

Appendix I. HIV Drug Resistance Mutations (DRM) included in EpiMolBio v 0.1 2024

1. HIV-1 acquired DRM

Mutations and classification according to the Stanford HIV Drug Resistance Database v9.6.0 (latest update on 20-03-2024). Information available at <https://hivdb.stanford.edu/> in the "Resistance Notes" section under "Comments."

A) Protease Inhibitors (PI)

MAJOR		ACCESSORY	OTHER
D30N	V82C	L10F	L10I
V32I	V82F	K20T	L10R
M46I	V82L	L23I	L10V
M46L	V82M	L24F	L10Y
I47A	V82S	L24I	V11I
I47V	V82T	L24M	V11L
G48A	I84A	L33F	K20I
G48L	I84C	K43T	K20M
G48M	I84V	M46V	K20R
G48Q	N88G	F53L	K20V
G48S	N88S	F53Y	L33I
G48T	N88T	Q58E	L33V
G48V	L90M	G73A	A71I
I50L		G73C	A71L
I50V		G73D	A71T
I54A		G73S	A71V
I54L		G73T	T74S
I54M		G73V	V82I
I54S		T74P	I85V
I54T		N83D	
I54V		N88D	
L76V		L89T	
V82A		L89V	

Available at <https://hivdb.stanford.edu/dr-summary/comments/PI/>.

B) Nucleoside Reverse Transcriptase Inhibitors (NRTI)

NRTI				OTHER
E40F	D67T	K70T	M184I	T69A
M41L	S68G	L74I	M184V	T69E
E44A	S68D	L74V	L210W	T69I
E44D	S68N	V75A	T215F	T69N
A62V	S68R	V75I	T215Y	T69S
K65E	T69D	V75T	K219E	V118I
K65N	T69G	V75M	K219N	
K65R	K70E	V75S	K219Q	
D67E	K70G	F77L	K219R	
D67G	K70N	Y115F	K219W	
D67H	K70Q	F116Y		
D67N	K70R	Q151L		
D67S	K70S	Q151M		

Available at <https://hivdb.stanford.edu/dr-summary/comments/NRTI/>

C) Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)

NNRTI					OTHER
A98G	V106A	V179F	Y188L	F227L	K101A
L100I	V106I	V179L	G190A	F227V	K101N
L100V	V106M	V179T	G190C	M230I	K101Q
K101E	V106L	Y181C	G190E	M230L	K101T
K101H	V108I	Y181F	G190Q	L234I	K103R
K101P	E138A	Y181G	G190S	P236L	I132L
K103E	E138G	Y181I	G190T	K238N	I132M
K103H	E138K	Y181S	G190V	K238T	V179I
K103N	E138Q	Y181V	H221Y	Y318F	V90I
K103Q	E138R	Y188C	P225H	N348I	
K103S	V179D	Y188F	F227C		
K103T	V179E	Y188H	F227I		

Available at <https://hivdb.stanford.edu/dr-summary/comments/NNRTI/>

D) Integrase Inhibitors (INSTI)

MAJOR			ACCESORY		OTHER
T66A	G140C	Q146R	A49G	S153Y	M50I
T66I	G140S	S147G	H51Y	E157Q	L74I
T66K	G140R	Q148H	L74F	G163K	S119R
E92G	Y143A	Q148K	L74M	G163R	E138D
E92Q	Y143C	Q148N	V75A	S230R	V151I
E92V	Y143G	Q148R	Q95K	D232N	S230N
G118R	Y143H	V151L	T97A		
F121C	Y143K	N155H	T122N		
F121Y	Y143R	N155S	A128T		
E138A	Y143S	N155T	G149A		
E138K	P145S	R263K	V151A		
E138T	Q146L		S153A		
G140A	Q146P		S153F		

Available at <https://hivdb.stanford.edu/dr-summary/comments/INSTI/>

E) Capsid inhibitors (CAI)

MAJOR	ACCESORY
L56I	N57S
M66I	A105T
Q67H	A105S
Q67Y	A105E
Q67N	T107N
Q67K	T107S
K70N	T107A
K70H	
K70R	
K70S	
N74D	
N74S	

Available at <https://hivdb.stanford.edu/dr-summary/comments/CAI/>

2. Transmitted HIV-1 DRM or SDRM

Mutations and classification according to the Stanford HIV Drug Resistance Database v9.5.0 (latest update on 22-08-2023). List of SDRM (mutations for drug resistance surveillance) for PI, NRTI, and NNRTI according to the WHO list¹. List of SDRM for INSTI according to Tzou et al. 2020².

