# Technical Report on the Global HPV LabNet DNA Genotyping Proficiency Panel 2022

**Carina Eklund[1], Camilla Lagheden[1], Emel Yilmaz[1], Sara Arroyo Mühr[1], Marina Lilja[2], Ola Forslund[3] & Joakim Dillner[1]**

1 HPV International Reference Center, Department of Clinical Science, Intervention and Technology, Karolinska Institute and Karolinska University Hospital, Stockholm, Sweden
2 Equalis, Uppsala, Sweden
3 Clinical Microbiology, Skåne Regional and University Laboratories, Lund Sweden

# Table of Contents

# Tables



# Figures

# Abbreviations

| | |
|---|---|
| AFR | African Region |
| 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 |
| WHO | World Health Organization |
| WPR | Western Pacific Region |

# Global HPV DNA genotyping proficiency panel 2022

***Distributed in October 2022***

## 1. Introduction

Accurate and internationally comparable HPV DNA detection and typing methodology is an essential component both for research and evaluation of HPV vaccines and in effective implementation and monitoring of HPV vaccination programmes. The WHO started a WHO Global HPV Laboratory Network (LabNet) in 2006 to support the world-wide development and implementation of HPV vaccines through improved laboratory standardization and quality assurance of HPV testing and typing methods used for research and evaluation of HPV vaccines, for HPV surveillance and monitoring of HPV vaccination programmes (*http://www.who.int/biologicals/vaccines/hpv/en/index.html*). A major method for achieving progress towards this goal was development, preparation and validation of proficiency panels (PP) to qualify methods and laboratories.

Call for participation in this 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 typing assays when routinely used in laboratories worldwide
2. To evaluate the sensitivity and type-specificity of HPV detection of the different HPV 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 PP. 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: 6, 11, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68a (HPV 68 prototype) and 68b (ME 180 isolate). Three additional samples, A, B and C were cell lines used as controls for the DNA extraction step in the testing. The composition of the panel is shown in Table 1.

**Table 1:** 2022 HPV PP composition by randomised sample ID

| HPV types | HPV genome equivalents (GE) or international unit (IU) (for HPV 16, 18) per 5 µl | Randomised Panel ID |
|---|---|---|
| 16 | 50 | 12 |
| 16 | 5 | 21 |
| 18 | 50 | 5 |
| 18 | 5 | 32 |
| 6 | 500 | 41 |
| 6 | 50 | 18 |
| 11 | 500 | 26 |
| 11 | 50 | 6 |
| 31 | 500 | 13 |
| 31 | 50 | 37 |
| 33 | 500 | 1 |
| 33 | 50 | 22 |
| 35 | 500 | 17 |
| 35 | 50 | 33 |
| 39 | 500 | 14 |
| 39 | 50 | 40 |
| 45 | 500 | 27 |
| 45 | 50 | 7 |
| 51 | 500 | 10 |
| 51 | 50 | 38 |
| 52 | 500 | 30 |
| 52 | 50 | 19 |
| 56 | 500 | 23 |
| 56 | 50 | 2 |
| 58 | 500 | 34 |
| 58 | 50 | 25 |
| 59 | 500 | 15 |
| 59 | 50 | 28 |
| 68a | 500 | 39 |
| 68a | 50 | 3 |
| 68b | 500 | 8 |
| 68b | 50 | 35 |
| 6, 33, 39, 59 | 500 | 16 |
| 6, 33, 39, 59 | 50 | 24 |
| 11, 16, 51, 68a | 500 | 36 |
| 11, 16, 51, 68a | 50 | 4 |
| 18, 31, 35, 45 | 500 | 29 |
| 18, 31, 35, 45 | 50 | 11 |

| | | |
|---|---|---|
| 52, 56, 58, 68b | 500 | 31 |
| 52, 56, 58, 68b | 50 | 20 |
| TE buffer with 10 ng/µl human placenta DNA | 0 | 9 |
| HPV 16 positive SiHa cells | 2500 | C |
| HPV 16 positive SiHa cells | 25 | A |
| HPV- negative C33A cells | 0 | B |

## 3.2 Validation of the PP

The PP 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.

## 3.3 Distribution of the PP

After pre-test validation by the International HPV Reference center in Sweden, the PP was compiled in September 2022 and distributed to laboratories throughout five WHO regions in October 2022, following the call for participation and requests received from the laboratories. The fee for participation was for commercial entities 1000 Euros, whereas academic and public health entities had a fee of 500 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 PP, 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.

One hundred fifty-four datasets from 78 laboratories were obtained. The number (n) of laboratories submitting results per WHO Region is shown in Figure 1. These are EUR (n = 27), SEAR (n = 2), WPR (n = 40), AFR (n = 1) and AMR (n = 8). Forty-four laboratories submitted a data set from one assay, twelve laboratories submitted data sets from 2 different assays, two laboratories submitted data sets from 3 assays and twenty laboratories submitted data sets from 4 different assays.


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

## 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 154. 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 in-house assays (Table 2). The proportion of correct HPV typing results, reported by the laboratory, was analyzed as data sets by laboratory and according to assay used.

A data set was considered proficient when it detected at least 50 international units (IU) of HPV 16 and HPV 18 in 5 µl and 500 genome equivalents (GE) in 5 µl of the other HPV types, in both single and multiple infection. For proficiency, it was required that no false positive type was detected.

# 4. Results

Seventy-eight participating laboratories submitted one hundred fifty-four data sets. Twenty seven data sets were generated using assays that either did not discriminate specific HPV types or reported results as HPV 16, 18 and "other" High Risk HPV types (Hybribio 14 HR, In-house Realtime PCR, Realquality, Harmonia HPV, and Sansure and YanengBio 16/18). These data sets are only analyzed for the specific types tested for individually.

Detection of 5 IU of HPV16 and HPV18 and 50 GE of the other HPV types was not required for proficiency - these samples are intended for training and for providing information on whether the test just barely met the requirements or whether it exceeded them.

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 137 data sets were obtained using commercially available tests. The most commonly used assays were the Hybribio 37 HPV Genoarray (Hybribio) that was used in 21 laboratories. Two other Hybribio assays were used by 20 laboratories Anyplex II HPV 28 (Seegene) was used in 17 laboratories (Table 2).

### *4.1.2 In-house assays*

Seventeen of the data sets had been obtained using a variety of in-house assays (Table 2).

## 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 2. The distribution of different assays in different WHO regions is shown in Figure 2.

