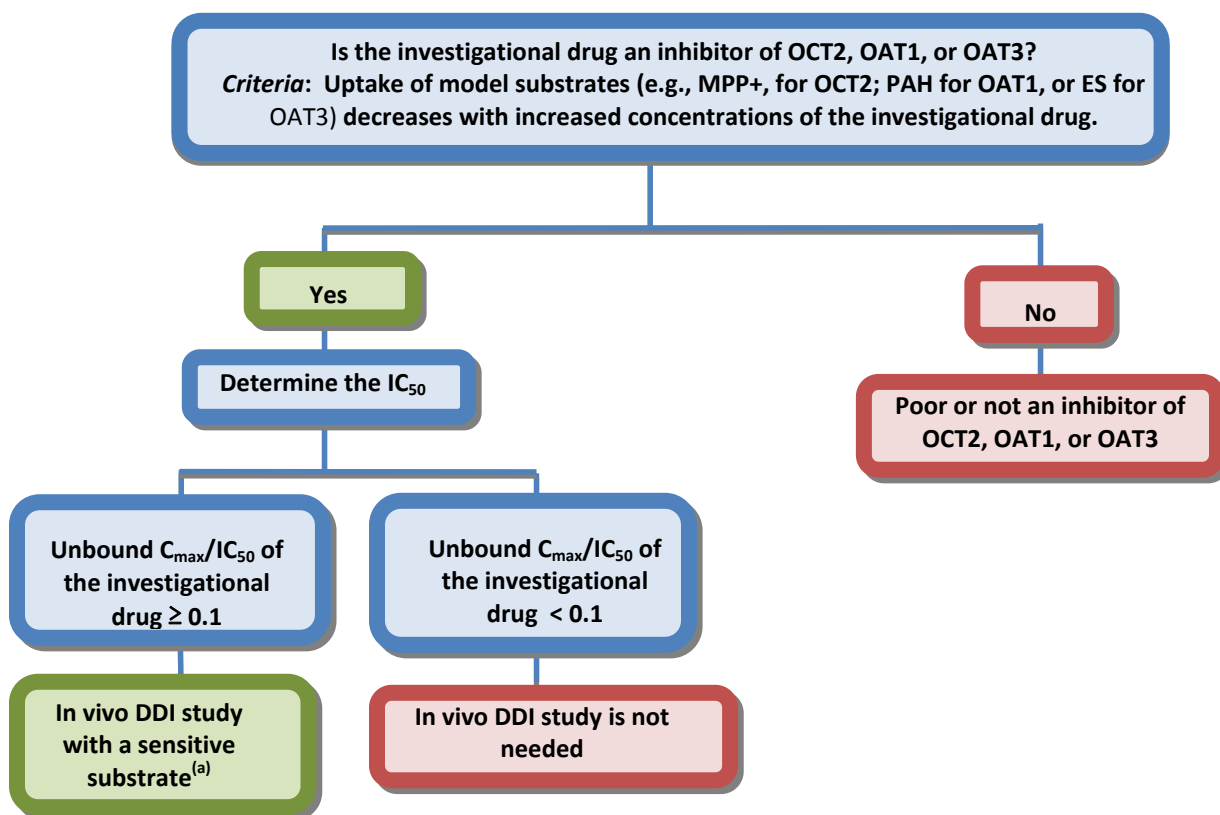


**Figure 11. Decision tree to determine whether an investigational drug is an inhibitor of OCT2, OAT1, or OAT3 and when an in vivo clinical study is needed — (Modified From Figures in Giacomini KM, *et al*, *Nat. Rev Drug Discov.* 9: 215-236, 2010)**



MPP<sup>+</sup>, 1-methyl-4-phenylpyridinium; PAH, *para*-aminohippuric acid; ES, estrone-3-sulfate.

<sup>(a)</sup> For the investigational drug that is an OCT2 inhibitor, metformin may be used as the substrate for the clinical drug interaction study.

For investigational drugs that are OAT1 or OAT3 inhibitors, multiple OAT1 or OAT3 substrates could be used in clinical DDI studies, including zidovudine, acyclovir, ciprofloxacin, tenofovir, or methotrexate.