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## **Hepatitis B Virus Resistance Testing**

Nucleoside/Nucleotide analogues are routinely used in the management of Hepatitis B positive patients. They act by inhibiting the reverse transcriptase activity of HBV's endogenous polymerase, resulting in decreased viral replication within infected cells.

They are administered orally and mostly have an excellent tolerance and safety profile. However, a major consideration with the long-term use of these antiviral products is the selection of antiviral-resistant mutations.

Resistance should be identified as early as possible, before clinical breakthrough (increased ALT), by monitoring HBV DNA levels and identifying the pattern of resistance mutations.

We use a well-established in-house method to detect sequence changes associated with antiviral drug resistance. Briefly, this comprises semi-nested amplification of part of the polymerase gene, followed by direct sequencing using ABI BigDye-3 dye terminator technology on an ABI 3130xl genetic analyzer. The resultant sequence data is then analysed both manually and by software comparison to wild-type sequence. A resistance profile can then be derived using data in the table below.

## HBV Resistance Patterns

Antiviral	Resistance Group Number	Reverse Transcriptase Mutations
Lamivudine	1	L180M + M204V/I/S
	2	M204I
	3	L80V/I + M204I [non-A genotype]
	4	V173L + L180M + M204V
	5	I169 T + V173L + L180M + M204V
	6	A181T
	7	T184S+ L180M+ M204V
	8	Q215S + L180M + M204V
Adefovir	1	N236T
	2	A181V/T
	3	V84M, S85A, L80V/I
	4	V214A, Q215S
Entecavir [3TC backbone*]	1	I169T + V173L + L180M + <b>T184G</b> + <b>S202I</b> + M204V
	2	I169T + V173L + L180M + M204V + <b>M250V</b>
	3	Various combinations of mutations at codons <b>184, 202, and 250</b>
Tenofovir	1	L180M + A194T + M204V
	2	V214A, Q215S
	3	A181IV + M204I
Famciclovir		V/G173L, L180M, V/L/M207I

Please note: L80V/I, V84M, S85A Adefovir associated mutations are not encompassed by our assay.