**Table 2:** Assays used for testing and typing of HPV.

| HPV assay type | Number of data sets | HPV region targeted (primers) |
|---|---|---|
| **All assays** | **154** | **L1/L2/E1/E2/E4/E5/E6/E7** |
| Hybribio 37 array HPV (Hybribio) | 21 | L1 (MY09/11) |
| HPV-23 Genotyping (Hybriobio) | 20 | L1/L2/E1/E2/E4/E6/E7 |
| Hybribio 21 array HPV (Hybribio) | 20 | L1 (MY09/11) |
| Hybribio 14 HR (Hybribio) | 19 | E6 / E7 |
| Anyplex II HPV 28 (Seegene) | 17 | L1 |
| HPV Genotyping 23 (Yaneng Bioscience) | 9 | |
| In-house realtime PCR | 8 | L1/E6/E7 |
| InnoLiPA Extra (Fujirebio) | 5 | L1 (SPF10) |
| In-house PCR Luminex | 4 | L1/E7 |
| Allplex HPV28 (Seegene) | 3 | L1 |
| Realquality (AB Analitica) | 3 | E6 / E7 |
| In-house NGS | 3 | L1 / E6 / E7 |
| Lineblot (different) | 3 | L1 / E1 |
| HPV Direct Flow-chip (Master Diagnostica) | 2 | L1 (GP) |
| In-house PGMY-CHUV | 2 | L1 (PGMY) |
| VisionArray HPV (ZytoVision) | 2 | L1 |
| Other Commercial assays [a)] | 13 | L1/L2/E1/E2/E4/E6/E7 |

a) Other commercial assays include one laboratory using each of: Venus HPV, Harmonia HPV, Sansure S3057, Sansure S3027, NeoPlex HPV 29, Ampliquality, GenoFlow HPV Array, DiagCor Realtime PCR, ScreenFire, F-HPV typing, Yaneng BIOscience Multicolour, Yaneng BIOscience HPV16/18 genotyping, HPV DNA-Array Autoimmun Diangnostika GmbH.

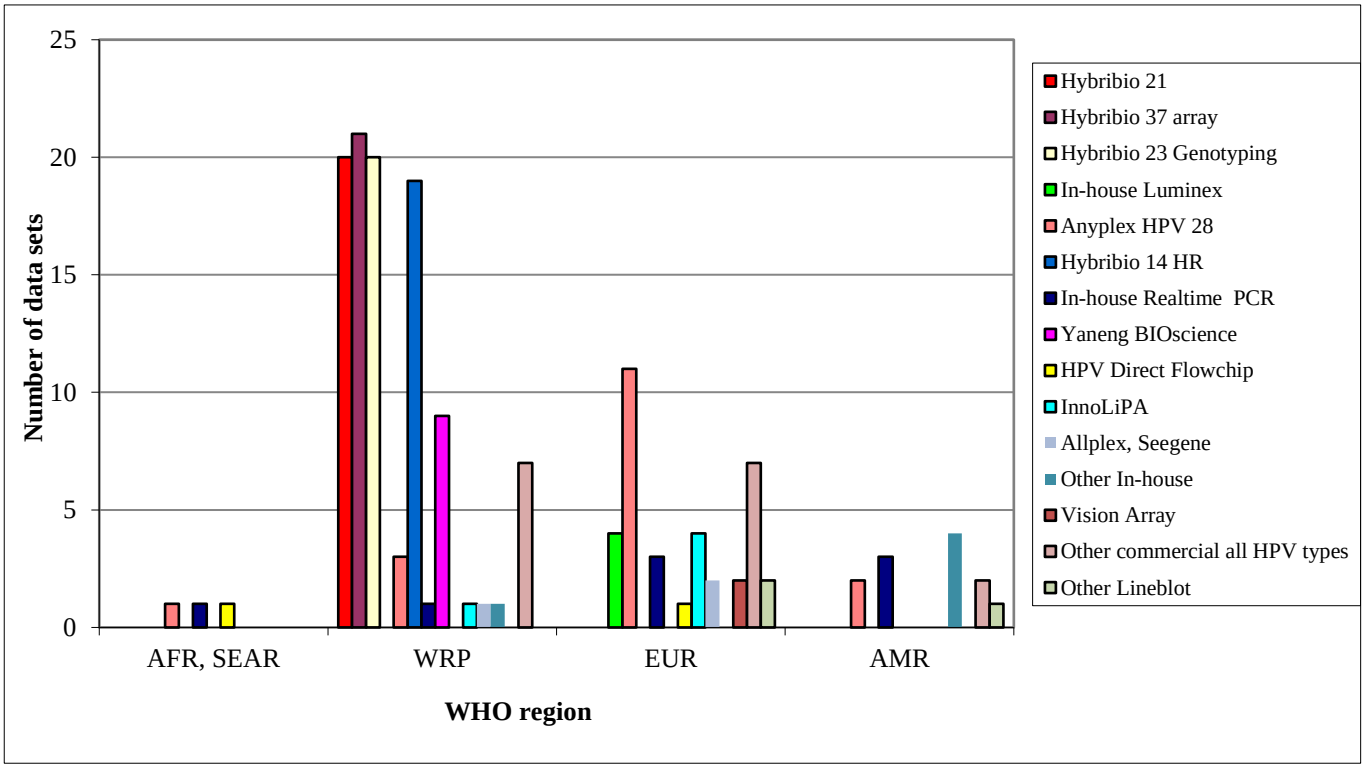


**Figure 2:** Type of assay in use for HPV DNA typing by WHO region, data for AFR and SEAR region are combined.

### 4.2.2 Results achieved by participating laboratories

The criteria for proficiency was since the panel issued 2019 no false positive results allowed (in previous years, a maximum of one false positive had been allowed for proficiency). According to the criteria described in 3.4, 119 (77 %) data set out of the 154 data sets that typed for at least one HPV type were 100 % proficient for the types claimed to be detected by the test.

Of these, 110 data set correctly identified the content of all samples, including the samples with copy number amounts that were lower than required for proficiency. 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).

