Technical Report on the Global HPV LabNet DNA Screening Proficiency Panel 2022

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Abbreviations

AMR	Region of the Americas
EMR	Eastern Mediterranean Region
Equalis	External Quality Assessment in Laboratory Medicine in Sweden
EUR	European Region
GE	Genome Equivalent
GRL	Global Reference Laboratory
HPV	Human Papilloma Virus
HPV LabNet	HPV Laboratory Network
IU	International Unit
PP	Proficiency Panel
SEAR	South East Asian Region
SP	Screening Panel
WHO	World Health Organization
WPR	Western Pacific Region

Global HPV DNA screening proficiency panel 2022

Distributed in October 2022

1. Introduction

The elimination of cervical cancer is a globally prioritized health policy goal, formulated by the World Health Organization (WHO). An essential part of the elimination strategy is high coverage population-based cervical screening programs implemented worldwide with testing for the human papillomavirus (HPV), the main cause of cervical cancer. Evaluation of HPV testing assays, as actually applied in different laboratories, is fundamental to ensure the quality, reliability, and accuracy of HPV-based cervical screening programs.

A major method for achieving progress towards the elimination goal is development, preparation and validation of proficiency panels (PP) to qualify methods and laboratories. Therefore, we designed a proficiency panel tailored to assess the quality of HPV testing services used for cervical screening.

Call for participation in this screening proficiency study was sent to all laboratories that had participated in the HPV LabNet proficiency panels in previous years (Annex 1, 2).

2. Aims

The aims of this panel were:

1. To assess the proficiency of HPV screening assays when routinely used in laboratories worldwide.
2. To evaluate the sensitivity and type-specificity of HPV detection of the different HPV screening assays when routinely used in laboratories worldwide.
3. Identify problems with any assays routinely used.

3. Methods

3.1 Panel composition

Complete genomes of HPV cloned into plasmid vectors had been provided to the International HPV Reference Center by the respective proprietors with written approval for use in this SP. All samples were purified plasmids diluted in TE buffer (10 mM TRIS-HCl, 0.1 mM EDTA, pH 8.0) with 10

ng/µl of human placental DNA (Sigma-Aldrich no 7011). The HPV types included were:16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68a (HPV 68 prototype) and 68b (ME 180 isolate).
The composition of the panel is shown in Table 1.

Table 1: 2022 HPV Screening panel composition by randomised sample ID

HPV types	HPV genome equivalents (GE) or international unit (IU) (HPV 16, 18) per µl	Randomised Panel ID
16	1 IU	9
16	10 IU	2
18	1 IU	4
18	10 IU	7
31	1000 GE	1
33	1000 GE	8
45	1000 GE	11
52	1000 GE	3
58	1000 GE	12
31/33/45/52/58	100[a] GE	5
35/39/51/56/59/68	100[a] GE	10
Negative (TE buffer with 10 ng/µl human placenta DNA)	0	6

[a]*100 copies of each HPV type. IU: international units, GE: genome equivalents*

3.2 Validation of the SP

The SP was pre-tested at GRL Sweden using a modified GP5+/6+ PCR followed by Luminex-based typing for HPV types 6, 11, 16, 18, 26, 30, 31, 33, 35, 39, 40, 42, 43, 45, 51, 52, 53, 54, 56, 58, 59, 61, 66, 67, 68a, 68b, 69, 70, 73, 74, 81, 82, 86, 87, 89, 90 and 91. As a second validation the SP was pre-tested using BD-COR Onclarity and Roche Cobas 4800.

3.3 Distribution of the PP

After pre-test validation by the International HPV Reference center in Sweden, the SP was compiled in September 2022 and distributed to laboratories throughout four WHO regions in October 2022, following the call for participation and requests received from the laboratories. The fee for participation was for commercial entities 330 Euros, whereas academic and public health entities had a fee of 140 Euros. Participants from low and lower-middle income countries could apply for waiving of the fee. As in previous years the HPV reference laboratory in Sweden prepared

the materials for the 2022 HPV DNA SP, but subcontracted the administration and distribution of the PP to Equalis (External quality assessment of laboratory medicine in Sweden; https://www.equalis.se/en/ a public, non-profit company that administrates the external quality assessment for public health care laboratories in Sweden) that handled the logistics and distribution of the panel. This model has continued to work well and is a possible mode of operation of a sustainable long-term activity with global distribution of an HPV DNA typing proficiency panel. National Reference Laboratories, appointed by their government were invited to receive panels for free to organize a quality control program in their country. The reference laboratories in Norway, Germany and Argentina did order panels to organize local quality control programs.

One hundred fifty-eight datasets from 84 laboratories were obtained. The number (n) of laboratories submitting results per WHO Region is shown in Table 2. These are EUR (n = 29), SEAR (n = 2), WPR (n = 26) and AMR (n = 27). Fifty-three laboratories submitted a data set from one assay, eleven laboratories submitted data sets from 2 different assays, nineteen laboratories submitted data sets from 4 different assays and one laboratory submitted results from 7 different assays.

