SAFETY PANELS: Combining the Conventional and Novel Toxicity Biomarkers

The notion of biomarker is not new. The FDA defines a biomarker as the measurable endpoint that can be used as an indicator of a physiological or pathological process. In particular, toxicity biomarkers are those capable of detecting liver, kidneys, bone marrow, and other target organs injuries. In the process of drug development, most drug candidates are discontinued because of induced organ toxicity and half of them owe this to liver toxicity[4].

What are the Characteristics of an Ideal Biomarker?

The current literature describes the "ideal" biomarker as: accessible, non-invasive, sensitive, specific, inexpensive, translational (able to cross the bridge between basic and clinical research), predictive of the extent of injury, and accurate. Tremendous research efforts in detecting novel biomarkers for kidneys and liver toxicity resulted in discovering few promising biomarkers, which come closer to the ideal model than the traditional ones do.

Combining Conventional and Novel Biomarkers in Safety Panels

The "ideal" biomarkers have yet to be discovered, therefore laboratories cannot completely stop testing for conventional biomarkers and switch to the new ones. We also cannot ignore the fact that the conventional biomarkers have their limitations. Parallel testing is critical, starting as early as Phase I and II of the clinical trials, in which the conventional biomarkers would be compared with some of the novel ones best suited for the purpose of each study. Research shows that sensitivity and specificity for diagnosing acute kidney injury increased when a combination of novel biomarkers was used[2,5,6]. It also points to the advantages of adding novel valuable biomarkers to the alanine transaminase (ALT) to improve detection of drug-induced liver injury[4].

Modern technology allows central laboratories to test for these novel biomarkers, along with the conventional ones, in a form of a "toxicity biomarkers panel," or "safety panel." This panel can be optimized in collaboration with the sponsor, according to the specificity of the study, in order to maintain low costs and to develop better and safer drugs.

While limited by the number of subjects, the results from a well-planned Phase I or Phase II toxicity biomarker testing could depict host genetic factors, elucidated by in more depth testing or by genetic analysis of the affected patients [1, 3]. It could also mean designing a better Phase III trial with increasing chances of achieving post marketing success. One of the drawbacks is that most of the novel biomarkers assays are enzyme-linked immunosorbent assays (ELISA) and only few are automated, thus increasing the costs. While initially this can be viewed as an extra expense, in the end, correctly interpreted data can prove very useful to drug developing companies, patients, clinical laboratories, and to science.

The Role of a Clinical Trial Central Laboratory

A clinical laboratory's responsibility is to ensure the quality of testing, which is very important with all tests, but vital for novel safety biomarkers in order for the data to be credible, accurately interpreted and for the correct decision to be made. Clinical trials laboratories need to make sure that the assays testing for the novel biomarkers are validated and globally standardized, in order to minimize errors. PV

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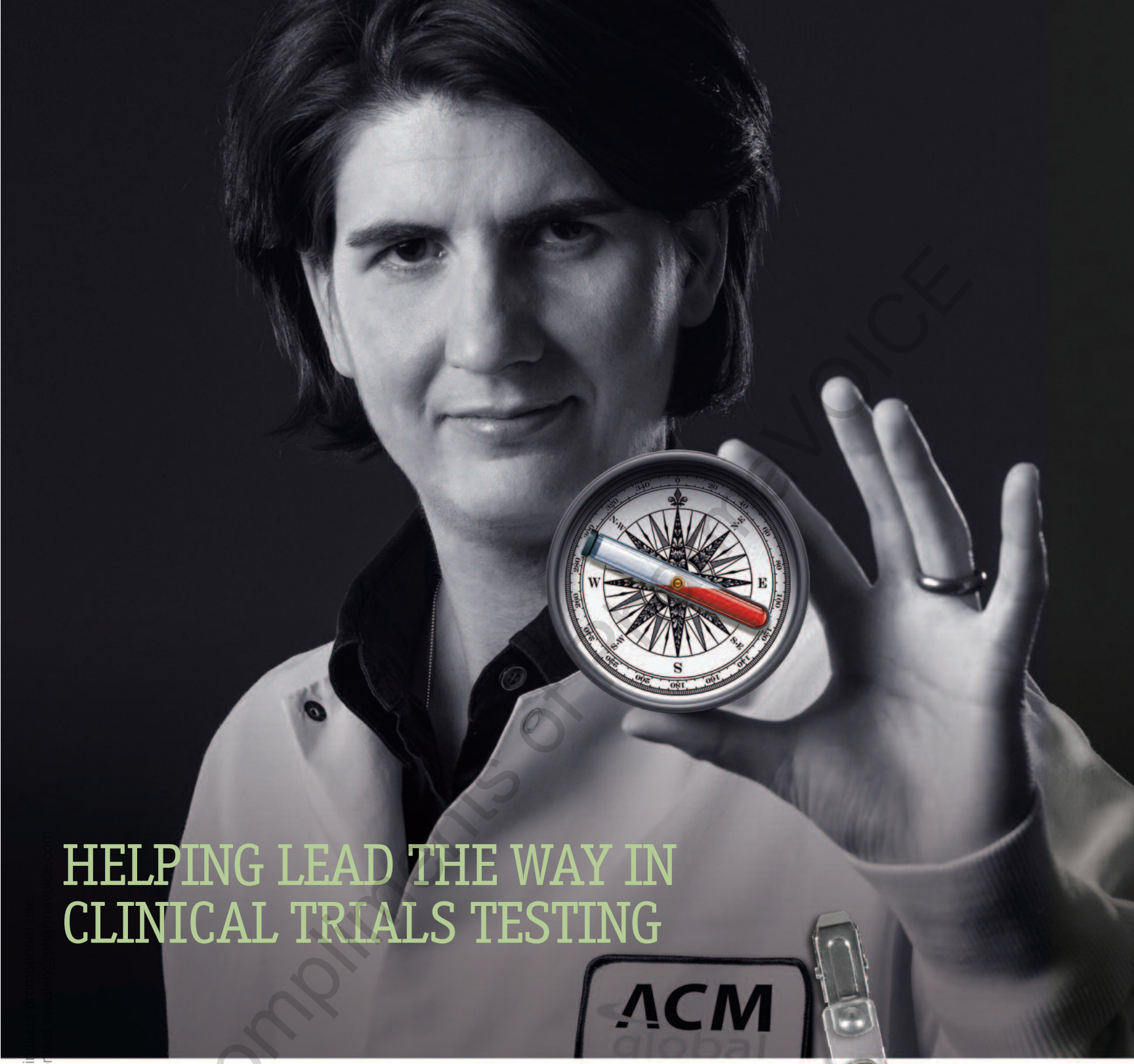

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