Overview of the College of American Pathologists (CAP) inspection process for assisted reproductive technology (ART) laboratories

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Abstract
The College of American Pathologists (CAP) serves over 300 reproductive laboratories in four countries. The goal of CAP is to improve laboratory conditions for the patient and the personnel who work in the laboratory. CAP accomplishes this goal through proficiency testing and inspections. Qualified inspectors will arrive, at a prearranged time, to inspect a laboratory. They will review procedure manuals, inspect reagents, instruments and equipment, and verify calibration of instruments/equipment. In addition, they will inspect the laboratory to insure the safety of the patients, their gametes, and the safety of the laboratory personnel. A summary report will be generated by the inspectors as to their findings with written reports given to the laboratory director and to CAP. It is through such organizations as CAP that the quality of patient results and the safety and well-being of the patient and the laboratory personnel have been improved over the years.

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Introduction
The College of American Pathologists (CAP) was established in 1961 and has provided a solid foundation for ensuring excellence in patient safety and compliance. During this half century, field teams with mixed language capabilities have been established in the Middle East, South America, India, Europe, Mexico, and other regions. These teams cover 45 different countries and over 7,000 laboratories, including 300 international laboratories.

More specifically, CAP inspects over 300 reproductive laboratories located in the United States, Germany, Saudi Arabia, and Russia. It is for the people in these laboratories and future laboratories that this manuscript is written, with the hope of explaining the inspection process.

Pre-inspection

Educational Resources
The CAP organization offers a variety of educational resources for its members. These resources include proficiency testing, on-site inspections, interim self-inspections, and technical/regional resources. This organization also offers resources in the form of documents/manuals, seminars, a website and scientific resource committees.

Proficiency Testing
Proficiency testing allows the personnel in one laboratory to compare their results of an unknown specimen to those of other laboratories performing the same procedure. In the case of reproductive laboratories, personnel can evaluate their proficiency with semen analyses and, more recently, embryo grading. If external tests are not available, however, split sample testing or testing of
known specimens are accepted as alternative methods of determining competency.

To make the proficiency test reflect the actual performance within the laboratory, several procedures must be followed. The proficiency test must be integrated with the routine workload and must be rotated among technicians. Furthermore, once the comparisons have been made between a laboratory and the summary of all laboratories, the laboratory director must follow through with corrective actions, if his/her laboratory is out of compliance. The laboratory director must document the corrective actions.

**Quality Control**

There are requirements for every analyte that undergoes an analysis in a laboratory. There must be a written procedure for each of these analytes. In addition, there must be a documented system for every analyte instrument. The system must include valid target ranges that have been defined. Furthermore, there must be documentation of a review and corrective actions that are performed, when necessary.

An example of quality control of an analyte is the evaluation of the instruments needed to perform a semen analysis. When semen analyses are performed in a 37°C environment, all instruments used in the analysis must be maintained at approximately this temperature. This would include the incubator in which the specimen is placed until it has undergone complete liquefaction. Heating blocks and microscopes that have heating elements also must be maintained at this temperature. Any instruments that are out of the acceptable range must be corrected and the correction documented. The documentation must be reviewed, signed and dated by the laboratory director or his/her designee.

**Procedure Manual**

The procedure manual must cover pre-analytic, analytic and post-analytic methodology. Items that need to be included in each procedure are the principle of the procedure, specimen requirements, and media/reagents to be used in the procedure. In addition to these items, the procedure needs to cover other supplies that are needed, such as the calibration procedures for the instruments, quality control issues associated with the procedure, and the procedure itself. Furthermore, calculations, normal values, and how results are to be reported need to be included for each analyte evaluated. Finally, hazardous waste disposal, procedural notes, and references also must be included for each method.

An annual review of the procedure manual must be performed by a knowledgeable person. In addition, technical staff who perform the procedures must be familiar with each of the procedures.

**Reagents**

Reagent labeling and testing must be performed. The label on each reagent container must include the content and quantity/concentration/titer. In addition, the label must contain the storage requirements, date of preparation and reconstitution as well as the expiration date. Furthermore, precautionary notes related to hazards must be included on the label. Finally, validation tests and acceptable criteria must be documented.