PI		NRTI		NNRTI	INSTI	
L23I	G73S	M41L	L210W	L100I	T66A	Q148R
L24I	G73T	K65R	T215Y	K101E	T66I	N155H
D30N	G73C	D67N	T215F	K101P	T66K	S230R
V32I	G73A	D67G	T215I	K103N	E92Q	R263K
M46I	L76V	D67E	T215S	K103S	E92G	
M46L	V82A	T69D	T215C	V106M	G118R	
I47V	V82T	K70R	T215D	V106A	F121Y	
I47A	V82F	K70E	T215V	V179F	E138A	
G48V	V82S	L74V	T215E	Y181C	E138K	
G48M	V82C	L74I	K219Q	Y181I	E138T	
I50V	V82M	V75M	K219E	Y181V	G140A	
I50L	V82L	V75T	K219N	Y188L	G140C	
F53L	N83D	V75A	K219R	Y188H	G140S	
F53Y	I84V	V75S		Y188C	Y143C	
I54V	I84A	F77L		G190A	Y143H	
I54L	I84C	Y115F		G190S	Y143R	
I54M	I85V	F116Y		G190E	Y143S	
I54A	N88D	Q151M		P225H	S147G	
I54T	N88S	M184V		M230L	Q148H	
I54S	L90M	M184I			Q148K	

Available at <https://hivdb.stanford.edu/page/who-sdrm-list/>

¹*Drug Resistance Mutations for Surveillance of Transmitted HIV-1 Drug-Resistance: 2009 Update.* Bennett DE, Camacho RJ, Otelea D, Kuritzkes DR, Fleury H, Kiuchi M, Heneine W, Kantor R, Jordan MR, Schapiro JM, Vandamme AM, Sandstrom P, Boucher CA, van de Vijver D, Rhee SY, Liu TF, Pillay D, Shafer RW. **PLoS One.** 2009;4(3):e4724. doi: 10.1371/journal.pone.0004724. Epub 2009 Mar 6. PMID: 1926609.

²*Integrase strand transfer inhibitor (INSTI)-resistance mutations for the surveillance of transmitted HIV-1 drug resistance.* Tzou PL, Rhee SY, Descamps D, Clutter DS, Hare B, Mor O, Grude M, Parkin N, Jordan MR, Bertagnolio S, Schapiro JM, Harrigan PR, Geretti AM, Marcelin AG, Shafer RW; WHO HIVResNet Working Groups. *J Antimicrob Chemother.* 2020 Jan 1;75(1):170-182. doi: 10.1093/jac/dkz417. PMID: 31617907.

3. HIV-2 DRM

HIV-2 DRM included in HIV-2 EU Tool v.2 2015³ (Charpentier et al. 2015) and Tzou et al. 2020⁴. Classification according to Stanford HIV Drug Resistance Database v9.4. Unclassified mutations in Stanford (HIVdb HIV-2 program is still in beta) are classified as “Other”.

A) Protease Inhibitors (PI)

MAJOR	ACCESSORY	OTHER
D30N	V10I	L23I
V47A	V33I	V62A
G48V	K45R	I64V
G48A	F53Y	
I50L	T56V	
I50V	V71I	
I54M	A73G	
I54L	F85L	
I82F	N88D	
I82L	M95V	
I82M	L99F	
I84V		
L90M		

B) Nucleoside Reverse Transcriptase Inhibitors (NRTI)

MAJOR	ACCESSORY	OTHER
K65R	K40R	T41L
K65N	A62V	D67N
K65E	N69S	D67GESTH
K70R	L74V	N69T
K70N	L74I	S215A
Y115F	I75V	S215C
Q151M	F77L	S215L
M184V	V111I	K223R
M184I	F116Y	
S215F	D195N	
S215Y	F214L	

C) Integrase Inhibitors (INSTI)

MAJOR		ACCESSORY	OTHER
H51Y	G140S	I84V	Q91R
T66A	Y143C	T97A	V119T
T66I	Y143R		V141I
T66K	S147G		Y143G
E92G	Q148K		N155R
E92A	Q148R		H156R
E92Q	Q148H		
G118R	A153G		
F121Y	N155H		
G140A	R263K		
G140C			

³*HIV-2EU: supporting standardized HIV-2 drug resistance interpretation in Europe.* Charpentier C, Camacho R, Ruelle J, Kaiser R, Eberle J, Gürtler L, Pironti A, Stürmer M, Brun-Vézinet F, Descamps D, Obermeier M. Clin Infect Dis. 2013 Jun;56(11):1654-8. doi: 10.1093/cid/cit104. Epub 2013 Feb 19. PMID: 23429380.

⁴*Expanded Spectrum of Antiretroviral-Selected Mutations in Human Immunodeficiency Virus Type 2.* Tzou PL, Descamps D, Rhee SY, Raugi DN, Charpentier C, Taveira N, Smith RA, Soriano V, de Mendoza C, Holmes SP, Gottlieb GS, Shafer RW. J Infect Dis. 2020 Jun 11;221(12):1962-1972. doi: 10.1093/infdis/jiaa026. PMID: 31965175; PMCID: PMC7289557.