Table S1 WHO International Standards for NAT that have been replaced

Preparation	Standard (code number)	Year of establishment	Material (accesion no.)	Unitage (IU/vial)	Reference
Hepatitis A virus RNA	1st IS (00/560)	2003	Viremic human plasma, genotype IA diluted in pooled plasma. 00/560 and 00/562 were prepared from the same single donation and the same diluent and lyophilized separately.	50,000	1
	2nd IS (00/562)	2013		27,000	2
	3rd IS (15/276) – current IS	2017	Viremic human plasma, a new genotype IB strain diluted in pooled plasma (KY003229)	15,451	3
Hepatitis B virus DNA	1st IS (97/746)	1999	Viremic human plasma - Eurohep R1; genotype A, HBsAg subtype adw2 diluted in pooled plasma. 97/746 were prepared from the same original bulk but lyophilized separately; 10/264 and 10/266 were prepared as separate bulks using the same strain with new pooled plasma diluent (KY003230).	500,000	4
	2nd IS (97/750)	2006		500,000	5
	3rd IS (10/264)	2011		425,000	6
	4th IS (10/266)- current IS	2016		477,500	7
Hepatitis C virus RNA	1st IS (96/790)	1997	HCV genotype 1a viremic human plasma diluted in pooled human cryosupernatant. 96/790 and 96/798 were prepared from the same original bulk but lyophilized separately	50,000	8
	2nd IS (96/798)	2003		50,000	9

Preparation	Standard (code number)	Year of establishment	Material (accesion no.)	Unitage (IU/vial)	Reference
	3rd IS (06/100)	2007	HCV genotype 1a viremic human plasma (distinct from 96/790 and 96/798) diluted in pooled human plasma. 06/100 and 06/102 were prepared from the same original bulk but lyophilized separately.	77,440	10
	4th IS (06/102)	2011		130,000	11
	5th IS (14/150) – current IS	2015	HCV genotype 1a viremic human plasma, distinct from previous standards.	100,000	12
HIV-1 RNA	1st IS (97/656)	1999	HIV-1 subtype B viremic human plasma diluted in pooled human cryosupernatant.	100,000	13
	2nd IS (97/650)	2006	Cultured subtype B isolate diluted in pooled human cryosupernatant (KJ019215) - isolate distinct from 97/656).	363,078	14
	3rd IS (10/152)	2011	Cultured and heat inactivated subtype B isolate (the same strain as 97/650) diluted in human plasma prepared as separate bulks from the same stock.	185,000	15
	4th IS (16/194) – current IS	2017		125,893	16
Parvovirus B19	1st IS (99/800)	2000	B19V genotype 1a1 viremic human	500,000	17

Preparation	Standard (code number)	Year of establishment	Material (accesion no.)	Unitage (IU/vial)	Reference
	2nd IS (99/802)	2008	plasma diluted in pooled plasma; 99/800 and 99/802 were prepared from the same original bulk but lyophilized separately (KM065414).	500,000	18
	3rd IS (12/208) – current IS	2013	B19V genotype 1 viremic human plasma of a new strain diluted in pooled plasma.	705,000	19

Table S2 Observed variation in molecular testing in EQA/PT schemes

Target Pathogen	IS available (year of establishment)	SD range of geometric mean (log_{10})*	Units of measurement reported by participants
HIV-1	Yes (1999)	0.17 – 0.24	Copies/mL
HCV	Yes (1997)	0.20 – 0.32	IU/mL
HBV	Yes (1999)	0.30 – 0.45	IU/mL
CMV	Yes (2010)	0.30 – 0.53	IU/mL Copies/mL
EBV	Yes (2011)	0.46 – 0.63	IU/mL Copies/mL
HAV	Yes (2003)	>1.0	Copies/mL
BKV	Yes (2015)	0.50 – 0.60	Copies/mL IU/mL
JCV	Yes (2015)	0.62 – 0.73	Copies/mL IU/mL

Herpes simplex virus	No	0.60 – 0.70	Copies/mL C_T values
Varicella zoster virus	No	0.66 – 0.85	Copies/mL
HHV6B	Yes (2016)	0.50 – 0.80	Copies/mL
Human adenovirus**	No	0.49 – 0.84	Copies/mL
Enterovirus	No	>1.30	C_T values
Gastroenteritis (bacterial, viral, parasitic pathogens)	No	>1.25	C_T values

*Where IU/mL and copies/mL are provided then the SD relates to the IU/mL only.

