(e) Failure to identify the same antibody in two consecutive or two out of three consecutive testing events is unsuccessful performance.

(f) Failure to achieve an overall testing event score of satisfactory for two consecutive testing events or two out of three consecutive testing events is unsuccessful performance.

Subpart I—Proficiency Testing Programs for Nonwaived Testing

SOURCE: 57 FR 7151, Feb. 28, 1992, unless otherwise noted.

§ 493.901 Approval of proficiency testing programs.

In order for a proficiency testing program to receive HHS approval, the program must be offered by a private non-profit organization or a Federal or State agency, or entity acting as a designated agent for the State. An organization, Federal, or State program seeking approval or reapproval for its program for the next calendar year must submit an application providing the required information by July 1 of the current year. The organization, Federal, or State program must provide technical assistance to laboratories seeking to qualify under the program, and must, for each specialty, subspecialty, and analyte or test for which it provides testing—

(a) Assure the quality of test samples, appropriately evaluate and score the testing results, and identify performance problems in a timely manner;

(b) Demonstrate to HHS that it has—

(1) The technical ability required to—

(i) Prepare or purchase samples from manufacturers who prepare the samples in conformance with the appropriate good manufacturing practices required in 21 CFR parts 606, 640, and 820; and

(ii) Distribute the samples, using rigorous quality control to assure that samples mimic actual patient specimens when possible and that samples are homogeneous, except for specific subspecialties such as cytology, and will be stable within the time frame for analysis by proficiency testing participants;

(2) A scientifically defensible process for determining the correct result for each challenge offered by the program;

(3) A program of sufficient annual challenge and with the frequency specified in §§ 493.909 through 493.958 to establish that a laboratory has met minimum performance requirements;

(4) The resources needed to provide Statewide or nationwide reports to regulatory agencies on individual’s performance for gynecologic cytology and on individual laboratory performance on testing events, cumulative reports and scores for each laboratory or individual, and reports of specific laboratory failures using grading criteria acceptable to HHS. These reports must be provided to HHS on a timely basis when requested;

(5) Provisions to include on each proficiency testing program report form used by the laboratory to record testing event results, an attestation statement that proficiency testing samples were tested in the same manner as patient specimens with a signature block to be completed by the individual performing the test as well as by the laboratory director;

(6) A mechanism for notifying participants of the PT shipping schedule and for participants to notify the proficiency testing program within three days of the expected date of receipt of the shipment that samples have not arrived or are unacceptable for testing. The program must have provisions for replacement of samples that are lost in transit or are received in a condition that is unacceptable for testing; and

(7) A process to resolve technical, administrative, and scientific problems about program operations;

(c) Meet the specific criteria for proficiency testing programs listed by specialty, subspecialty, and analyte or test contained in §§ 493.901 through 493.958 for initial approval and thereafter provide HHS, on an annual basis, with the information necessary to assure that the proficiency testing program meets the criteria required for approval; and

(d) Comply with all applicable packaging, shipment, and notification requirements of 42 CFR part 72.

§ 493.903 Administrative responsibilities.

The proficiency testing program must—

(a) (1) Provide HHS or its designees and participating laboratories with an electronic or a hard copy, or both, of reports of proficiency testing results and all scores for each laboratory’s performance in a format as required by and approved by CMS for each CLIA-certified specialty, subspecialty, and analyte or test within 60 days after the date by which the laboratory must report proficiency testing results to the proficiency testing program.

(2) Provide HHS with reports of PT results and scores of individual performance in cytology and provide copies of reports to participating individuals, and to all laboratories that employ the individuals, within 15 working days of the testing event;

(b) Furnish to HHS cumulative reports on an individual laboratory’s performance and aggregate data on CLIA-certified laboratories for the purpose of establishing a system to make the proficiency testing program’s results available, on a reasonable basis, upon request of any person, and include such explanatory information as may be appropriate to assist in the interpretation of the proficiency testing program’s results;

(c) Provide HHS with additional information and data upon request and submit such information necessary for HHS to conduct an annual evaluation to determine whether the proficiency testing program continues to meet the requirements of §§ 493.901 through 493.959;

(d) Maintain records of laboratories’ performance for a period of five years or such time as may be necessary for any legal proceedings; and

(e) Provide HHS with an annual report and, if needed, an interim report which identifies any previously unrecognized sources of variability in kits, instruments, methods, or PT samples, which adversely affect the programs’ ability to evaluate laboratory performance.


§ 493.905 Nonapproved proficiency testing programs.

If a proficiency testing program is determined by HHS to fail to meet any criteria contained in §§ 493.901 through 493.959 for approval of the proficiency testing program, CMS will notify the program and the program must notify all laboratories enrolled of the non-approval and the reasons for non-approval within 30 days of the notification.

§ 493.909 Microbiology.

The subspecialties under the specialty of microbiology for which a program may offer proficiency testing are bacteriology, mycobacteriology, mycology, parasitology and virology. Specific criteria for these subspecialties are found at §§ 493.911 through 493.919.

§ 493.911 Bacteriology.

(a) Types of services offered by laboratories. In bacteriology, for proficiency testing purposes, there are five types of laboratories:

(1) Those that interpret Gram stains or perform primary inoculation, or both; and refer cultures to another laboratory appropriately certified for the subspecialty of bacteriology for identification;

(2) Those that use direct antigen techniques to detect an organism and may also interpret Gram stains or perform primary inoculation, or perform any combination of these;

(3) Those that, in addition to interpreting Gram stains and performing primary inoculations, and using direct antigen tests, also isolate and identify aerobic bacteria from throat, urine, cervical, or urethral discharge specimens to the genus level and may also perform antimicrobial susceptibility tests on selected isolated microorganisms;

(4) Those that perform the services in paragraph (a)(3) of this section and also isolate and identify aerobic bacteria from any source to the species level and may also perform antimicrobial susceptibility tests; and

(5) Those that perform the services in paragraph (a)(4) of this section and also...
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isolate and identify anaerobic bacteria from any source.