Table 2: Distribution of participating laboratories and submitted datasets in each WHO region.

WHO region	Participating laboratories (n)	Submitted datasets(n)
Total	**84**	**158**
AMR	27	35
EUR	29	36
SEAR	2	2
WPR	26	85

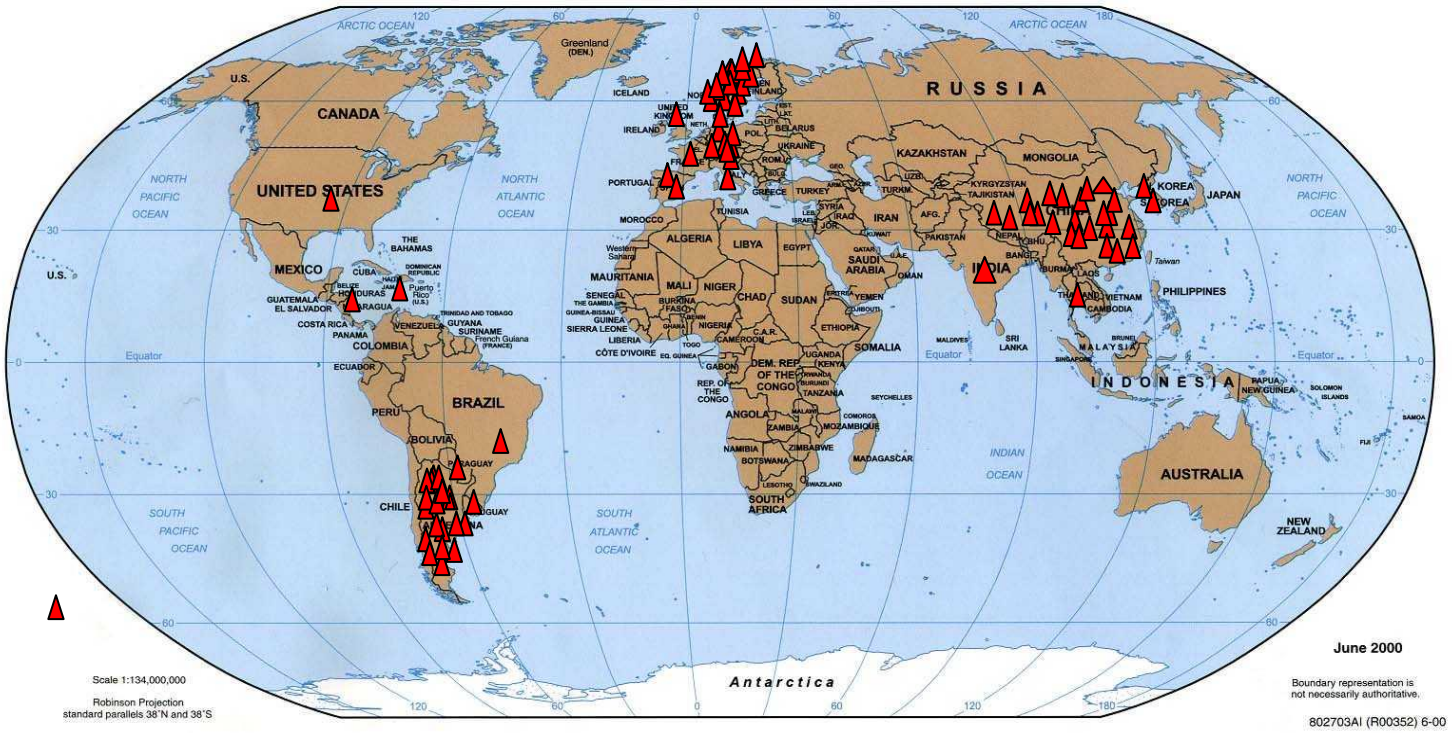

Figure 1: Global distribution of laboratories that submitted results for the 2022 HPV DNA SP.

3.4 Data analysis

Results analysed in this report include all results returned prior to the 5th of February 2022. Data was compiled by Equalis and transferred to the HPV reference laboratory in Sweden for analyses. Each data set was designated a number from 1 to 158. The data were analysed by region of the laboratory, by assay used and by HPV type.

From the data sets submitted, it was noted that participating laboratories used a range of commercial assays as well as 9 datasets submitted using in-house assays (Table 3). The proportion of correct HPV typing results, reported by the laboratory, was analyzed as data sets by laboratory and according to assay used.

This was the first screening proficiency panel, the requirements for proficiency were established by comparing data from the genotyping proficiency panel and a longitudinal cohort study with type-

specific quantitation of HPV in cervical samples taken up to 8.5 years before development of invasive cervical cancer.

