



COLLEGE of AMERICAN PATHOLOGISTS

June 4, 2019

Seema Verma
Administrator
U.S. Centers for Medicare & Medicaid Services
7500 Security Boulevard,
Baltimore, MD 21244

Re: Clinical Laboratory Improvement Amendments of 1988 (CLIA) Proficiency Testing
Regulations Related to Analytes and Acceptable Performance (CMS- 3355–P)

Dear Ms. Verma:

The College of American Pathologists (CAP) appreciates the opportunity to comment on the Centers for Medicare and Medicaid Services (CMS) proposed rule entitled, **Clinical Laboratory Improvement Amendments of 1988 (CLIA) Proficiency Testing Regulations Related to Analytes and Acceptable Performance**. As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide. We laud CMS's effort to modernize PT regulations reflecting the evolution of clinical laboratory testing offered today since the inception of CLIA.

Since 1947, the CAP strongly supports the principle that interlaboratory comparisons of performance creates an environment that contributes to "Advancing Excellence" in laboratory science and therefore is critical to quality patient care. Our program allows laboratories to evaluate their performance regularly and improve the accuracy of the patient results they provide for methods and analytes for specific clinical indications. PT represents a "snapshot" and is not intended to provide a comprehensive evaluation of a laboratory's quality assurance processes. We believe fundamentally that proficiency testing (PT) is only one of many tools needed to maintain laboratory quality in addition to quality assurance, laboratory director involvement, competency assessment, qualified personnel and quality control. Moreover, PT is one mechanism to alert laboratories to problems and indicate changes to avoid future errors. As the largest PT program, it is open and available to any laboratory that offers clinical laboratory testing in the world.

The CAP supports the agency's effort to update the list of regulated analytes by proposing the addition of the 29 and the deletion of six current analytes, allow PT programs more autonomy to establish peer-groups and parameters for PT offerings, and protect the integrity of the program by ensuring non-profit status for administrative activities. In addition, we propose the agency consider addition of analytes in the specialty of toxicology. However, before this rule is finalized, we believe CMS needs to clarify the administrative



responsibilities required to be non-profit and the peer-group requirements applicable to non-regulated analytes. Likewise, we believe the agency should rescind several proposals from the rule because of the potential burden and cost to laboratories. These proposals include laboratories' declaration of patient reporting practices to PT programs, reporting microbiology organisms to PT programs at the highest level, and the one-time online submission of PT data. Lastly, we believe a key to modernizing the PT regulations is to fix the cytology PT program and allow electronic signatures with electronic PT submissions for regulated analytes.

The CAP also requests the opportunity to share with CMS all peer group data sets which will demonstrate comprehensively the effect of the proposed grading criteria. It is recognized that abridged data sets have previously been provided; however, we feel that provision of complete data sets will better allow CMS to gauge impacts prior to rule finalization. This would need to be done after the regular PT evaluation cycles during the year and may occur after the formal comment period has ended.

Detailed comments on the above topics are provided in the "Specific Comment" section of this letter. Also, comments on the proposed regulated analytes and performance criteria are provided in the "Proposed Analytes Appendices". The appendices are labeled as followed:

Proposed Analytes Appendices

Appendices	Subspecialty/sub-specialty
Appendix A	Microbiology
Non-Microbiology Regulated Analytes	
Appendix B	General immunology
Appendix C	Routine Chemistry
Appendix D	Endocrinology
Appendix E	Toxicology
Appendix F	Hematology
Appendix G	Immunohematology



Cytology PT

The CAP appreciates CMS's efforts to ensure and protect women's health. However, the CAP believes that the current regulation continues to demonstrate the problems with embedding professional standards into federal regulations and fails to achieve the stated objective. In short, CMS efforts to regulate in this manner have resulted in a program that inadequately measures competency, is not supported by science, and does not support improved health outcomes. Therefore, we urge you to consider meaningful alternatives.

