

Psi\_CYP4V -----SY-----S-VSVLGLISLLIAAVTYLTYRLLSDVYHKWFV-----MKPIPPQAGTYPFIGNAHQFKNAGDF-----F-----RQIEDLTIIEFSGEPLFKLWIGPFP-F  
Psi\_CYP46A2 -----MKFWSAE-----F-VGLLLLVGCVGTVILRRTLWLVWPKPKLEKLQSQGIGKGP-YTILFGDLRKLIVQTKAEVSRPIDPFSNDILRRASPFFSQVVED-----CGGKLCYLWLGTSPI-I  
Psi\_CYP46A1 -----MA-----LFGVFLSWTAACLFAAFL-I-----LCIGYCLVQVQH-H-MK-----YDHIPGPRDSFLFGHSATYAMRMDG-----D-----I-IHDRF-LEWAE--KYGPVCRQNFHLHYV-V  
Psi\_CYP5A METLVLDVNLVFIKTSKGSVTLSSLVLF-LGLLWYYSIFPYSVL-----S-----RCGKHP-KPVFPLGNIFMFRGFFNP-----I-----NDLIK--THGRVCYYLGRKRP-V  
Psi\_CYP3C1 -----MFLFD-LFSATSW-----TLLALF-FLLMLYGIWYPRFF-----K-----HLGKGP-RPLPFIGTLLYFRGWVGF-----D-----RECQA-KYGDVWGTDFDARLP-V  
Psi\_CYP3A69 -----MGYFL-FFSVETW-----LLITF-ICLFVIYKQWTHGVF-----E-----NLGIPGP-KPYTYWGTGRHSVYVED-----D-----QCCA-KYGVVWGMYEFRSP-M  
Psi\_CYP3A -----MGFLP-ELSVETW-----TLIVFF-VTLVTYGYAPYGF-----K-----KLGIPGP-KPLPFIGTFLYRGIHNF-----D-----TECYE-KYGVVWGIYDGRTP-V  
Psi\_CYP3C2 -----MGFSL-FPSAETW-----TLLVAL-VTLLFVYVVCWNGFIF-----K-----KLGVPGP-KPIPFPGTMLAYRGTNF-----D-----EDCSK-KYGRVWGIYDGRTP-V  
Psi\_CYP4F2 -----SLLPLVLSWTGPCQVLLVLSGLGAVVAFWITRLLLRHAWYTHR-----L-----LSCFSKPHANSWLLGHLGQMQSEEGL-----D-----QVD-DLVQ-KYTHSCSWFLGPIYHL  
Psi\_CYP4B1 -----WPRTHHWAAYTALCLVAA-----VYKLAALLAQRHALRN-----D-----AESFPGP-RAHWLFGVNRERKDGNDL-----D-----RVV-KWGK-HDPYAFPIWFGPIVCF

A

B

**SRS1** **SRS2**  
Psi\_CYP4V LILFHAETVEAILTN--SVHMKSYSY----TFLHPWLKGLLTS-TGNKWQRKRLMPTTFHFSILTDFLDMNEQAQAVLVEKLEKQ-AGG-EFDSFSHITLICALDIICETAMGKKIHAQSHS--DSEYVVSV  
Psi\_CYP46A2 VIVTDPKLVREIMCDKS-GH-IDKTPS-----HPLGGYLLNGLVNI--CGQKWDYDRRRIINPVFHVLDKLLKMYGAFSCCCESELIDRWEKL-LDS-ESVELDWVPELENLTGDIISRSAFGSSYLEGRRI--F-QL  
Psi\_CYP46A1 TLVSCPEGTKELIIMSQKYS--KDRFFYKKIFSLFGQRFLGNGLVTISQNHQWYKQRRIIMDPAFSSLYLRGLIGTFNERVERLMTKLSDV-ADN-T--EAGMLKLVNFLTLDVIKAVAFGVDLDRLKDRSL--FPKAV  
Psi\_CYP5A VVIADPDMLRQVMVRD-FSSFNRMTL--RFASKPMTDCLLM--RNERWKRVRSLTLPFSFAAKMREMVPINTVTDSLMSNLNV--AESV--AFDIHKCFGCFMTMDIASVAFGTQVDSQKNFDD-PFVCHA  
Psi\_CYP3C1 LHMADPEIIKTVLVEKCFVFTNRRDN--PAA-GPLADAITAV--KDERWKRMRSTLSPCFTSGRMKQFPIVARYADRLTENLGG--TV--PIDVKQFMAPYSLDVVTSASFGEIANAMNDD-PLNCHA  
Psi\_CYP3A69 LAVMDPDMKLTILVKECFYFTNRRNI--RLN-GDYDSVSTV--EDDHWRRIRNVLTPSFTSGHIKEMPRIMKHLSSKLTASLQSK-AQNV--VVTIKDYFGAYSVLDMASCAFQVMDLNNFSS-PIVCHA  
Psi\_CYP3A LATMDTAMIKSILVKECYSNFTNRRDF--GLN-GALRDAITVY--EDEEWKRIRSLSPSFTSGRLKEMYSIMLQHSNLIKSLHKK-AEAE--VVDVKDIFGPGYMDVVTSTAFSVDIDSINNSD-PFVANI  
Psi\_CYP3C2 LCITDPAMIKTILIKECYSLFTNRRNF--RLN-GQLYDAVSI-A-EDDQWKRIRSVLSPSFTSGRLKEMFDMKHHSANLTSSMKKK-ADK--PELLEKFFGPGYMDVVTSTAFSVDIDSINNSD-PFVANI  
Psi\_CYP4F2 VRI FHPDYVVKPLMAPASITMDELIVY--GHLRFPWLGQSLLS--NGEEWKRIRRLTPAFHFLDKTYVAKFTSTNLTLDHNRHAVAEGSA--ALEMFDHVTMLTDLSSLRCAFSSVDSNCRQST--SEYVSAL  
Psi\_CYP4B1 LNIHHPDYVKTWTS--SEPKDRVAV--SFEI EWIGEGLVLS-GKQKWFRHRRLTPGFHYEVLKPYVDLMSDSTV TMLDKWERY-AKSE--SFELFEHVSLMTLDSILKCAFSDSHCQTESGTNAYIAV

