Documentation List to accompany CLIA application, CMS-116, for Toxicology Laboratories

Please provide responses and documents for the following questions. If the information is not provided, the application will not be processed.

1. Is this laboratory a pain clinic, only testing their patients or a reference laboratory, taking in patients from throughout the state or country?
   1. Pain clinic \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
   2. Reference lab \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
2. Is your laboratory performing only screening, only confirmatory, or both?
   1. Screening (qualitative)\_\_\_\_\_\_\_\_\_\_\_
   2. Confirmatory \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
   3. Both \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
   4. List which instrument(s) are for screening, confirmatory or both
3. Please submit credentials for the laboratory director:
   1. Current medical license (physicians)
   2. Grade transcripts and/or diplomas (PhD)
   3. Board Certification (pathologists, PhD)
   4. Documentation of clinical /work experience
4. If requesting a Certificate of Accreditation, please provide confirmation of enrollment with an accreditation organization.
5. Enrollment in Proficiency Testing for each analyte and specimen type.
6. What date does the lab anticipate to begin patient testing?\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
7. Has staff been hired? If not, anticipated date. \_\_\_\_\_\_\_\_\_\_\_\_\_
8. Please list the instrument(s) along with the reagents.   Please provide documentation.
   1. Are the instruments and reagents purchased?
   2. Are the instruments and reagents currently in-house?
      1. If no, what is the date of delivery?
   3. What is the specimen type: serum\_\_\_\_\_\_\_ urine\_\_\_\_\_\_\_\_ oral fluids\_\_\_\_\_\_\_\_\_
   4. How many of each instrument will be used in the lab? Specify qualitative and/or quantitative instrument and type of specimen on each analyzer
   5. Package Inserts and instrument manual(s)
9. The instruments and reagents will determine which studies to be performed: verification or establishment studies.
   1. Establishment studies must be performed on the following: non-FDA approved instruments/reagents; modified FDA approved instruments/reagents, research-only or forensic instruments/reagents, etc.
      1. Any modification(s) made to method(s)/instrument(s) are defined as a Laboratory Developed Test. The laboratory must perform the studies as if the laboratory was the manufacturer.
      2. CLIA regulations: §493.1251; §493.1253 (b)(2) and b(3);
      3. Exact Regulation text and interpretive guidelines can be found at <http://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Downloads/apcsubk1.pdf>
   2. Verification studies must be performed on either moderate or high complexity tests that are FDA approved with no modification to method or reagents.

**Establishment Study Requirement**:

1. Please provide documentation for:
   1. Lab must have a developed plan for conducting studies.
   2. Were these studies performed in your laboratory?
   3. Who performed your studies? Your laboratory or the instrument manufacturer or laboratory consultant service?
   4. Were these studies performed on your instruments/reagents using laboratory staff?
   5. Studies include:
      1. All performance specifications must be obtained from clinical scientific literature for toxicology (research or forensic may not be used).
      2. Provide the scientific literature for establishment of cut-off points for each test method/instrument/specimen type.
      3. Specimen Collection and handling
         1. Stability of the specimen
         2. Determine allowed time span between sample collection and analysis
         3. Studies should be conducted under real sample storage conditions
            1. Affected by storage, chemical properties of the drug, matrix, and container
            2. Long and short term storage (frozen, then thawed to room temperature, freeze thaw cycles)
            3. Assess degradation of samples based on elevated temperature, humidity or light,
            4. Assess degradation of the sample based on human intervention; tests include pH, creatinine, etc.
            5. Please include studies for storage of samples during transportation of sample as well as storage requirements for testing.
         4. Rejection Criteria
         5. Client service manual
      4. Establishment of quality control parameters. Based on clinical scientific literature for toxicology, acceptance rates for quality control is 20%, not 30%.
         1. Qualitative
         2. Quantitative
         3. Define quality control parameters; and how the system will be monitored over time.
         4. Corrective action policies and remediation of patient for failed quality control
      5. Dilution Recovery and Linearity
      6. Precision – run-to-run; within-run; reproducibility
      7. Accuracy – to include extraction phase
      8. Specificity/Selectivity – Interference
      9. Carryover studies
      10. Sensitivity-Limit of Blank (analytical sensitivity)
          1. Limit of Quantitation (LOQ)
          2. Limit of Detection (LOD)
      11. Linearity and reference range
          1. Require clinical toxicology scientific literature for cut-off points
2. A signed and dated summary of acceptance is required by the lab director.  What were the performance acceptability criteria and did your studies meet the criteria. The laboratory director must approve the methods prior to patient testing.   A program such as EP Evaluator should be used to evaluate the data.
   1. Additionally, this full review/summary of the work completed should represent the timeline and data analysis, as it helps better show what actually took place during this verification and what the conclusions were made by the laboratory.
   2. If the test is laboratory developed, the reagents/supplies in use most likely have manufacturer's specifications. This information should be considered when developing the procedure, and provided as part of the complete study.

**Verification Study Requirements:**

1. Performed on either moderate or high complexity tests that are FDA approved. Should include the following:
   1. Were these studies performed in your laboratory?
   2. Were these studies performed on your instruments/reagents using your staff?
   3. Who performed the studies? Your laboratory staff or the instrument manufacturer or a laboratory consultant service?
   4. Studies to be performed:
      1. Verification data of manufacturer’s instructions for Specimen Collection and handling
         1. Rejection Criteria
         2. Client service manual
      2. Establishment of quality control parameters. Based on clinical scientific literature for toxicology, acceptance rates for quality control is 20%, not 30%.
         1. Qualitative
         2. Quantitative
         3. Define quality control parameters; and how the system will be monitored over time.
         4. Corrective action policies and remediation of patient for failed quality control
      3. Precision – run-to-run; within-run; reproducibility
      4. Accuracy – to include extraction phase
      5. Carryover studies
      6. Linearity and reference range
         1. Require toxicology clinical scientific literature for cut-off points
2. A signed and dated summary of acceptance is required by the lab director.  What were the performance acceptability criteria and did your studies meet the criteria. The laboratory director must approve the methods prior to patient testing.   A program such as EP Evaluator should be used to evaluate the data.
   1. Additionally, this full review/summary of the work completed should represent the timeline and data analysis, as it helps better show what actually took place during this verification and what the conclusions were made by the laboratory.
3. Have staff been hired and trained?
4. When resubmitting information, please remember to submit:
   1. Package inserts for test kit methodology, reagent, quality control (etc.)and/or manufacturer's instructions, cut-off points, etc.