**It is anticipated that the 1st ISs human adenovirus will be established in 2018.

Table S3 Standards in development

Viral targets	**Parasitic targets**	**Bacterial targets**
Crimean Congo hemorrhagic fever*	*Babesia microti**	*Mycobacterium tuberculosis*
Enterovirus (A71, D68, coxsackie A and B)*	*Leishmania spp*	
Herpes simplex virus type 1 and type 2	*Plasmodium vivax*	
HIV-1 CRF panel extension*	*Trypanosma cruzi*	
Human adenovirus**		
Human papilloma virus[#]		
Influenza virus (A and B)		
Lassa virus*		
Marburg virus*		
Middle East respiratory syndrome coronavirus		
Nipah virus*		
Respiratory syncytial virus		
Sudan virus*		
Varicella zoster virus		

West Nile virus		

*The proposals for these reference materials are expected to be endorsed by the WHO ECBS in October 2018 http://www.who.int/biologicals/BS.2018.2342_Requests_to_initiate_new_WHO_reference_material_projects_for_biologicals.pdf

**N.B. It is expected that the human adenovirus standard will be established at the 1st IS by the WHO ECBS in October 2018

#Several preparations are being evaluated for HPV (types 6, 11, 31, 33, 45, 52 and 58) and similar to the established standard for HPV 16 and HPV 18 are based on recombinant plasmids (20) diluted in human genomic DNA.

Sequence information - International Reference Panels

1st International Reference Panel for Hepatitis B Virus genotypes - (5086/08)

Sequence information (PreS/S region) for the individual panel members available under https://www.pei.de/SharedDocs/Downloads/EN/who/5086-08-additional-information.pdf?__blob=publicationFile&v=1

Table S4 2nd International Reference Panel for HIV-1 subtypes (12/224)

Subtype/group	Strain	Code Number	Accession Number
A	92UG037	11/150	U51190
B	92TH014	11/152	U86572
C	98TZ017	11/154	AF286235
D	94UG114	11/156	U88824
AE	92TH001	11/158	U86565 (near full length)
F	93BR020	11/160	AF005494
G	RU570	11/162	U08368 (partial)
AG-GH	VI525	11/164	L11792 + U09665 + AJ277822 (partial)
N	YBF30	11/166	AJ006022
O	MVP5180	11/168	L20571

Table S5 1st International Reference Panel for HIV-1 circulating recombinant forms (13/214)

Subtype/group	Strain	Code Number	Accession Number
Group O	BCF01	11/144	AY713425
CRF 11 GJ	MP1307	11/148	AF460972
CRF 02 AG	P1261	11/140	EU786671
CRF01 AE	CM244	11/102	AY494 972
CRF01, A, G, J, U	96CM1849	12/146	AJ291720
CRF BG 24	X2456	12/144	FJ670526
Subtype J	SE9173	11/100	*NA
Subtype C	X1936	12/142	EU786673
Subtype G	P962	11/138	EU786670
CRF ADG	24203	11/146	*NA

*Not available

Table S6 1st International Reference Panel for Hepatitis E Virus RNA Genotypes (8578/13)

Genotype	Strain	Code Number	Accession Number
1a		8567/13	NA*
1a	Kol 15	8568/13s	NA*
1e		8569/13	NA*
3b	JRC-HE3	8570/13	AB6300971
3c	Oct 8	8571/13	JN995569 (partial)
3e	Oct 3	8572/13	JN995564 (partial)
3f**	Oct 12	8573/13	JN995573 (partial)
3 (rabbit)		8574/13s	MG211750
4c	HRC-HE15	8575/13	LC387631
4g	HRC-HE58	8576/13	LC387631
2a	Mex 14	8577/13s	KX578717