The CAP asked an expert panel of members to review the current proficiency testing model and to develop an alternative model of Cytopathology PT. This panel felt that there is no proven efficacy for requiring annual individual PAP PT but does make the distinction that individuals interpreting cervical cytology specimens be required to participate in gynecologic interlaboratory educational programs annually. This participation would be monitored by each laboratory and remediation for missed challenges would occur as per laboratory policies for competency assessment. Records of participation and any additional education and remediation for those individuals missing challenges in these educational programs could be verified during laboratory accreditation site visits. Individually mandated gynecologic proficiency testing, if necessary, could occur no more often than every three years. Data from 2005 to present show that individuals who are already competent do not have these skills change in a short time period. Individuals evaluating cervical cytology specimens in the U.S. have been performing extremely well in the CMS-mandated gynecologic proficiency tests over the past several years.

Electronic signature

The CAP requests that CMS permit the use of verified electronic signatures to attest the review and approval of both PT results and evaluations, consistent with the Electronic Signatures in Global and National Commerce Act and in accordance with the Government Paperwork Elimination Act¹. The Act specifically states that electronic records and their related electronic signatures are not to be denied legal effect, validity, or enforceability merely because they are in electronic form, and encourages Federal government use of a range of electronic signature alternatives. Moving to electronic transactions and electronic signatures can reduce transaction costs for the agency and its partners. Transactions are quicker and information access can be more easily tailored to the specific questions that need to be answered. As a result, data analysis is easier.

SPECIFIC COMMENTS

§ 493.801 (b). Declaration of Patient Reporting Practices

CMS is proposing that laboratories declare their patient reporting practices for organisms included in each PT challenge. The CAP opposes this proposal because we believe it is the

¹ GPEA, Pub.L. 105-277 Title XVII



inspecting agency's responsibility to review and act on laboratories patient reporting practices for organisms. The CAP agrees that laboratories must examine or test, as applicable, the PT samples it receives from the PT program in the same manner as it tests patient specimens. The PT Programs can include a statement in the PT kit instructions on behalf of the CMS that laboratories must report organisms at the highest level. However, CAP disagrees that laboratories should declare their patient reporting practices for organisms included in each PT challenge. As stated in the proposed rule, "PT programs should only gather this information as it is the inspecting agency's responsibility to review and take action if necessary". Gathering such information serves no purpose for the PT Programs as stated in the proposed rule that it is the responsibility of the inspecting agency to review and act if necessary.

§ § 493.801 (b), 493.911(b), 493.913(b), 493.915(b), 493.917(b). Reporting Microbiology Organisms

CMS states in the proposed rule "that 10% of the 36,777 laboratories (total of 3680 laboratories) are not reporting microbiology organisms to the highest level, and it would take 20 minutes for labs to fill the information out three times a year." In the March 1990 CLIA regulations extent classifications for microbiology laboratories were defined. The CAP attempted to implement these extent levels for PT grading. The extent classification requirements proved to be unimplementable due to the varied testing practices among participating laboratories. In the 1992 revised CLIA regulations, the Department of Health and Human Services (HHS) removed the extent classification definitions from the regulations presumably because of implementation was not possible. Since 1992, verifying that PT specimens are being tested to the same degree as patient samples has been the inspecting organizations' responsibility. Therefore, we oppose PT providers collecting this data and recommend no change to the current convention. Further, we believe that by verification of this aspect of testing being done through the inspecting agency, nuances of reporting can best be explained and understood in that forum.

§ 493.901(a). Peer-Group Minimum Requirement

CMS proposes to require that each HHS- approved PT program have a minimum of ten laboratory participants before offering any PT analyte. The CAP supports this but would like the agency to clarify that this proposal is applicable to regulated analytes only.

