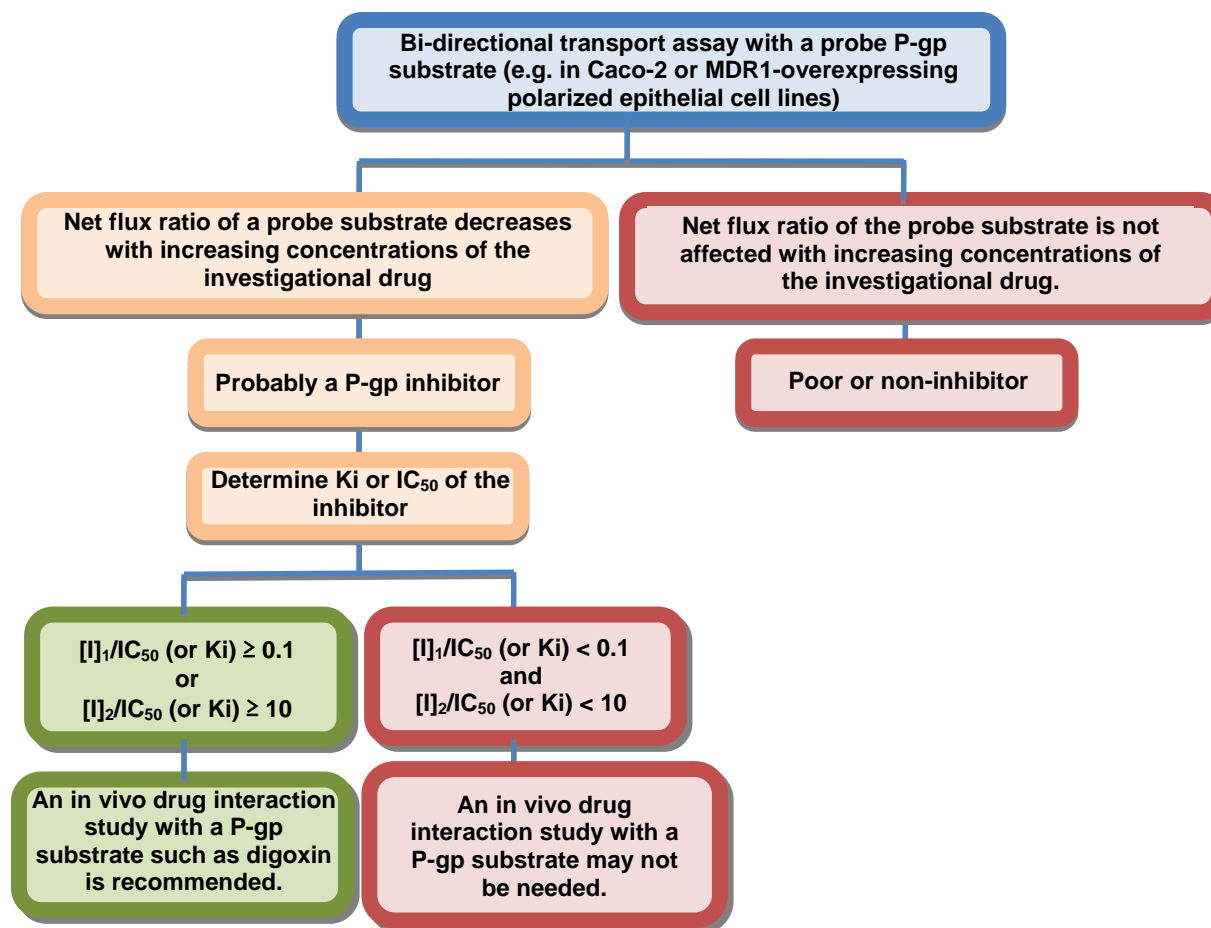


Figure 7. Decision tree to determine whether an investigational drug is an inhibitor of P-gp and when an in vivo clinical study is needed. A similar model can be applied to a BCRP inhibitor) — (Modified From Figures in Giacomini KM, *et al*, Nat. Rev Drug Discov. 9: 215-236, 2010)



[I]₁ represents the mean steady-state total (free and bound) C_{max} following administration of the highest proposed clinical dose. [I]₂= Dose of inhibitor (in mol)/250 mL (if IC₅₀ is in a molar unit). For IC₅₀ determination, a unidirectional assay (e.g., B to A) based on the probe substrate can also be considered.