Pharmacokinetic drug-drug interaction can significantly impact drug safety and efficacy. Prediction of this drug-drug interaction risk is a requisite in the development plan of a new drug candidate to the submission of the registration dossier. In vitro identification and measurement of the contribution of the major cytochrome P450 enzymes involved in the human metabolism of a new drug candidate, also called “CYP phenotyping assay”, allows predicting the impact of another co-administered drug (perpetrator) on the pharmacokinetics of the new chemical entity (victim). Up to now, a battery of in vitro tests (recommended by the regulatory agencies) is required for this CYP phenotyping assay. Each of these tests suffers from numerous inconveniences: no direct quantitative measurement of the contribution of each CYP in the metabolism of a drug, biologic system not fully representative of the liver situation (eg human recombinant CYP450), lack of specificity (eg antibody anti-CYP450), too specific conditions of use (eg chemical competitive CYP specific inhibitors). A new in vitro model, called, Silensomes™ has been developed to encounter the disadvantages of the current methodologies. Silensomes™ correspond to human pooled liver microsomes chemically desactivated for one specific CYP450. CYP3A4 Silensomes™ were chosen as a proof of concept of this new model. Following their preparation, the cryopreserved batches of desactivated-CYP3A4 and control pooled liver microsomes were incubated with CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4 specific substrates to measure their respective activities. Results showed that CYP3A4 Silensomes™ abolished CYP3A4 activities of testosterone, nifedipine and midazolam to more than 80 % with no impact on the other CYP450 activities tested showing the high specificity and potency of the inhibition. Silensome™ CYP3A4 desactivation was preserved after storage at -80° C. Moreover, CYP3A4 contribution measured for known multi CYP substrates, following their incubation with CYP3A4 Silensomes™ were similar to the fm values observed in vivo or in vitro. These results showed that the CYP3A4 Silensomes™ model responds to the different criteria of specificity, potency, stability and predictability to ensure a good extrapolation of the risk of pharmacokinetic drug-drug interaction. Moreover, this new "ready to use" in vitro model is very easy to handle and can be easily fully automated. This approach will be extended to all the human major CYP450 in order to provide a complete kit ready to use for the CYP450 phenotyping assay. It is therefore the model of choice for a rapid and robust determination of the CYP contribution all along the development plan of a new chemical entity.