A data set was considered proficient when it detected at least 10 international units (IU) / µl of HPV 16 and HPV 18, and 1000 genome equivalents (GE) / µl of HPV 31, 33, 45, 52 and 58. Two samples with HPV16 and 18 at 1 IU/µl and a pool with 100 GE/µl for HPV types 31, 33, 45, 52, 58 were also included but detection of these low virus amounts was not required for proficiency.
In addition, the specificity of the reported types should be 100 % (no false positive result).

4. Results

Eighty-four participating laboratories submitted one hundred fifty-eight data sets.
Each data set submitted by each laboratory was analyzed and a feedback letter was sent to all participating laboratories that had paid the fee in February 2023.

4.1 Results by assays used

4.1.1 Commercial assays

A total of 149 data sets were obtained using commercially available tests. The most commonly used assays were the Hybribio Genotyping with Real-time PCR that was used in 21 laboratories. Two other Hybribio assays were used by 20 and 19 laboratories, Hybrid Capture 2 (Qiagen) was used in 19 laboratories (Table 3).

4.1.2 In-house assays

Nine of the data sets had been obtained using a variety of in-house assays (Table 3).

4.2 Results analysed by assay

4.2.1 Assay details

The different assays used for testing and typing of HPV as well as the number of submitted data sets and different part of the HPV genome targeted by each assay is shown in Table 3. The distribution of different assays in different WHO regions is shown in Figure 2.

Table 3: Assays used for analyzing the HPV screening panel.

HPV assay	Number of data sets	HPV region targeted (primers)
All assays	**158**	**L1/L2/E1/E2/E4//E6/E7**
Abbott/Abbott Alinity m (Abbott)	6	L1
Allplex HPV 28/Allplex HPV HR (Seegene)	2	
Ampfire HPV screen	2	E6 / E7
Anyplex II HPV28/Anyplex II HPV HR (Seegene)	8	
BD_Onclarity/Viper (BD)	7	E6 / E7
Cobas4800/6800 (Roche)	12	L1
Genotyping with Real-time PCR (Hybribio)	21	L1/L2/E1/E2/E4/E6/E7
Hybrid Capture 2 (Qiagen)	19	
14 High-risk (Hybribio)	19	E6 / E7
21 HPV GenoArray (Hybribio)	20	L1 (MY09)
37 HPV GenoArray (Hybribio)	19	L1 (MY09)
ScreenFire HPV RS	2	
TypeSeq/TypeSeq2	5	L1 / E6 / E7
Other commercial assays[a]	12	L1/L2/E1/E2/E4/E6/E7
Other In-house assays[b]	4	

[a]*In the other commercial assays category, the following assay types are included: Line Probe assay, Screen +, Ampliquality HPV-type, HPV Screening real-time PCR, Alias: Harmonia HPV, Alias: Venus HPV, Cepheid Xpert HPV, NeoPlex, Sacace HPV screen and type, HPV Direct-Flow Chip, INNO-LiPA HPV and Acon Biotech High risk.*

[b]*In the other in-house assays category, the following assay types are included: multiplex qPCR, real-time PCR, MALDI-TOF, RFLP.*