(b) Program content and frequency of challenge. To be approved for proficiency testing for bacteriology, the annual program must provide a minimum of five samples per testing event. There must be at least three testing events at approximately equal intervals per year. The samples may be provided to the laboratory through mailed shipments or, at HHS’ option, may be provided to HHS or its designee for on-site testing. For the types of laboratories specified in paragraph (a) of this section, an annual program must include samples that contain organisms that are representative of the six major groups of bacteria: anaerobes, Enterobacteriaceae, gram-positive bacilli, gram-positive cocci, gram-negative cocci, and miscellaneous gram-negative bacteria, as appropriate. The specific organisms included in the samples may vary from year to year. The annual program must include samples for bacterial antigen detection, bacterial isolation and identification, Gram stain, and antimicrobial susceptibility testing.

(1) An approved program must furnish HHS with a description of samples that it plans to include in its annual program no later than six months before each calendar year. At least 50 percent of the samples must be mixtures of the principal organism and appropriate normal flora. The program must include other important emerging pathogens (as determined by HHS) and either organisms commonly occurring in patient specimens or opportunistic pathogens. The program must include the following two types of samples; each type of sample must meet the 50 percent mixed culture criterion:

(i) Samples that require laboratories to report only organisms that the testing laboratory considers to be a principal pathogen that is clearly responsible for a described illness (excluding immuno-compromised patients). The program determines the reportable isolates, including antimicrobial susceptibility for any designated isolate; and

(ii) Samples that require laboratories to report all organisms present. Samples must contain multiple organisms frequently found in specimens such as urine, blood, abscesses, and aspirates where multiple isolates are clearly significant or where specimens are derived from immuno-compromised patients. The program determines the reportable isolates.

(2) An approved program may vary over time. For example, the types of organisms that might be included in an approved program over time are—

Anaerobes:
- Bacteroides fragilis group
- Clostridium perfringens
- Peptostreptococcus anaerobius
- Enterobacteriaceae
- Citrobacter freundii
- Enterobacter aerogenes
- Escherichia coli
- Klebsiella pneumoniae
- Proteus mirabilis
- Salmonella typhimurium
- Serratia marcescens
- Shigella sonnei
- Yersinia enterocolitica

Gram-positive bacilli:
- Listeria monocytogenes
- Corynebacterium species CDC Group JK

Gram-positive cocci:
- Staphylococcus aureus
- Streptococcus Group A
- Streptococcus Group B
- Streptococcus Group D (S. bovis and enterococcus)
- Streptococcus pneumoniae

Gram-negative cocci:
- Branhamella catarrhalis
- Neisseria gonorrhoeae
- Neisseria meningitidis

Miscellaneous Gram-negative bacteria:
- Campylobacter jejuni
- Haemophilus influenzae, Type B
- Pseudomonas aeruginosa

(3) For antimicrobial susceptibility testing, the program must provide at least one sample per testing event that includes gram-positive or gram-negative strains that have a predetermined pattern of sensitivity or resistance to the common antimicrobial agents.

(c) Evaluation of a laboratory’s performance. HHS approves only those programs that assess the accuracy of a laboratory’s responses in accordance with paragraphs (c) (1) through (7) of this section.

(1) The program determines staining characteristics to be interpreted by Gram stain. The program determines the reportable bacteria to be detected by direct antigen techniques or isolation. To determine the accuracy of a laboratory’s response for Gram stain
§ 493.913 Mycobacteriology.

(a) Types of services offered by laboratories. In mycobacteriology, there are five types of laboratories for proficiency testing purposes:

(1) Those that interpret acid-fast stains and refer specimen to another laboratory appropriately certified in the subspecialty of mycobacteriology;

(2) Those that interpret acid-fast stains, perform primary inoculation, and refer cultures to another laboratory appropriately certified in the subspecialty of mycobacteriology for identification;

(3) Those that interpret acid-fast stains, isolate and perform identification and/or antimycobacterial susceptibility of Mycobacterium tuberculosis, but
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refer other mycobacteria species to another laboratory appropriately certified in the subspecialty of mycobacteriology for identification and/or susceptibility tests;

(4) Those that interpret acid-fast stains, isolate and identify all mycobacteria to the extent required for correct clinical diagnosis, but refer antimycobacterial susceptibility tests to another laboratory appropriately certified in the subspecialty of mycobacteriology; and

(5) Those that interpret acid-fast stains, isolate and identify all mycobacteria to the extent required for correct clinical diagnosis, and perform antimycobacterial susceptibility tests on the organisms isolated.

(b) Program content and frequency of challenge. To be approved for proficiency testing for mycobacteriology, the annual program must provide a minimum of five samples per testing event. There must be at least two testing events per year. The samples may be provided through mailed shipments or, at HHS' option, provided to HHS or its designee for on-site testing events. For types of laboratories specified in paragraphs (a)(1) and (a)(3) through (5) of this section, an annual program must include samples that contain species that are representative of the 5 major groups (complexes) of mycobacteria encountered in human specimens. The specific mycobacteria included in the samples may vary from year to year.

(1) An approved program must furnish HHS and its agents with a description of samples that it plans to include in its annual program no later than six months before each calendar year. At least 50 percent of the samples must include samples that contain species that are representative of the 5 major groups (complexes) of mycobacteria encountered in human specimens. The specific mycobacteria included in the samples may vary from year to year.