§ 493.493.901 (c)(6). Online Submission of PT Data

CMS proposes to add the requirement of PT programs limiting the participants' online submission of PT data to one submission or that a method be provided to track changes made to electronically reported results. The CAP opposes this requirement. Instead, the CAP urges CMS to not limit the electronic submissions prior to the PT event due date. The CAP believes that the proposed requirement will unnecessarily complicate the submission process, introducing potential obstacles and creating opportunities for errors. For example, there are many patient tests that are routinely batched and analyzed during different



days/shifts, and for proficiency testing specimens to be tested with the laboratory's regular workload, laboratories will require submission of those results as completed. Limiting the electronic submission to one time or alternatively having the PT provider collect the reasons for subsequent submissions will create an additional burden and confusion for laboratories, as well as significant costs to the PT providers to provide administrative support and update program functionality. The CAP recommends that the laboratory internally maintain documentation, as appropriate and warranted, for any updates to approved data."

§ 493.901(e). CMS On-Site Visits to PT Programs

CMS proposes to implement on-site visits to PT Programs by CMS staff. We support on-site visits from CMS officials.

§ 493.2 Assignment of Peer Group

CMS proposes define peer groups as a group of laboratories whose testing process uses similar instruments, methodologies, and/or reagent systems and is not to be assigned using the reagent lot number. PT programs assign peer groups based on their policies/procedures and not based on any manufacturer directions. We support this definition and believe PT programs should assign peer groups based on their policies and procedures.

§ 493.901(c)(8). Non-profit Status for PT programs

CMS proposes any contractor performing administrative responsibilities as described in this section and § 493.903 must be a private nonprofit organization or a Federal or State agency, or an entity acting as a designated agent for the Federal or State agency. We agree but believe clarification is needed. What activities does CMS consider administrative activities?

§ 493.903. Administrative Responsibilities

CMS proposes to disallow changes to submitted laboratory data and results for any proficiency testing event. We support this proposal but recommend the following language be added, "except in those instances where the laboratory has clearly demonstrated that the error was on the receiving end of the PT provider, therefore, a revision was warranted."

§ § 493.20 and 493.25. Waived Testing

CMS proposes to amend the regulations to reflect that if moderate and high complexity laboratories also perform waived tests, the laboratories are not required to enroll in PT for waived testing. However, if the laboratories elect to participate in PT, the laboratories must comply with all PT requirements as outlined in the regulations and are subject to PT referral sanctions. The CAP believes waived testing should be subjected to PT since no tests is so simple not to cause harm. Therefore, we believe CMS should encourage laboratories to participate in PT since it is a good indicator that can help laboratories identify potential problems. We remain concerned that CMS's intent to punish laboratories with draconian PT referral sanctions discourages laboratories from participating in PT. We encourage CMS to



consider imposing alternative sanctions against laboratories for any PT referral violations for waived testing.

§ § 493.911(b)(1), 493.913 (b)(1), 493.915(b)(1)...493.927(c)(1),493.931(c)(1). Ungradable Specimens.

The CAP seek clarification on CMS's intent to amend these provisions. CMS is proposing to amend these provisions to clarify that for the purpose of achieving consensus, PT programs must attempt to grade using both participant and referee laboratories before determining that the sample is ungradable. CMS believes this change will enhance consistency among the PT programs when grading samples. The current regulations noted above allow for scoring either with participants or with referees before calling a sample ungradable. The CAP interprets that if there is no participants' consensus, a challenge must be graded by referee consensus. If there is no consensus either by the participants or the referees, only then, a specimen is considered ungradable.

Thank you for the opportunity to submit these comments. The CAP looks forward to working with the CMS to ensure quality of clinical laboratory testing by modernizing the PT regulations. Please direct questions on these comments to Helena Duncan at (202) 354-7131 or hduncan@cap.org.

Closing,

R. Bruce Williams, MD, FCAP
President



**CAP Comments to the
CMS Proposed CLIA Regulated Analytes
Appendices**



Appendix A – Microbiology

§ 493.911 (a) Bacteriology

CMS Proposal: (a) 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 provided to the laboratory at approximately equal intervals per year. The samples may be provided to the laboratory through mailed shipments. The specific organisms included in the samples may vary from year to year.

