Commentary



# The impact of preanalytical variability in clinical trials: are we underestimating the issue?

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The essential contribution that the preanalytical phase plays to the reliability of the total testing process and the quality of diagnostic information is now clear to most laboratory professionals (1). The recent release of the 2015 STARD guidelines has further contributed to catalyze the attention on this topic (2-4), also emphasizing the importance of preanalytical activities in the quality of diagnostic studies (5). Nevertheless, the familiarity of many scientists and clinicians with extra-analytical issues remains vague, at best. The role and active involvement of experts or national and international organizations of laboratory medicine has propelled the generation of a consistent literature, culminating in robust and sizeable recommendations aimed to define best practice criteria for accurate and appropriate handling of biological specimens before analysis. Such a huge scientific effort has been paralleled by a number of technological advances in the materials used for drawing blood and in the procedures for collection, transport, centrifugation, separation and storage of biological materials. The high degree of complexity and heterogeneity in the preanalytical phase is mainly attributable to the analysis of different biological fluids (e.g., whole blood, serum, plasma, urine), less frequently used biological materials such as saliva, hairs, stools, and even of specimens necessitating special preparations (i.e., nucleic acids, supernatants or cell cultures). Additional sources of vulnerability emerge from the use of different procedures and materials for collection of biological specimens (1).

Notably, the interest of academic, professional and industrial is increasingly merging to provide best practices for obtaining reliable laboratory data. An essential part of clinical medicine, i.e., experimental and translational medicine, develops through clinical trials, and is largely based on laboratory data to verify the putative beneficial effects of innovative drugs, new medical or surgical procedures, which may ultimately translate into cost-effective treatment of patients. Clinical trials are frequently sponsored or directly organized by companies manufacturing drugs or medical devices, often involving specialized companies (e.g., contract research organizations), but can else be spontaneously proposed by physicians, scientists and even patients associations. In large and multicenter trials, laboratory analyses are frequently centralized to reduce the impact of analytical variability due to the use of different methods, reagents and instrumentation. Indeed, the process of centralization may be effective to decrease the analytical variability, but the impact of preanalytical variables (especially preparation, storage and transportation of the specimens) is dramatically magnified when accurate procedures are not defined and followed. A large number of randomized clinical trials entail multicenter and international studies. The fulfillment of transport and storage criteria of biological materials is hence crucial to prevent the generation of inaccurate results and misinterpretation of data which, in turn, could mistakenly enhance or reduce the clinical efficacy of a given drug or medical devices. Importantly, many promising treatment may "be lost in translation" from basic research to routine practice due to undue bias emerging from extra-analytical activities. To date, little information is available on this issue. Specifically, a limited number of comments or reports has been published to emphasize the focus of scientists and clinicians on many sources of preanalytical variability (6,7), thus adding more fuel to the fire in the basic and applied

 

research involving laboratory diagnostics (8).

It is now undeniable that recommendations and guidelines released by national or international organizations of laboratory medicine should be integrated (or adopted to be used) into the quality prerequisites of clinical trials. Moreover, the expertise of laboratory professionals should be seen as an add value and exploited for evaluating clinical trials results and, consequently, for supporting patients and healthcare agencies to obtain best outcomes.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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