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

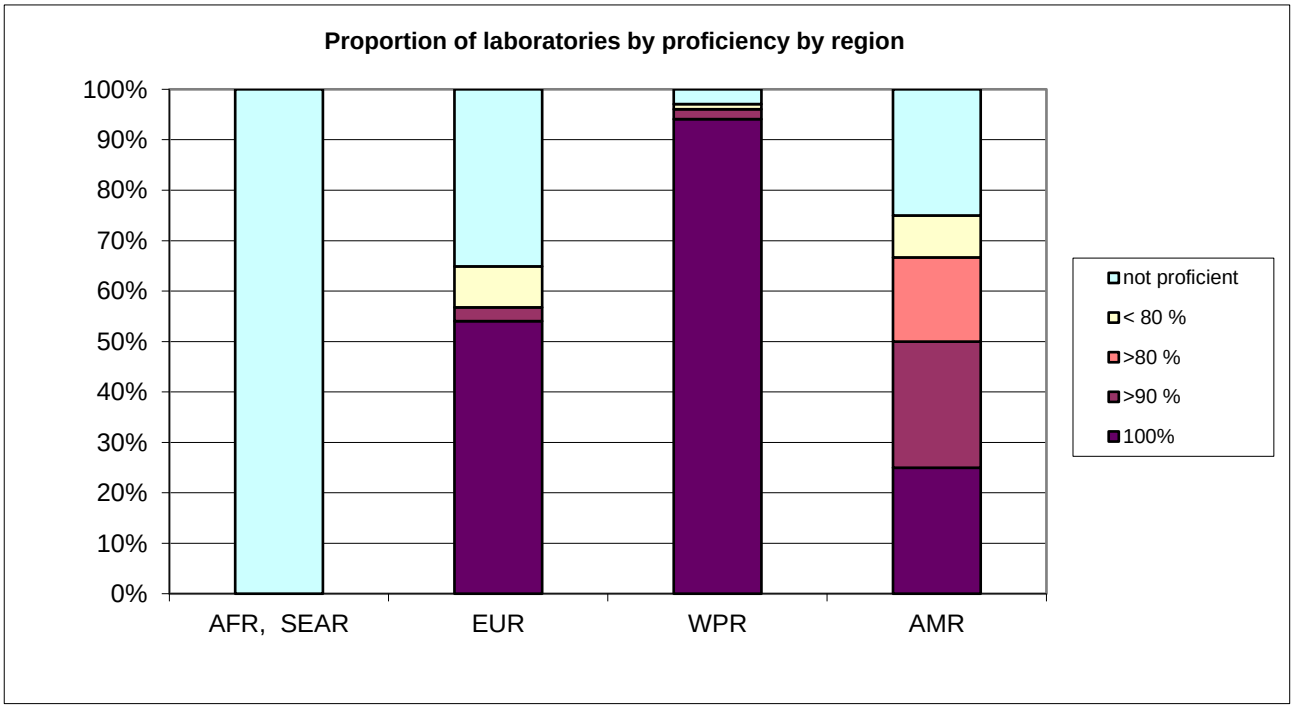


**Figure 3**: Proficiency for HPV DNA typing by WHO region. The figure includes 154 data set.

**Table 3:** 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 (37) | 54 % | 57 % |
| AFR, SEAR (3) | 0 % | 0 % |
| AMR (12) | 25 % | 50 % |
| WPR (102) | 94 % | 96 % |

**Table 4:** Proficiency for detection of specific HPV types by assay used.

| HPV assay type | Number of data sets | No. of proficient data sets | | | | |
|---|---|---|---|---|---|---|
| | | 100 % proficient | 99-90 % proficient | 89-80 % proficient | <80 % proficient | Not proficient |
| **All assays** | **154** | **119** | **6** | **2** | **5** | **22** |
| Hybribio 37 array HPV (Hybribio) | 21 | 21 | 0 | 0 | 0 | 0 |
| HPV-23 Genotyping (Hybriobio) | 20 | 20 | 0 | 0 | 0 | 0 |
| Hybribio 21 array HPV (Hybribio) | 20 | 20 | 0 | 0 | 0 | 0 |
| Hybribio 14 HR (Hybribio) | 19 | 18 | 0 | 0 | 0 | 1 |
| Anyplex II HPV 28 (Seegene) | 17 | 14 | 1 | 0 | 0 | 2 |
| HPV Genotyping 23 (Yaneng Bioscience) | 9 | 8 | 1 | 0 | 0 | 0 |
| In-house realtime PCR | 8 | 1 | 1 | 2 | 1 | 3 |
| InnoLiPA Extra (Fujirebio) | 5 | 2 | 0 | 0 | 0 | 3 |
| In-house PCR Luminex | 4 | 4 | 0 | 0 | 0 | 0 |
| Allplex HPV28 (Seegene) | 3 | 3 | 0 | 0 | 0 | 0 |
| Realquality (AB Analitica) | 3 | 0 | 0 | 0 | 0 | 3 |
| In-house NGS | 3 | 1 | 1 | 0 | 0 | 1 |
| Lineblot (3 different) | 3 | 0 | 1 | 0 | 1 | 1 |
| HPV Direct Flow-chip (Master Diagnostica) | 2 | 1 | 0 | 0 | 0 | 1 |
| In-house PGMY-CHUV | 2 | 1 | 0 | 0 | 0 | 1 |
| VisionArray HPV (ZytoVision) | 2 | 0 | 0 | 0 | 0 | 2 |
| Other Commercial assays [a)] | 13 | 5 | 1 | 0 | 3 | 4 |

a) Other commercial assays include one laboratory using each of; Venus HPV, Harmonia HPV, Sansure S3057, Sansure S3027, NeoPlex HPV 29, Ampliquality, GenoFlow HPV Array, DiagCor Realtime PCR, ScreenFire, F-HPV typing, Yaneng BIOscience Multicolour, Yaneng BIOscience HPV16/18 genotyping, HPV DNA-Array Autoimmun Diangnostika GmbH.

### 4.2.3 HPV types detected

The sensitivity to detect each HPV type, as percent of laboratories detecting the different copy number (IU / GE) of the HPV types is shown in Figure 4. This data includes laboratories with

multiple false positives. In table 5 and 6 the lowest detected GE / IU grouped by assay used are shown.

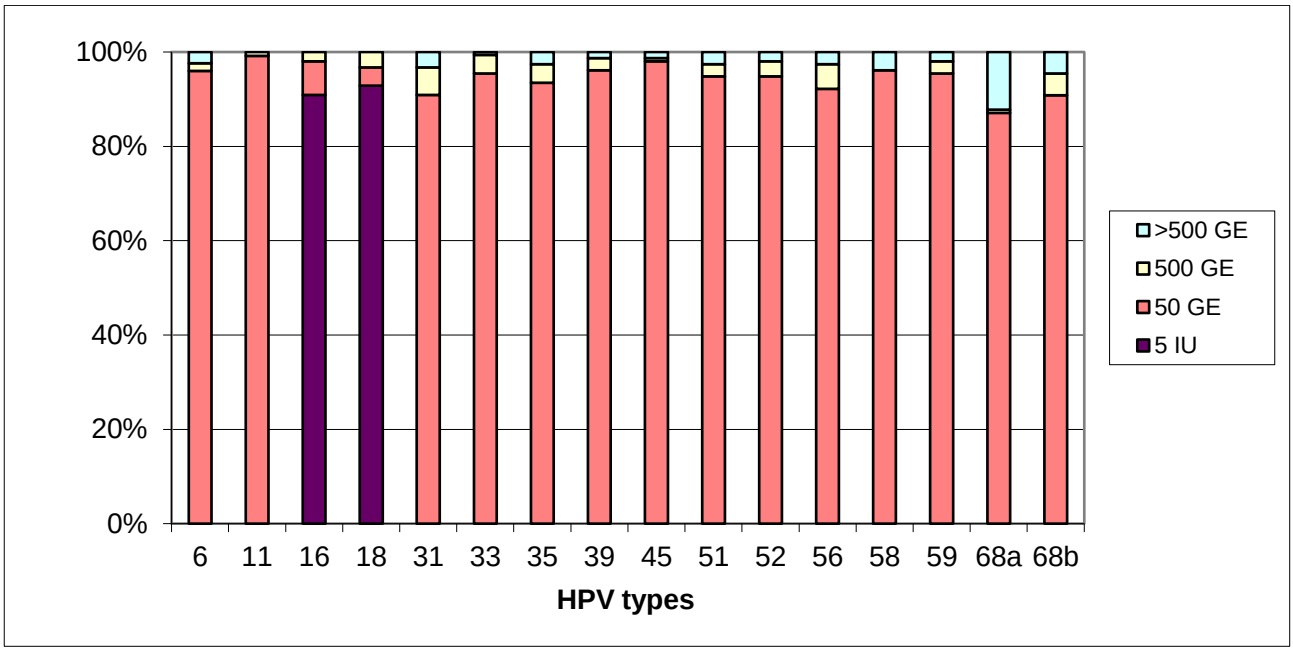


**Figure 4**: HPV Genome Equivalents (GE) or International Units (IU) detected per 5 µl in both single and multiple infections. Please note that only HPV16 and 18 were diluted to 5 IU (not all data sets analyze all HPV types).