*Partial sequence data included in original study report for 1a and 1e http://apps.who.int/iris/bitstream/handle/10665/197775/WHO_BS_2015.2264_eng.pdf;jsessionid=31DC19F99562D2722A9B88594D83AF51?sequence=1, whole genome sequencing of panel has been performed (manuscript in preparation)

**3f – tentatively assigned as 3l using the HEVnet criteria

Table S7 1st International Reference Panel for Parvovirus B19 Genotypes - 09/110; CBER Parvovirus B19 Genotype Panel 1

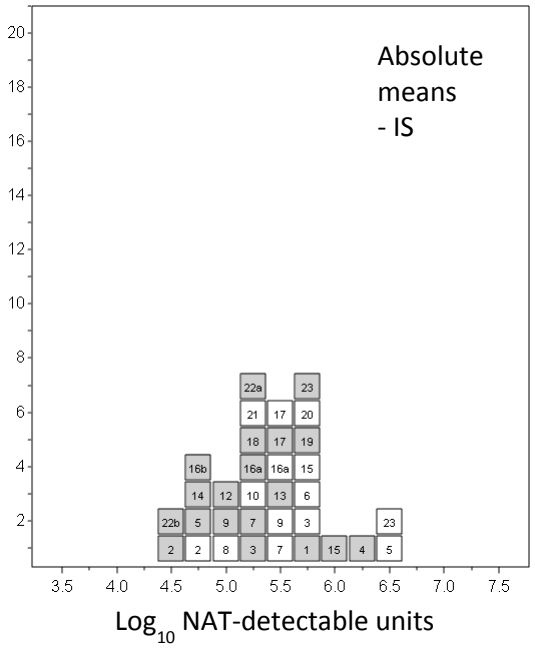
Genotype	Strain	Code Number	Accession Number
1a1	NA	09/110 member 1	KM065414
2	IM-81	09/110 member 22	AY903437
3a	P1	09/110 member 3	FJ265736

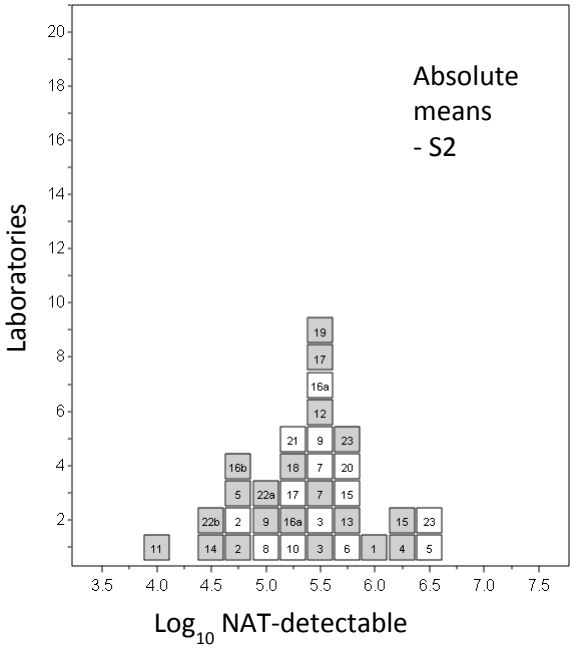
Panel member 4 – negative plasma

Panel supplied by both NIBSC (code number 09/110) also supplied by CBER/FDA (code number Parvovirus B19 Genotype Panel 1)

Figure S1 Relative potency analysis

Relative potency of the sample S2 included in the study to establish the 1st IS for HEV RNA. White indicates quantitative assays (log_{10} copies/mL); gray indicates qualitative assays (log_{10} NAT–detectable units/mL). Number of laboratories is indicated on the vertical axis. Laboratory code numbers are indicated in the respective boxes. Reproduced, in modified form, with the permission of *Emerging Infectious Diseases* (21).