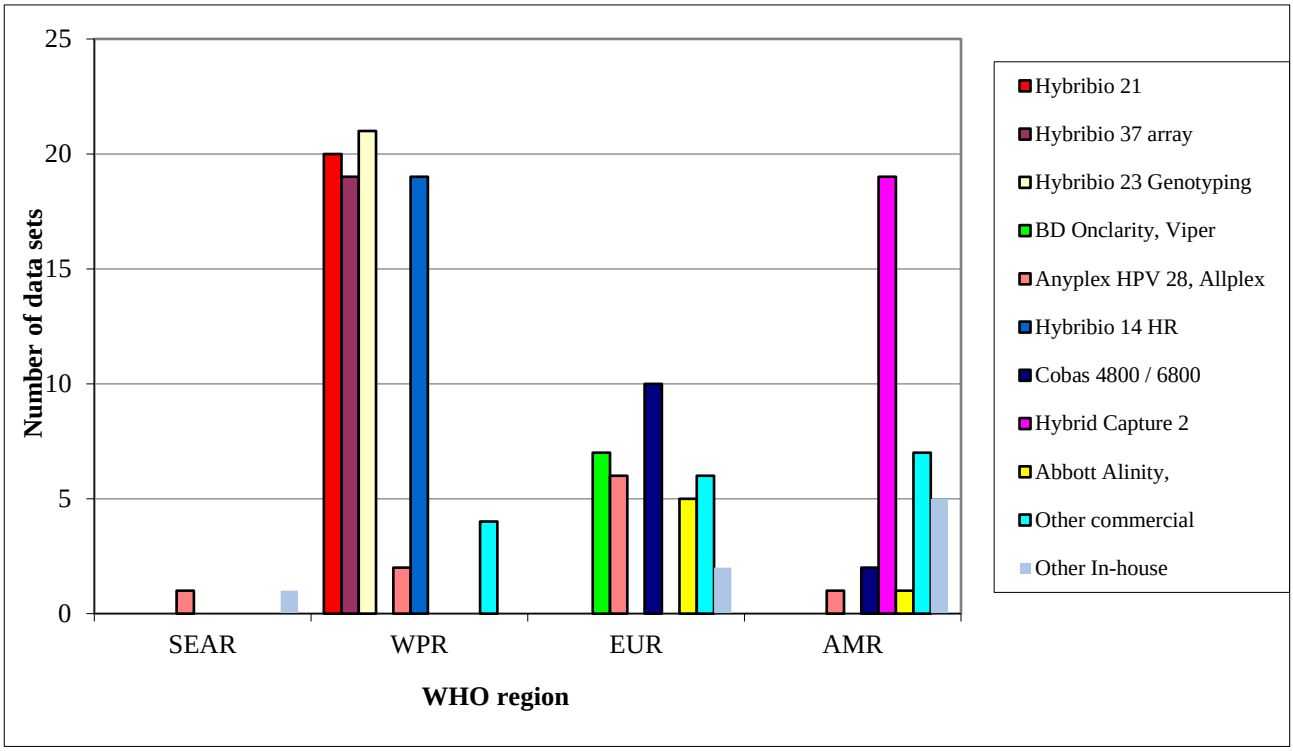

Figure 2: Type of assay in use for HPV DNA screening by WHO region.

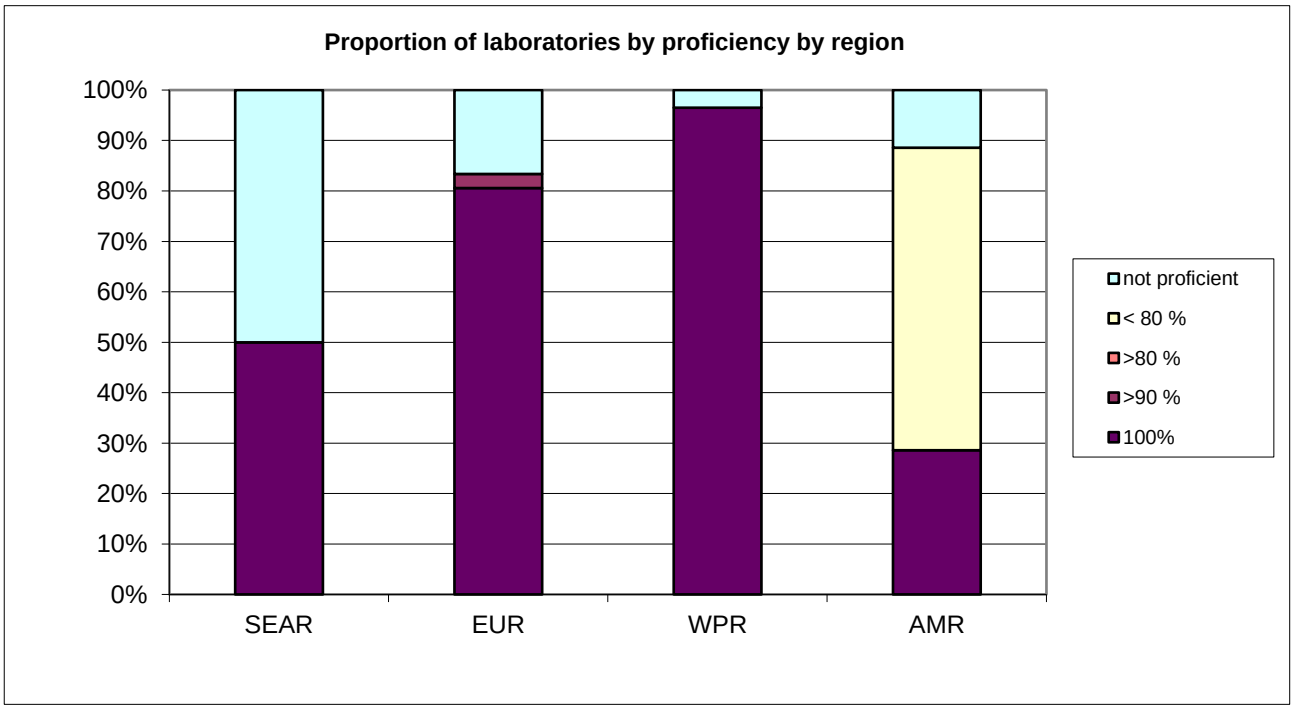

Figure 3: Proficiency for HPV DNA screening by WHO region. The figure includes 158 data set.

Table 4: Proportion of data sets submitted by WHO region with ≥90 % proficient HPV typing results.