(2) An approved program may vary over time. For example, the types of mycobacteria that might be included in an approved program over time are—

\[\text{TB} \]
\[\text{Mycobacterium tuberculosis} \]
\[\text{Mycobacterium bovis} \]
\[\text{Group I} \]
\[\text{Mycobacterium kansasii} \]
\[\text{Group II} \]
\[\text{Mycobacterium szulgai} \]
\[\text{Group III} \]
\[\text{Mycobacterium avium-intracellulare} \]
\[\text{Mycobacterium terrae} \]
\[\text{Group IV} \]
\[\text{Mycobacterium fortuitum} \]

(3) For antimycobacterial susceptibility testing, the program must provide at least one sample per testing event that includes mycobacterium tuberculosis that has a predetermined pattern of sensitivity or resistance to the common antimycobacterial agents.

(4) For laboratories specified in paragraphs (a)(1) and (a)(2), the program must provide at least five samples per testing event that includes challenges that are acid-fast and challenges which do not contain acid-fast organisms.

(c) Evaluation of a laboratory's performance. HHS approves only those programs that assess the accuracy of a laboratory's response in accordance with paragraphs (c)(1) through (6) of this section.

(1) The program determines the reportable mycobacteria to be detected by acid-fast stain, for isolation and identification, and for antimycobacterial susceptibility. To determine the accuracy of a laboratory's response, the program must compare the laboratory's response for each sample with the response that reflects agreement of either 80 percent of ten or more referee laboratories or 80 percent or more of all participating laboratories.

(2) To evaluate a laboratory's response for a particular sample, the program must determine a laboratory's type of service in accordance with paragraph (a) of this section. A laboratory must interpret acid-fast stains and isolate and identify the organisms to the same extent it performs these procedures on patient specimens. A laboratory's performance will be evaluated on the basis of the average of its scores as determined in paragraph (c)(6) of this section.

(3) Since laboratories may incorrectly report the presence of organisms in addition to the correctly identified
§ 493.915 Mycology.

(a) Types of services offered by laboratories. In mycology, there are four types of laboratories for proficiency testing purposes that may perform different levels of service for yeasts, dimorphic fungi, dermatophytes, and aerobic actinomycetes:

(1) Those that isolate and identify only yeasts and/or dermatophytes to the genus level;

(2) Those that isolate and identify yeasts and/or dermatophytes to the species level;

(3) Those that isolate and perform identification of all organisms to the genus level; and

(4) Those that isolate and perform identification of all organisms to the species level.

(b) Program content and frequency of challenge. To be approved for proficiency testing for mycology, the annual program must provide a minimum of five samples per testing event. There must be at least three testing events at approximately equal intervals per year. The samples may be provided through mailed shipments or, at HHS’ option, may be provided to HHS or its designee for on-site testing. An annual program must include samples that contain organisms that are representative of five major groups of fungi: Yeast or yeast-like fungi; dimorphic fungi; dematiaceous fungi; dermatophytes; and saprophytes, including opportunistic fungi. The specific fungi included in the samples may vary from year to year.

(1) An approved program must, before each calendar year, furnish HHS with a description of samples that it plans to include in its annual program no later than six months before each calendar year. At least 50 percent of the samples must be mixtures of the principal organism and appropriate normal background flora. Other important emerging pathogens (as determined by HHS) and organisms commonly occurring in patient specimens must be included periodically in the program.

(2) An approved program may vary over time. As an example, the types of organisms that might be included in an approved program over time are—

Candida albicans
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§ 493.917 Parasitology.

(a) Types of services offered by laboratories. In parasitology there are two types of laboratories for proficiency testing purposes—

(1) Those that determine the presence or absence of parasites by direct observation (wet mount) and/or pinworm preparations and, if necessary, refer specimens to another laboratory appropriately certified in the subspecialty of parasitology for identification;

(2) Those that identify parasites using concentration preparations and/or permanent stains.

(b) Program content and frequency of challenge. To be approved for proficiency testing in parasitology, a program must provide a minimum of five samples per testing event. There must be at least three testing events at approximately equal intervals per year. The samples may be provided through mailed shipments or, at HHS’s option, may be provided to HHS or its designee for on-site testing. An annual program must include samples that contain parasites that are commonly encountered in the United States as well as those recently introduced into the United States. Other important emerging pathogens (as determined by HHS) and parasites commonly occurring in patient specimens must be included periodically in the program.

(1) An approved program must, before each calendar year furnish HHS with a description of samples that it plans to include in its annual program no later than six months before each calendar year. Samples must include both formalinized specimens and PVA (polyvinyl alcohol) fixed specimens as well as blood smears, as appropriate for a particular parasite and stage of the parasite. The majority of samples must contain protozoa or helminths or a combination of parasites. Some samples must be devoid of parasites.

(5) The score for a testing event is the average of the sample scores as determined under paragraph (c)(3) or (c)(4), or both, of this section.


§ 493.917 Parasitology.

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§ 493.917 Parasitology.

(c) Evaluation of a laboratory’s performance. HHS approves only those programs that assess the accuracy of a laboratory’s response, in accordance with paragraphs (c)(1) through (5) of this section.

(1) The program determines the reportable organisms. To determine the accuracy of a laboratory’s response, the program must compare the laboratory’s response for each sample with the response that reflects agreement of either 80 percent of ten or more referee laboratories or 80 percent or more of all participating laboratories.

(2) To evaluate a laboratory’s response for a particular sample, the program must determine a laboratory’s type of service in accordance with paragraph (a) of this section. A laboratory must isolate and identify the organisms to the same extent it performs these procedures on patient specimens.

(3) Since laboratories may incorrectly report the presence of organisms in addition to the correctly identified principal organism(s), the grading system must deduct credit for additional erroneous organisms reported. Therefore, the total number of correct responses submitted by the laboratory divided by the number of organisms present plus the number of incorrect organisms reported by the laboratory must be multiplied by 100 to establish a score for each sample in each shipment or testing event. For example, if a sample contained one principal organism and the laboratory reported it correctly but reported the presence of an additional organism, which was not present, the sample grade would be 1/(1+1) x 100 = 50 percent.