**Instrument/Equipment Maintenance**

Instruments/equipment must be maintained in order to perform the procedure accurately. This includes checking automatic pipettors for accuracy and reproducibility. Thermometers must be certified or checked and tolerance limits for all temperature-dependent equipment must be maintained. In addition, centrifuges must be checked for speed verification.

Calibration of instruments and equipment must be performed according to manufacturer’s instructions and must be performed at least every six months to insure accuracy and reproducibility. Other times that calibration must be performed are when reagents are changed, when indicated by quality control data, after major maintenance, or when recommended by the manufacturer. The calibration/verification materials can be provided by 1) the manufacturer, 2) proficiency testing material that has been validated, or 3) previously tested patient material. The
calibration/verification also can be performed with the use of standards, reference materials, or calibrators.

**Competency Assessment**
Each technician that performs an analysis on a specific analyte must meet minimum standards to perform the assay. Evaluations must be specific for each job description. Records must indicate what, how and when skills were assessed. If problems are identified, retraining and reassessment must occur.

**Safety**
Patient safety, as well as laboratory safety, is at the highest level of concern for CAP, with patient and specimen identification being essential. If errors are found, they must be corrected. Patient and specimen safety must be integrated and coordinated throughout the organization. As for the safety of laboratory personnel, hazardous and flammable reagents must be handled appropriately. This includes biohazardous materials and radioactive materials. Items such as air quality, storage space, and ergonomics also must be addressed.

**Laboratory Personnel**
Positions within the laboratory include the laboratory director and the support staff. The laboratory director must be a physician or a doctoral scientist in the field of biological, physical, or chemical science. This individual must have at least two years of documented experience in the reproductive laboratory and be familiar with total quality management, inspections, accreditation, licensing procedures, and detailed knowledge of assisted reproductive technology and andrology. The support staff consists of technical supervisors, general supervisors, and technicians. These positions have various levels of education and skill requirements.

**Standards and Checklists**
Standards are the broad principles that the laboratory must meet in order to achieve accreditation. The checklists provide detailed requirements that inspectors use to determine whether or not the laboratory meets the standards. The checklists guide the inspector by assisting with the interpretation of the Laboratory Accreditation Program (LAP) standards. The checklists provide guidelines for development of laboratory policies and procedures and help to ensure accurate and reliable test results. Furthermore, the checklists ensure a focus on patient safety as well as laboratory safety. For reproductive laboratories, there is a team leader checklist, a laboratory general checklist, and an embryology and andrology checklist. The checklists are constantly being revised by CAP to incorporate new technology, eliminate outdated technology, and allow for more appropriate technology.

**Inspection**

**Assignment and Preparation**
While CAP inspections are normally conducted as unannounced inspections, international laboratories and reproductive laboratories are prearranged. In the case of foreign laboratories, prearrangements must be made for travel, which may include obtaining visas. Visas require laboratory officials in international facilities to agree to accept foreign visitors and must be confirmed by their government. As for prearranging inspections of reproductive laboratories, these are often small laboratories that require all members be present if procedures are being performed, thus not allowing time for laboratory personnel to be distracted by outside inspectors.

Laboratory inspectors will be sent a packet of information from the CAP office months prior to the inspection to allow sufficient time to prepare for the inspection. Inside the packet will be laboratory demographics that provide information about the laboratory personnel and their organization plan along with a curriculum vitae of the laboratory director. The information also contains the annual test volume as well as the previous on-site inspection report for the laboratory. In addition, the packet contains the activity menu, which describes the tests and methods in each section, and the proficiency testing required. Furthermore, within the packet will be a list of the instruments that are in the laboratory, a floor plan of the laboratory and CAP checklists for each section of the laboratory.
**Inspection Team**

The inspection team consists of individuals that are of equal standing to those in the laboratory. These are laboratory professionals who have first-hand knowledge of how reproductive laboratories should operate. These individuals should be able to offer constructive feedback to the personnel who work in the laboratory being inspected. The size of the laboratory usually dictates the number of inspectors needed for the inspection team.