**Table 5**: HPV GE or IU detected and typed per 5 µl in samples in both single and multiple HPV infections among the most commonly used commercial assays. Lowest detected GE / IU are indicated.

| HPV type | HPV IU /GE | All Assays (%) | Hybribio 37 | Anyplex II HPV 28 | Hybribio 21 | HPV 23 Genotyping Hybribio | Hybribio 14 | InnoLiPA | Allplex HPV 28 | Yaneng Bioscience |
|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 5 | 140/154 (91) | 21 / 21 | 17 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 2 / 3 | 8 / 9 |
| 16 | 50 | 150/154 (97) | | | | | | | 3 / 3 | |
| 16 | 500 | 154/154 (100) | | | | | | | | 9 / 9 |
| 18 | 5 | 143/154 (93) | 21 / 21 | 16 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 9 / 9 |
| 18 | 50 | 149/154 (97) | | 17 / 17 | | | | | | |
| 18 | 500 | 154/154 (100) | | | | | | | | |
| 6 | 50 | 120 / 125 (96) | 21 / 21 | 17 / 17 | 20 / 20 | 20 / 20 | nt [a)] | 5 / 5 | 3 / 3 | 9 / 9 |
| 6 | 500 | 122 / 125 (98) | | | | | | | | |
| 11 | 50 | 124 / 125 (99) | 21 / 21 | 17 / 17 | 20 / 20 | 20 / 20 | nt [a)] | 5 / 5 | 3 / 3 | 9 / 9 |
| 11 | 500 | 124 / 125 (99) | | | | | | | | |
| 31 | 50 | 139 / 154 (90) | 21 / 21 | 16 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 8 / 9 |
| 31 | 500 | 149 / 154 (97) | | 17 / 17 | | | | | | 9 / 9 |
| 33 | 50 | 147 / 154 (95) | 21 / 21 | 17 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 9 / 9 |
| 33 | 500 | 153 / 154 (99) | | | | | | | | |
| 35 | 50 | 144 / 154 (94) | 21 / 21 | 17 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 9 / 9 |
| 35 | 500 | 150 / 154 (97) | | | | | | | | |
| 39 | 50 | 148 / 154 (96) | 21 / 21 | 17 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 9 / 9 |
| 39 | 500 | 154 / 154 (100) | | | | | | | | |
| 45 | 50 | 151 / 154 (98) | 21 / 21 | 17 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 9 / 9 |
| 45 | 500 | 152 / 154 (99) | | | | | | | | |
| 51 | 50 | 146 / 154 (95) | 21 / 21 | 17 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 9 / 9 |
| 51 | 500 | 150 / 154 (97) | | | | | | | | |
| 52 | 50 | 145 / 154 (94) | 21 / 21 | 15 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 9 / 9 |
| 52 | 500 | 150 / 154 (97) | | 17 / 17 | | | | | | |
| 56 | 50 | 142 / 154 (92) | 21 / 21 | 14 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 4 / 5 | 3 / 3 | 9 / 9 |
| 56 | 500 | 150 / 154 (97) | | 17 / 17 | | | | 5 / 5 | | |
| 58 | 50 | 148 / 154 (96) | 21 / 21 | 17 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 9 / 9 |
| 58 | 500 | 148 / 154 (96) | | | | | | | | |
| 59 | 50 | 147 / 154 (95) | 21 / 21 | 16 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 9 / 9 |
| 59 | 500 | 151 / 154 (98) | | 17 / 17 | | | | | | |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 68a | 50 | 128 / 146 (88) | 21 / 21 | 17 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 8 / 9 |
| 68a | 500 | 131 / 146 (90) | | | | | | | | 9 / 9 |
| 68b | 50 | 140 / 153 (92) | 21 / 21 | 16 / 17 | 20 / 20 | 20 / 20 | 19 / 19 | 5 / 5 | 3 / 3 | 8 / 9 |
| 68b | 500 | 147 / 153 (96) | | 17 / 17 | | | | | | 9 / 9 |

a) Nt: Not tested

**Table 6**: HPV GE or IU detected and typed per 5 µl in samples with in both single and multiple HPV infections among in-house assays and commercial assays used by 3 laboratories and less. Lowest detected GE / IU are indicated.

| HPV type | HPV IU /GE | In-house Luminex | In-house Realtime PCR | In-house NGS | Lineblot | Realquality (AB Analitica) | HPV Direct Flow-chip | In-house PGMY-CHUV | Vision Array HPV | Other Commercial[a)] |
|---|---|---|---|---|---|---|---|---|---|---|
| 16 | 5 | 4 / 4 | 6 / 8 | 2 / 3 | 2 / 3 | 3 / 3 | 1 / 2 | 2 / 2 | | 9 / 13 |
| 16 | 50 | | 8 / 8 | 3 / 3 | | | 2 / 2 | | 2 / 2 | 12 / 13 |
| 16 | 500 | | | | 3 / 3 | | | | | 13 / 13 |
| 18 | 5 | 4 / 4 | 4 / 8 | 2 / 3 | 3 / 3 | 3 / 3 | 1 / 2 | 1 / 2 | | 12 / 13 |
| 18 | 50 | | 6 / 8 | 3 / 3 | | | 2 / 2 | 2 / 2 | | 13 / 13 |
| 18 | 500 | | 8 / 8 | | | | | | 2 / 2 | |
| 6 | 50 | 4 / 4 | 4 / 5 | 3 / 3 | 2 / 3 | 2 / 2 | 2 / 2 | 2 / 2 | | 7 / 7 |
| 6 | 500 | | | | | | | | 2 / 2 | |
| 11 | 50 | 4 / 4 | 5 / 5 | 3 / 3 | 2 / 3 | 2 / 2 | 2 / 2 | 2 / 2 | 2 / 2 | 7 / 7 |
| 11 | 500 | | | | | | | | | |
| 31 | 50 | 3 / 4 | 6 / 8 | 2 / 3 | 1 / 3 | 3 / 3 | 2 / 2 | 1 / 2 | | 9 / 13 |
| 31 | 500 | 4 / 4 | 7 / 8 | | 2 / 3 | | | 2 / 2 | 2 / 2 | 10 / 13 |
| 33 | 50 | 4 / 4 | 7 / 8 | 2 / 3 | 2 / 3 | 3 / 3 | 2 / 2 | 2 / 2 | | 11 / 13 |
| 33 | 500 | | 8 / 8 | | 3 / 3 | | | | 2 / 2 | 13 / 13 |
| 35 | 50 | 4 / 4 | 6 / 8 | 2 / 3 | 2 / 3 | 3 / 3 | 2 / 2 | 2 / 2 | | 10 / 13 |
| 35 | 500 | | 7 / 8 | | | | | | 2 / 2 | 12 / 13 |
| 39 | 50 | 3 / 4 | 7 / 8 | 2 / 3 | 2 / 3 | 3 / 3 | 2 / 2 | 2 / 2 | | 13 /13 |
| 39 | 500 | 4 / 4 | 8 / 8 | | | | | | 2 / 2 | |
| 45 | 50 | 4 / 4 | 6 / 8 | 3 / 3 | 3 / 3 | 3 / 3 | 2 / 2 | 2 / 2 | 2 / 2 | 12 / 13 |
| 45 | 500 | | 7 / 8 | | | | | | | |
| 51 | 50 | 4 / 4 | 7 / 8 | 2 / 3 | 2 / 3 | 3 / 3 | 2 / 2 | 2 / 2 | 2 / 2 | 10 / 13 |
| 51 | 500 | | 7 / 8 | | | | | | | 11 / 13 |
| 52 | 50 | 4 / 4 | 7 / 8 | 2 / 3 | 2 / 3 | 3 / 3 | 2 / 2 | 2 / 2 | 2 / 2 | 12 / 13 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 52 | 500 | | 7 / 8 | | | | | | | 13 / 13 |
| 56 | 50 | 3 / 4 | 8 / 8 | 3 / 3 | 2 / 3 | 3 / 3 | 2 / 2 | 1 / 2 | | 9 / 13 |
| 56 | 500 | | | | | | | 2 / 2 | | 12 / 13 |
| 58 | 50 | 4 / 4 | 8 / 8 | 3 / 3 | 2 / 3 | 3 / 3 | 2 / 2 | 2 / 2 | | 11 / 13 |
| 58 | 500 | | | | | | | | | |
| 59 | 50 | 4 / 4 | 8 / 8 | 3 / 3 | 2 / 3 | 3 / 3 | 2 / 2 | 2 / 2 | | 10 / 13 |
| 59 | 500 | | 7 / 7 | | | | | | 2 / 2 | 11 / 13 |
| 68a | 50 | 3 / 3 | 1 / 3 | 1 / 3 | | | 2 / 2 | 2 / 2 | | 5 / 12 |
| 68a | 500 | | 2 / 3 | 2 / 3 | | | | | | |
| 68b | 50 | 3 / 4 | 5 / 7 | 1 / 3 | 2 / 3 | 3 / 3 | 2 / 2 | 2 / 2 | | 10 / 13 |
| 68b | 500 | 4 / 4 | 6 / 7 | | | | | | | 13 / 13 |