C

C-Helix region

D

E

**SRS3** **SRS4**  
Psi\_CYP4V YKMSDIVSRRQRTPWFWDVYVYCFGE----GREHRTLVKLVHSFTHKVIQEKAASVS-AGDPDSDEEQCAKRRPAFLDMLLK-----TTYDDGSRMSH  
Psi\_CYP46A2 QTEQVELLIQAVRSIYIPGLKFPTR--NRRRKEIDSEVCDLRLGRIKKREQSIA--TNPASTSSASHDDLGLFLMDS-----NSNQETTGITT  
Psi\_CYP46A1 QTCLKGMVFSV-----RDSFFAVNPKNRPFIVEV--REACRLLRTTGAQWKDRKTAME--NGIDVNPNDITQIIKTSVK-----EESMTEEDE  
Psi\_CYP5A --QMFSSPFFRPIML--FFAFPFITAPLARFLPNKRRDQMNHFFINIQIKIQREE--QPAEERRRDFLQMLDARTSKECVSLEHFDASATHAADQQTPAASQDDRLPPQEPSSRRPQKMKITE  
Psi\_CYP3C1 --KNILNFRWP--II--IL--IFPFGARLLTLLKLEMDRVSVDFYDVIKRFKHQH-G--KDIATRADFLQVMIQNEIQETDIKS--EEDQPCKGLTE  
Psi\_CYP3A69 --SRFFKIP--KFVFI--LQ--IFPLLPLFELLGFSFFSPTSTAFFKTLAKIKAEREG--SSCKNSGDLQSMINSKTA--NDPSKGLTD  
Psi\_CYP3A --KKLVKFTFPLPLV--LL--LFPFLPVLKMDVTLFAELDDFFYNFLKKIKSDRNK--NEFKNRVDIQLMVDSSQPET--SK--DNPSSHKGLSD  
Psi\_CYP3C2 --KKMLKFDFFSPIFL--IV--FPFPLGPMVEKMEFSPFPKSVTDFFYAALQKIKSNRVH--SEQKSRVDFLQMLMDSQKNSD--L--SKEESNKGLSD  
Psi\_CYP4F2 VELSERIERRHKLHHWDFYVYKTEQ----GRRFRKALGIVHSFTREVVQKRRALINQQTKSDADLTRAQQRKKDFVDILL--SKDADGRLTD  
Psi\_CYP4B1 YELSYLINLRFRTFPYHSDLIF--LSPH--GFRFRKARKVAHSHTEEVIRKRKEALKGVNRPDG--TRAKRNLDFLIDILLS--ARDENQGLSD

