

**S1 Table. Reaction List.** The individual reactions for both models: the *in vitro* hepatocyte and the *in vivo* PBPK/PD model. The column with R# and Cell Compartment depict the reactions that are present in the *in vitro* hepatocyte model and where. The columns with M# and multi-scale compartment do the same for the *in vivo* PBPK/PD model. The column reactions describe the modelled pathway along with the column kinetic rate law which gives insight on the kinetics used to model each step.

#	Cell Compartment	Multiscale Compartment	Reaction	Kinetic rate law	
R1	-	Cell Intracellular	-	$IFN \rightarrow \emptyset$	$k1 \cdot S$
R2	M1	Cell Intracellular	Liver Interstitial	$IFNA + IFNAR2 \rightleftharpoons IFNA\text{-}IFNAR\ 2\ \text{Complex}$	$k1 \cdot S1 \cdot S2 - P/keq$
R3	M2	Cell Intracellular	Liver Interstitial	$IFNA\_R2\_Complex + IFNAR1 \rightleftharpoons \text{Activated Receptor Complex}$	$k1 \cdot S1 \cdot S2 - P/keq$
R4	M3	Cell Intracellular	Liver Interstitial	$\text{Activated Receptor Complex} \rightleftharpoons SOCS1\ IFNAR1 + IFNAR2$	$\frac{V \cdot S \cdot A}{(Kms+S)(Ka+A)}$
-	M4	-	Liver Interstitial	$\emptyset \rightarrow IFNAR1$	$rel\_exp\_out \cdot AF \cdot f_o \cdot k_t \cdot S \cdot k_t$
-	M5	-	Liver Interstitial	$\emptyset \rightarrow IFNAR2$	$rel\_exp\_out \cdot AF \cdot f_o \cdot k_t \cdot S \cdot k_t$
R5	M6	Cell Intracellular	Liver Intracellular	$\text{Activated Receptor Complex} + STAT2c \rightarrow Rec2$	$k1 \cdot S$
R6	M7	Cell Intracellular	Liver Intracellular	$Rec2 + STAT1c \rightarrow Rec21$	$k1 \cdot S$
R7	M8	Cell Intracellular	Liver Intracellular	$Rec21 + IRF9c \rightarrow \text{ISGF-3c} + \text{Activated Receptor Complex}$	$k1 \cdot S$
R8	M9	Cell Intracellular	Liver Intracellular	$\emptyset \xrightleftharpoons[\text{binding sites}]{\text{Occupied ISGF-3n}} mRNAc\_SOCS$	$k1 \cdot M$
R9	M10	Cell Intracellular	Liver Intracellular	$mRNAc\_SOCS \rightarrow \emptyset$	$k1 \cdot S$
R10	M11	Cell Intracellular	Liver Intracellular	$\emptyset \xrightleftharpoons[\text{binding sites}]{\text{Occupied ISGF-3n}} mRNAc$	$k1 \cdot M$
R11	M12	Cell Intracellular	Liver Intracellular	$mRNAc \rightarrow \emptyset$	$k1 \cdot S$
R12	M13	Cell Intracellular	Liver Intracellular	$\emptyset \xrightleftharpoons{mRNAc} IRF9c$	$(k_{const} + k_{act})M - P \cdot IRF9_{deg}$
R13	M14	Cell Intracellular	Liver Intracellular	$\emptyset \xrightleftharpoons{mRNAc\_SOCS} SOCS\ 1$	$k_{act} \cdot M - K_{deg} \cdot P$
R14	M15	Exchange	Exchange	$STAT1n \rightleftharpoons STAT1c$	$k1 \cdot S - P/keq$
R15	M16	Exchange	Exchange	$STAT2n \rightleftharpoons STAT2c$	$k1 \cdot S - P/keq$
R16	M17	Exchange	Exchange	$IRF9n \rightleftharpoons IRF9c$	$k1 \cdot S - P/keq$
R17	M18	Exchange	Exchange	$ISGF-3c \rightleftharpoons ISGF-3n$	$k1 \cdot S$
R18	M19	Cell Nucleus	Liver Nucleus	$\text{Open ISGF-3n binding sites} + ISGF-3n \rightleftharpoons \text{Occupied ISGF-3n binding sites}$	$k1 \cdot S1 \cdot S2 - P/keq$
R19	M20	Cell Nucleus	Liver Nucleus	$\text{Occupied ISGF-3n binding sites} \rightarrow \text{STAT 1n} + \text{STAT 2n} + \text{IRF 9n} + \text{Open ISGF-3n binding sites}$	$k1 \cdot S$
R20	M21	Cell Nucleus	Liver Nucleus	$IRF9n \rightarrow \emptyset$	$k1 \cdot S$