Improving human papillomavirus (HPV) testing in the cervical cancer elimination era: The 2021 HPV LabNet international proficiency study

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ABSTRACT

Background: Proficient Human Papillomavirus (HPV) genotyping services are essential to support HPV and cervical cancer elimination strategies, in particular to support HPV vaccine research.

Objectives: To perform a global HPV genotyping proficiency study, with evaluation in relation to previous proficiency studies.

Study design: The proficiency panel contained 44 coded samples (40 samples containing one or more purified HPV types (HPV6/11/16/18/31/33/35/39/45/51/52/56/58/59/68a/68b) in human DNA, 1 human DNA control and 3 DNA extraction controls). Proficiency required detection of both single and multiple infections of 50 International Units of HPV 16/18, of 500 genome equivalents for other HPV types and no false positivity.

Results: One hundred and thirty-two laboratories submitted 211 datasets. Most assays used (182/211 datasets) were commercially available. An all-time high of 75% of the datasets were 100% proficient. One or more false positives were found in 17.5% of datasets. Among laboratories who participated in the 2019 proficiency study, full proficiency increased from 25% in 2019 to 60% in 2021. The high overall proficiency was mostly attributable to a large number of new laboratories, which used similar assays.

Conclusions: The worldwide deterioration in comparability and reliability of HPV testing found in 2019 is now reversed and an overall increase in proficiency is found.

WPRO   Western Pacific Regional Office.

1. Introduction

In the era of cervical cancer elimination, many laboratories perform Human Papillomavirus (HPV) detection and the number of different assays used has increased exponentially. [1] In 2012 there were already 125 different commercial HPV tests on the global market and in 2020, there were 254 distinct HPV assays and 425 assay variants. [2, 3]

Accurate and internationally comparable HPV detection is a must for both research and evaluation of HPV vaccination, as well as for screening programs. [4] A recent meta-review of publications validating the different HPV assays found that only 11 HPV DNA assays had published in the peer-reviewed literature with analytical/clinical evaluation. [3]

Abbreviations
AFRO   African Regional Office
EMRO   Eastern Mediterranean Regional Office
EURO   European Regional Office
Equalis   External quality assessment of laboratory medicine in Sweden
GE   Genome equivalents
HPV   Human papillomavirus
International HPV Reference Center   IHRC
IU   International units
LabNet   Laboratory Network
PAHO   Pan American Health Organization
PP   Proficiency panel
SEARO   South-East Asian Regional Office
WHO   World Health Organization

the fee before February 2022.

3. Results

The 2021 proficiency study was distributed to 144 subscribing laboratories. A total of 132 laboratories returned 211 datasets (every laboratory could submit more than one dataset if several different HPV typing methods were used – one dataset per method). Ninety-six laboratories submitted 1 dataset, 13 laboratories submitted 2 datasets, 4 laboratories submitted 3 datasets, 18 laboratories submitted 4 datasets and 1 laboratory submitted 5 datasets.

There were 126 participating laboratories that provided data on type of laboratory. There were 83 diagnostic and screening laboratories, 26 laboratories performing HPV surveillance, 8 clinical trial laboratories and 9 diagnostic test manufacturers. The annual number of samples analysed for HPV per laboratory varied from 100 to > 100,000 per year, with 15 laboratories performing 10,000 tests or more.

Among datasets that typed for at least one HPV type 158/211 (75%) were 100% proficient for the types claimed to be detected by the test. Of these, 119/158 datasets not only correctly identified the content of all required samples, but also correctly identified the content of the training samples that contained amounts that were lower than required for proficiency (samples that contained only 5IU of HPV16/18 and 50GE of other HPVs). Tests that did not type for all the types in the panel could still be 100% proficient, as the denominator was the number of types claimed to be detected by the test (not the number of types included in the panel).

3.1. Proficiency by HPV type

The number of laboratories reporting correct HPV types, with no false positivity, are shown in Table 1. Median percent of 100% proficient datasets for the different coded samples was 94.8% (minimum 75.9%, maximum 99.0%). All datasets showed >90% proficiency for all coded samples containing 50 UI or 500 GE/ 5ul except for HPV 68a, where 75.9% and 78.9% of the datasets had detected HPV 68a at 50 GE/5 ul and 500 GE/5 ul, respectively.

