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In Vivo Genotoxicity Testing Strategies: Report of the International Workshop on Genotoxicity Testing (IWGT)

Carol Beevers^{1*}, Yoshifumi Uno², Krista Meurer³, Shuichi Hamada⁴, Kiyohiro Hashimoto⁵, Ludovic Le Hegarat⁶, David Kirkland⁷, Matthew J. LeBaron⁸, Frank Le Curieux⁹, Hans-Joerg Martus¹⁰, Kenichi Masumura¹¹, Wakako Ohyama¹², Daniel J. Roberts¹³, Marie Vasquez¹⁴, James Whitwell¹⁵, Kristine L. Witt¹⁶

¹Corteva Agriscience, Oxford, UK

²LSI Medience, Tokyo, Japan

³BASF SE, Limburgerhof, Germany

⁴BoZo Research Center Inc., Tokyo, Japan

⁵Takeda Pharmaceutical Co., Ltd., Tokyo, Japan

⁶ANSES, Fougères, France

⁷Kirkland Consulting, Tadcaster, UK

⁸The Dow Chemical Company, Midland, MI, USA

⁹ECHA, Helsinki, Finland

¹⁰Novartis Institutes for BioMedical Research, Basel, Switzerland

¹¹National Institute of Health Sciences, Kanagawa, Japan

¹²Yakult Honsha Co., Ltd., Tokyo, Japan

¹³Toxys Inc., NY, USA

¹⁴Helix3 Inc., Morrisville NC, USA

¹⁵Labcorp Drug Development, Harrogate, UK

¹⁶National Institute of Environmental Health Sciences, RTP, USA

*carol.beevers@corteva.com

The in vivo testing strategies working group (WG) at the International workshop on genotoxicity testing (IWGT) discussed topics related to in vivo testing. Key conclusions from the group will be discussed.

The majority of the WG group agreed that it is unacceptable to reject the conclusions of a negative in vivo erythrocyte MN study solely on the basis of test substance concentrations in blood or plasma falling below the concentration that induced positive results in vitro. Consensus on the evidence required to demonstrate systemic exposure was not reached.

The WG members agreed that the liver MN test is sufficiently validated to develop this test into an OECD Test Guideline, however, the impact of age at the time of dosing warrants further study. The WG agreed that Ki-67 is a reliable marker for mitotic activity, however, the evaluation of longer-lived cell proliferation markers would be valuable. The WG agreed that comparison of comet study results to historical control data (HCD) for determination of biological relevance should not be performed unless the laboratory can demonstrate stability of their HCD, and that animal (but not study) factors are the predominant source of variance in the HCD. The WG agreed that methodological differences could influence the risk of both false positive and false negative results.

Keywords:

In vivo, Genetic toxicology, Test strategies.