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Determination of point of departures based on high throughput *in vitro* metabolomics

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Metabolomics *in vitro* poses a high potential for a biologically driven risk assessment approach. We recently developed a platform for high throughput in vitro testing based on LC-MS targeted metabolomics in HepG2 cells. This screening platform was optimized for various parameters such as cell seeding density, passage number, sample preparation, analytical method, etc. and could be used to identify different liver toxicity mode of actions. To determine biologically relevant dose concentrations useful for *in vitro* to *in vivo* extrapolation, it is required to determine a point-of-departure (PoD). We present here an approach to determine PoD from a dose response curve determined from multivariate metabolomics data. This approach establishes an important connection for translating results from *in vitro* systems to *in vivo* and thus human relevance. Taken together, our metabolomics *in vitro* system demonstrates applicability for mode of action identification in vitro as well as POD determination.

Keywords:
Metabolomics; metabolomics in vitro; point of departure; PoD.