3.2. Proficiency by WHO region

Laboratories submitting datasets belonged to 6 WHO regions, with Western Pacific Regional Office (WPRO) showing the highest number of participating laboratories ($n = 59$), followed by European Regional Office (EURO, $n = 49$), Pan American Health Organization (PAHO, $n = 10$), African Regional Office (AFRO, $n = 7$), Eastern Mediterranean Regional Office (EMRO, $n = 5$) and South-East Asian Regional Office (SEARO, $n = 2$).

The proportion of laboratory proficiency including all datasets grouped by WHO region is shown in Fig. 1 and Table 2. WPRO showed the highest number of proficient laboratories (93%) and EURO was the region with the highest number of non-proficient laboratories, with only 49% of laboratories being 100% proficient.

3.3. Proficiency by assay used

The different assays used are displayed in Fig. 2 and the number of proficient datasets, false positivity, and HPV targets per assay in Table 3.

A total of 182 datasets were obtained using commercially available tests, with the most commonly assays used being Hybribio 21 array (Hybribio, 39 laboratories), Anyplex II HPV 28 (Seegene, 21 laboratories) and 3 other Hybribio assays (20 laboratories) (Table 4). Twenty-

Table 2
Proportion of datasets submitted by WHO region with ≥90% proficient HPV typing results.

Region (datasets)	Proportion of laboratories with 100% correct typing	Proportion of laboratories with ≥90% correct typing
EURO (65)	49%	52%
AFRO, EMRO, SEARO (17)	65%	65%
PAHO (12)	50%	50%
WPRO (117)	93%	96%

AFRO: African Regional Office, EMRO: Eastern Mediterranean Regional Office, EURO: European Regional Office, PAHO: Pan American Health Organization, SEARO: South-East Asian Regional Office, WPRO: Western Pacific Regional Office.
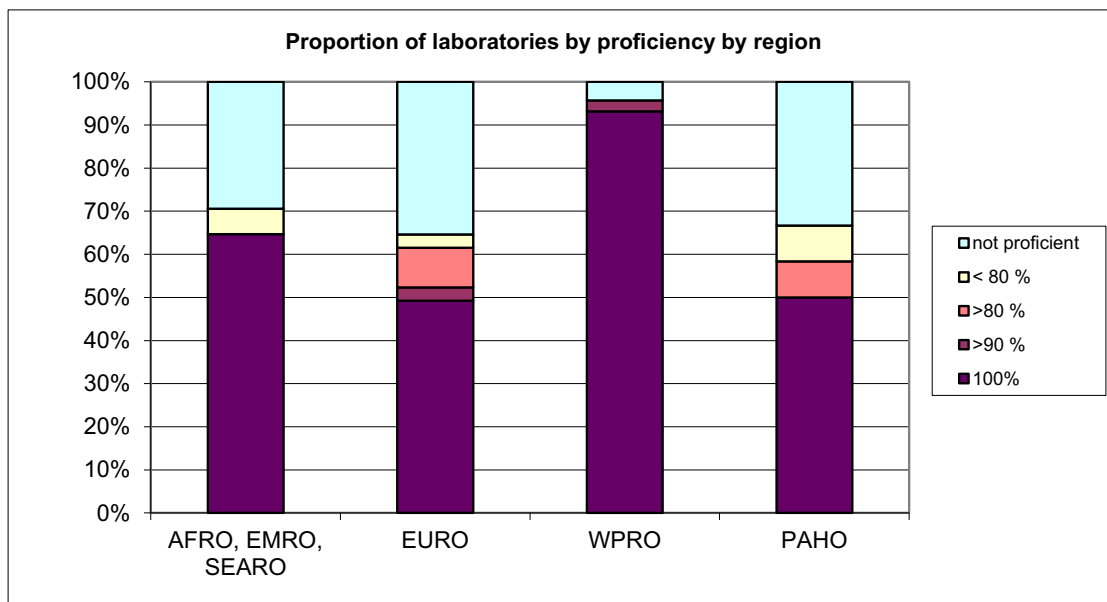
Fig. 1. Proficiency for HPV DNA typing by WHO region. Proficiency criteria were: i) detection at least 50 international units (IU) per 5 ul of HPV 16 and HPV 18, in both single and multiple HPV infections, ii) detection of at least 500 genome equivalents (GE) in 5 ul of the other HPV types (not HPV 16 nor HPV 18) in both single and multiple HPV infections and iii) no false positivity detection. AFRO: African Regional Office, EMRO: Eastern Mediterranean Regional Office, EURO: European Regional Office, PAHO: Pan American Health Organization, SEARO: South-East Asian Regional Office, WPRO: Western Pacific Regional Office.
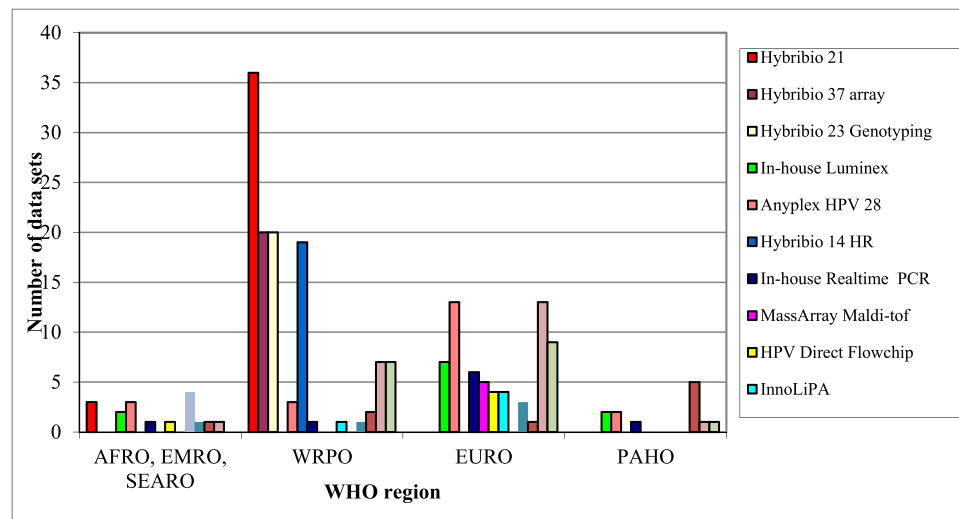
Fig. 2. Type of assay in use for HPV DNA typing by WHO region. AFRO: African Regional Office, EMRO: Eastern Mediterranean Regional Office, EURO: European Regional Office, PAHO: Pan American Health Organization, SEARO: South-East Asian Regional Office, WPRO: Western Pacific Regional Office. Data for AFRO, EMRO and SEARO region are combined.