a) Other commercial assays include: Venus HPV, Harmonia HPV, Sansure S3057, Sansure S3027, NeoPlex HPV 29, Ampliquality, GenoFlow HPV Array, DiagCor Realtime PCR, ScreenFire, F-HPV typing, Yaneng BIOscience Multicolour, Yaneng BIOscience HPV16/18 genotyping, HPV DNA-Array Autoimmun Diangnostika GmbH.

## 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:** Percentage of laboratories reporting correct HPV type as claimed and with **no false** positive HPV type detected, including test that type HPV 16 and HPV 18 and other HR, reported by sample number.

| HPV types | HPV genome equivalents per 5 µl | Percent correct data sets (N) |
|---|---|---|
| 16 | 50 | **99.3 (151 / 152)** |
| 16 | 5 | 91.4 (139 / 152) |
| 18 | 50 | **97.4 (148 / 152)** |
| 18 | 5 | 93.4 (143 / 153) |
| 6 | 500 | **97.6 (120 / 123)** |
| 6 | 50 | 96.7 (119 / 123) |
| 11 | 500 | **99.2 (122 / 123)** |
| 11 | 50 | 99.2 (122/ 123) |
| 31 | 500 | **96.7 (147 / 152)** |
| 31 | 50 | 90.8 (138 / 152) |
| 33 | 500 | **99.3 (151 / 152)** |
| 33 | 50 | 95.4 (146 / 153) |

| | | |
|---|---|---|
| 35 | 500 | **97.3 (149 / 153)** |
| 35 | 50 | 93.4 (143 / 153) |
| 39 | 500 | **98.7 (150 / 152)** |
| 39 | 50 | 96.0 (146 / 152) |
| 45 | 500 | **98.7 (149 / 151)** |
| 45 | 50 | 98.0 (149 / 152) |
| 51 | 500 | **97.4 (148 / 152)** |
| 51 | 50 | 95.4 (145 / 152) |
| 52 | 500 | **100.0 (153 / 153)** |
| 52 | 50 | 97.4 (148/ 152) |
| 56 | 500 | **97.4 (148/ 152)** |
| 56 | 50 | 94.6 (142 / 150) |
| 58 | 500 | **96.7 (148 / 153)** |
| 58 | 50 | 96.7 (148 / 153) |
| 59 | 500 | **98.0 (149 / 152)** |
| 59 | 50 | 96.0 (146 / 152) |
| 68a | 500 | **93.7 (136 / 145)** |
| 68a | 50 | 91.1 (133 / 146) |
| 68b | 500 | **96.7 (147 / 152)** |
| 68b | 50 | 93.4 (141 / 151) |
| 6, 33, 39, 59 | 500 | **98.7 (149 / 151)** |
| 6, 33, 39, 59 | 50 | 95.4 (145 / 152) |
| 11, 16, 51, 68a | 500 | **91.5 (140 / 153)** |
| 11, 16, 51, 68a | 50 | 88.8 (135 / 152) |
| 18, 31, 35, 45 | 500 | **96.0 (144 / 150)** |
| 18, 31, 35, 45 | 50 | 90.1 (137 / 152) |
| 52, 56, 58, 68b | 500 | **98.0 (150 / 153)** |
| 52, 56, 58, 68b | 50 | 91.5 (140 / 153) |
| TE buffer with 10 ng/µl human placenta DNA | 0 | **98.7 (152 / 154)** |
| HPV 16 positive SiHa cells | 2500 | 99.3 (150 / 151) (3 false positive) |
| HPV 16 positive SiHa cells | 25 | 84.8 (128 / 151) (3 false positive) |
| . HPV-negative C33A cells | 0 | 95.4 (147 / 154) (7 false positive) |

[a] Data sets known not to detect the HPV 68a plasmids in this panel are considered as correct when the other HPV types in the sample are detected.

## 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 type | Number of data sets | No. of false positive samples per data set | | | | |
|---|---|---|---|---|---|---|
| | | 0 samples | 1 sample | 2 samples | 3 samples | > 3 samples |
| **All assays** | **154** | **132** | **15** | **4** | **0** | **3** |
| Hybribio 37 array HPV (Hybribio) | 21 | 21 | 0 | 0 | 0 | 0 |
| HPV-23 Genotyping (Hybriobio) | 20 | 20 | 0 | 0 | 0 | 0 |
| Hybribio 21 array HPV (Hybribio) | 20 | 20 | 0 | 0 | 0 | 0 |
| Hybribio 14 HR (Hybribio) | 19 | 18 | 1 | 0 | 0 | 0 |
| Anyplex II HPV 28 (Seegene) | 17 | 15 | 1 | 1 | 0 | 0 |
| HPV Genotyping 23 (Yaneng Bioscience) | 9 | 9 | 0 | 0 | 0 | 0 |
| In-house realtime PCR | 8 | 5 | 2 | 0 | 0 | 1 |
| InnoLiPA Extra (Fujirebio) | 5 | 2 | 2 | 1 | 0 | 0 |
| In-house PCR Luminex | 4 | 4 | 0 | 0 | 0 | 0 |
| Allplex HPV28 (Seegene) | 3 | 3 | 0 | 0 | 0 | 0 |
| Realquality (AB Analitica) | 3 | 0 | 3 | 0 | 0 | 0 |
| In-house NGS | 3 | 2 | 0 | 0 | 0 | 1 |
| Lineblot (3 different) | 3 | 2 | 0 | 1 | 0 | 0 |
| HPV Direct Flow-chip (Master Diagnostica) | 2 | 1 | 1 | 0 | 0 | 0 |
| In-house PGMY-CHUV | 2 | 1 | 1 | 0 | 0 | 0 |
| VisionArray HPV (ZytoVision) | 2 | 0 | 2 | 0 | 0 | 0 |
| Other Commercial assays [a)] | 13 | 9 | 2 | 1 | 0 | 1 |

