WHITE PAPER

Benefits of metabolomics-based quality control of human plasma samples for clinical biobanking

metanomicshealth

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Content

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Executive Summary

Proper specimen collection and biobanking are recognized as critical success factors in the identification of clinically useful biomarkers of disease and disease progression, discovery of new drug targets, and understanding the underlying mechanisms of diseases.

Researchers continue to report that there are problems associated with obtaining sufficient high-quality, well-annotated samples of diseased and control tissue, blood, and other biological materials. At the same time, funders of biobanks are looking to obtain the best value from their investments in sample and data collection.

In most cases, unacceptable sample quality results from failures in the pre-analytical phase. Consequently, in relation to plasma samples, there is a pressing need for greater quality control measures in the processes utilized for 1) blood withdrawal, 2) blood and plasma processing and 3) storage of samples. To accomplish this, quality control biomarkers are needed which are ubiquitous, easy to test, and able to deliver quantitative values.

Metabolite levels in blood and plasma are very reactive and responsive to disturbances from a wide range of physiological and chemical processes. Thus, this makes metabolite levels in blood and plasma suitable as biomarkers; their responsiveness to pre-analytical variations allows for comprehensive and sensitive quality control biomarkers.

The metabolomics-based MxP® Quality Control Plasma assay from Metanomics Health is the only quality control assay that provides information about the presence of pre-analytical deviations, where they occur in the process, and/or improper storage conditions.

The MxP® Quality Control Plasma assay reports a quantitative Quality Score (QS) that provides color-coded quality categories and recommendations for sample utilization. Therefore, using this assay can improve the quality of plasma sample deposits of Biobanks and, in the long run, serve as a source of confidence in the investment made in samples. Providing high quality samples is critical for thereputation of any biobanking organization.

Quality issues of specimen in clinical R&D

Today, many published research results cannot be replicated. This is a critical issue as leading biopharmaceutical companies report they can only reproduce a quarter or even less of landmark studies, and many scientific journals are also increasingly sensitive to the impact of results that cannot be reproduced [1]. One reason is the competitiveness of science, i.e., the need to publish first. However, another major source of failures in studies is quality issues of specimen used, as only quality defined biological samples will lead to reliable, reproducible data.

As any clinical research and development study depends on specimen collection to hunt for new targets and biomarkers, access to high quality specimen like human plasma samples is important. Specimens that are collected and stored in adherence to best-in-class sampling SOPs minimize the risk of confounder's effect during the pre-analytical phase. This will increase the chance of successful drug target or biomarker identification, validation and delivery of reproducible data.

Challenges in clinical biobanking

Academic and commercial biobanks play a crucial role in today's biomedical research and clinical trials. Moreover, the number of samples being deposited continues to grow.

A well-managed biobank with proper collection, processing, storage, and tracking processes require professional quality management in order to offer high quality specimens at reasonable numbers and fuller representation of populations and diseases.

Biobank stakeholders at all levels can agree that quality of samples and related data should be consistent and standardized. Today, quality assurance (QA) and quality control (QC) systems are part of the biobank best practices, which include technical, legal, ethical and, managerial issues [2].

These biobank QA/QC systems are not standardized. If samples do not meet established standards, then reputation of the biobank and ultimately clinical research of its clients suffers. Thus, biobank leaders should view additional QA and QC measures as an added benefit, an investment which returns in increasing sample deposits and good reputation.

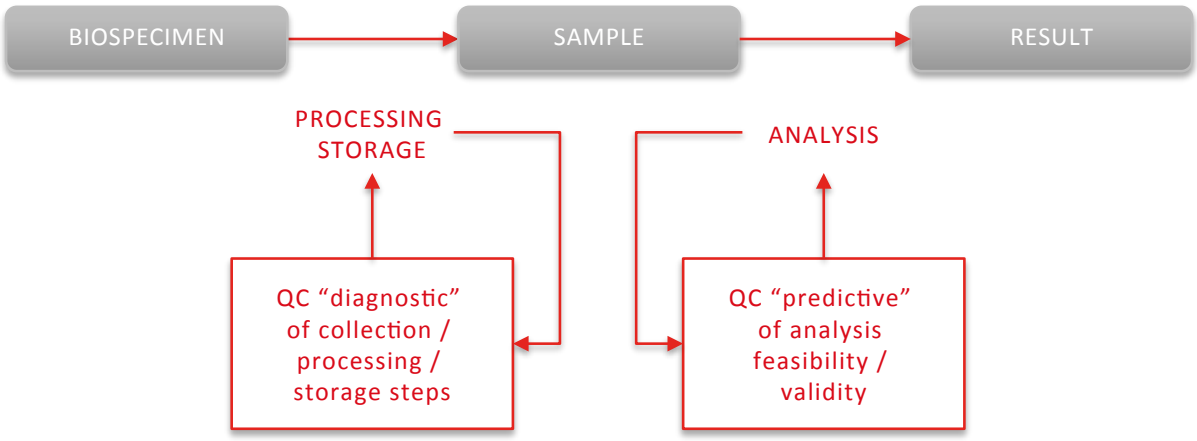

Figure 1: Challenges in biospecimen quality control [2]

Standardization in clinical biobanking

Key stakeholders from institutions like the National Cancer Institute Office of Biorepositories and Biospecimen Research (BBRB) and the International Society for Biological And Environmental Repositories (ISBER) have pushed for standard operation procedures (SOPs), guidelines oversight, and accreditation. Ideally, each sample should be properly identified beyond labeling, but also including sample quality assessment and recommendation of usage.

