P0137 HIV 125 copies/mL subtype reference panel

RUO

REF P0137

The kit insert contains a detailed protocol and should be read carefully before testing the reference panel to ensure optimal performance

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Intended Use

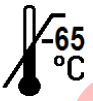
P0137 HIV 125 copies/mL subtype reference panel is composed of a series of cross calibrated HIV-RNA standard dilutions covering most of the genetic variants of the virus, i.e. HIV-1 group M subtypes A-H, circulating recombinant forms (CRF's) AE and AG, some group O isolates and HIV-2 subtypes A and B. The panel can be used to investigate the sensitivity of qualitative and quantitative nucleic acid amplification technology (NAT) methods for detection of different subtypes of Human Immunodeficiency Virus (HIV) RNA type I and 2 and group O in plasma samples. The panel can be used to compare the quantification of low concentrations (of 125 copies/mL) of HIV subtypes by viral load assays is product can be used with amplification methods, including TMA and real-time PCR assays and is useful for development and validation of nucleic acid test systems. It also can be used as a release panel for new batches of HIV-RNA test reagents. This product is not for diagnostic use.

Key to Symbols Used


Manufacturer

Lot number

Catalogue number



Store below -65°C

Biological substance Category B

Research use only


Expiry date

Contents


Caution


Read instructions for use

Summary and Explanation

The HIV subtype panel for blood screening is designed for testing the analytical sensitivity or quantification limits of HIV-RNA tests. The reference panel helps ensure that procedures for HIV-RNA testing are properly validated, and that test results with an unknown group, subtype are consistent across manufacturers, testing laboratories, operators, platforms and assay formats. The bioQControl tissue culture HIV-RNA virus standards have been diluted in a pool of plasma units that tested negative for viral markers in individual donation NAT and serology testing. All viral standards were quantified by testing in the Siemens Versant bDNA 3.0 assays[1,2]. The group O and HIV-2 RNA materials were calibrated against the group M subtype B standard by comparing the HIV-Ag reactivity using the Murex HIV-Ag assay and comparing the reactivity on dilution series in Roche s201 MPX 1.0[3] and Grifols Procleix Ultrio Elite[4]. The group- and subtype was determined by sequencing the V3 region. The viral concentrations in the plasma pool are ensured by gravimetrically recorded dilutions from calibrated viral stock solutions stored at –70°C. The concentration was verified by testing 1:4 dilutions in Grifols Procleix Ultrio Elite[4].

