We report here on a novel exogenous metabolic negative control: Metabolic deactivation system. Cytotoxicity of protoxicants in the metabolically incompetent target cell line MetMax™ human hepatocytes (inactivated by heating for 15 minutes) was compared to the metabolically competent group 1. To group 2, 10 μL of MetMax™ human hepatocytes was added. To group 3, 10 μL of inactive hepatocyte medium but without MetMax™ human hepatocytes was added. To group 4, 10 μL of inactive hepatocyte medium but without MetMax™ human hepatocytes was added. Heat inactivation of the MetMax™ human hepatocytes (MMHH) was prepared from a pool of 10 (5 male and 5 female) human donors using proprietary procedures (patent pending). MetMax™ can be stored and used similarly to HLM and S9, without the complicated storage and use procedures of cryopreserved hepatocytes.

**Results**

MetMax™ Hepatocytes and intact hepatocytes contain complete hepatic drug metabolizing enzyme pathways due to the presence of all cellular organelles. Metabolic activation of protoxicants by MetMax™ human hepatocytes was eliminated by heat inactivation.

**Summary and Conclusion**

Four protoxicants – acetylsalicylic, cyclophosphamide, ifosfamide and 2-naphthylamine were evaluated for their cytotoxicity in HEK293 cells in the presence and absence of MetMax™ Human Hepatocytes. The cytotoxicity of all four protoxicants was increased by MetMax™ Human Hepatocytes. Metabolic activation of protoxicants by MetMax™ Human Hepatocytes was eliminated by heat inactivation.