- (1) The annual program must include, as applicable, samples for:
 - (i) Gram stain including bacterial morphology;
 - (ii) Direct bacterial antigen detection;
 - (iii) Bacterial toxin detection; and,
 - (iv) Detection and identification of bacteria which includes one of the following:
 - (A) Detection of growth or no growth in culture media;
 - (B) Identification of bacteria; and
 - (v) Antimicrobial susceptibility or resistance testing.

CAP Response: The CAP supports the addition of bacterial toxin detection; but we would like clarification on the following:

- ***Bacterial toxin detection***
 - ***Clarify bacterial toxin detection. Does this include other toxins, such as, Shiga toxin or only C. difficile toxin?***
 - ***Clarify whether bacterial toxin detection by molecular methods can be used to fulfill PT requirements for bacterial toxin detection.***
 - ***Clarify whether molecular methods can be used to fulfill PT requirements for bacterial detection and identification.***
- ***Detection of growth or no growth in culture media***

Clarify whether detection of growth or no growth in culture media applies to all Microbiology specialty/sub-specialty programs. This may be adequate for sources such as urine, however, from sterile sites or from sites that contain normal flora such as throat cultures, reporting just growth or no growth are not appropriate responses, and are not of any clinical value to the clinicians.

§ 493.911(a)(2) Bacteriology.

CMS Proposal: CMS proposed to decrease the required mixed cultures from 50 percent to



25 percent for culture challenges that require laboratories to report only the principal pathogen and those that require laboratories to report all organisms present.

CAP Response:

The CAP agrees with the proposal to decrease the required mixed cultures from 50 percent to 25 percent for culture challenges.

§ 493.911(a)(3)(iii) Bacteriology

CMS Proposal: (3) The content of an approved program must vary over time, as appropriate. The types of bacteria included annually must be representative of the following major groups of medically important aerobic and anaerobic bacteria, if appropriate for the sample sources:

- (vi) Gram-negative bacilli.
- (vii) Gram-positive bacilli.
- (viii) Gram-negative cocci.
- (ix) Gram-positive cocci.

CAP Response:

The CAP seek clarification on whether gram-negative cocci and gram-positive cocci include coccobacilli and diplococci (e.g. *Neisseria*, *Moraxella*, *Gardnerella*, and *Streptococcus pneumoniae*).

§ 493.911(a)(4) Bacteriology

CMS Proposal: For antimicrobial susceptibility or resistance testing, the program must provide at least two samples per testing event that include one Gram-positive and one Gram-negative organism that have a predetermined pattern of susceptibility or resistance to the common antimicrobial agents.

CAP Response:

The CAP seeks clarification on the term “resistance testing”. Does this mean molecular genetic testing for resistance markers? If so, does this only apply to FDA approved/cleared tests, since these are limited for most of these groups of organisms?

§ 493.911(b)(4) Bacteriology.

CMS Proposal: The performance criteria for Gram stain including bacterial morphology is staining reaction, that is, Gram positive or Gram negative and morphological description for each sample. The score is the number of correct responses for Gram stain reaction plus the number of correct responses for morphological description divided by 2 then divided by the number of samples to be tested, multiplied by 100.

CAP Response:

The CAP would like clarification on the following:



- ***Bacterial morphology responses for Gram stain. Is grading bacterial morphology reporting limited to cocci and bacilli, as indicated in 493.911(a)(3)(iii)?***
- ***If no, are detailed morphology responses such as clusters, chains, diplococci, coccobacilli etc. also gradable choices?***

§ 493.913 Mycobacteriology.

CMS Proposal: 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 provided to the laboratory at approximately equal intervals per year. The samples may be provided through mailed shipments. The specific organisms included in the samples may vary from year to year.