eight datasets were generated using assays that either did not discriminate specific HPV types or reported results as HPV 16, 18 and "other" HPV types (Hybribio 14 HR, Roche Cobas 4800/6800 test, Abbot Realtime PCR, High risk HPV Screen, Harmonia HPV, and Oncopredict Screen). These datasets were only analyzed for the specific types tested for individually.

Twenty-nine datasets were obtained using a variety of in-house assays.

Overall, 74.88% of datasets (158/211) were 100% proficient and 82.46% (174/211) of datasets showed no false positivity. There were several assays with all the datasets provided showing 100% proficiency (Hybribio 37 array HPV (Hybribio), HPV-23 Genotyping (Hybribio), Hybribio 14 HR (Hybribio), Real-time PCR MehrViru, Tellgen 27plex 14HR, GenoFlow HPV array (DiagCor) and OncoPredict HPV-DNA (Hiantis)), followed by Hybribio 21 array HPV (Hybribio) with 97.44% of datasets being 100% proficient. None of the datasets obtained with HPV SPF10-LiPA25 (Labo-bio), Abbott m2000 / Alinity M (Abbott), Ampliquality (AB Analitica) and VisionArray HPV (ZytoVision) were fully proficient.

Up to 11 assays (all commercial) showed no false positivites, including Abbott m2000 / Alinity M (Abbott), VisionArray HPV (ZytoVision), MassArray MALDITOF (Agena), Onclarity (BD) and Hybribio 37 array HPV (Hybribio), in addition to the assays that were 100% proficient as listed above. Only HPV SPF10-LiPA25 (Labo-bio) showed all datasets (n = 3) non-proficient (all of which due to false positivity).