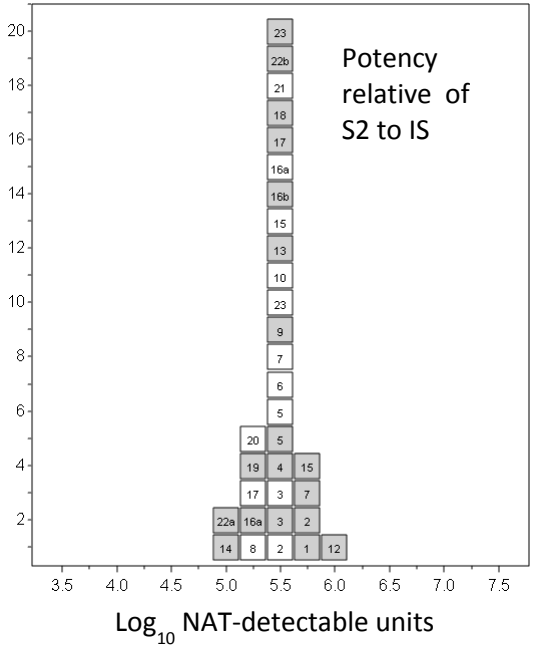


Figure S2 Change in qualitative versus quantitative reporting for the CMV EQA programme between 2002 and 2018.

