

Virus Safety Studies (VSS)

Introduction

VSS, as part of the Sanquin Business Unit 'Sanquin Pharmaceutical Services', has more than twenty years experience in performing virus validation studies for plasma derivatives and other biologicals (including bone, milk and animal sera). As a Sanquin unit, VSS is well aware of the most recent blood safety issues and has ample experience in validation of a range of process steps, including column and nanofiltration steps. VSS is highly experienced in providing tailor-made programmes for virus validation studies using efficient experimental designs to obtain accurate insight into viral safety or to demonstrate robustness of a given process step. VSS offers services for customers throughout the world and is well known for its active project support and moreover for performing studies in the timeframes agreed upon.

Facilities and Accreditation

VSS test systems meets the latest requirements of national and international regulatory bodies (i.e. EMEA and FDA). VSS has state-of-the-art Biosafety Level 3 facilities, including strict separation between virus negative and virus positive areas.

The Food and Consumer Product Safety Authority (VWA) of the Dutch authorities have granted an Endorsement of Compliance with the OECD principles of GLP on December 9, 2005, based on assessments performed according to the Netherlands GLP Compliance Monitoring Programme and according to Directive 2004/9/EC.

Virus Validation Studies

Validation studies performed by VSS typically include suitability testing and spiking experiments.

Suitability testing includes:

- Cytotoxicity testing
- Testing for valid stop and storage conditions
- Interference assay
- pH check
- Sterility testing

Virus stocks for spiking experiments:

- Qualified high-titre virus stocks; typically 7-8 log TCID₅₀/ml
- Both serum containing and serum-free virus stocks are available for spiking; typically non-concentrated stocks are used to minimise virus aggregation
- No aggregation detected for CPV, PPV, and HAV stocks by 35 nm filtration and for BVDV, HIV, and PSR by 0.22 µm filtration

Virus assays are performed in real time:

- Samples are tested immediately, typically within 10 minutes after collection
- Minimal handling of samples after collecting; e.g. cytotoxicity of samples is prevented by a rapid one-step dilution with culture medium; no ultra-centrifugation or column steps are used to avoid cytotoxicity and there is no freezing and thawing of samples prior to testing for infectivity
- TCID₅₀ assays testing 3-fold serial dilutions in 8-12 replicates according to the EU-regulations
- Bulk culture tests are used for ultra sensitive detection of residual infectivity
- Extended culture times are used to prevent false negative results and for ultra sensitive detection of viruses

VSS offers these services for a wide range of virus systems (see Table 1).

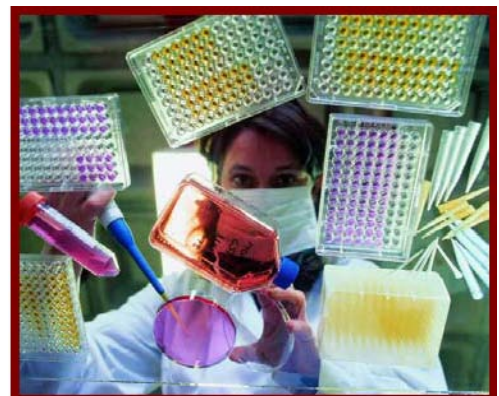


Table 1: Overview of virus systems available at VSS

Virus-system ¹	Virus strain	Cell line	Titre of virus stocks [log TCID50/ml]	Read-out	Total assay time [days]
HIV-1	HTLV-IIIb	MT-2	7.5-8.5	CPE	14
HAV	HM175/18F	BSC-1	7.0-8.0	ELISA	14+14
BPV	Haden	MDBK	6.5-7.5	CPE	14
BVDV	NADL	EBTr	7.0-8.0	CPE	6+6
CPV	780916	A72	7.5-8.5	CPE	7+7
EMC	EMC	VERO	7.0-8.0	CPE	6
MuLV	1-1-A	SC-1/XC	6.0-7.0	PFU	6-10
MVM	MVMi	NB324K	6.5-7.5	CPE	7+7
PPV	NADL2	ST	7.0-8.0	CPE	7+7
PSR	Bartha K61	PD5	8.0-9.0	CPE	5
SV40	PML-2	BSC-1	7.0-8.0	CPE	21
TGEV	Purdue	ST	7.5-8.5	CPE	4
VSV	Indiana	BHK-21	7.0-8.0	CPE	4

¹ Abbreviations: HIV-1, human immunodeficiency virus type 1; HAV, hepatitis A virus; BPV, bovine parvovirus (model virus for B19); BVDV, bovine viral diarrhoea virus (model virus for hepatitis C virus); CPV, canine parvovirus (model virus for B19); EMC, encephalomyocarditis virus (model virus for HAV); MVM, minute virus of mice (model virus for B19); MuLV, murine leukemia virus (general model for retroviruses); PPV, porcine parvovirus (model virus for human parvovirus B19); PSR, pseudorabies virus (herpesvirus, general model virus for lipid enveloped and double stranded DNA viruses); SV40, simian virus type 40 (general model for non-lipid enveloped double stranded DNA viruses); TGEV, transmissible gastroenteritis virus (model virus for coronaviruses); VSV, vesicular stomatitis virus (general model virus for lipid enveloped single-stranded RNA viruses); B19, human parvovirus B19. PFU, Plaque Forming Units.

¹ The B19 titre is expressed as log IU/ml.

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