The biobank´s reputation and future growth as trusted resource depends to a large extent on the integrity of its deposits. Thus, being able to monitor SOP adherence or identify low-quality collection sites in order to provide the highest quality samples, gives the biobank a competitive edge and helps to maintain the integrity of clinical studies.

The importance of pre-analytics on poor sample quality

It is generally accepted that a major source for poor sample quality is pre-analytical factors that are outside the control of the biobank like methodology and consistency in sample collection, sample processing and shipping [3,4].

A specimen may pass as many as 20 hands prior to biobank deposit, introducing a high risk for pre-analytical errors including labeling errors, resulting in the fact that 98% of errors happen before a sample reaches the biobank [5].

Pre-analytical processing steps such as incorrect choice of sample tube, prolonged storage of blood or plasma and incubation at improper temperatures can have negative effects on the quality of human plasma samples, which in turn influences analytic reliability and reproducibility of clinical results.

Therefore, quality control of plasma samples in addition to quality assurance is important for biobanks to implement

Advantages of metabolomics-based quality control

Metabolomics is the systematic study of the metabolome, the unique biochemical fingerprint of all cellular processes. This deep insight into the actual phenotype of any biological system is metabolomics' advantage over other -omics technologies.

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Cellular processes and the physiological status are most closely reflected by the patterns of metabolites, the small endogenous and exogenous molecules (<1.5 kDa) such as nucleotides, carbohydrates, amino acids and lipids, whose levels are highly responsive to both genetic and environmental factors.

Metabolite levels in blood cover a wide range of physiological and chemical processes and they are very reactive to disturbances. Analysis of the responsiveness of the human plasma metabolome to pre-analytical variations allows the most comprehensive and sensitive read-out of human plasma sample quality [6].

MxP® Quality Control Plasma Assay

MxP® Quality Control Plasma is a novel metabolomics-based profiling assay that provides a holistic control of EDTA human plasma sample quality for the first time. One can gain information about presences of pre-analytical deviations and where they occur in the process. This allows biobanks to upgrade their quality management system from quality assurance to quality control, safeguarding their investment.

HOW IT WORKS

The *MxP Quality Control Plasma* assay measures specifically-developed and validated multiple metabolic biomarkers in a single read-out. By applying proprietary algorithms, three different test results are calculated which not only provides precise assessment of sample quality but also recommendations of sample utilization.