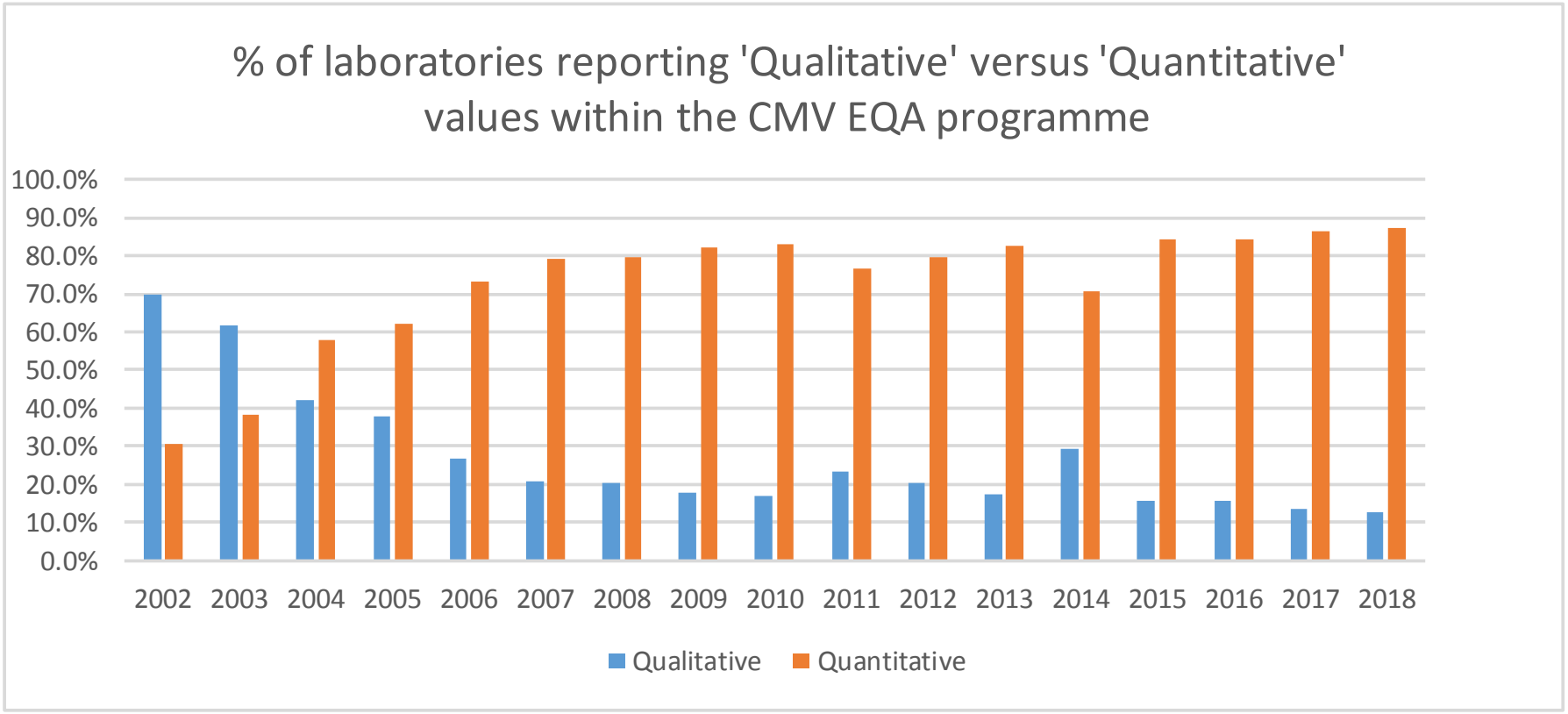


Figure S3 Increase in reporting in IU/mL versus copies/mL or other units for CMV in the EQA programme between 2002 and 2018.