(4) The score for the antigen tests is the number of correct responses divided by the number of samples to be tested for the antigen, multiplied by 100.

1Note: Provided as a nonviable sample.
§493.919  Virology.

(a) Types of services offered by laboratories. In virology, there are two types of laboratories for proficiency testing purposes—

(1) Those that only perform tests that directly detect viral antigens or structures, either in cells derived from infected tissues or free in fluid specimens; and

(2) Those that are able to isolate and identify viruses and use direct antigen techniques.

(b) Program content and frequency of challenge. To be approved for proficiency testing in virology, a program must provide a minimum of five samples per testing event. There must be at least three testing events at approximately equal intervals per year. The samples may be provided to the laboratory through mailed shipments or, at HHS’s option, may be provided to HHS or its designee for on-site testing. An annual program must include viral species that are the more commonly
identified viruses. The specific organisms found in the samples may vary from year to year. The annual program must include samples for viral antigen detection and viral isolation and identification.

(1) An approved program must furnish HHS with a description of samples that it plans to include in its annual program no later than six months before each calendar year. The program must include other important emerging viruses (as determined by HHS) and viruses commonly occurring in patient specimens.

(2) An approved program may vary over time. For example, the types of viruses that might be included in an approved program over time are the more commonly identified viruses such as Herpes simplex, respiratory syncytial virus, adenoviruses, enteroviruses, and cytomegaloviruses.

(c) Evaluation of laboratory’s performance. HHS approves only those programs that assess the accuracy of a laboratory’s response in accordance with paragraphs (c)(1) through (5) of this section.

(1) The program determines the reportable viruses to be detected by direct antigen techniques or isolated by laboratories that perform viral isolation procedures. To determine the accuracy of a laboratory’s response, the program must compare the laboratory’s response for each sample with the response that reflects agreement of either 80 percent of ten or more referee laboratories or 80 percent or more of all participating laboratories.

(2) To evaluate a laboratory’s response for a particular sample, the program must determine a laboratory’s type of service in accordance with paragraph (a) of this section. A laboratory must isolate and identify the viruses to the same extent it performs these procedures on patient specimens.

(3) Since laboratories may incorrectly report the presence of viruses in addition to the correctly identified principal virus, the grading system must provide a means of deducting credit for additional erroneous viruses reported. Therefore, the total number of correct responses determined by virus culture techniques submitted by the laboratory divided by the number of viruses present plus the number of incorrect viruses reported by the laboratory must be multiplied by 100 to establish a score for each sample in each testing event. For example, if a sample contained one principal virus and the laboratory reported it correctly but reported the presence of an additional virus, which was not present, the sample grade would be 1/(1+1)×100=50 percent.

(4) The performance criterion for qualitative antigen tests is presence or absence of the viral antigen. The score for the antigen tests is the number of correct responses divided by the number of samples to be tested for the antigen, multiplied by 100.

(5) The score for a testing event is the average of the sample scores as determined under paragraph (c)(3) and (c)(4) of this section.


§ 493.921 Diagnostic immunology.

The subspecialties under the specialty of immunology for which a program may offer proficiency testing are syphilis serology and general immunology. Specific criteria for these subspecialties are found at §§ 493.923 and 493.927.

§ 493.923 Syphilis serology.

(a) Program content and frequency of challenge. To be approved for proficiency testing in syphilis serology, a program must provide a minimum of five samples per testing event. There must be at least three testing events at approximately equal intervals per year. The samples may be provided through mailed shipments or, at HHS’ option, may be provided to HHS or its designee for on-site testing. An annual program must include samples that cover the full range of reactivity from highly reactive to non-reactive.

(b) Evaluation of test performance. HHS approves only those programs that assess the accuracy of a laboratory’s responses in accordance with paragraphs (b)(1) through (4) of this section.

(1) To determine the accuracy of a laboratory’s response for qualitative and quantitative syphilis tests, the
§ 493.927 General immunology.

(a) Program content and frequency of challenge. To be approved for proficiency testing for immunology, the annual program must provide a minimum of five samples per testing event. There must be at least three testing events at approximately equal intervals per year. The annual program must provide samples that cover the full range of reactivity from highly reactive to nonreactive. The samples may be provided through mailed shipments or, at HHS’ option, may be provided to HHS or its designee for on-site testing.

(b) Challenges per testing event. The minimum number of challenges per testing event the program must provide for each analyte or test procedure is five. Analytes or tests for which laboratory performance is to be evaluated include:

- **Analyte or Test Procedure**
  - Alpha-1 antitrypsin
  - Alpha-fetoprotein (tumor marker)
  - Antinuclear antibody
  - Antistreptolysin O
  - Anti-human immunodeficiency virus (HIV)
  - Complement C3
  - Complement C4
  - Hepatitis markers (HBsAg, anti-HBc, HBeAg)
  - IgA
  - IgG
  - IgE
  - IgM
  - Infectious mononucleosis
  - Rheumatoid factor
  - Rubella

(c) Evaluation of a laboratory’s analyte or test performance. HHS approves only those programs that assess the accuracy of a laboratory’s responses in accordance with paragraphs (c)(1) through (5) of this section.

(1) To determine the accuracy of a laboratory’s response for quantitative and qualitative immunology tests or analytes, the program must compare the laboratory’s response for each analyte with the response that reflects agreement of either 80 percent of ten or more referee laboratories or 80 percent or more of all participating laboratories. The proficiency testing program must indicate the minimum concentration that will be considered as indicating a positive response. The score for a sample in general immunology is either the score determined under paragraph (c)(2) or (3) of this section.

(2) For quantitative immunology analytes or tests, the program must determine the correct response for each analyte by the distance of the response from the target value. After the target

\[
\text{Testing event score} = \left( \frac{\text{Number of acceptable responses for all challenges}}{\text{Total number of all challenges}} \right) \times 100
\]
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§ 493.931 Routine chemistry.

