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Qualification of Safety Biomarkers for use in Drug Development: what has been achieved and what is the path forward?

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Abstract: There are multiple categories of biomarkers (such as safety, diagnostic, prognostic, susceptibility/risk, predictive, monitoring, pharmacodynamic/response or surrogate) giving rise to many applications in clinical medicine and drug development. The scope of this article is limited to the development and evaluation of novel safety biomarkers, leading to their regulatory qualification for use in the different phases of drug development, from early preclinical safety assessment to clinical trials. The goal is that, once these additional safety biomarkers are adequately demonstrated to perform translationally across the common animal test species (rat, mouse, dog and nonhuman primate) and in humans, they will enhance the efficiency and utility of both the animal toxicology studies that are used to support the safe conduct of clinical drug trials, as well as the safety of clinical trials themselves. From a regulatory perspective, the actions of the US Food and Drug Administration (FDA) have been highlighted because, although other regulatory agencies, notably the European Medicines Agency, have also been very active in this sphere, the FDA stands out for the sustained leadership it has given. The barriers to progress and necessary refinements to expedite a complex and resource intensive regulatory qualification process are discussed.

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Abbreviations to be included as first page footnote: FDA = US Food and Drug Administration; EMA = European Medicines Agency; PMDA = Pharmaceuticals and Medical Devices Agency of Japan; FNIH = Foundation for the National Institutes of Health; PSTC = Predictive Safety Testing Consortium; IMI Safe-T = Innovative Medicines Initiative Safe and Effective Evidence-Based Translation; ILSI HESI = International Life Sciences Institute, Health and Environmental Sciences Institute