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APPLICATION OF *IN VITRO* METHODS FOR ASSESSMENT OF CARCINOGENIC POTENTIAL OF CHEMICALS

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Modern toxicology around the world is undergoing significant changes and is increasingly moving away from traditional research methods using laboratory animals. This process is dictated by international requirements for testing, which provide for the gradual replacement and even abandonment of the use of animals for research purposes. Testing of chemical products, as well as micro- and nanosized particles, in accordance with harmonized international requirements, includes several stages. At the first stage of the study, screening experimental studies using alternative *in vitro* test models are envisaged. And only with the existing effects obtained at the screening stage, is it supposed to switch to research using experimental models *in vivo*, while the use of testing on animals implies in this case a strict limitation in the number of animals and justification of the need for the selected methods.

The first test that began to be used to identify the genotoxicity of compounds was the Ames test (Kirkland D., 2008). It has been shown that the predictive efficiency of this test is 75–80 % when testing a wide range of chemicals (Guyton K. Z., 2009). After reports of a high correlation between bacterial mutagenicity and carcinogenicity in mammals, a number of international reference studies were carried out for *in vitro* and *in vivo* tests using mutation analysis in yeast, fungi, rodent and other mammalian cells to identify mutagens (Huff J., 1999).

Based in part on these studies, the scientific and regulatory communities have settled on a limited number of *in vitro* and *in vivo* tests to assess mutations that have been incorporated into international regulations. It was found that chromosome damage and gene mutations are caused by different mechanisms (with some overlap), and that different substances can trigger different pathways. Therefore, an *in vitro* test battery must include tests for all known mechanisms. Typically, such an *in vitro* test battery for evaluating chemicals consists of a gene mutation test in bacteria (Ames test), a gene mutation or DNA damage test in mammalian cells, and a chromosome damage test in mammalian cells.

A number of *in vitro* tests on microorganisms and mammals are available that analyze not mutation as such, but DNA damage: SOS chromotest on bacteria (Kirkland D., 2005), tests for DNA strand breaks - comet analysis (Fairbairn D. W., 1995). But, despite the fact that the existence of non-genotoxic carcinogens was recognized decades ago, the theory of cancer due to somatic mutations was generally viewed as the prevailing paradigm.

That is, the need to create short-term mutagenicity tests for the identification of mutagenic / genotoxic chemicals was recognized (Benigni R., 2010). The identification of non-genotoxic carcinogens is a weak point of existing testing strategies. Considering the fact that non-genotoxic carcinogens are inducers of oxidative stress, peroxisome proliferators, hormone modulators, including modulators of cell division and growth, tests for the induction of oxidative stress, cell cycle analysis, as well as a test were proposed for their detection. on neoplastic cell transformation. The latter mimics some *in vivo* stages of multistage carcinogenesis and can reveal non-genotoxic carcinogens in culture (Tice R. R., 2011).