Table 1 reactivity in Grifols Procleix Ultrio Elite

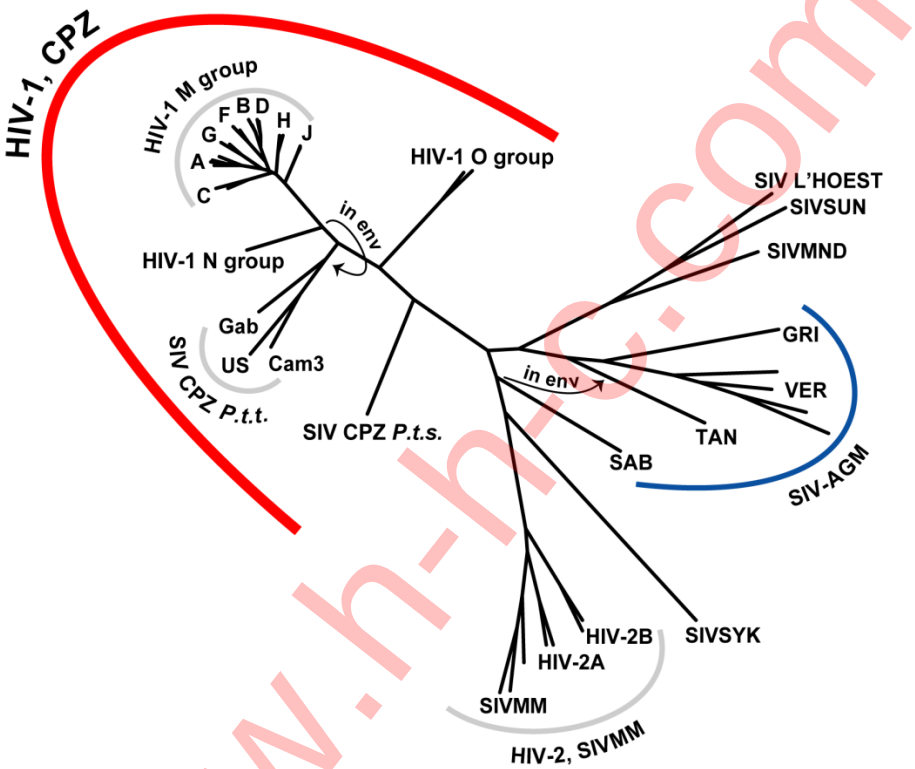
Member	HIV-1 geno, subtype	50% LOD (CI) copies/mL	95% LOD (CI) copies/mL	Ultrio Elite response*
1	A	2.6 (1.6-4.1)	12.8 (7.7-24.7)	4/4
2	B	2.7 (1.9-3.9)	18.4 (11.7-33.8)	4/4
3	C	1.6 (1.1-2.3)	10.9 (6.9-20.2)	4/4
4	D	2.2 (1.3-3.7)	19.1 (10.0-49.4)	4/4
5	F	nd	nd	4/4
6	F	nd	nd	4/4
7	G	nd	nd	4/4
8	G	nd	nd	4/4
9	H	nd	nd	4/4
10	CRF01_AE	1.4 (1.0-2.1)	11.8 (7.8-19.1)	4/4
11	CRF01_AE	nd	nd	4/4
12	CRF01_AG	nd	nd	4/4
13	group O	nd	nd	4/4
14	group O	nd	nd	4/4
15	group O	nd	nd	4/4
16	group O	nd	nd	4/4
17	HIV-2 gt A	2.2 (1.8-2.8)	9.3 (6.8-14.4)	4/4

* 1:4 dilution of 125 cps/mL panel members was tested

HIV genetic subtypes, CRF's and URF's

The Human Immunodeficiency Virus type 1 is characterized by extensive genetic heterogeneity. Due to this variability, HIV-1 variants are classified in three major phylogenetic groups: group M (main), a group O (outlier) as well as a group N (non-M/non-O)[5,6,7]. The group M, responsible for the majority of infections in the HIV-1 worldwide epidemic, can be further subdivided into 10 recognized phylogenetic subtypes (A – K), which are approximately equidistant from one another. Within the group M, the average inter-subtype genetic variability is 15%, for the gag gene, and 25% for the env gene [8, 9,10,11,12,13]. Moreover, within a subtype, it is possible to identify groups of viral isolates forming genetically related sister clades, termed sub-subtypes[14]. This is the case with the A and F clades, whose members are currently classified into A1 - A2 and F1 - F2 sub-subtypes, respectively [15]. However, with the increasing number of viral isolates available worldwide and improvement of sequencing methods, HIV-1 phylogenetic classifications are based either on nucleotide sequences derived from multiple subgenomic regions (gag, pol and env) of the same isolates or on full-length genome sequence analysis. This approach has revealed virus isolates in which phylogenetic relations with different subtypes switch along their genomes. These inter-subtype recombinant forms are thought to have originated in multiply infected individuals. When an identical recombinant virus is identified in at least three epidemiologically unlinked people it can be designated as circulating recombinant forms (CRFs)[16]. More than 20 CRFs have been reported. Nowadays the CRF's do account for 18 % of new infections[17,18] while CRF01_AE [17,19,20] and CRF02_AG[21,22] are dominant in respectively South-east Asia and West-

Central Africa. Group N viruses appear to be a recombination event between a SIVcpz-like and an HIV-1-like virus, and the high similarity to chimpanzee viruses may indicate a recent zoonotic cross-species transmission. These evidences suggest that cross-species zoonotic transmission to humans of additional primate lenti-viruses, and/or recombinations between HIV-1 viruses and primate lenti-viruses, may still evolve to new HIV-1 Groups with unpredictable virulence and incidence[23].



The picture present the genetic diversity of HIV in humans and several monkey related viruses[24].

Relation to 2nd WHO standard for HIV-RNA.