(1) The annual program must include, as applicable, samples for:

- (i) Acid-fast stain;
- (ii) Detection and identification of mycobacteria which includes one of the following:
 - (A) Detection of growth or no growth in culture media; or
 - (B) Identification of mycobacteria; and
- (iii) Antimycobacterial susceptibility or resistance testing.

CAP Response:

The CAP would like clarification on the following:

- ***Detection of growth or no growth in culture media – Growth or no growth in culture media is not an appropriate response to determine if mycobacteria are present. However, an appropriate response could be growth or no growth of acid fast bacilli.***
- ***Whether molecular methods can be used to fulfill PT requirements for detection and identification of mycobacteria.***
- ***Resistance testing in antimycobacterial susceptibility testing. Does this include molecular genetic testing for resistance?***

§ 493.913(a)(2) Mycobacteriology.

CMS Proposal: CMS proposed to decrease the mixed culture requirement from 50 percent to 25 percent.

CAP Response:

The CAP agrees with the proposal of at least 25 percent of the samples must be mixtures of the principal mycobacteria and appropriate normal flora.

§ 493.915 Mycology.

CMS Proposal: (a) 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 provided to the



laboratory at approximately equal intervals per year. The samples may be provided through mailed shipments. The specific organisms included in the samples may vary from year to year.

- (1) The annual program must include, as applicable, samples for:
 - (i) Direct fungal antigen detection;
 - (ii) Detection and identification of fungi and aerobic actinomycetes which includes one of the following:
 - (A) Detection of growth or no growth in culture media; or
 - (B) Identification of fungi and aerobic actinomycetes; and
 - (iii) Antifungal susceptibility or resistance testing.

CAP Response:

The CAP would like clarification on the following:

- ***Whether direct fungal antigen detection includes *Cryptococcus*, beta-D-glucan and galactomannan antigens.***
- ***Detection of growth or no growth in culture media. It is not clinically appropriate to only report growth without reporting to a level of yeast or mold. However, an appropriate response could be growth of yeast, growth of mold or specimen negative for fungi.***
- ***Whether molecular and mass spectrometry methods can be used to fulfill PT requirements for identification of fungi and aerobic actinomycetes.***

493.915(a)(2) Mycology.

CMS Proposal: CMS proposed to decrease the mixed culture requirement from 50 percent to 25 percent.

CAP Response: The CAP agrees with the proposal of at least 25 percent of the samples must be mixtures of the principal organism and appropriate normal background flora.

§ 493.915(a)(3)(c) Mycology.

CMS Proposal: The content of an approved program must vary over time, as appropriate. The fungi included annually must contain species representative of the following major groups of medically important fungi and aerobic actinomycetes, if appropriate for the sample sources:

- (iv) Yeast or yeast-like organisms;
- (v) Molds that include;
 - (A) Dematiaceous fungi;
 - (B) Dermatophytes;
 - (C) Dimorphic fungi;
 - (D) Hyaline hyphomycetes;
 - (E) Mucormycetes; and



(vi) Aerobic actinomycetes.

CAP Response:

The CAP would like clarification on what is included in dimorphic fungi as many fungi listed are of Biosafety Level III (BSL III). The Risk Management Profile of the CAP prohibits offering any PT challenge at BSL III. There are limited dimorphic fungi that are of BSL II.

§ 493.915(a)(4) Mycology.

CMS Proposal: For antifungal susceptibility or resistance testing, the program must provide at least two challenges per testing event that include fungi that have a predetermined pattern of susceptibility or resistance to the common antifungal agents.

CAP Response:

The CAP would like clarification on detecting resistance. There are no FDA cleared tests to detect anti-fungal resistance markers. However, there are methods to determine antifungal susceptibility, which are the MIC/MECs and zone diameters of disk diffusion susceptibility testing. The CAP disagrees with proposed requirement to provide at least two challenges per testing event that include fungi that have a predetermined pattern of susceptibility or resistance to the common antifungal agents. Extensive variability between breakpoints and test systems is evident from the results observed in the current CAP PT Surveys. There are very limited Candida species for which susceptibility or resistance can be determined by FDA-cleared test systems. Requiring additional susceptibility or resistance testing will not serve a purpose if challenges cannot be graded.