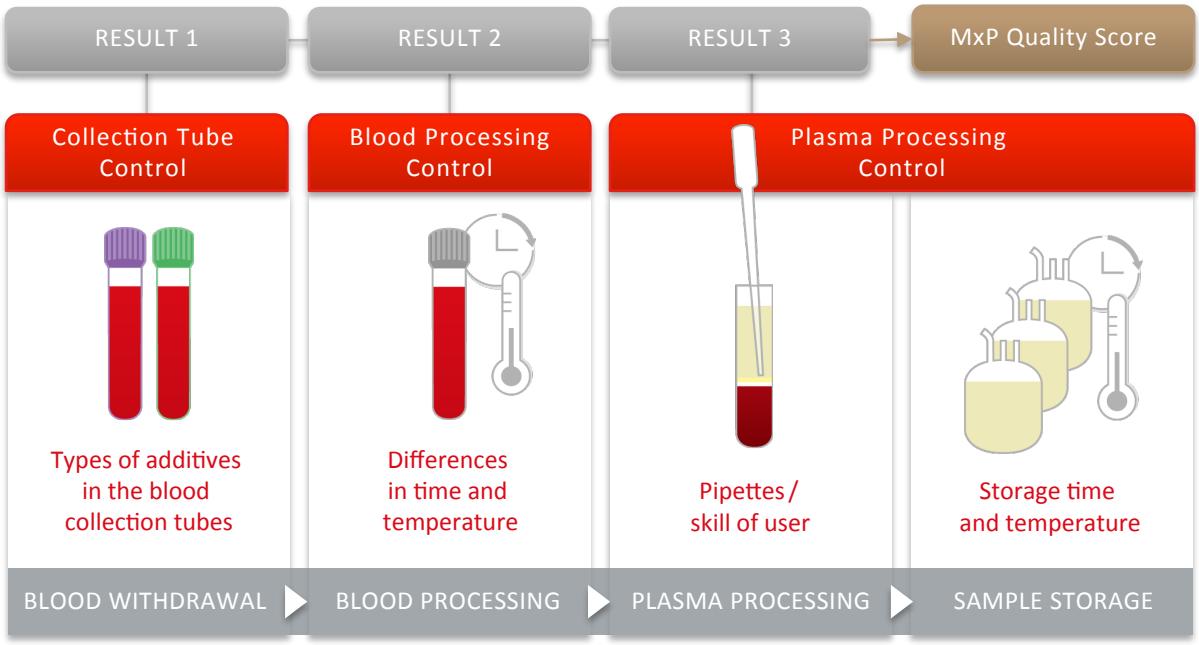

Figure 2: MxP® Quality Control Plasma controls EDTA plasma sample quality at three check points.

CLINICAL PERFORMANCE

The performance of the MxP Quality Control Plasma assay has been evaluated in a blinded study by *Bayer Pharma AG* with human blood samples addressing the following confounders in addition to a control group:

- Blood storage at room temperature for 6 h
- Plasma storage at room temperature for 6, 24, 48 h
- Five freeze-thaw-cycles of plasma samples

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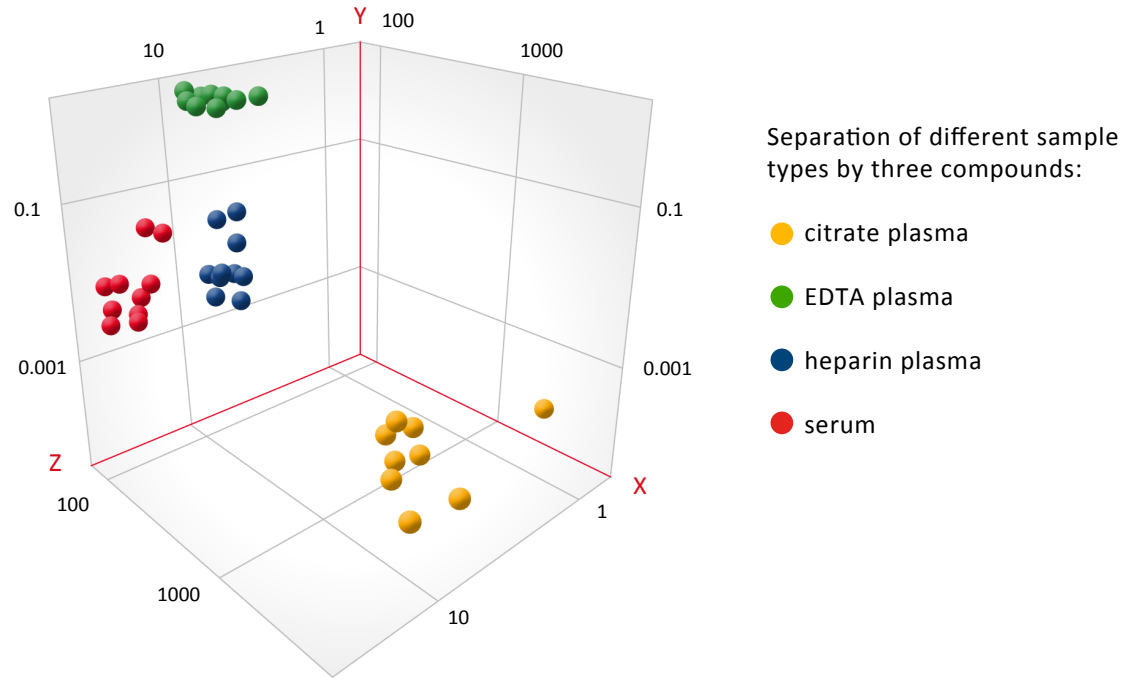

Figure 3: Control of correct choice of collection tube. The assay allows separation of sample types by tube compound.

MxP® QC TEST RESULT	CONTROL (20)	CONFOUNDERS (100)
Negative	18	2
Positive	2	98
	SPECIFICITY: 90 %	SENSITIVITY: 98 %

Table 1: Clinical sensitivity and specificity of results 2 and 3 of the MxP Quality Control Plasma assay. Results from Bayer Pharma AG.

Key benefits of the MxP® Quality Control Plasma assay for biobanks include the ability to deliver truly quality-controlled human plasma specimens, the establishment of active longitudinal quality management, the possibility to monitor compliance to sampling SOPs and to assess training needs of their employees.

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Conclusions

Superior sample quality is a key factor for the success and the future growth of a biobank. Pre-analytic errors, which occur before samples reach the biobank, are the major cause for poor sample quality. Biobanks can easily increase the value of their human plasma samples by using the metabolomics-based assay MxP® Quality Control Plasma offered by Metanomics Health.

To learn more about the MxP Quality Control Plasma assay, please visit www.metanomics-health.com or speak to a Metanomics Health business development representative.

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