Validation of an Analytical Method for Lentivirus Physical Concentration Using Videodrop (ILM) following **ICH Q2 Guidelines**

Marie Berger[1], Aurélie Perier *1. Myriade, Paris France 2. Ixaka, Villejuif, France*

Purpose & Protocol

Lentiviral vector (LV) clinical application involves large-scale **Good Manufacturing Practice (GMP)**, including production purification and quality controls.

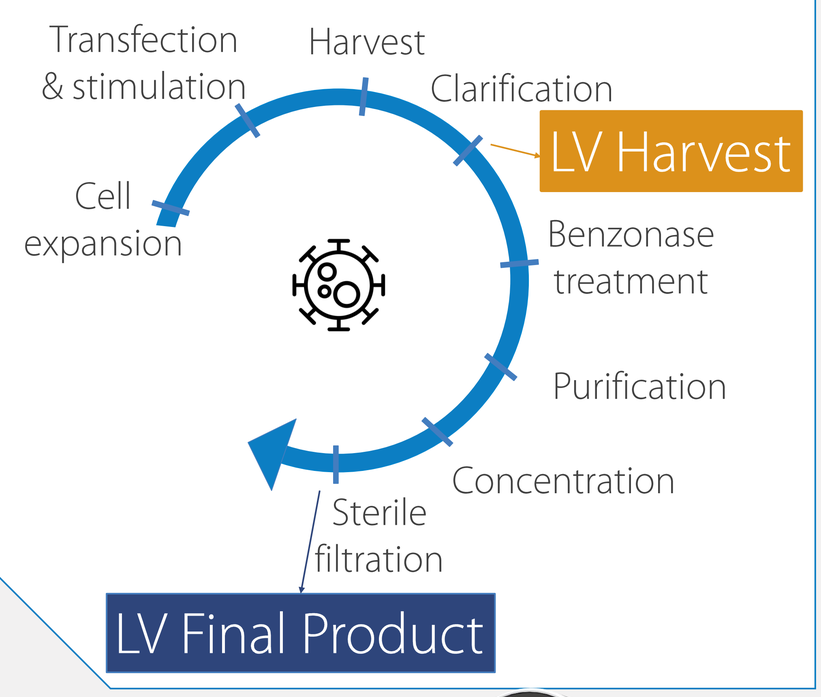
By rapidly measuring the size and physical titer of nanoparticles in solution, VIDEODROP can be integrated in lentiviral quality control strategy. GMP environment implies analytical method validation. Validation of an analytical method for viral vector production must be done according to International Conference on Harmonization Q2 (**ICH Q2**) Guidelines.

In this application note , we demonstrate how **Videodrop** is suitable for GMP environments, as a quality control method for physical titer monitoring of lentiviral vectors.

As described on ICH Q2, LV physical titer quantification method is evaluated on **linearity**, **precision**, **accuracy** and **accuracy compared to a standard method (p24 ELISA).**

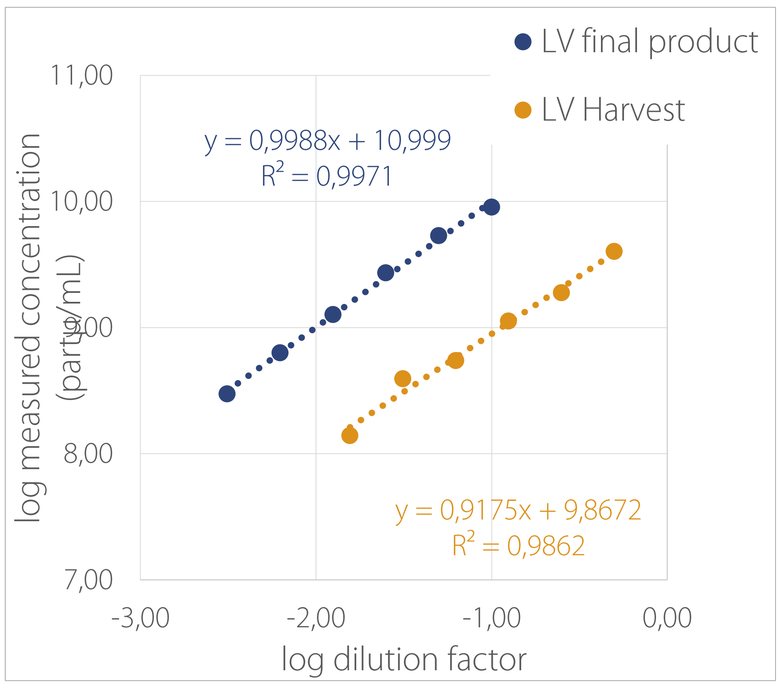
ICH Q2 parameter	Sample	Dilution factor	Replicate per sample
Linearity	LV1 Final product	1/10 ; 1/20 ; 1/40 ; 1/80 ; 1/160 ; 1/320	3
	LV1 Harvest	½ ; ¼ ; 1/8 ; 1/16 ; 1/32 ; 1/64	3
Precision	LV1 Final product	1/80	9
	LV1 Harvest	1/4	9
Accuracy	LV1 Final product	1/10 ; 1/20 ; 1/40 ; 1/80 ; 1/160 ; 1/320	3
Accuracy compared with p24 ELISA	2 batches LV1 : 6 fractions from Harvest to final product LV2 : 3 fractions from Harvest to final product	Linear range	3