§ 493.917 Parasitology.

CMS Proposal: Program content and frequency of challenge. To be approved for proficiency testing in parasitology, the annual program must provide a minimum of five samples per testing event. There must be at least three testing events provided to the laboratory at approximately equal intervals per year. The samples may be provided through mailed shipments. The specific organisms included in the samples may vary from year to year.

(1) The annual program must include, as applicable, samples for:

- i. Direct parasite antigen detection; and
- ii. Detection and identification of parasites which includes one of the following:
 - A. Detection of presence or absence of parasites; or
 - B. Identification of parasites.

CAP Response:

The CAP would like clarification on if molecular methods satisfy PT requirements for identification?



§ 493.919 Virology.

CMS Proposal: 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. The specific organisms included in the samples may vary from year to year.

(1) The annual program must include, as applicable, samples for:

- (i) Viral antigen detection;
- (ii) Detection and identification of viruses; and
- (iii) Antiviral susceptibility or resistance testing.

CAP Response:

The CAP would like clarification on the following:

- ***If molecular methods satisfy PT requirements for viral antigen detection, detection and identification of viruses, and antiviral susceptibility or resistance testing?***
- ***Clarify resistance testing – does this include HIV drug resistance testing to protease and reverse transcriptase inhibitors?***
- ***If this also includes CMV resistance markers?***

The CAP disagrees with proposed requirement to provide at least two challenges per testing event that have a predetermined pattern of susceptibility or resistance to the common anti-viral agents. There are very few laboratories that perform anti-viral susceptibility testing – either phenotypic or genotypic. The CAP proposes requiring viral loads as they are clinically important.



Appendix B: General Immunology

§ 493.927 General Immunology.

CMS Proposal: CMS proposes to Anti-HBs, Anti-HCV, C-reactive protein (high sensitivity) as regulated analytes.

CAP Response:

- *The CAP agrees with the addition of C-reactive protein (HS) to the list of the regulated analytes. According to the AHA/CDC Scientific Statement on Markers of Inflammation and Cardiovascular Disease, the hs-CRP results should be expressed as mg/L only. The criteria should be changed to +/- 1 mg/L or 30% (greater)*
- *The CAP agrees with the addition of Anti-HBs, Anti-HCV to the list of regulated analytes.*
- *The CAP proposes raising the acceptable performance criteria of target values for IgA and IgE to 20% and 25% respectively.*



Appendix C: General Chemistry

§ 493.931 Routine Chemistry - Criteria for acceptable performance

CMS proposal: For glucose, CMS proposes acceptable performance criteria of target value $\pm 8\%$ (greater).

CAP Response:

The limit was omitted. The CAP proposes to add ± 6 mg/dL in addition to $\pm 8\%$.

CMS Proposal: For Carbon dioxide – CMS proposes acceptable performance criteria of target value $\pm 20\%$.

CAP Response:

The CAP proposes to add ± 3 mmol/L in addition to $\pm 20\%$.

CMS proposal: For Hemoglobin A1c, CMS proposes acceptable performance criteria of target value $\pm 10\%$.

CAP Response:

The CAP offers for your consideration, two sets of criteria for Hemoglobin A1c. One for commutable (matrix effect free) whole blood material, where the criteria should be $\pm 6\%$. And the second criteria for other matrix, where the acceptable performance could be target value $\pm 10\%$. The CAP can accept use of $\pm 10\%$ for non-commutable material so long as the accuracy-based criteria of 6% is simultaneously implemented. Currently, the criteria for acceptable performance is target value $\pm 6\%$. The field methods have significantly improved.