The HIV-RNA Group M subtype B preparation was included in the WHO collaborative study[25,26] to establish the 1st and 2nd WHO standard for HIV-RNA. It was found one bDNA copy is equal to 2.08 IU of the second WHO HIV-RNA standard. The other Groups, Group M subtypes were calibrated on the Group M subtype B preparation. All panel members contain 208 IU/ml.

Principles of the Evaluation Procedure.

The HIV subtype panel for blood screening members have been carefully formulated to mimic human plasma specimens containing 125 copies/ml (208 IU/ml) or 50 virions/ml HIV-RNA. The HIV subtype panel for blood screening is suitable for evaluate the ability of

the assay specific primers and probes to recognise all HIV groups and subtypes. The composition of the panel covers world-wide most spread HIV-variants. HIV Group O and HIV-2 are more diverse to the other isolates and thereby more difficult to detect. For this reason several HIV group O isolates were included. As HIV is continuously evolving we recognise not all variants are included. Laboratories should find equal, positive responses for the different samples.

P0137 HIV 125 copies/ml subtype reference panel reagents

Each panel member is quantified at 125 copies/ml* and filled off with 4.3 ml.

Panel member	HIV group, subtype	Country of origin
01	Group M, subtype A	The Netherlands
02	Group M, subtype B	The Netherlands
03	Group M, subtype C	The Netherlands
04	Group M, subtype D	The Netherlands
05	Group M, subtype F	Brazil
06	Group M, subtype F	Romania
07	Group M, subtype G	Zaire
08	Group M, subtype G	Kenya
09	Group M, subtype H	Zaire
	Circulating rec. forms	
10	Group M, CRF01_AE	The Netherlands
11	Group M, CRF01_AE	Thailand
12	Group M, CRF01_AG	Ghana
	Group O preparations	
13	Group O	USA
14	Group O	Camaroon
15	Group O	Camaroon
16	Group O	Spain
	HIV-2 preparations	
17	HIV-2-RNA genotype A	The Netherlands
	Negative	
18	Negative samples	The Netherlands

The HIV-RNA standards has been diluted in a pool of plasma units that tested individually negative for HBsAg, anti-HBc, anti-HBs, anti-HCV, anti-HIV 1 and 2, HIV-RNA, HCV-RNA and HIV-1 RNA.

Storage Instructions

It is recommended that the panel is stored at below –65°C or lower to ensure highest quality. Discard any unused material after the first use. Any panel members that appear cloudy or contain precipitates after thawing should be discarded.

Warning and precautions

The P0137 HIV 125 copies/ml subtype reference panel members contain infectious *HIV* virions and are bio-hazardous. Observe the universal precautions for prevention of transmission of infectious agents when handling these materials[27,28,29]. Although the normal human plasma used in the production of this panel was negative for infectious disease markers the reference panel members should be handled as if capable of transmitting (unknown) infectious agents. Do not pipette by mouth. Use personal protective equipment, including lab coats, gloves and safety glasses. Do not eat, drink or smoke in areas where P0137 HIV 125 copies/ml subtype reference panel is handled. Disinfect liquids, materials or spills with a 0.5% sodium hypochlorite solution or

equivalent. Dispose of all materials and liquids used in the procedure as if they contained pathogenic agents.

- Do not pipette by mouth.
- Use personal protective equipment, including lab coats, gloves and safety glasses.
- Do not eat, drink or smoke in areas where P0137 HIV 125 copies/ml subtype reference panel and specimens are handled.
- Disinfect liquids, materials or spills with a 0.5% sodium hypochlorite solution or equivalent.
- Dispose of all materials and liquids used in the procedure as if they contained pathogenic agents.

Test procedure

- Thaw the panel members quickly in a water bath at 37°C to avoid formation of cryo-precipitates.
- Mix gently during thawing until ice clot has disappeared.
- Immediately after thawing, vortex briefly, and give a short spin before releasing screw cap from the vials.
- The panel members should be handled and tested in a manner identical to that required for clinical specimens run in the test procedure being evaluated.
- Follow the manufacturers or testing laboratory instructions and recommendations for the handling and testing of clinical specimens.

Limitations

The P0137 HIV 125 copies/ml subtype reference panel in not intended to replace the internal calibrators integral to in vitro diagnostic (IVD) test kits, but may be used as external, independent standards for the assessment of the performance of qualitative or quantitative NAT assays.

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