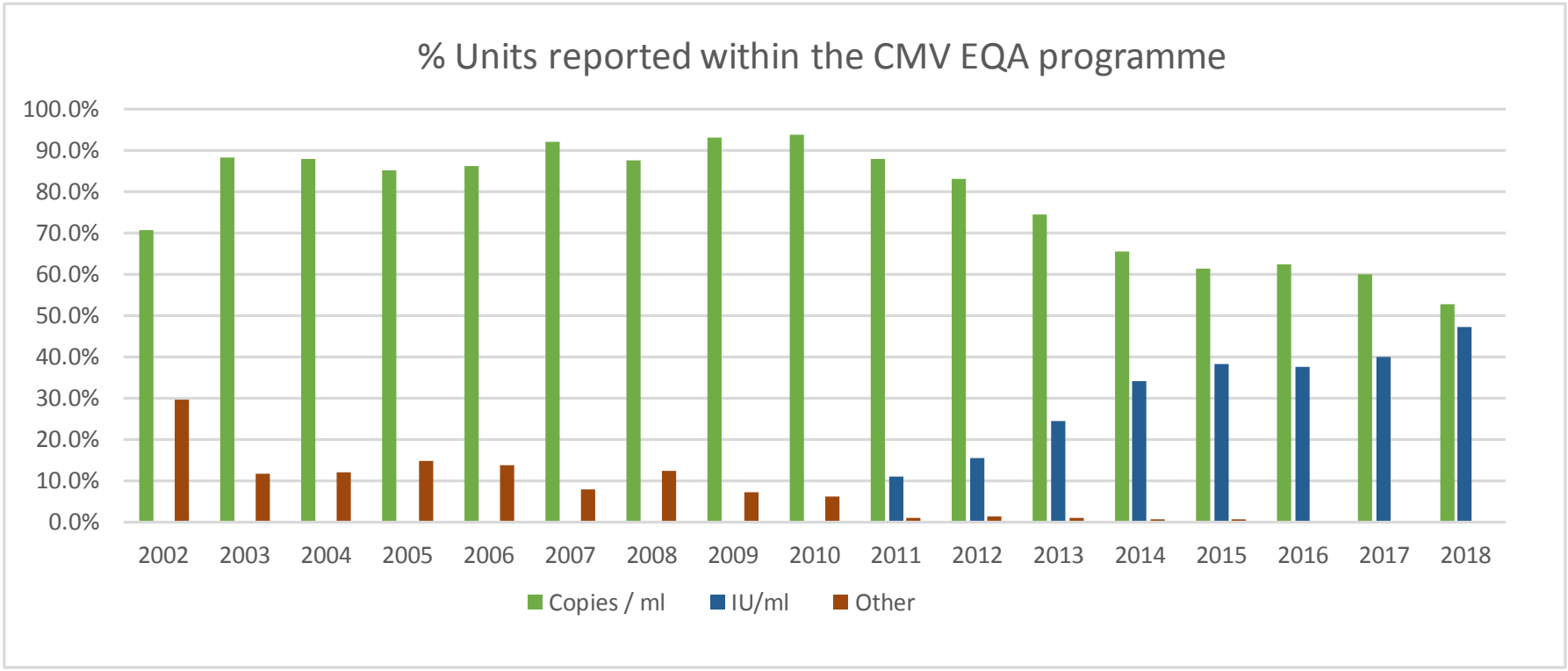
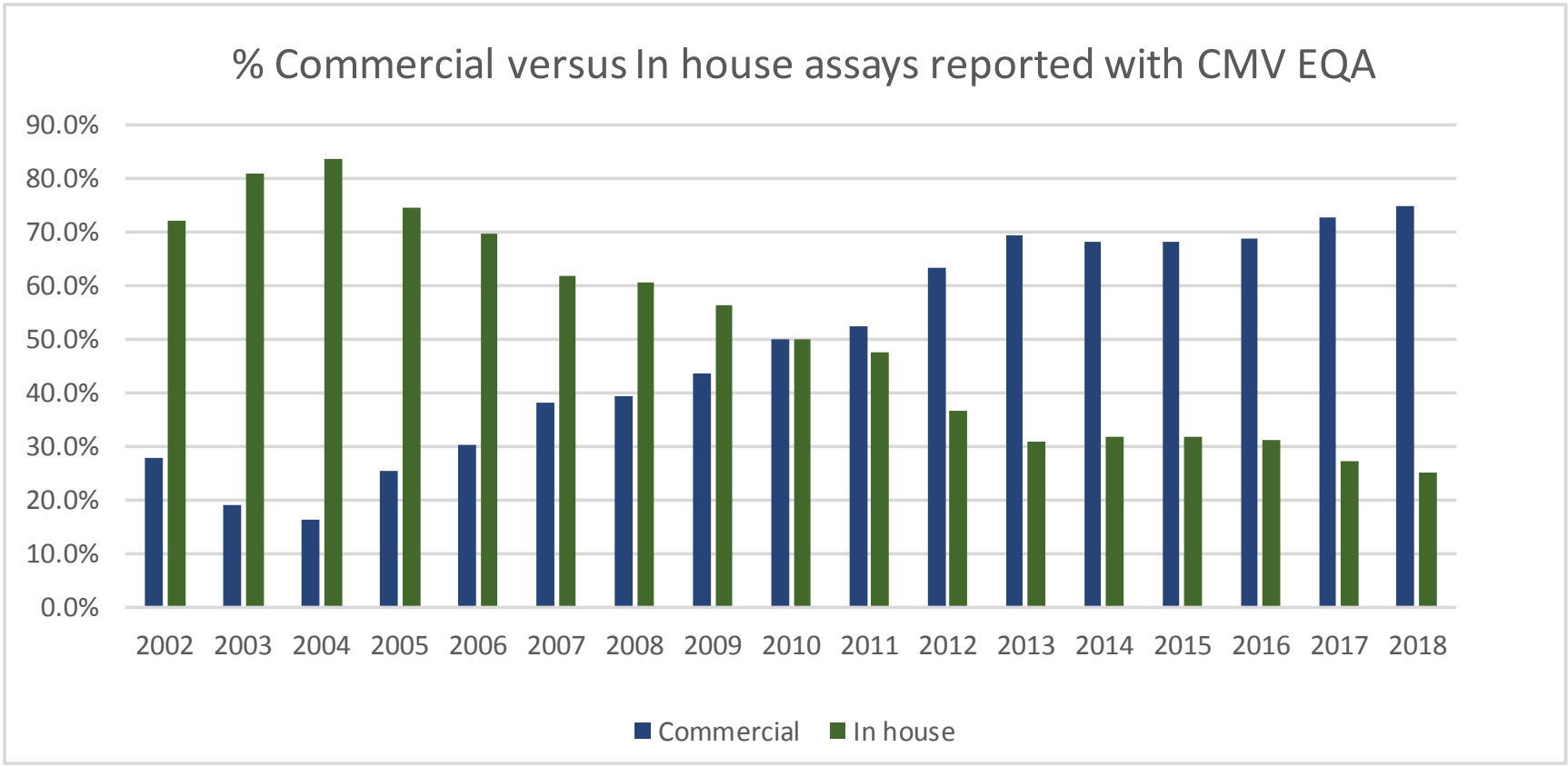


Figure S4 Increasing use of commercial CMV assays for the CMV EQA programme between 2002 and 2018.



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