CMS proposal: For Prostate Specific Antigen, total, CMS proposes acceptable performance criteria of target value ± 2 ng/dL or 20% (greater).

CAP Response:

The concentration should be in ng/mL.

CMS Proposal: For Troponin I, CMS proposes acceptable performance criteria of target value ± 0.9 ng/mL or 30% (greater).

CAP Response:



The availability of high sensitivity (HS) Troponin I was not taken into account when the criteria were reviewed. The CAP recommends adding HS Troponin I and it be reported in ng/L. Applying +/- 900 ng/L (0.9 ng/mL) is not useful for HS Troponin I. CAP recommends using +/- 30% or +/- 7 ng/L (whichever is greater) as criteria for acceptable performance for HS Troponin I.

CMS Proposal: For Troponin T, CMS proposes acceptable performance criteria of target value +/- 0.2 ng/mL or 30% (greater).

CAP Response:

The availability of high sensitivity (HS) Troponin T was not considered when the criteria were reviewed. The CAP recommends adding HS Troponin T and it be reported in ng/L. Applying +/- 200 ng/L (0.2 ng/mL) is not useful for HS Troponin T. CAP recommends using 30% or +/- 10 ng/L (whichever is greater) as criteria for acceptable performance for HS Troponin T.

§ 493.931 (b) CK-MB Isoenzymes.

CMS Proposal: CMS proposes a technical change to the description for creatine kinase isoenzymes to be CK-MB isoenzymes, which may be measured either by electrophoresis or by direct mass determination, for example using an immunoassay.

CAP Response:

The CAP proposes that CK-MB Isoenzymes should be analyzed using immunochemical methods, preferably monoclonal antibody assays. CK Isoenzyme assays which use electrophoretic methods should be discontinued and discouraged.

CMS Proposal: For CK-MB isoenzymes, CMS proposes acceptable performance criteria of target value +/- 25% (greater).

CAP Response:

The limit was omitted. At +/-25%, the low target specimen has consensus of 78%. The CAP proposes to add +/- 2 ng/mL in addition to +/- 25% (greater).

CMS Proposal: For Bilirubin, Total, CMS proposes acceptable performance criteria of target value +/- 20%.

CAP Response:

The CAP proposes to replace proposed +/- 20% with +/- 15% or 0.4 mg/dL, whichever is greater.



Appendix D: Endocrinology

CMS Proposal: For Human Chorionic Gonadotropin, CMS proposes acceptable performance criteria of target value \pm 18% or positive or negative.

CAP Response:

The CAP proposes to add \pm 3 mIU/mL in addition to \pm 18%.

CMS Proposal: For T3 Uptake, CMS proposes acceptable performance criteria of target value \pm 18%.

CAP Response:

The CAP proposes to remove T3 uptake from the list of regulated analytes due to lack of clinical utility.

CMS Proposal: For Vitamin B12, CMS proposes acceptable performance criteria of target value \pm 25%.

CAP Response:

The CAP proposes to add fixed limit in addition to \pm 25%. At \pm 25%, the consensus drops significantly for low target challenges from 98% to 61%. At \pm 25% or \pm 30 pg/mL, the consensus was 77%.



Appendix E: Toxicology

§ 493.937 Toxicology

CMS Proposal: CMS proposes to add Acetaminophen, Salicylate, and Vancomycin as regulated analytes.

CAP Response:

- ***The CAP agrees with the addition of new drugs and proposes immunosuppressant drugs be added as regulated analytes. Those drugs include everolimus, sirolimus, tacrolimus, and methotrexate. Immunosuppressant drugs are dose dependent and proper dosing/monitoring prevents severe/serious complications.***
- ***Phenytoin and Vancomycin concentrations should be in mcg/mL.***
- ***Suggest adding Fixed concentrations of +/- 2 mg/dL in addition to +/- 15% for Salicylate. The consensus drops dramatically for low target challenges from 98% to 80% with proposed criteria of +/-15%.***

CMS Proposal: For Lithium, CMS proposes acceptable performance criteria of target value +/- 15%.