We investigated if there was any specific sample or assay where false positivity was consistently detected. Overall, false positivity appeared to be essentially randomly distributed among samples, indicating that the problem with false positivity was not related to a specific sample nor an assay itself (e.g. cross-reactivity), but rather due to laboratory conditions of use (e.g. cross-contamination).

Comparison of results for laboratories that participated in 2021 as well as in 2008, 2010, 2011, 2013, 2014, 2017 and 2019.

In total, 65 laboratories that participated in 2021 had also participated in at least one of the previous proficiency studies. There were 15 laboratories that submitted results in 2021 that had been participating ever since the first PP was issued in 2008, with 10/15 having participated in all eight previous proficiency studies (2008, 2010, 2011, 2013, 2014, 2017, 2019 and 2021). Some laboratories used the same tests during all years, whereas some laboratories had changed at least one of the tests used.

Comparisons of these results were made for each laboratory using the current proficiency criteria for evaluating datasets obtained during all the years. At the outset in 2008 one false positivity had been allowed, but since 2019 no false positivity is required for 100% proficiency. We now retrieved all crude data from previous years and re-calculated proficiency using exactly the same criteria as used since 2019 (no false positivity allowed).

The proficiency trend for laboratories participating multiple times is shown in Table 3. The 2021 PP revealed an increase in 100% proficiency (from 25% to 60%) and a decrease in <80% proficiency (from 45.1% to 33.1%) when compared to 2019. Moreover, the highest overall proficiency (75% of datasets) was achieved in 2021 – higher than in any previous proficiency study.

4. Discussion

We report that the global proficiency in HPV genotyping services had increased in 2021. The increased proficiency is seen both in laboratories that had participated in previous studies as well as in laboratories participating for the first time. This improvement suggests that continuing proficiency testing is helpful to sustain accuracy and to avoid a deterioration in proficiency, as found in 2019. [10]

There are three major strengths of our proficiency study. [10] First, the use of the same PP design as in previous PPs enables a directly comparable estimate of the global development of proficiency in HPV genotyping services. Second, the panel contains all 13 HPV types established as oncogenic and the 2 non-oncogenic vaccine-targeted HPV types, reflecting the HPV genotyping requirements that are most important for HPV vaccine research, surveillance, and monitoring, and third, the broad worldwide distribution (132 laboratories worldwide) and variety of different HPV tests used that make generalizability possible.

Weakness of the study is that the PP was composed for evaluating the HPV genotyping services required to support HPV vaccine research and studies monitoring vaccination impact. However, HPV screening may not need to always separate all different HPV genotypes and the sensitivity requirement may also be different. Similar panels with screening-relevant concentrations of HPV genotypes will be developed to assess and validate the assays (and their use in laboratories) used in cervical screening and triage of high-risk HPV-positive subjects. Another weakness is that we do not have any explanation for the low detectability of HPV68a. Samples were diluted in human DNA as typically found in clinical samples. Further dilution of the samples may have led to a

Table 3
Assays used for testing and typing of HPV, HPV region targeted, proficiency and false positivity.