a) Other commercial assays include one laboratory using each of; Venus HPV, Harmonia HPV, Sansure S3057, Sansure S3027, NeoPlex HPV 29, Ampliquality, GenoFlow HPV Array, DiagCor Realtime PCR, ScreenFire, F-HPV typing, Yaneng BIOscience Multicolour, Yaneng BIOscience HPV16/18 genotyping, HPV DNA-Array Autoimmun Diangnostika GmbH.

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).

## 4.5 Comparison of results for laboratories that participated 2022 and in the years 2008, 2010, 2011, 2013, 2014, 2017, 2019 and 2021

In total 51 laboratories that participated in 2022 had also participated in the HPV LabNet PPs from at least one previous year. Fourteen laboratories that submitted results in 2022 participated from the start 2008 of these eight laboratories participated in all 9 PPs (2008, 2010, 2011, 2013, 2014, 2017, 2019, 2021 and 2022). Six laboratories analysed the PP in 8 years, 4 laboratories in 7 years, 2 laboratories in 6, 5 and 4 years respectively, 6 laboratories in 3 years and 21 laboratories analysed the panel in 2021 and 2022. Comparisons of these results were made for each laboratory. Some of the laboratories used the same tests during all years, whereas some laboratories had changed at least one of the tests used. Percent proficiency, for each year and compared with the results from all data sets submitted 2022 is shown in Table 9a and 9b, the sensitivity for individual HPV types in Table 10 and the specificity with number of false positive samples in Table 11a and 11b.

**Table 9a**: Proficiency of detecting HPV types by laboratories that participated in 2022 PP, using identical assays in 2008, 2010, 2011, 2013, 2014, 2017, 2019 and 2021 in comparison with all data sets submitted in 2022.

**Not proficient = One or more false positive results**

| Proficiency | All test by laboratories that participated in 2008, 2010, 2011, 2013, 2014, 2017, 2019, 2021 and 2022 using identical assays | | | | | | | | | All datasets 2022 (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2008 (%) | 2010 (%) | 2011 (%) | 2013 (%) | 2014 (%) | 2017 (%) | 2019 (%) | 2021 (%) | 2022 (%) | |
| **100 % proficient** | 0 / 4 (0) | 2 / 8 (25) | 8 / 15 (53) | 9 / 18 (50) | 10 / 18 (56) | 14 / 22 (64) | 14 / 37 (38) | 80 / 100 (80) | 80 / 104 (77) | 119 / 154 (77) |
| **99-90 % proficient** | 1 / 4 (25) | 1 / 8 (12) | 1 / 15 (6.7) | 1 / 18 (5.6) | 2 / 18 (11) | 2 / 22 (9.1) | 8 / 37 (22) | 2 /100 (2.0) | 5 /104 (4.8) | 6 / 154 (3.9) |
| **89-80 % proficient** | 0 / 4 (0) | 1 / 8 (12) | 2 / 15 (13) | 2 / 18 (11) | 1 / 18 (5.6) | 1 / 22 (4.6) | 2 / 37 (5.4) | 1 / 100 (1.0) | 0 / 104 (0) | 2 / 154 (1.3) |
| **<80 % proficient** | 2 / 4 (50) | 1 / 8 (12) | 1 / 15 (6.7) | 0 / 18 (0) | 0 / 18 (0) | 0 / 22 (0) | 1 / 37 (2.7) | 1 / 100 (1.0) | 1 / 104 (1.0) | 5 / 154 (3.2) |
| **Not proficient** | 1 / 4 (25) | 3 / 8 (38) | 3 / 15 (20) | 6 / 18 (33) | 5 / 18 (28) | 5 / 22 (23) | 12 / 37 (32) | 16 / 100 (16) | 18 / 104 (17) | 22 / 154 (14) |

**Table 9b**: Proficiency of detecting HPV types by laboratories that participated in 2022 PP, with data from 2008, 2010, 2011, 2013, 2014, 2017, 2019 and 2021 in comparison with all data sets submitted 2022

**Not proficient = false positive result**

| Proficiency | All test by laboratories that participated in 2008, 2010, 2011, 2013, 2014, 2017, 2019, 2021 and 2022 | | | | | | | | | All datasets 2022 (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2008 (%) | 2010 (%) | 2011 (%) | 2013 (%) | 2014 (%) | 2017 (%) | 2019 (%) | 2021 (%) | 2022 (%) | |
| **100 % proficient** | 5 / 15 (33) | 5 / 24 (21) | 16 / 29 (55) | 13 / 28 (46) | 15 / 28 (54) | 20 / 33 (61) | 16 / 45 (36) | 80 / 101 (79) | 81 / 105 (77) | 119 / 154 (77) |
| **99-90 % proficient** | 1 / 15 (6.7) | 1 / 24 (4.2) | 2 / 29 (6.9) | 3 / 28 (11) | 2 / 28 (7.1) | 3 / 33 (9.1) | 10 / 45 (22) | 2 /101 (2.0) | 5 /105 (4.8) | 6 / 154 (3.9) |
| **89-80 % proficient** | 0 / 15 (0) | 3 / 24 (12) | 2 / 29 (6.9) | 2 / 28 (7.1) | 2 / 28 (7.1) | 2 / 33 (6.1) | 3 / 45 (6.7) | 1 / 101 (1.0) | 0 / 105 (0) | 2 / 154 (1.3) |
| **<80 % proficient** | 2 / 15 (13) | 2 / 24 (8.3) | 2 / 29 (6.9) | 0 / 28 (0) | 1 / 28 (3.6) | 0 / 33 (0) | 1 / 45 (2.2) | 1 / 101 (1.0) | 1 / 105 (1.0) | 5 / 154 (3.2) |
| **Not proficient** | 7 / 15 (47) | 13 / 24 (54) | 7 / 29 (24) | 10 / 28 (36) | 8 / 28 (29) | 8 / 33 (24) | 15 / 45 (33) | 17 / 101 (17) | 18 / 105 (17) | 22 / 154 (14) |

**Table 10**: HPV GE or IU detected and typed per 5 µl in both single and multiple infections by laboratories participating in 2011, 2013, 2014, 2017, 2019, 2021 and 2022. Table includes samples with detection of false positive HPV types. Lowest detected GE/IU is indicated.