(a) Program content and frequency of challenge. To be approved for proficiency testing for routine chemistry, a program must provide a minimum of five samples per testing event. There must be at least three testing events at approximately equal intervals per year. The annual program must provide samples that cover the clinically relevant range of values that would be expected in patient specimens. The specimens may be provided through mailed shipments or, at HHS’ option, may be provided to HHS or its designee for on-site testing.

(b) Challenges per testing event. The minimum number of challenges per testing event a program must provide for each analyte or test procedure listed below is five serum, plasma or blood samples.

Analyte or Test Procedure

Alanine aminotransferase (ALT/SGPT)
Albumin
Alkaline phosphatase

(3) The criterion for acceptable performance for qualitative general immunology tests is positive or negative.

(4) To determine the analyte testing event score, the number of acceptable analyte responses must be averaged using the following formula:

\[
\text{Analyte score for the testing event} = \left( \frac{\text{Number of acceptable responses for the analyte}}{\text{Total number of challenges for the analyte}} \right) \times 100
\]

(5) To determine the overall testing event score, the number of correct responses for all analytes must be averaged using the following formula:

\[
\text{Testing event score} = \left( \frac{\text{Number of acceptable responses for all challenges}}{\text{Total number of all challenges}} \right) \times 100
\]
§ 493.931  

Amylase  
Aspartate aminotransferase (AST/SGOT)  
Bilirubin, total  
Blood gas (pH, pO2, and pCO2)  
Calcium, total  
Chloride  
Cholesterol, total  
Cholesterol, high density lipoprotein  
Creatine kinase  
Creatine kinase, isoenzymes  
Creatinine  
Glucose (Excluding measurements on devices cleared by FDA for home use)  
Iron, total  
Lactate dehydrogenase (LDH)  
LDH isoenzymes  
Magnesium  
Potassium  
Sodium  
Total Protein  
Triglycerides  
Urea Nitrogen  
Uric Acid  

(c) Evaluation of a laboratory’s analyte or test performance. HHS approves only those programs that assess the accuracy of a laboratory’s responses in accordance with paragraphs (c)(1) through (5) of this section.

(1) To determine the accuracy of a laboratory’s response for qualitative and quantitative chemistry tests or analytes, the program must compare the laboratory’s response for each analyte with the response that reflects agreement of either 80 percent of ten or more referee laboratories or 80 percent of all participating laboratories. The score for a sample in routine chemistry is either the score determined under paragraph (c)(2) or (3) of this section.

(2) For quantitative chemistry tests or analytes, the program must determine the correct response for each analyte by the distance of the response from the target value. After the target value has been established for each response, the appropriateness of the response must be determined by using either fixed criteria based on the percentage difference from the target value or the number of standard deviations (SDs) the response differs from the target value.

Criteria for Acceptable Performance

The criteria for acceptable performance are—

<table>
<thead>
<tr>
<th>Analyte or test</th>
<th>Criteria for acceptable performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine aminotransferase (ALT/SGPT)</td>
<td>Target value ±20%</td>
</tr>
<tr>
<td>Albumin</td>
<td>Target value ±10%</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>Target value ±30%</td>
</tr>
<tr>
<td>Amylase</td>
<td>Target value ±30%</td>
</tr>
<tr>
<td>Aspartate aminotransferase (AST/SGOT)</td>
<td>Target value ±20%</td>
</tr>
<tr>
<td>Bilirubin, total</td>
<td>Target value 0.4 mg/dL or ±20% (greater)</td>
</tr>
<tr>
<td>Blood gas pO2</td>
<td>Target value ±3 SD</td>
</tr>
<tr>
<td>pH</td>
<td>Target value ±0.04</td>
</tr>
<tr>
<td>Calcium, total</td>
<td>Target value ±1.0 mg/dL</td>
</tr>
<tr>
<td>Chloride</td>
<td>Target value ±15%</td>
</tr>
<tr>
<td>Cholesterol, total</td>
<td>Target value ±10%</td>
</tr>
<tr>
<td>Cholesterol, high density lipoprotein</td>
<td>Target value ±30%</td>
</tr>
<tr>
<td>Creatine kinase</td>
<td>Target value ±10%</td>
</tr>
<tr>
<td>Creatine kinase isoenzymes</td>
<td>Target value ±30%</td>
</tr>
<tr>
<td>Creatinine</td>
<td>Target value ±0.3 mg/dL or ±15% (greater)</td>
</tr>
<tr>
<td>Glucose (excluding glucose performed on monitoring devices cleared by FDA for home use)</td>
<td>Target value ±6 mg/dL or ±10% (greater)</td>
</tr>
<tr>
<td>Iron, total</td>
<td>Target value ±20%</td>
</tr>
<tr>
<td>Lactate dehydrogenase (LDH)</td>
<td>Target value ±20%</td>
</tr>
<tr>
<td>LDH isoenzymes</td>
<td>LDH1/LDH2 (+ or −) or Target value ±30%</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Target value ±25%</td>
</tr>
<tr>
<td>Potassium</td>
<td>Target value ±0.5 mmol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>Target value ±14 mmol/L</td>
</tr>
<tr>
<td>Total Protein</td>
<td>Target value ±10%</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>Target value ±25%</td>
</tr>
<tr>
<td>Urea nitrogen</td>
<td>Target value ±12 mg/dL or ±15% (greater)</td>
</tr>
<tr>
<td>Uric acid</td>
<td>Target value ±17%</td>
</tr>
</tbody>
</table>

(3) The criterion for acceptable performance for qualitative routine chemistry tests is positive or negative.