F

G

**SRS5**  
Psi\_CYP4V RDIQEVDVTFMF~~RGHDTT~~AASMNWAVHLLGSHPEAHSKVQQELQEVFGSSD-RPVIMEDLKKLYLECVIK~~EALRL~~ESVPPFARNIGEDCHI-NGFKVPKGANAIIVTYAVHRDPVY~~PE-PDAFRPERF~~LLEN-S  
Psi\_CYP46A2 DEMIGECLKFYF~~AGQETT~~SVLLNWTLVVLSMYPNQWHLARQEVLVQVGRKQ--PFSDMNQLKIVTMI~~YEVLR~~LYPPVFLFLARMAHMANI-GGYSFPGMEFRLPILTMHDDP~~LDVDDVKEFKPERF~~SGIGSK  
Psi\_CYP46A1 EIMLNDNFVTFI~~AGHETT~~ANQLAPCIMELTRRPDILEKMKKEVDVVGMMQ--DISYDDLKGLIYLSQVLK~~ETLRMY~~PTAPGTSRDVLEDVI-DGIIHPPGGVTCFSSYVCGRMD~~FFKD-PLTFDPRF~~HPDA--  
Psi\_CYP5A DEIIVGQAFVFLI~~AGYETS~~SNLAFATCYLLAINPECQRKVQEVDFFSRHE--SPYTNVQELKYLDVMI~~ISLTLRL~~YPPGFRFARDIDQDCVL-NGQFLPKGATLEIPAGFLHYDP~~HWTE-PERFIPERF~~TPEA-K  
Psi\_CYP3C1 HEILSQUALIFIF~~GGYETT~~STLTFLLYLNAINPDAMRTLQEEIDANIPRDA--PLYEDVVLQYLVDQVLL~~ESQRL~~ITAPRLERVKCKTTQV-HGLTIKGTLVGIPVNLHTDP~~FWSS-PQLFRPERF~~SKEG-G  
Psi\_CYP3A69 HEILTQATMFMV~~AGYETS~~ATLAFLAYNLARNPEVMKRLQEEIDATFPDKG--AVYEELVQMEYLDVSVN~~ESLRL~~YPPAGRLDRVAKTVEI-RGITIPKDMIVVIVPYALHRDP~~DLWPE-PBEFRPERF~~SKQN-K  
Psi\_CYP3A SEILSQAMIFIF~~AGYETS~~SSGLGFLAYNLATHPDIQKTLQEEIDETFPNKA--RPIYDALMQMEYLDVMI~~INESMLR~~YPSGNRLDRVSKSSVEI-EGVTIPKGTVMIVPYTLHREP~~DLWPE-PDAFKPERF~~SKEN-K  
Psi\_CYP3C2 HEILSQAMIFIF~~AGYETS~~SSLTFLAYNLATNPDIMKRLQEEVDSFPNKG--PVYQALMQMEYLDVSI~~INESLRL~~YIAPRLERVAKATVEI-NGIVIPKGMVVMVPTWPLHRDP~~DLWPE-PEAFKPERF~~SKEN-K  
Psi\_CYP4F2 BEVQAEANTFMF~~AGHDTT~~ASATCWTLYNLARHEHYQEKCRQEVMDLMQGRDRHKLWEDLSNLPPTTMCIR~~ESLRL~~HAPVQAVTRKYITRDMALPGHRTVPAAGICLVSYGTHHNP~~VWTD-PHFBNPERF~~DPAR-S  
Psi\_CYP4B1 EDLRAEVDVTFMF~~EGHDTT~~ASGLSFLYSLACQPEHQRLCREEILRTLDCGRD--TLWEDLGTKIPYTTMCIK~~ESLRL~~YPPVPGTSRVITKPMTFDGRTEAGCLVGTSVFGIHRNA~~VWEN-PNVFDLRF~~LLEN-V

H I-Helix region

I

J

K-Helix region

PERF motif region

**SRS6**  
Psi\_CYP4V AGRPPYAYIP~~FSAGLRNCTG~~QRFALMEEKVVLAAILRNFNIEACQK----REELR~~YV~~GELTLR~~PENGI~~WIKLEKRKRQT-----  
Psi\_CYP46A2 ATKNKMIFFP~~FGAGSRCTIG~~QSFAMTEARLGLAMILQRFKFELSPSYLH-----APFFFLTLP~~YQHG~~-----  
Psi\_CYP46A1 --PKPYFCYYP~~FALGPRACLG~~KNFAGQMEAKVFMAKLIGRFEFNLLPGQTF-----DELDCGTLR~~PKSGVVCSVRHR~~-----  
Psi\_CYP5A ASRHFPVYLP~~FGAGPRNCVG~~MRLAQLIEIKMALVRLFHRFSIVACSETKV-----PLE~~KS~~SSTL~~GKNGIFVKIQRRDL~~SEGRVNSPPDD  
Psi\_CYP3C1 EEVNPYAYMP~~FGLGPRNCVG~~MRYALLTMKAVLVRLQLSINVTCKDXTMI-----PLEINWK--AG~~VPKI~~KLQFVPRE  
Psi\_CYP3A69 PSINPYTYLPL~~FMGPRNCLG~~MRFALVYVVKLALVEVLGHYSFSVCAETEI-----PLTMEPAGLVG~~PLKPI~~KLKVTTTR  
Psi\_CYP3A DSIDPYSYLP~~FGAGPRNCIG~~MRFALLMMLSMVEILQSFVFTCKETQI-----PLE~~STD~~GFTN~~PKGPINL~~KLPRGA--VADPP--  
Psi\_CYP3C2 DTIDPYTYMP~~FGAGPRNCIG~~MRFALVMMKLAMVEILQRFSFSVCKETEI-----PLE~~MDI~~QGLM~~PKRP~~IKLKLVS  
Psi\_CYP4F2 ADRPSHAFIP~~FSSGPRNCIG~~QKFFALQRLVVVALTLRFRILTPGENPDPGTRSGGVRLPQLVLR~~AEGLL~~WLRVEEL  
Psi\_CYP4B1 SKRSPHAFVFP~~FSAGPRNCIG~~QTFAMNELKVATALTLKRYQLIEDPTQRP-----K~~L~~LAQLVLR~~SINGI~~HIRIKPVD

Heme-binding region

K

L