CAP Response:

The CAP suggests that the fixed limit of +/- 0.3 mmol/L be added in addition to target value +/- 15%.

CMS Proposal: For blood lead, CMS proposes acceptable performance criteria of target value +/- 10% or 2 mcg/dL (greater).

CAP Response:

The CAP believes the current criteria should be retained since the tighter criteria will result in more failures for certain platforms.

CMS Proposal: CMS proposes to remove ethosuximide, quinidine, primidone, and procainamide (and its metabolite, N-acetyl procainamide) from the list of regulated analytes.

CAP Response:

The CAP agrees with removal of ethosuximide, quinidine, primidone, and procainamide (and its metabolite, N-acetyl procainamide) due to the limited clinical utility and advent of newer and more targeted drug therapy.



Appendix F: Hematology

§ 493.941 Hematology

CMS Proposal: CMS proposes to require laboratories that perform both cell counts and differentials to conduct PT for both (that is, the “or” would be changed to an “and”)

CAP Response:

The CAP would like clarification on whether it would require reporting of PT for both manual and automated flow through differentials for those platforms that can report flow through differentials.

CMS Proposal: For cell identification, CMS proposes acceptable performance criteria for cell identification of 80% or greater consensus on identification.

CAP Response:

The CAP agrees with the proposed change that will bring consistency in both consensus and performance of acceptability on identification.

CMS proposal: For white blood cell differential, CMS proposes acceptable performance criteria of target $\pm 3SD$ on the percentage of different types of white blood cells in the sample.

CAP Response:

The CAP proposes to add ± 1.0 (whichever is greater) for low target values/absolute values (i.e.) basophils.

CMS Proposal: For leukocyte counts, CMS proposes acceptable performance criteria target of $\pm 5\%$.

CAP Response:

The CAP proposes changing target to $\pm 10\%$. At 5%, there will be significant failures on some platforms.

CMS Proposal: For hematocrit/hemoglobin, CMS proposes acceptable performance criteria target of $\pm 4\%$.

CAP Response:

With proposed target, the CAP believes there will be some increase in failures for some platforms.



CMS Proposal: For International Normalized Ratio (INR), CMS proposes if a laboratory reports prothrombin time in both INR and seconds, the INR should be reported to the PT provider program.

CAP Response:

The CAP proposes that INR specifically be listed as standalone Regulated Analyte.



Appendix G: Immunohematology

§ 493.959 Immunohematology

CMS Proposal: For unexpected antibody detection CMS proposes CMS proposes acceptable performance criteria of 100%.

CAP Response:

The CAP disagrees with the change in requiring 100% for performance criteria with regards to unexpected RBC antibody detection [i.e., RBC antibody screening]. We agree that “it is critical for laboratories to detect any unexpected antibody when cross-matching blood” –assuming this is referring to clinically significant RBC antibodies. However, we are concerned with the proposed change for the following reasons:

- 1. To our knowledge, immunohematology is the only laboratory section in which 100% performance in PT is required for any regulated analytes, namely ABO group, D (Rho) typing and compatibility testing. Extending this requirement to another test presumes that test must be extremely accurate.*
- 2. However, proficiency testing challenges for unexpected antibody detection contain both positive and negative unknown specimens, like regular laboratory specimens, so that laboratories do not know what result is expected for each specimen. The new proposed rule does not separate false positive results from false negative results. A false positive antibody detection result would not cause harm to a patient but would result in unsatisfactory PT performance under the proposed rule.*
- 3. As with any sensitive screening test, false positive results for unexpected antibody detection occasionally occur and should be expected from time to time.*
- 4. There are several different FDA-approved testing methodologies being used for unexpected antibody detection. Some RBC antibodies react more strongly in one method versus another method. The proposed change increases the possibility of method-dependent unsuccessful performance in PT.*



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