(4) To determine the analyte testing event score, the number of acceptable analyte responses must be averaged using the following formula:

\[
\text{Analyte score for the testing event} = \frac{\text{Number of acceptable responses for the analyte}}{\text{Total number of challenges for the analyte}} \times 100
\]
(5) To determine the overall testing event score, the number of correct responses for all analytes must be averaged using the following formula:

\[
\text{Number of acceptable responses for all challenges} \times \frac{100}{\text{Total number of all challenges}} = \text{Testing event score}
\]

§ 493.933 Endocrinology.

(a) Program content and frequency of challenge. To be approved for proficiency testing for endocrinology, a program must provide a minimum of five samples per testing event. There must be at least three testing events at approximately equal intervals per year. The annual program must provide samples that cover the clinically relevant range of values that would be expected in patient specimens. The samples may be provided through mailed shipments or, at HHS’ option, may be provided to HHS or its designee for on-site testing.

(b) Challenges per testing event. The minimum number of challenges per testing event a program must provide for each analyte or test procedure is five serum, plasma, blood, or urine samples.

(c) Evaluation of a laboratory’s analyte or test performance. HHS approves only those programs that assess the accuracy of a laboratory’s responses in accordance with paragraphs (c)(1) through (5) of this section.

(1) To determine the accuracy of a laboratory’s response for qualitative and quantitative endocrinology tests or analytes, a program must compare the laboratory’s response for each analyte with the response that reflects agreement of either 80 percent of ten or more referee laboratories or 80 percent or more of all participating laboratories. The score for a sample in endocrinology is either the score determined under paragraph (c)(2) or (c)(3) of this section.

(2) For quantitative endocrinology tests or analytes, the program must determine the correct response for each analyte by the distance of the response from the target value. After the target value has been established for each response, the appropriateness of the response must be determined by using either fixed criteria based on the percentage difference from the target value or the number of standard deviations (SDs) the response differs from the target value.

Criteria for Acceptable Performance

The criteria for acceptable performance are—

<table>
<thead>
<tr>
<th>Analyte or Test</th>
<th>Criteria for acceptable performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol</td>
<td>Target value ±25%</td>
</tr>
<tr>
<td>Free Thyroxine</td>
<td>Target value ±3 SD or greater</td>
</tr>
<tr>
<td>Human Chorionic gonadotropin (excluding urine pregnancy tests done by visual color comparison categorized as waived tests)</td>
<td>Target value ±3 SD or greater</td>
</tr>
<tr>
<td>T3 Uptake</td>
<td>Target value ±3 SD or greater</td>
</tr>
<tr>
<td>Triiodothyronine</td>
<td>Target value ±20% or 1.0 mcg/dL (greater)</td>
</tr>
<tr>
<td>Thyroid-stimulating hormone</td>
<td>Target value ±3 SD or greater</td>
</tr>
<tr>
<td>Thyroxine</td>
<td>Target value ±20% or 1.0 mcg/dL (greater)</td>
</tr>
</tbody>
</table>

(3) The criterion for acceptable performance for qualitative endocrinology tests is positive or negative.

(4) To determine the analyte testing event score, the number of acceptable analyte responses must be averaged using the following formula:
§ 493.937 Toxicology.

(a) Program content and frequency of challenge. To be approved for proficiency testing for toxicology, the annual program must provide a minimum of five samples per testing event. There must be at least three testing events at approximately equal intervals per year. The annual program must provide samples that cover the clinically relevant range of values that would be expected in specimens of patients on drug therapy and that cover the level of clinical significance for the particular drug. The samples may be provided through mailed shipments or, at HHS’ option, may be provided to HHS or its designee for on-site testing.

(b) Challenges per testing event. The minimum number of challenges per testing event a program must provide for each analyte or test procedure is five serum, plasma, or blood samples.

(c) Evaluation of a laboratory’s analyte or test performance. HHS approves only those programs that assess the accuracy of a laboratory’s responses in accordance with paragraphs (c)(1) through (4) of this section.

(1) To determine the accuracy of a laboratory’s responses for quantitative toxicology tests or analytes, the program must compare the laboratory’s response for each analyte with the response that reflects agreement of either 80 percent of ten or more referee laboratories or 80 percent or more of all participating laboratories. The score for a sample in toxicology is the score determined under paragraph (c)(2) of this section.

(2) For quantitative toxicology tests or analytes, the program must determine the correct response for each analyte by the distance of the response from the target value. After the target value has been established for each response, the appropriateness of the response must be determined by using fixed criteria based on the percentage difference from the target value.

Criteria for Acceptable Performance

The criteria for acceptable performance are:

<table>
<thead>
<tr>
<th>Analyte or Test Procedure</th>
<th>Criteria for acceptable performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol (blood)</td>
<td>Target Value ±25%</td>
</tr>
<tr>
<td>Blood lead</td>
<td>Target Value ±10% or 4 mcg/dL (greater).</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Target Value ±25%</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Target Value &lt;25% or &gt;±0.2 ng/mL (greater).</td>
</tr>
<tr>
<td>Ethosuximide</td>
<td>Target Value ±25%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Target Value ±25% or ±0.3 mmol/L or &lt;±20% (greater).</td>
</tr>
<tr>
<td>Lithium</td>
<td>Target Value ±25%</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Target Value ±25%</td>
</tr>
<tr>
<td>Primidone</td>
<td>Target Value ±25%</td>
</tr>
<tr>
<td>Procainamide (and metabo-lite)</td>
<td>Target Value ±25%</td>
</tr>
<tr>
<td>Quinidine</td>
<td>Target Value ±25%</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>Target Value ±25%</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Target Value ±25%</td>
</tr>
</tbody>
</table>