| HPV type | HPV IU /GE | All test by laboratories participating both in 2011, 2013, 2014, 2017, 2019, 2021 and 2022 | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 2011 (%) | 2013 (%) | 2014 (%) | 2017 (%) | 2019 (%) | 2021 (%) | 2022 (%) |
| 16 | 5 | 19 / 27 (70) | 22 / 28 (79) | 21 / 28 (75) | 26 / 33 (79) | 40 / 45 (89) | 95 / 101 (94) | 99 / 105 (94) |
| 16 | 50 | 27 / 27 (100) | | 25 / 28 (89) | 29 / 33 (88) | 44 / 45 (98) | 100 / 101 (99) | 102 / 105 (97) |
| 16 | 500 | | 28 / 28 (100) | 28 / 28 (100) | 32 / 33 (97) | 45 / 45 (100) | 101/ 101 (100) | 105 / 105 (100) |
| 18 | 5 | 17 / 27 (63) | 23 / 28 (82) | 19 / 27 (70) | 23 / 33 (70) | 40 / 45 (89) | 95 / 101 (94) | 96 / 105 (91) |
| 18 | 50 | 25 / 27 (93) | 24 / 28 (86) | 21 / 27 (78) | 28 / 33 (85) | 45 / 45 (100) | 101/ 101 (100) | 103 / 105 (98) |
| 18 | 500 | 26 / 27 (96) | 28 / 28 (100) | 27 / 27 (100) | 33 / 33(100) | | | 105 / 105 (100) |
| 6 | 50 | 19 / 25 (76) | 18 / 26 (69) | 18 / 26 (69) | 22 / 28 (79) | 35 / 39 (90) | 80 / 84 (95) | 84 / 88 (95) |
| 6 | 500 | 24 / 25 (96) | 24 / 26 (92) | 24 / 26 (92) | 28 / 28 (100) | 39 / 39 (100) | 81 / 84 (96) | 86 / 88 (98) |
| 11 | 50 | 21 / 25 (84) | 21 / 26 (81) | 22 / 26 (85) | 24 / 28 (86) | 38 / 39 (97) | 81 / 84 (96) | 87 / 88 (99) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 11 | 500 | 24 / 25 (96) | 25 / 26 (96) | 26 / 26 (100) | 28 / 28 (100) | 39 / 39 (100) | 84 / 84 (100) | |
| 31 | 50 | 16 / 27 (59) | 20 / 28 (71) | 19 / 28 (68) | 25 / 33 (76) | 38 / 45 (84) | 96 / 101 (95) | 98 / 105 (93) |
| 31 | 500 | 26 / 27 (96) | 27 / 28 (96) | 27 / 28 (96) | 32 / 33 (97) | 42 / 45 (93) | 101/ 101 (100) | 104 / 105 (99) |
| 33 | 50 | 22 / 27 (81) | 24 / 28 (86) | 21 / 28 (75) | 28 / 33 (85) | 43 / 45 (96) | 99 / 101 (98) | 102 / 105 (97) |
| 33 | 500 | 25 / 27 (93) | 28 / 28 (100) | 27 / 28 (96) | 33 / 33 (100) | 45 / 45 (100) | 101/ 101 (100) | 105 / 105 (100) |
| 35 | 50 | 22 / 27 (81) | 23 / 28 (82) | 22 / 28 (79) | 28 / 33 (85) | 43 / 45 (96) | 98 / 101 (97) | 99 / 105 (94) |
| 35 | 500 | 26 / 27 (96) | 28 / 28 (100) | 26 / 28 (93) | 31 / 33 (98) | 44 / 45 (97) | 100 / 101 (99) | 105 / 105 (100) |
| 39 | 50 | 18 / 27 (67) | 23 / 28 (82) | 21 / 28 (75) | 29 / 33 (88) | 44 / 45 (97) | 97 / 101 (96) | 101 / 105 (96) |
| 39 | 500 | 24 / 27 (89) | 28 / 28 (100) | 26 / 28 (93) | 32 / 33 (97) | 45 / 45 (100) | 100/ 101 (99) | 104 / 105 (99) |
| 45 | 50 | 21 / 27 (78) | 23 / 28 (82) | 22 / 28 (79) | 30 / 33 (91) | 45 / 45 (100) | 99 / 101 (98) | 105 / 105 (100) |
| 45 | 500 | 26 / 27 (99) | 27 / 28 (96) | 26 / 28 (93) | 33 / 33 (100) | | 101/ 101 (100) | |
| 51 | 50 | 23 / 27 (85) | 23 / 28 (82) | 23 / 28 (82) | 27 / 33 (82) | 44 / 45 (97) | 96 / 101 (95) | 101 / 105 (96) |
| 51 | 500 | 27 / 27 (100) | 28 / 28 (100) | 27 / 28 (96) | 30 / 33 (91) | 45 / 45 (100) | 100 / 101 (99) | 103 / 105 (98) |
| 52 | 50 | 20 / 28 (71) | 23 / 28 (82) | 22 / 28 (79) | 30 / 33 (91) | 45 / 45 (100) | 99 / 101 (98) | 100 / 105 (95) |
| 52 | 500 | 27 / 28 (96) | 27 / 28 (96) | 27 / 28 (96) | 33 / 33 (100) | | 101/ 101 (100) | 104 / 105 (99) |
| 56 | 50 | 21 / 27 (78) | 24 / 28 (86) | 23 / 28 (82) | 26 / 33 (79) | 41 / 45 (91) | 94 / 101 (93) | 95 / 105 (90) |
| 56 | 500 | 26 / 27 (99) | 28 / 28 (100) | 27 / 28 (96) | 32 / 33 (97) | 43 / 45 (96) | 98 / 101 (97) | 102 / 105 (97) |
| 58 | 50 | 19 / 27 (70) | 20 / 28 (71) | 21 / 28 (75) | 25 / 33 (76) | 42 / 45 (93) | 96 / 101 (95) | 102 / 105 (97) |
| 58 | 500 | 25 / 27 (93) | 27 / 28 (96) | 26 / 28 (93) | 32 / 33 (97) | 45 / 45 (100) | 98 / 101 (97) | |
| 59 | 50 | 20 / 27 (74) | 21 / 28 (75) | 22 / 28 (79) | 26 / 33 (79) | 42 / 45 (93) | 98 / 101 (97) | 100 / 105 (95) |
| 59 | 500 | 24 / 27 (89) | 26 / 28 (93) | 27 / 28 (96) | 33 / 33 (100) | 44 / 45 (97) | 101/ 101 (100) | 104 / 105 (99) |
| 68a | 50 | 8 / 18[a)] (44) | 8 / 19 (42) | 10 / 17 (59) | 17 / 29 (59) | 29 / 42 (69) | 87 / 101 (86) | 88 / 100 (88) |
| 68a | 500 | 11 / 18 (61) | 10 / 19 (53) | 12 / 17 (71) | | 32 / 42 (76) | 89 / 101 (88) | 89 / 100 (89) |
| 68b | 50 | 19 / 27 (70) | 20 / 27 (74) | 21 / 27 (78) | 28 / 32 (88) | 3 / 44 (6.8) | 94 / 101 (93) | 98 / 104 (94) |
| 68b | 500 | 25 / 27 (93) | 27 / 27 (100) | 26 / 27 (96) | 30 / 32 (94) | 15 / 44 (34) | 98 / 101 (97) | 100 / 104 (96) |

a) 68a cannot be detected by PGMY based primers except version 2 of PGMY-CHUV, the plasmid used contains the L1 fragment only.