Region (data sets)	Proportion of laboratories with 100 % correct typing	Proportion of laboratories with ≥90 % correct typing
EUR (36)	81 %	83 %
SEAR (2)	50 %	50 %
AMR (35)	29 %	50 %
WPR (85)	96 %	96 %

4.2.2 Results achieved by participating laboratories

The criteria for proficiency was no false positive results. According to the criteria described in 3.4, 122 (77 %) data set out of the 158 data sets were 100 % proficient. All the datasets with HPV analysis results reported from BD Onclarity/Viper, Cobas4800/6800, Genotyping with Real-time PCR (Hybribio), Hybribio 14 High-risk, and Hybribio 21 HPV GenoArray showed 100% proficiency (Table 5).

The proportion of laboratory proficiency including all datasets grouped by WHO region is shown in Figure 3 and Table 4. The percent proficiency of detecting HPV types grouped by assay used for testing is shown in Table 5.

A total of 54/84 laboratories provided at least one fully proficient dataset. The performance of assays detecting HPV types at low concentrations where HPV detection was not required for proficiency is summarized in Table 6. The low concentration HPV18 sample (1 IU/µl) was detected by 80% of the datasets (126/158) and the low concentration HPV16 (1 IU/µl) was detected by 84% (133/158) of datasets. The low amounts of HPV 31/33/45/52/58 (100 GE/ul) and HPV 35/39/51/56/59/68 (100 GE/ul) were detected in 91% (143/158) and in 94% (148/158) of datasets, respectively (Table 6).

Table 5: Overall proficiency of 2022 screening panel by assay type.

HPV assay	Number of data sets	No. of proficient data sets				
		100 % proficient	99-90 % proficient	89-80 % proficient	<80 % proficient	Not proficient
All assays	**158**	**122**	**11**	**15**	**9**	**1**
Abbott/Abbott Alinity m (Abbott)	6	5	1	0	0	0
Allplex HPV 28/Allplex HPV HR (Seegene)	2	1	1	0	0	0
Ampfire HPV screen	2	1	1	0	0	0
Anyplex II HPV28/Anyplex II HPV HR[a] (Seegene)	8	5	2	1	0	0
BD_Onclarity/Viper (BD)	7	7	0	0	0	0
Cobas4800/6800 (Roche)	12	12	0	0	0	0
Genotyping with Real-time PCR	21	21	0	0	0	0
Hybrid Capture 2 (Qiagen)	19	0	0	13	6	0
14 High-risk (Hybribio)	19	19	0	0	0	0
21 HPV GenoArray (Hybribio)	20	20	0	0	0	0
37 HPV GenoArray (Hybribio)	19	18	1	0	0	0
ScreenFire HPV RS	2	0	2	0	0	0
TypeSeq/TypeSeq2	5	3	2	0	0	0
Other commercial assays[a]	12	9	0	1	2	0
Other In-house assays[b]	4	1	1	0	1	1

[a]In the other commercial assays category the following assay types are included: Line Probe assay, Screen +, Ampliquality HPV-type, HPV Screening real-time PCR, Alias: Harmonia HPV, Alias: Venus HPV, Cepheid Xpert HPV, NeoPlex, Sacace HPV screen and type, HPV Direct-Flow Chip, INNO-LiPA HPV and Acon Biotech High risk.

[b]In the other in-house assays category, the following assay types are included: multiplex qPCR, real-time PCR, MALDI-TOF, RFLP.

Table 6: Number of datasets that have detected all HPV types in optional samples.

HPV assay	Number of data sets	HPV types in panel			
		16 (1 IU/ µl)	18 (1 IU/ µl)	31/33/45/52/58 (100 GE/ µl)	35/39/51/56/59/68 (100 GE/ µl)
All assays	**158**	**133**	**126**	**144**	**148**
Abbott/Abbott Alinity m (Abbott)	6	6	6	6	6
Allplex HPV 28/Allplex HPV HR (Seegene)	2	2	2	2	2
Ampfire HPV screen	2	1	0	1	2
Anyplex II HPV28/Anyplex II HPV HR[a] (Seegene)	8	8	8	5	5
BD_Onclarity/Viper (BD)	7	7	3	7	7
Cobas4800/6800 (Roche)	12	12	9	12	12
Genotyping with Real-time PCR	21	21	21	21	21
Hybrid Capture 2 (Qiagen)	19	0	0	14	18
14 High-risk (Hybribio)	19	19	19	19	19
21 HPV GenoArray (Hybribio)	20	20	20	20	20
37 HPV GenoArray (Hybribio)	19	19	19	19	18
ScreenFire HPV RS	2	0	0	2	2
TypeSeq/TypeSeq2	5	5	5	5	5
Other commercial assays[a]	12	11	12	9	9
Other In-house assays[b]	4	2	2	2	2

[a]*In the other commercial assays category, the following assay types are included: Line Probe assay, Screen +, Ampliquality HPV-type, HPV Screening real-time PCR, Alias: Harmonia HPV, Alias: Venus HPV, Cepheid Xpert HPV, NeoPlex, Sacace HPV screen and type, HPV Direct-Flow Chip, INNO-LiPA HPV and Acon Biotech High risk.*
[b]*In the other in-house assays category, the following assay types are included: multiplex qPCR, real-time PCR, MALDI-TOF, RFLP.*

4.3 Results by sample number

The numbers of laboratories typing for and reporting correct HPV type, with **no false positive** HPV type detected are shown in table 7. The number of datasets without false positive results differs for each sample.