(5) To determine the overall testing event score, the number of correct responses for all analytes must be averaged using the following formula:

\[
\text{Analyte score for the testing event} = \frac{\text{Number of acceptable responses for the analyte} \times 100}{\text{Total number of challenges for the analyte}}
\]

\[
\text{Testing event score} = \frac{\text{Number of acceptable responses for all challenges} \times 100}{\text{Total number of all challenges}}
\]
(3) To determine the analyte testing event score, the number of acceptable analyte responses must be averaged using the following formula:

\[
\frac{\text{Number of acceptable responses for the analyte}}{\text{Total number of challenges for the analyte}} \times 100 = \text{Analyte score for the testing event}
\]

(4) To determine the overall testing event score, the number of correct responses for all analytes must be averaged using the following formula:

\[
\frac{\text{Number of acceptable responses for all challenges}}{\text{Total number of all challenges}} \times 100 = \text{Testing event score}
\]

(1) An approved program for cell identification may vary over time. The types of cells that might be included in an approved program over time are—

- Neutrophilic granulocytes
- Eosinophilic granulocytes
- Basophilic granulocytes
- Lymphocytes
- Monocytes
- Major red and white blood cell abnormalities
- Immature red and white blood cells

(2) White blood cell differentials should be limited to the percentage distribution of cellular elements listed above.

(c) Evaluation of a laboratory’s analyte or test performance. HHS approves only those programs that assess the accuracy of a laboratory’s responses in accordance with paragraphs (c) (1) through (5) of this section.

(1) To determine the accuracy of a laboratory’s responses for qualitative and quantitative hematology tests or analytes, the program must compare the laboratory’s response for each analyte with the response that reflects agreement of either 80 percent of ten or more referee laboratories or 80 percent or more of all participating laboratories. The score for a sample in hematology is either the score determined under paragraph (c) (2) or (3) of this section.

(2) For quantitative hematology tests or analytes, the program must determine the correct response for each
analyte by the distance of the response from the target value. After the target value has been established for each response, the appropriateness of the response is determined using either fixed criteria based on the percentage difference from the target value or the number of standard deviations (SDs) the response differs from the target value.

Criteria for Acceptable Performance

The criteria for acceptable performance are:

<table>
<thead>
<tr>
<th>Analyte or test</th>
<th>Criteria for acceptable performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell identification</td>
<td>90% or greater consensus on identification.</td>
</tr>
<tr>
<td>Erythrocyte count</td>
<td>Target ±3SD based on the percentage of different types of white blood cells in the samples.</td>
</tr>
<tr>
<td>Hematocrit (Excluding spun hematocrit)</td>
<td>Target ±16%.</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Target ±16%.</td>
</tr>
<tr>
<td>Leukocyte count</td>
<td>Target ±15%.</td>
</tr>
<tr>
<td>Platelet count</td>
<td>Target ±20%.</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>Target ±15%.</td>
</tr>
<tr>
<td>Partial thromboplastin time</td>
<td>Target ±15%.</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>Target ±15%.</td>
</tr>
</tbody>
</table>

(3) The criterion for acceptable performance for the qualitative hematology test is correct cell identification.

(4) To determine the analyte testing event score, the number of acceptable analyte responses must be averaged using the following formula:

\[
\frac{\text{Number of acceptable responses for the analyte}}{\text{Total number of challenges for the analyte}} \times 100 = \text{Analyte score for the testing event}
\]

(5) To determine the overall testing event score, the number of correct responses for all analytes must be averaged using the following formula:

\[
\frac{\text{Number of acceptable responses for all challenges}}{\text{Total number of all challenges}} \times 100 = \text{Testing event score}
\]


§ 493.945 Cytology; gynecologic examinations.

(a) Program content and frequency of challenge. (1) To be approved for proficiency testing for gynecologic examinations (Pap smears) in cytology, a program must provide test sets composed of 10- and 20-glass slides. Proficiency testing programs may obtain slides for test sets from cytology laboratories, provided the slides have been retained by the laboratory for the required period specified in §§493.1105(a)(7)(i)(A) and 493.1274(d)(2). If slide preparations are still subject to retention by the laboratory, they may be loaned to a proficiency testing program if the program provides the laboratory with documentation of the loan of the slides and ensures that slides loaned to it are retrievable upon request. Each test set must include at least one slide representing each of the response categories described in paragraph (b)(3)(ii)(A) of this section, and test sets should be comparable so that equitable testing is achieved within and between proficiency testing providers.

(2) To be approved for proficiency testing in gynecologic cytology, a program must provide announced and unannounced on-site testing for each individual at least once per year and must provide an initial retesting event for each individual within 45 days after...
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(b) Evaluation of an individual’s performance. HHS approves only those programs that assess the accuracy of each individual’s responses on both 10- and 20-slide test sets in which the slides have been referenced as specified in paragraph (b)(1) of this section.

(1) To determine the accuracy of an individual’s response on a particular challenge (slide), the program must compare the individual’s response for each slide preparation with the response that reflects the predetermined consensus agreement or confirmation on the diagnostic category, as described in the table in paragraph (b)(3)(ii)(A) of this section. For all slide preparations, a 100% consensus agreement among a minimum of three physicians certified in anatomic pathology is required. In addition, for premalignant and malignant slide preparations, confirmation by tissue biopsy is required either by comparison of the reported biopsy results or re-evaluation of biopsy slide material by a physician certified in anatomic pathology.

(2) An individual qualified as a technical supervisor under §493.1449 (b) or (k) who routinely interprets gynecologic slide preparations only after they have been examined by a cytotechnologist can either be tested using a test set that has been screened by a cytotechnologist in the same laboratory or using a test set that has not been screened. A technical supervisor who screens and interprets slide preparations that have not been previously examined must be tested using a test set that has not been previously screened.