HPV assay type	No. of datasets	HPV region targeted (primers)	No. of proficient data sets					No. of false positive samples per data set				
			100% proficient	99–90% proficient	89–80% proficient	<80% proficient	Not proficient	0 samples	1 sample	2 samples	3 samples	> 3 samples
All assays	211	L1/L2/E1/E2/E4/E5/E6/E7	158	5	7	4	37	174	19	7	1	10
Hybribio 21 array HPV (Hybribio)	39	L1 (MY09/11)	38	0	0	0	1	38	1	0	0	0
Anyplex II HPV 28 (Seegene)	21	L1	15	1	0	0	5	16	3	1	0	1
Hybribio 37 array HPV (Hybribio)	20[c,f]	L1 (MY09/11)	20	0	0	0	0	20	0	0	0	0
HPV-23 Genotyping (Hybribio)	20[c,f]	L1/L2/E1/E2/E4/E6/E7	20	0	0	0	0	20	0	0	0	0
Hybribio 14 HR (Hybribio)	19[c,f]	E6 / E7	19	0	0	0	0	19	0	0	0	0
In-house PCR Luminex	11	L1 / E7	7	0	0	0	4	7	3	1	0	0
In-house realtime PCR	9[e,h]	L1/E1/E4/E6/E7	4	0	0	0	5	4	3	1	0	1
MassArray MALDITOF (Agena)	5[f]	E6 / E7	2	0	3	0	0	5	0	0	0	0
HPV Direct Flow-chip (Master Diagnostica)	5[e,h]	L1 (GP)	4	0	0	0	1	4	0	1	0	0
InnoLiPA Extra (Fujirebio)	5	L1 (SPF10)	2	0	0	0	3	2	2	1	0	0
Anyplex HR HPV (Seegene)	5	L1	3	1	0	0	1	4	0	0	0	0
Real-time PCR MehrViru	4[c,f]	E6/E7/L1/L2	4	0	0	0	0	4	1	0	0	0
In-house PGMY-CHUV	3	L1 (PGMY)	2	0	0	0	1	2	0	0	0	1
HPV SPF10-LiPA25 (Labo-bio)	3[d,g,h]	L1 (SPF10)	0	0	0	0	3	0	0	2	1	0
Cobas 4800 / 6800 (Roche)	3	L1	2	0	0	0	1	2	1	0	0	0
Abbott m2000 / Alinity M (Abbott)	3[f]	L1	0	2	1	0	0	3	0	0	0	0
Tellgen 27plex, 14HR	3[c]	L1 / L2	3	0	0	0	0	3	0	0	0	0
Realquality (AB Analitica)	3[e,h]	E6 / E7	1	0	0	0	2	1	2	0	0	0
In-house NGS	2	L1	1	0	0	0	1	1	1	0	0	0
Onclarity (BD)	2[f]	E6 / E7	1	0	0	1	0	2	0	0	0	0
GenoFlow HPV array (DiagCor)	2[c,f]	L1 (PGMY)	2	0	0	0	0	2	0	0	0	0
Ampliquality (AB Analitica)	2	L1	0	1	0	0	1	1	0	0	0	1
OncoPredict HPV-DNA (Hiantis)	2[c,f]	E6 / E7	2	0	0	0	0	2	0	0	0	0
VisionArray HPV (ZytoVision)	2[f]	L1	0	0	1	1	0	2	0	0	0	0
Other Commercial assays[a]	14	L1/E1/E2/E6/E7	5	0	2	1	6	8	3	0	0	3
Other In-house assays[b]	4	L1 / E6 / E7	1	0	0	1	2	2	0	0	0	2

[a]Other commercial assays include one laboratory using each of: Venus HPV, Harmonia HPV, Molgentix, Papilloplex, AmpFire, OncoPredict Screen, GeneProof, HPV Operon, HPV screen, SACACE HPV screen, yd-diagnostics, aid-diagnostika, Cephid GeneXpert, CLART 4 Genomica.
[b]Other In-house assays include one laboratory using each of: In-house RFLP, In-house Blot, In-house gel-electroforesis and In-house Mass-array.
[c]All datasets provided using the assay were classified as 100% proficient.
[d]All datasets provided using the assay were classified non-proficient.
[e]Most datasets provided using the assay were classified as non-proficient.
[f]All datasets provided using the assay did not report false positivity.
[g]All datasets provided using the assay reported false positivity.
[h]Most datasets provided using the assay reported false positivity.

Table 4

Proficiency of detecting HPV types and number of false positive results by laboratories that participated in 2021 PP, with data from 2008, 2010, 2011, 2013, 2014, 2017 and 2109 in comparison with all data sets submitted 2021.