Table 7:
Proficiency of each sample. To achieve 100% proficiency full detection of HPV types 16 and 18 with 10 IU/ µl, HPV types 31, 33, 45, 52 and 58 with 1000 genome equivalents/ µl and no false positivity is required.

HPV types	HPV genome equivalents per 5 µl	Percent correct data sets (N)
16	1 IU	99.37 (157/158)
16	10 IU	86.08 (136/158)
18	1 IU	99.37 (157/158)
18	10 IU	86.08 (136/158)
31	1000 GE	93.67 (148/158)
33	1000 GE	98.10 (155/158)
45	1000 GE	93.04 (147/158)
52	1000 GE	96.20 (152/158)
58	1000 GE	97.47 (154/158)
31/33/45/52/58	100[a] GE	98.73 (156/158)
35/39/51/56/59/68	100[a] GE	98.10 (155/158)
Negative (TE buffer with 10 ng/µl human placenta DNA)	0	99.37 (157/158)

[a]100 copies of each HPV type. IU: international units, GE: genome equivalents

4.4 Analysis of false positive results

To be considered as proficient for HPV testing no false positive result was accepted. The number of false positive samples by assay is shown in Table 8.

Table 8: Number of false positive HPV types detected per data set reported by assay used.

HPV assay	Number of data sets	No. of false positive samples per data set			
		0 samples	1 sample	2 samples	> 3 samples
All assays	**158**	**144**	**11**	**1**	**2**
Abbott/Abbott Alinity m (Abbott)	6	6	0	0	0
Allplex HPV 28/Allplex HPV HR (Seegene)	2	1	1	0	0
Ampfire HPV screen	2	2	0	0	0
Anyplex II HPV28/Anyplex II HPV HR[a] (Seegene)	8	5	2	1	0
BD_Onclarity/Viper (BD)	7	7	0	0	0
Cobas4800/6800 (Roche)	12	12	0	0	0

Genotyping with Real-time PCR	21	21	0	0	0
Hybrid Capture 2 (Qiagen)	19	19	0	0	0
14 High-risk (Hybribio)	19	19	0	0	0
21 HPV GenoArray (Hybribio)	20	20	0	0	0
37 HPV GenoArray (Hybribio)	19	18	1	0	0
ScreenFire HPV RS	2	0	2	0	0
TypeSeq/TypeSeq2	5	3	2	0	0
Other commercial assays[a]	12	10	1	0	1
Other In-house assays[b]	4	1	2	0	1

[a]*In the other commercial assays category, the following assay types are included: Line Probe assay, Screen +, Ampliquality HPV-type, HPV Screening real-time PCR, Alias: Harmonia HPV, Alias: Venus HPV, Cepheid Xpert HPV, NeoPlex, Sacace HPV screen and type, HPV Direct-Flow Chip, INNO-LiPA HPV and Acon Biotech High risk.*

[b]*In the other in-house assays category, the following assay types are included: multiplex qPCR, real-time PCR, MALDI-TOF, RFLP.*

We searched the data sets for patterns of consistent false positivity for any specific sample in the panel. The false positivities appeared to be essentially randomly distributed among the samples, indicating that the problem with false positives is usually not related to a property of the assays itself (e.g. cross-reactivity), but rather with the laboratory conditions of use (e.g. contamination).

5. Discussion

A total of 84 laboratories applied for participation in the 2022 screening proficiency study. The 2022 proficiency panels were distributed to all solicitants and a total of 158 datasets from 84 laboratories were returned before the deadline (January 2023).

We here report the results of the first international HPV screening proficiency study providing an overview of the performance of laboratories using various HPV testing methodologies in the screening setting. We have found that the majority of laboratories were highly competent, providing accurate results according to the preliminary proficiency criteria.

The main strengths of this study are that i) the content of the proficiency panel is traceable to international standards and ii) the wide participation from many laboratories makes it internationally comparable. The datasets submitted have been obtained from a variety of tests performed in many different settings, thus providing insights into the robustness of test performance when used in different laboratories.

Nevertheless, it seems that continued research is required in particular to define the optimal type of composition and analytical sensitivity for optimal clinical specificity.