LV production process



Results

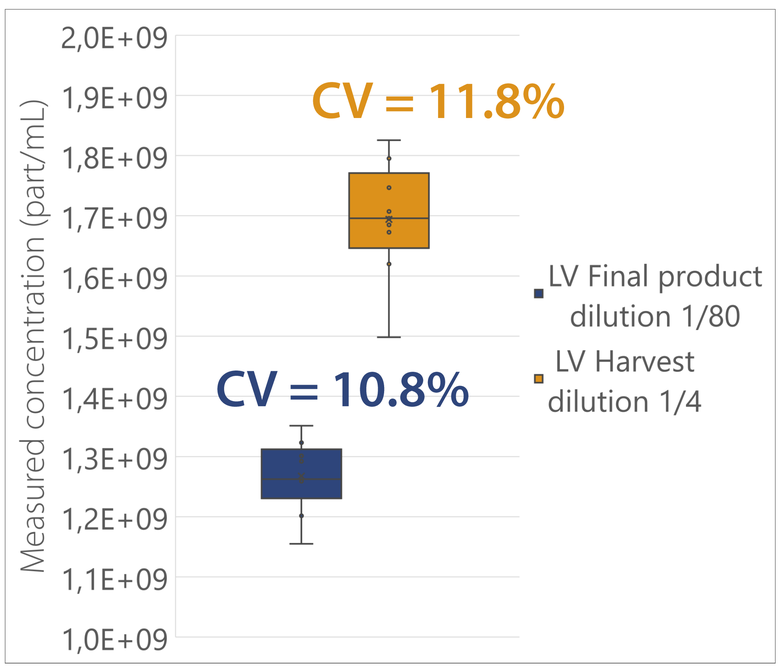
Linearity



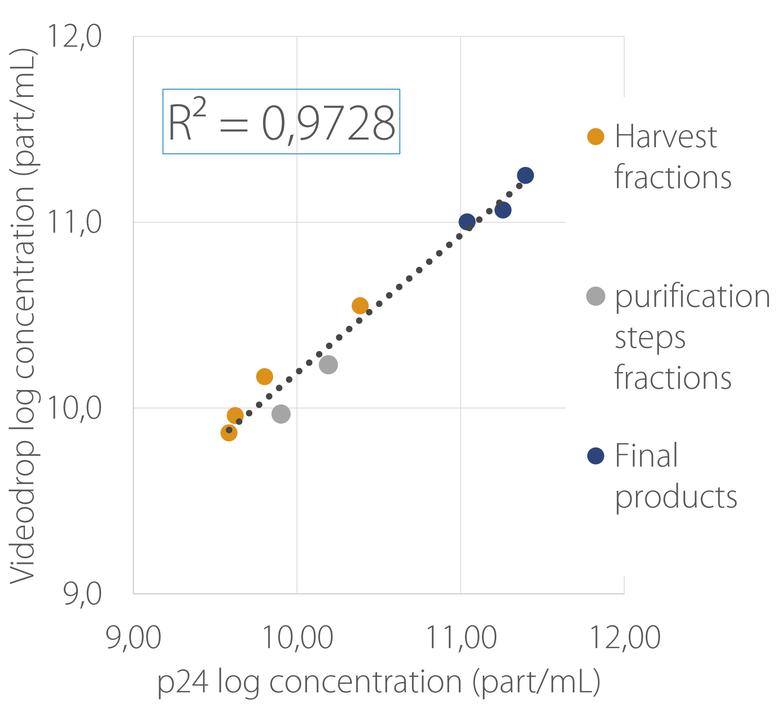
Accuracy

	Dilution factor	Measured Concentration (part/mL)	Theoretical concentration (part/mL)	Recovery (%)
LV Final product 1.00E11 part/mL	1/10	9.00E+09	1.00E+10	**89.7**
	1/20	5.34E+09	5.02E+09	**106.4**
	1/40	2.71E+09	2.51E+09	**108.1**
	1/80	1.26E+09	1.25E+09	**100.8**
	1/160	6.30E+08	6.27E+08	**100.4**
	1/320	2.97E+08	3.14E+08	**94.7**

Precision



Accuracy compared to p24 ELISA



Conclusion

Validation parameter	Results
linearity	R^2>0.98 a>0.9
Precision	CV<12%
Accuracy	Recovery [90-110%]
Accuracy compared to p24 ELISA	R^2=0.97

The **validation** parameters considered in the ICH Q2 guidelines as linearity, precision and accuracy show very good performances for LV physical titer analysis using Videodrop. Videodrop can fit in **GMP bioprocessing of lentivirus**, that are commonly used for ex-vivo engineered cell therapy as CAR-T cells[7] or Hematopoietic Stem Cells[8]

Contact information - Email : Marie.berger@myriadelab.com