		All test by laboratories that participated in 2008, 2010, 2011, 2013, 2014, 2017, 2019 and 2021								All datasets 2021 (%)
		2008 (%)	2010 (%)	2011 (%)	2013 (%)	2014 (%)	2017 (%)	2019 (%)	2021 (%)	
N total participating laboratories / datasets[a]		54/85	98/132	96/134	96/136	121/148	114/141	78/110	132/211	132/211
Overall proficiency[b]		25%	22%	40%	44%	59%	73%	50%	75%	75%
N participating laboratories / datasets[c]		NA	16/27	19/33	21/38	28/43	32/65	43/77	64/94	64/94
Data proficiency comparison*	100% proficient	5 / 17 (29)	5 / 27 (19)	16 / 33 (48)	15 / 38 (39)	26 / 43 (60)	35 / 65 (54)	19 / 77 (25)	56 / 94 (60)	158 / 211 (75)
	99–90% proficient	1 / 17 (5.9)	1 / 27 (3.7)	2 / 33 (6.1)	3 / 38 (7.9)	2 / 43 (4.7)	5 / 65 (7.7)	17 / 77 (22)	5 /94 (5.3)	5 / 211 (2.4)
	89–80% proficient	1 / 17 (5.9)	3 / 27 (11)	3 / 33 (9.1)	4 / 38 (11)	3 / 43 (7.0)	6 / 65 (9.2)	6 / 77 (7.8)	2 / 94 (2.1)	7 / 211 (3.3)
	<80% proficient	3 / 17 (18)	3 / 27 (11)	2 / 33 (6.1)	0 / 38 (0)	1 / 43 (2.3)	2 / 65 (3.1)	2 / 77 (2.6)	2 / 94 (2.1)	4 / 211 (0.9)
	Not proficient	7 / 17 (41)	15 / 27 (56)	10 / 33 (30)	16 / 38 (42)	11 / 43 (26)	17 / 65 (26)	33 / 77 (43)	29 / 94 (31)	37 / 211 (17)
False positivity	0 samples	9 / 17 (53)	12 / 27 (44)	23 / 33 (70)	22 / 38 (58)	32 / 43 (74)	48 / 65 (74)	44 / 77 (57)	65 / 94 (69)	174 / 211 (82)
	1 sample	1 / 17 (5.9)	2 / 27 (7.4)	5 / 33 (15)	7 / 38 (18)	2 / 43 (4.7)	8 / 65 (12)	16 / 77 (26)	17 /94 (18)	19 / 211 (9.0)
	2 samples	4 / 17 (24)	5 / 27 (18)	3 / 33 (9.1)	1 / 38 (2.6)	2 / 43 (4.7)	2 / 65 (3.1)	5 / 77 (6.5)	6 / 94 (6.4)	7 / 211 (3.3)
	3 samples	1 / 17 (5.9)	5 / 27 (18)	0 / 33 (0)	3 / 38 (7.9)	3 / 43 (2.3)	1 / 65 (1.5)	6 / 77 (7.8)	1 / 94 (1.1)	1 / 211 (0.5)
	>3 samples	2 / 17 (12)	3 / 27 (11)	2 / 33 (6.1)	5 / 38 (13)	4 / 43 (9.3)	6 / 65 (9.2)	6 / 77 (7.8)	5 / 94 (5.3)	10 / 211 (4.7)

[a] Number of total laboratories and datasets that have been included for each of the corresponding proficiency panels (not considering if they participated other years).
[b] Overall proficiency detected for each proficiency panel not considering if laboratories had participated other years.
[c] Number of total laboratories and datasets laboratories that have participated in the corresponding year as well as in previous proficiency panels. For 2008, the value is non-applicable as it was the first panel study.
*Proficiency detected from datasets belonging to laboratories that had participated in more than one proficiency panel. NA: non-applicable.
Comparison of proficiency and false positivity over the years for laboratories that have participated in at least in two proficiency panels.

decrease in proficiency. As these samples were readily detectable by a majority of labs, it is unlikely that the low detectability could be caused by a problem with the samples.

The proportion of commercial assays has increased over time, from 57% in 2011, 80% in 2019, and now 86% in 2021 (182/211). Surprisingly, only 13/211 datasets had used any one of the 11 assays that in systematic reviews of the literature had been found to have had published validation data fulfilling all validation criteria (Abbott RealTime High Risk HPV, $n = 3$; Anyplex II HPV HR Detection, $n = 5$; BD Onclarity HPV Assay, $n = 2$; Cobas 4800 HPV Test, $n = 3$). [11] Both Anyplex II HPV HR Detection and Cobas 4800 showed false positivity in one dataset, and none of the 4 other validated assays were fully proficient in more than 2/3ds of datasets. Only 1/3 HPV assays that have been pre-qualified by WHO was used by any laboratory (Xpert HPV from Cepheid, used by one laboratory). [12]

A common finding, seen also in previous studies, is that the laboratory performing the test has a big impact on the performance of the test itself in particular for certain assays. An example is Anyplex II HPV 28, where 15/21 datasets were fully proficient, but 5/21 datasets were not proficient with 1 to 3 false positive results. An example of assays with robust performance in many laboratories is the assays by Hybribio. These were fully proficient in nearly all datasets (97/98 datasets) from different laboratories, comprising >50% of all fully proficient datasets in the 2021 proficiency study. The widespread use of these assays in laboratories in the WPRO region appears to be a reason why the proficiency was highest in this region. Hybribio was used in 59/132 laboratories, with most of them (44/47) belonging to the WPRO region.