A major limitation is that the proficiency criteria established in this study were provisional. Indeed, the results indicate that there is a need for additional research regarding the required analytical sensitivity, in particular for HPV16 and 18. We provisionally used the same requirement as for HPV genotyping proficiency studies (10 IU/µl) which was agreed on at an international WHO consensus workshop 2009. However, the fact that none of the 19 laboratories using the Hybrid Capture 2 (HC2) assay were able to detect HPV16/18 in this amount implies that the proficiency criteria for these two HPV types, HPV16 and 18, may need to be reconsidered. HC2 assay has been evaluated in several classic randomized controlled trials and is FDA approved. The reported sensitivity of the assay (detection limit) is 100 copies. Hortlund et al. found that only 3/49 (6%) HPV18 positive (HPV16 negative) invasive cancers that were preceded by viral amounts lower than 100 IU/µl, implying that maybe this analytical sensitivity (100 IU/µl) is sufficient. On the other hand, almost all assays used worldwide were able to detect HPV16/18 at 1 IU/µl.

The lack of established requirements for specificity was reflected in the results of this study. Particularly, this was clearly seen in the results obtained from the samples contained HPV types of lower oncogenicity (not HPV 16/18) at low viral loads, among which almost no cases of cervical cancer are found. and highest false positivity (5.75%) found for HPV35/39/51/56/58/59/66/68 in the

reference screening. As global HPV screening programs are implemented, a lack of consideration for specificity of the test may result in very large numbers of women unnecessarily being labelled as screen-positive.

Some of the HPV assays performed better than others, in agreement with what has already been reported in previous HPV DNA genotyping proficiency reports. However, the high proportion of datasets that were fully proficient already in this first round of proficiency test for HPV screening implies that the problems are limited and that a continued HPV screening proficiency program will readily be able to arrive at quite reliable performance of the global HPV screening laboratories.

In conclusion, a global proficiency study of HPV testing services for cervical screening programs has found that, although the results were mostly satisfactory, continued research on the required analytical sensitivity for optimal clinical sensitivity and clinical specificity is needed.

6. Conclusions and recommendations

This technical report summarizes the results obtained from the 1st HPV LabNet HPV DNA proficiency study targeting HPV screening assays. The study was open for participation to all laboratories across the globe.

The proficiency panel provided the possibility to evaluate the specificity and sensitivity for different HPV typing assays to correctly identify 13 high risk HPV types and 2 low risk HPV types, the HPV types that are the most important for HPV vaccine research as well as for HPV surveillance and monitoring.

We report that the global proficiency in HPV genotyping services had increased in the 2022 proficiency study. The increased proficiency is seen both in laboratories that had participated in previous studies as well as in laboratories participating for the first time. An increase in submitted datasets from the WPRO (102 datasets) was seen, surpassing the EURO region (38 datasets) which usually was the region with more laboratories participating in the previous proficiency studies.

The 2022 Global HPV LabNet HPV DNA proficiency panel further supports that it is possible to perform global studies comparing the sensitivity and specificity of different HPV typing assays, as well as the performance of participating laboratories, in a consistent manner that allows comparison of results generated by different laboratories worldwide and over time. Comparing the results from 2008, 2010, 2011, 2013, 2014, 2017, 2019, 2021 and 2022 Global HPV DNA PPs, we can see overall improvements.

Moreover, the highest overall proficiency (77% of datasets) was achieved in this proficienty study, 2022 – higher than in any previous proficiency study. We suggest that recommendations for HPV laboratory testing should continue to include a strong emphasis on the use of negative controls in the assays.

It is possible to achieve a global improvement in proficiency of HPV genotyping services. The improvement in proficiency seen in the 2021 and 2022 proficiency study suggests that continuing proficiency testing is helpful to sustain and improve accuracy and to avoid a deterioration in

proficiency, as seen in the last proficiency study in 2019. In the efforts to eliminate cervical cancer, the International HPV Reference Center will continue to issue PP yearly to promote proficiency in HPV testing services. Starting in 2022, we did also issue HPV screening panels (with screening-relevant concentrations of the HPV genotypes important for screening) to promote proficiency in HPV screening services as well.

Annex 1:

Call for participation:
HPV DNA screening proficiency study 2022 (597)

External quality assessment for laboratories that perform **HPV screening**.
Testing for oncogenic HPV in cervical cancer screening is a globally recommended health policy. For HPV screening, it is important to detect the most carcinogenic viruses (HPV16 and 18) at high sensitivity, but for less carcinogenic viruses it is not important to determine the exact type. Complete HPV genotyping is particularly important for vaccinology, but as the HPV genotyping proficiency panel contains 44 challenge samples, many laboratories have asked for a smaller proficiency panel tailored to what is important for assessing the quality of HPV screening services.

Participant laboratories will be asked to perform HPV screening using one or more of their usual HPV screening assays on the 12 challenge samples in this panel. The panel will evaluate the detection of the major oncogenic HPV types as well as detection of other oncogenic HPV types in groups.

