to establish procedures to properly identify lab specimens.⁵⁰ CMS's list of the top 10 deficiencies among Certificate of Compliance labs, released in October 2018, did not include any of the deficiencies we identified as related to preventing specimen source errors.⁵¹

⁴⁹State survey agencies surveyed the majority of labs with deficiencies reported here; a specialized cytology organization surveyed the remainder. Because labs are generally surveyed biennially, only a portion were surveyed in 2018 and reported here. In addition, deficiencies identified by accreditation organizations are not reported here because deficiencies from their surveys may not be directly comparable to the standard-level deficiencies cited by state survey agencies.

⁵⁰That is, 52 labs had deficiencies related to specimen identification and integrity (42 C.F.R. §493.1232). Fifty-one of the labs had corrected this deficiency as of May 2020. CMS had not documented whether one lab corrected this error because the lab no longer conducts tests where this requirement is applicable. Labs have at most 12 months to correct a standard-level deficiency. CMS officials noted that the acceptable time frame to correct a deficiency may be shorter than 12 months, depending upon the severity of the issue.

⁵¹The most common standard-level deficiency was found in 4.8 percent of labs and related to lab criteria for storing specimens.

Figure 2: Certificate of Compliance Lab Survey Findings, 2018



Source: Centers for Medicare & Medicaid Services data. | GAO-21-59

^aThese labs had a deficiency related to at least one of the following regulations: 42 C.F.R. §§ 493.1232 (specimen identification and integrity), 493.1234 (communications), 493.1239 (general laboratory systems quality assessment), 493.1242(a) or 493.1242(d) (specimen submission, handling, and referral), or 493.1249 (preanalytic systems quality assessment).

^bThese labs had a deficiency related to 42 C.F.R. § 493.1232 (specimen identification and integrity), which is most directly related to preventing specimen source errors.

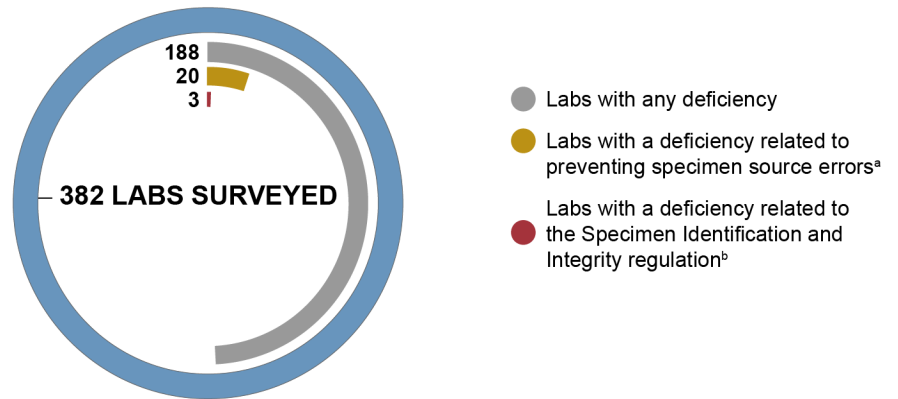
Certificate of Accreditation Labs

CMS data also show that 5.2 percent (20 out of 382) of Certificate of Accreditation labs surveyed by surveyors acting on behalf of CMS had a deficiency related to preventing specimen source errors in 2018.⁵² (See fig. 3.) More specifically, 0.8 percent (3 out of 382) were found to be deficient in meeting the regulation related to specimen identification and integrity, which requires labs to establish procedures to properly identify lab specimens.⁵³

⁵²In 2018, there were 15,867 Certificate of Accreditation labs. State survey agencies conduct surveys of these labs if they receive a complaint about the lab or to validate that accreditation organizations are identifying lab deficiencies appropriately.

⁵³That is, three labs had deficiencies related to specimen identification and integrity (42 C.F.R. §493.1232). All three of the labs had corrected this deficiency as of May 2020.

Figure 3: Certificate of Accreditation Lab Survey Findings, 2018



Source: Centers for Medicare & Medicaid Services data. | GAO-21-59

^aThese labs had a deficiency related to at least one of the following regulations: 42 C.F.R. §§ 493.1232 (specimen identification and integrity), 493.1234 (communications), 493.1239 (general laboratory systems quality assessment), 493.1242(a) or 493.1242(d) (specimen submission, handling, and referral), or 493.1249 (preanalytic systems quality assessment).

^bThese labs had a deficiency related to 42 C.F.R. § 493.1232 (specimen identification and integrity), which is most directly related to preventing specimen source errors.

Agency Comments

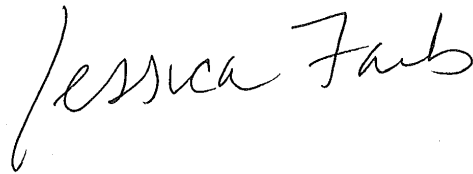
We provided a draft of this report to the Department of Health and Human Services for review and comment. The department provided technical comments, which we incorporated as appropriate.

As agreed with your office, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time, we will send copies to the Secretary of the Department of Health and Human Services. In addition, the report will be available at no charge on the GAO website at <https://www.gao.gov>.

If you or your staff have any questions about this report, please contact me at (202) 512-7114 or at farbj@gao.gov. Contact points for our Offices

of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made key contributions to this report are listed in appendix I.

Sincerely yours,

A handwritten signature in black ink that reads "Jessica Farb". The signature is written in a cursive, flowing style.

Jessica Farb
Director, Health Care

Appendix I: GAO Contact and Staff Acknowledgments

GAO Contact

Jessica Farb, (202) 512-7114 or farbj@gao.gov.

Staff Acknowledgments

In addition to the contact named above, Leslie V. Gordon, Assistant Director; Hannah Marston Minter, Analyst-in-Charge; Kerry Casey; Sarah Garcia; Ethiene Salgado-Rodriguez; and Caitlin Scoville made key contributions to this report. Also contributing were George Bogart, Cynthia Khan, and Pamela Snedden.

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