The 2021 Global HPV LabNet HPV DNA proficiency study further enables improving and sustaining sensitivity and specificity of different HPV typing assays. Comparing the results in the 2008, 2010, 2011, 2013, 2014, 2017, 2019 and 2021 global HPV DNA PPs, we can both see that it is possible to achieve a global improvement in proficiency of HPV genotyping services and that regular issuing of PPs is needed for sustaining and improving HPV detection. In the efforts to eliminate cervical cancer, the IHRC will continue to issue PP yearly to promote proficiency in HPV testing. Starting in 2022, we will also be issuing HPV screening panels (with screening-relevant concentrations of the HPV genotypes important for screening) to specifically promote proficiency in HPV screening services.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper

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References

[1] P.J. Maver, M. Poljak, Primary HPV-based cervical cancer screening in Europe: implementation status, challenges, and future plans, Clin. Microbiol. Infect. 26 (2020) 579–583.
[2] M. Poljak, J. Cuzick, B.J. Kocjan, T. Iftner, J. Dillner, M. Arbyn, Nucleic acid tests for the detection of alpha human papillomaviruses, Vaccine 30 (5) (2012) F100–F106. Suppl.
[3] M. Poljak, A. Ostrbenk-Valencak, G. Gimpelj-Domjanic, L. Xu, M Arbyn, Commercially available molecular tests for human papillomaviruses: a global overview, Clin. Microbiol. Infect. 26 (2020) 1144–1150.
[4] M. Ferguson, D.E. Wilkinson, T. Zhou, WHO meeting on the standardization of HPV assays and the role of the WHO HPV Laboratory Network in supporting vaccine introduction held on 24-25 January 2008, Geneva, Switzerland, Vaccine 27 (2009) 337–347.

[5] International HPV Reference Center. Technical report on the global HPV LabNet DNA genotyping proficiency panel. 2017. https://www.hpvcenter.se/wp-content/uploads/2021/06/Global-HPV-DNA-PP-2017-summary-report.pdf, (accessed 6 June 2021).

[6] C. Eklund, O. Forslund, K.L. Wallin, J. Dillner, Global improvement in genotyping of human papillomavirus DNA: the 2011 HPV LabNet International Proficiency Study, J. Clin. Microbiol. 52 (2014) 449–459.

[7] C. Eklund, O. Forslund, K.L. Wallin, J. Dillner, Continuing global improvement in human papillomavirus DNA genotyping services: the 2013 and 2014 HPV LabNet international proficiency studies, J. Clin. Virol. 101 (2018) 74–85.

[8] C. Eklund, O. Forslund, K.L. Wallin, T. Zhou, J. Dillner, The 2010 global proficiency study of human papillomavirus genotyping in vaccinology, J. Clin. Microbiol. 50 (2012) 2289–2298.

[9] C. Eklund, T. Zhou, J. Dillner, Network WHOHPL. Global proficiency study of human papillomavirus genotyping, J. Clin. Microbiol. 48 (2010) 4147–4155.

[10] C. Eklund, L.S.A. Muhr, C. Lagheden, O. Forslund, K.D. Robertsson, J. Dillner, The 2019 HPV Labnet international proficiency study: need of global Human Papillomavirus Proficiency Testing, J. Clin. Virol. 141 (2021), 104902.

[11] M. Arbyn, M. Simon, E. Peeters, et al., 2020 List of human papillomavirus assays Suitable for primary cervical cancer screening, Clin. Microbiol. Infect. (2021).

[12] World Health Organization. Prequalified In vitro diagnostics. https://extranet.who.int/pqweb/vitro-diagnostics/vitro-diagnostics-lists (accessed 14 May 2022).