**The Day of the Inspection**

The actual inspection usually only takes a day for most reproductive laboratories, unless the laboratory is large, is undergoing its initial inspection, or has a history of numerous deficiencies. The inspection will include a review of the procedure manuals, an inspection of reagents, instruments and equipment, and verification of calibration of the instruments/equipment. In addition, there will be an inspection of the laboratory to insure safety of the patients, their gametes, as well as the laboratory personnel.

When reviewing the procedure manual, the inspector will be looking for four major points. First, the manual must show annual review by those who perform the procedures as well as reviewed by the laboratory director. Second, the tests that are performed must be scientifically valid and third, clinically relevant. Finally, the fourth point is that the practice must match the policy and procedure.

As for the reagents used in the reproductive laboratory, they must meet specific requirements. The reagents cannot be used if they are past the expiration date. Each new reagent lot must show proof of being validated. If the reagents are placed in a second container, the second container must be labeled appropriately. All chemicals which reside in the laboratory must be labeled appropriately. Finally, all reagents must be store under appropriate conditions.

Instruments and equipment must undergo scrutiny to insure that they operate properly and pass appropriate calibration and verification tests. If glassware is used, it cannot be chipped or cracked. Thermometers must be certified and recertified when appropriate. Equipment maintenance charts must be reviewed and corrective action documented. The maintenance/repair records must be kept for the life of the instrument. Manufacturer’s guidelines must be followed and corrective action documented. In addition, normal ranges for each instrument must be established and adherence verified. Finally, patient data generated from these instruments/equipment, must fit within an acceptable range, with dilutions being performed, if necessary.

**Safety**

Laboratory safety is a high priority for CAP. When an inspector reviews the laboratory, this individual will observe proper warning labels for chemicals and how they are stored. The inspector will determine if exits are blocked or not. In addition, the inspector will evaluate fire extinguisher locations and determine the last inspection date for each of the extinguishers. Furthermore, alarms and evacuations routes will be studied. Appropriate signages for biohazardous materials as well as radioactivity will be determined. Likewise, electrical checks, availability of personal protective equipment and eyewashes must be convenient. In addition, lighting, space and availability of material safety data sheets will be evaluated.

**Summation of the Inspection**

At the end of the inspection, a summary report will be filled out by the inspection team and discussed with the laboratory director and others whom he/she directs to hear the results. It is here that deficiencies are reviewed again (they should be discussed as the inspection progresses and not left for the laboratory personnel to hear them for the first time at the summary meeting) with the laboratory director and his/her team.

When an inspector finds an incident that needs to be addressed, he/she can cite the laboratory for a Phase I or a Phase II deficiency or he/she can make a recommendation. A Phase I deficiency may not seriously affect patient care or the safety/welfare of the laboratory personnel. This type of deficiency must be addressed
by the laboratory, but supporting documentation of that correction need not be provided to CAP. If the laboratory receives a Phase II deficiency, the incident may have a serious affect on patient care or may seriously affect safety/welfare of the laboratory worker. These types of deficiencies must be corrected with documentation of the corrective action, prior to being accredited. However, the incident that needs to be addressed might only require a recommendation that some action be considered. For example, the laboratory in question currently might have sufficient storage space, but if their laboratory is undergoing growth, they will need to consider investigating future storage space.

There are two parts to the Summation report – Part A and Part B. Part A includes the general observations and conclusions along with a summary of the laboratory's overall quality and any confidential feedback that the inspectors have for CAP. Part B contains the list of deficiencies and the recommendations. A copy of Part B is to be left with the laboratory director at the time of the inspection.

The deficiencies must be addressed, in writing, by the laboratory director. If a deficiency requires a new or revised policy or procedure, it must be submitted to CAP for their approval. If there is a deficiency in how documents are being reviewed, they must be submitted and show evidence of review. If new equipment or instruments must be ordered to correct the deficiency, purchase orders and photographs must be submitted to CAP. Once these documents have been reviewed by CAP, an accreditation decision will be made.

Conclusion

The College of American Pathologists has a long-standing record for improving laboratory conditions for the patient as well as the laboratory personnel. It is through organizations such as CAP that the quality of patient results has been greatly improved over the years. Adherence to CAP standards by laboratory personnel not only improves quality of patient care, but improves the safety and well-being of the patient and the laboratory personnel that take care of the patient.