Three 2023 news regarding ‘Statistics in in-vitro Toxicology’

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I like to discuss some consequence from the recently released:
i) FDA 2nd modernization act: no-vivo data more needed
ii) Zeiger E. Determination of a positive response in the Ames Salmonella mutagenicity assay. Environ Mol. Mutag (2023)
iii) M. Hayashi “Statistical significance” and other important considerations in genotoxicity safety testing . Mut Res. (2023)

The old contradiction between significance and relevance breaks out again in full. There is none- only inappropriately formulated tests. Therefore are recommended:

i) non-inferiority tests within the proof-of-safety framework instead of point-zero-H0 tests within the common used proof-of-hazard,
ii) a delta-value threshold of 'yet to be tolerated effect’ is inherently needed.

The definition of the randomized unit is essential in inference. Based on the paradigm ‘a rat is a little man’ it is available in in-vivo bioassays. It is not obvious in in-vitro assays- with dramatic consequences. Assay-specific proposals are discussed.

Sometime k-fold is used for interpretation in in-vitro assays. But the statical tests based on the difference-to-control effect size. This basic contradiction can be overcome be using ratio-to-control tests and confidence intervals.

Related examples are demonstrated and their evaluation by means of CRNA packages.