(3) The criteria for acceptable performance are determined by using the scoring system in paragraphs (b)(3)(i)(C) and (D) of this section, for technical supervisors and cytotechnologists, respectively, provide a maximum of 10 points for a correct response and a maximum of minus five (−5) points for an incorrect response on a 10-slide test set. For example, if the correct response on a slide is “high grade squamous intraepithelial lesion” (category “D” on the scoring system chart) and an examinee calls it

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A ..........</td>
<td>Unsatisfactory for diagnosis due to:</td>
</tr>
<tr>
<td></td>
<td>(1) Scant cellularity.</td>
</tr>
<tr>
<td></td>
<td>(2) Air drying.</td>
</tr>
<tr>
<td></td>
<td>(3) Obscuring material (blood, inflammatory cells, or lubricant).</td>
</tr>
<tr>
<td>B ..........</td>
<td>Normal or Benign Changes—includes:</td>
</tr>
<tr>
<td></td>
<td>(1) Normal, negative or within normal limits.</td>
</tr>
<tr>
<td></td>
<td>(2) Infection other than Human Papillomavirus (HPV) (e.g., Trichomonas vaginalis, changes or morphology consistent with Candida spp., Actinomyces spp. or Herpes simplex virus).</td>
</tr>
<tr>
<td></td>
<td>(3) Reactive and reparative changes (e.g., inflammation, effects of chemotherapy or radiation).</td>
</tr>
<tr>
<td>C ..........</td>
<td>Low Grade Squamous Intraepithelial Lesion—includes:</td>
</tr>
<tr>
<td></td>
<td>(1) Cellular changes associated with HPV.</td>
</tr>
<tr>
<td></td>
<td>(2) Mild dysplasia/CIN±1.</td>
</tr>
<tr>
<td></td>
<td>(3) High Grade Lesion and Carcinoma—includes:</td>
</tr>
<tr>
<td></td>
<td>(1) High grade squamous intraepithelial lesions which include moderate dysplasia/CIN–2 and severe dysplasia/carcinoma in-situ/CIN–3.</td>
</tr>
<tr>
<td></td>
<td>(2) Squamous cell carcinoma.</td>
</tr>
<tr>
<td></td>
<td>(3) Adenocarcinoma and other malignant neoplasms.</td>
</tr>
</tbody>
</table>

(B) In accordance with the criteria for the scoring system, the charts in paragraphs (b)(3)(ii)(C) and (D) of this section, for technical supervisors and cytotechnologists, respectively, provide a maximum of 10 points for a correct response and a maximum of minus five (−5) points for an incorrect response on a 10-slide test set. For example, if the correct response on a slide is “high grade squamous intraepithelial lesion” (category “D” on the scoring system chart) and an examinee calls it
§ 493.959 Immunohematology.

(a) Types of services offered by laboratories. In immunohematology, there are four types of laboratories for proficiency testing purposes—

1. Those that perform ABO group and/or D (Rh) typing;
2. Those that perform ABO group and/or D (Rh) typing, and unexpected antibody detection;
3. Those that in addition to paragraph (a)(2) of this section perform compatibility testing; and
4. Those that perform in addition to paragraph (a)(3) of this section antibody identification.

(b) Program content and frequency of challenge. To be approved for proficiency testing for immunohematology, a program must provide a minimum of five samples per testing event. There must be at least three testing events at approximately equal intervals per year. The annual program must provide samples that cover the full range of interpretation that would be expected in patient specimens. The samples may be provided through mailed shipments or, at HHS’ option, may be provided to HHS or its designee for on-site testing.

(c) Challenges per testing event. The minimum number of challenges per testing event a program must provide for each analyte or test procedure is five.

Analyte or Test Procedure

- ABO group (excluding subgroups)
- D (Rh) typing
- Unexpected antibody detection
- Compatibility testing
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§ 493.1101

Antibody identification

(d) Evaluation of a laboratory's analyte or test performance. HHS approves only those programs that assess the accuracy of a laboratory's response in accordance with paragraphs (d)(1) through (5) of this section.

(1) To determine the accuracy of a laboratory's response, a program must compare the laboratory's response for each analyte with the response that reflects agreement of either 100 percent of ten or more referee laboratories or 95 percent or more of all participating laboratories except for unexpected antibody detection and antibody identification. To determine the accuracy of a laboratory's response for unexpected antibody detection and antibody identification, a program must compare the laboratory's response for each analyte with the response that reflects agreement of either 95 percent of ten or more referee laboratories or 95 percent or more of all participating laboratories.

(2) Criteria for acceptable performance. The criteria for acceptable performance are—

<table>
<thead>
<tr>
<th>Analyte or test</th>
<th>Criteria for acceptable performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABO group</td>
<td>100% accuracy.</td>
</tr>
<tr>
<td>D (Rh) typing</td>
<td>100% accuracy.</td>
</tr>
<tr>
<td>Unexpected antibody detection</td>
<td>80% accuracy.</td>
</tr>
<tr>
<td>Compatibility testing</td>
<td>100% accuracy.</td>
</tr>
<tr>
<td>Antibody identification</td>
<td>80% accuracy.</td>
</tr>
</tbody>
</table>

(3) The criterion for acceptable performance for qualitative immunohematology tests is positive or negative.

(4) To determine the analyte testing event score, the number of acceptable analyte responses must be averaged using the following formula:

\[
\frac{\text{Number of acceptable responses for the analyte}}{\text{Total number of challenges for the analyte}} \times 100 = \text{Analyte score for the testing event}
\]

(5) To determine the overall testing event score, the number of correct responses for all analytes must be averaged using the following formula:

\[
\frac{\text{Number of acceptable responses for all challenges}}{\text{Total number of all challenges}} \times 100 = \text{Testing event score}
\]

Subpart J—Facility Administration for Nonwaived Testing

Source: 68 FR 3703, Jan. 24, 2003, unless otherwise noted.

§ 493.1100 Condition: Facility administration.

Each laboratory that performs nonwaived testing must meet the applicable requirements under §§ 493.1101 through 493.1105, unless HHS approves a procedure that provides equivalent quality testing as specified in Appendix C of the State Operations Manual (CMS Pub. 7).