Composition of sample material
The panel consists of 12 samples containing purified whole genomic plasmids of **HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68a** and **68b** in a background of human cellular DNA. Each sample may contain either no HPV, a single HPV type or a mixture of HPV types at varying concentrations.

Participation fee
The price for one panel (12 samples as described above) is 330 Euros for commercial entities and 140 Euros for academic entities. Participants from low and lower middle-income counties (World Bank classification with GNI (gross national income) per capita: <4045 USD) can apply for waiving of fee. Laboratories that have outstanding payments from past Global HPV LabNet proficiency studies will need to clear their debts before their registration is accepted.

Data submission
The International HPV Reference Laboratory in Sweden is organizing this study in collaboration with the Swedish external quality assurance provider Equalis AB, who is responsible for management and distribution. Laboratories that have more than one assay are encouraged to provide results on each assay they commonly use. Data submitted will become the property of the organizers and may be analyzed for publication by the Global HPV LabNet either as an internal document or peer reviewed manuscript. All results will be handled in a coded anonymous fashion, with summaries grouped by method. The code linking data to originating laboratories will be kept confidential. Laboratories that provide data within the required time-frame will receive a copy of their own results and the summary data.

Scientific issues
Dr. Joakim Dillner
HPV International Reference Laboratory, Sweden

Center for Cervical Cancer Prevention
E-mail: joakim.dillner@ki.se or www.hpvcenter.se

Registration

Application forms for the 2022 study can be found at: equalis.se

Preliminary dates

15th of June 2022: Registration for participation opens.
26th of August 2022: Registration for participation closes.
September/October 2022: Dispatch of panels begins.

Participation, management and practical issues

Equalis AB, Sweden www.equalis.se
E-mail: HPV@equalis.se

Annex 2: Application for participating in The 2022 Global HPV LabNet DNA Screening Study

Fee for commercial entities: 330 Euros, Fee for academic entities: 140 Euros. Participants from low and lower middle-income countries (World Bank classification with GNI (gross national income) per capita: <3 975 USD) can apply for waiving of fee.	
Delivery address:	
Lab ID (from previous participation):	
Department /Laboratory	
Address	
City	Postal code
Province /State	Country
E-mail	Fax
Phone	
Invoice address (if different from above):	
VAT number:	
Department /Laboratory	
Address	
City	Postal code
Province /State	Country
Mode of payment (please check the preferred choice):	
By Credit Card/PayPal:	
By Invoice:	
Principal Investigator:	
First Name	
Surname (Title)	
HPV DNA typing experience in your laboratory	
Methodology used (may be more than one)	
Annual number of HPV typing tests performed	
Brief description of involvement in HPV surveillance or HPV vaccine development	

Return registration form by email or fax to: info@equalis.se. **Fax: +46 18 69 31 46**

Annex 3:

Source of panel material.

Complete genomes of HPV cloned into plasmid vectors had been provided to the Lund University by the respective proprietors with a written approval to be used in this proficiency panel: Dr Ethel-Michele de Villiers (HPV types 16, 18 and 45), Dr Gérard Orth (HPV types 33, 39 and 68a prototype), Dr Elisabeth Schwarz (HPV 68b), Dr Saul Silverstein (HPV type 51), Dr Attila Lörincz (HPV types 31, 35 and 56), Dr Wayne Lancaster (HPV type 52) and Dr Toshihiko Matsukura (HPV types 58 and 59).

The HPV genomes are cloned into different cloning vectors: HPV 16 in pBR322 at position 6152, HPV 18 in pGEM-5Zf vector in the L2 region, HPV 31 in pT713 at position 3362, HPV 33 in pBR322 at position 2797, HPV 35 are cloned in two fragments 5012-956 and 956-5012 in pT713, HPV 39 in pGEM4z at position 1714, HPV 45 in pGEM4Z at position 75, HPV 51 in pGEM4z at position 4511, HPV 52 in pUC19 at position 7559, HPV 56 in pT713 at position 5521, HPV 58 in pGEM4Z at position 1158, HPV 59 in pUC9 at position 69, HPV 68a prototype in a bluescript vector, and HPV68b (ME180) of about 7 kb containing L1, L2, E1, E2, E4, E5, E6, E7 with an incomplete E2 gene in pCR4-TOPO.

The nucleic acid sequences for each of these HPV genomes have been reported previously and are available in Gene Bank with the following accession numbers; HPV 16 nr K02718; HPV 18 nr X05015; HPV 31 nr J04353; HPV 33 nr M12732; HPV 35 nr M74117; HPV 39 nr M62849; HPV 45 nr X74479; HPV 51 nr M62877; HPV 52 nr X74481; HPV 56 nr X74483; HPV 58 nr D90400; HPV 59 nr X77858; HPV 68a nr X67161 and HPV 68b nr FR751039.

Annex 4:

List of participants in the HPV LabNet Proficiency Study of HPV DNA Screening, 2022

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