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Development of External Quality Assurance Programs for Biorepositories

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Introduction

Differences in biorepository methods and practices can result in sample variation that has the potential to impact research results derived from those samples. The establishment of common quality assurance (QA) and quality control (QC) tools has been difficult due to the wide variety of specimens and intended uses of the collections in biorepositories.

The development and adoption of the ISBER *Best Practices for Repositories* (*Best Practices*), the latest edition of which was published in *Biopreservation and Biobanking* this past April, has been an important advancement in the field. *Best Practices* provides guidance on management practices and technical aspects, and addresses repository development, facilities and equipment, cost management, security, and training, while taking regulatory compliance and the ethical, legal, and social issues relevant to repositories into account.

Although many biorepository institutions have adopted these *Best Practices*, dissemination of information on sample preparation methods and sample quality assessment practices across biorepositories remains a significant issue for the repository community. External quality assurance (EQA) programs are utilized throughout the world to control interlaboratory variation in the clinical diagnostic arena and are excellent models to apply for standardization of key quality assessment processes in the biorepository industry.

Common Quality Practices

Most organizations today have established quality management systems designed to provide early indications of problems via a continuous improvement environment. The quality management systems ensure that actual practices conform to established management and standard operating procedures using continual monitoring. In addition, quality management takes process outputs and customer feedback into consideration to improve organizational performance.

While an effective quality management system (QMS) is essential in ensuring consistent quality practices within an organization, the ideal QMS would also incorporate comparisons of practices across different organizations serving the same customer base. This comparison requires the application of standards and tools that can be applied in a uniform manner over multiple organizations.

Certification and Accreditation Programs

One mechanism for EQA is certification or accreditation to a standard by an independent, external institution. Repositories generating diagnostic results that are returned to an individual participant are governed under state or federal regulations in most countries [e.g., Clinical Laboratory Improvement Amendments (CLIA) in the United States]. Many repository organizations fall outside the purview of the regulatory agencies as they focus on pre-analytical activities and do not produce diagnostic results.

One voluntary standard applicable to all customer-focused organizations is the International Organization of Standards' *ISO 9001, Quality Management Systems—Requirements*. This standard outlines the requirements needed to ensure an organization provides consistent quality products or services to their customers while striving to meet or exceed their expectations. Another common set of guidelines applied to biorepositories is ISO/IEC 17025, General Requirements for the Competence of Testing and Calibration Laboratories. However, as the name implies, 17025 standards only apply to biorepositories generating test results.

France was the first country to generate a national standard for biorepositories, NF S 96-900. This is a voluntary standard, but any repository that is receiving funding from the French government for its biorepository activities must be certified to this standard.

The College of American Pathologists (CAP) recently launched its Biorepository Accreditation Program (BAP). The goal of the CAP BAP is to improve and standardize the collecting, processing, storing, distributing and cataloguing of biospecimens while ensuring the quality of those biospecimens (e.g., serum, urine, blood, and tissue) and genetic material (e.g., RNA and DNA) remains at the highest possible level.

Proficiency Testing

Proficiency testing (PT), as defined in ISO/IEC 17043, Conformity Assessment—General Requirements for Proficiency Testing, provides a powerful tool to help laboratories

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demonstrate competence in performing an assay. PT enables laboratories and repositories to monitor their QC tests over time, identify longer term trends and consider any necessary corrective actions. This common EQA tool has been used effectively for several decades in the diagnostic laboratory testing arena.

ISBER recently developed a PT program focused on biospecimen characterization. The overall PT program develops, coordinates, and implements individual PT programs for QC assays and biomolecular characterization of biospecimens. The individual PT programs include assays performed by repositories and/or end-users for the validation or characterization of biospecimens and their cellular and molecular derivatives. The ISBER PT program allows biorepositories to assess the accuracy of their quality control assays and their biospecimen characterization and to compare results with other laboratories around the world. The global comparison allows identification of testing problems that may be related to individual staff performance or to calibration of the instruments used in biospecimen quality control.

Like other diagnostic assay PT programs, a fundamental mission of the ISBER PT program is education. The program provides guidance to biorepositories on appropriate remedial action for accurate testing. In addition, the PT program is a necessary External Quality Assessment tool for biorepositories that wish to seek accreditation (ISO 17025, CAP, or equivalent).

ISBER's PT Program launched in 2011 with DNA Quantification and Purity Assessment and RNA Integrity Assessment schemes. This year, ISBER expects to add schemes to assess Cellular Viability, Tissue Histology, and/or Tissue Antigenicity. Broad participation by individual biorepositories is essential to the effectiveness of these PT programs.

Conclusion

In the past year there have been major advancements in the EQA tools available to the repository industry. Biorepository-specific accreditation programs and PT programs have been established and are available for incorporation into repository quality management systems. Adoption of these programs throughout the biorepository community will allow true standardization of quality practices. Specimens collected, processed, characterized, stored and disseminated using these standardized practices will be more consistent and will enable new discoveries by the research community.