**Table 11a**: Number of false positive HPV types detected per data set reported by laboratories using identical assays in 2008, 2010, 2011, 2013, 2014, 2017, 2019, 2021 and 2022 years proficiency studies in comparison with all data sets submitted 2022.

| No of false positive samples | All test by laboratories that participated in 2008, 2010, 2011, 2013, 2014, 2017, 2019, 2021 and 2022 using identical assays | | | | | | | | | All datasets 2022 (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2008 (%) | 2010 (%) | 2011 (%) | 2013 (%) | 2014 (%) | 2017 (%) | 2019 (%) | 2021 (%) | 2022 (%) | |
| **0 samples** | 3 / 4 (75) | 5 / 8 (62) | 12 / 15 (80) | 12 / 18 (67) | 13 / 18 (72) | 17 / 22 (77) | 25 / 37 (68) | 84 / 100 (84) | 86 / 104 (83) | 132 / 154 (86) |
| **1 sample** | 1 / 4 (25) | 0 / 8 (0) | 1 / 15 (6.7) | 3 / 18 (17) | 1 / 18 (5.6) | 2 / 22 (9.1) | 7 / 37 (19) | 10 /100 (10) | 13 /104 (13) | 15 / 154 (9.7) |
| **2 samples** | 0 / 4 (0) | 2 / 8 (25) | 1 / 15 (6.7) | 0 / 8 (0) | 0 / 18 (0) | 1 / 22 (4.6) | 0 / 37 (0) | 4 / 100 (4.0) | 4 / 104 (3.8) | 4 / 154 (2.6) |
| **3 samples** | 0 / 4 (0) | 0 / 8 (0) | 0 / 15 (0) | 2 / 18 (11) | 1 / 18 (5.6) | 1 / 22 (4.6) | 4 / 37 (11) | 0 / 100 (0) | 0 / 104 (0) | 0 / 154 (0) |
| **>3 samples** | 0 / 4 (0) | 1 / 8 (12) | 1 / 15 (6.7) | 1 / 18 (5.6) | 3 / 18 (17) | 1 / 22 (4.6) | 1 / 37 (2.7) | 2 / 100 (2.0) | 1 / 104 (1.0) | 3 / 154 (1.9) |

**Table 11b**: Number of false positive HPV types detected per data set reported by laboratories participating in 2008, 2010, 2011, 2013, 2014, 2017, 2019, 2021 and 2022 years proficiency studies in comparison with all data sets submitted 2022.

| No of false positive samples | All test by laboratories that participated in 2008, 2010, 2011, 2013, 2014, 2017, 2019, 2021 and 2022 | | | | | | | | | All datasets 2022 (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | 2008 (%) | 2010 (%) | 2011 (%) | 2013 (%) | 2014 (%) | 2017 (%) | 2019 (%) | 2021 (%) | 2022 (%) | |
| **0 samples** | 8 / 15 (53) | 11 / 24 (46) | 22 / 29 (76) | 18 / 28 (64) | 20 / 28 (71) | 25 / 33 (76) | 30 / 45 (67) | 84 / 101 (83) | 87 / 105 (83) | 132 / 154 (86) |
| **1 sample** | 2 / 15 (13) | 2 / 24 (8.3) | 5 / 29 (17) | 6 / 28 (21) | 2 / 28 (7.1) | 3 / 33 (9.1) | 9 / 45 (20) | 11 /101 (11) | 13 /105 (12) | 15 / 154 (9.7) |
| **2 samples** | 3 / 15 (20) | 4 / 24 (17) | 1 / 29 (3.4) | 0 / 28 (0) | 2 / 28 (7.1) | 2 / 33 (6.1) | 1 / 45 (2.2) | 4 / 101 (4.0) | 4 / 105 (3.8) | 4 / 154 (2.6) |
| **3 samples** | 1 / 15 (6.7) | 5 / 24 (21) | 0 / 29 (0) | 3 / 28 (11) | 1 / 28 (3.6) | 1 / 33 (3.0) | 4 / 45 (8.9) | 0 / 101 (0) | 0 / 105 (0) | 0 / 154 (0) |
| **>3 samples** | 1 / 15 (6.7) | 2 / 24 (8.3) | 1 / 29 (3.4) | 1 / 28 (3.4) | 3 / 28 (11) | 2 / 33 (6.1) | 1 / 45 (2.2) | 2 / 101 (2.0) | 1 / 105 (0.9) | 3 / 154 (1.9) |

# 5. Discussion

A total of 78 laboratories applied for participation in the 2022 proficiency study. The 2021 proficiency panels were distributed to all solicitants and a total of 154 datasets from 78 laboratories were returned before the deadline (January 2023).

Gladly, the global deterioration in HPV typing proficiency that was seen and reported in the 2019 PP has significantly reversed, with a total of 77% (119/154) datasets showing 100% proficiency. Again, this is the highest percentage of 100% proficient datasets seen in all proficiency studies. The highest percentage was seen in 2021 with 75% (158/211) datasets being 100% proficient.

Proficiency criteria was defined as: 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. The criteria for proficiency since the 2019 PP includes no false positivity (in previous years, a maximum of one false positive had been allowed for proficiency). Not all assays tested for every HPV type included in the panel. Twenty-seven datasets were generated using assays that either did not discriminate specific HPV types or reported results as HPV 16, 18 and "other" High Risk HPV types (Hybribio 14 HR, In-house Realtime PCR, Realquality, Harmonia HPV, and Sansure and YanengBio 16/18). These data sets are only analyzed for the specific types tested for individually. In the analyses for proficiency only the HPV types tested for were included. E.g., if an assay did not include HPV 68, laboratories using such an assay were considered as not testing for HPV 68. According to these criteria, 119/154 (77%) datasets that typed for at least one HPV type were 100 % proficient for the types claimed to be detected by the test. Of these, 110/154 datasets correctly identified the content of all samples, including the samples with copy number amounts that were lower than required for proficiency.

HPV 16, 18 and 45 (most prevalent ones in cervical cancer) were detected in more than 97% datasets.

Most datasets were provided using commercially available assays (137/154), being Hybribio 37 HPV Genoarray (Hybribio, 21 laboratories), two other Hybribio assays (20 laboratories) and Anyplex II HPV 28 (Seegene, 17 laboratories) the most commonly assays used. Seventeen datasets were obtained using a variety of in-house assays. The proportion of commercial assays used in the proficiency studies has exponentially increased over time, from 57% in 2011, 80% in 2019, 86% in 2021 and now 89% (137/154 datasets using commercial assays in 2022).

There were several assays from which all the datasets provided showed 100% proficiency (Hybribio 37 array HPV (Hybribio), HPV-23 Genotyping (Hybriobio), Hybribio 21 array HPV (Hybribio), Seegene Allplex HPV 28). On the contrary, none of the datasets obtained with Ampliquality (AB Analitica) and VisionArray HPV (ZytoVision) were 100% proficient.

Overall, 85.7% (132/154) of datasets showed no false positivity. Up to 6 assays showed no false positivity including the assays being 100% proficient and described above, the (Yaneng) HPV 23 Genotyping and In-house Luminex assays.

We aimed to investigate if there was any specific sample or assay where false positivity was consistently detected. Results from false positivity investigation revealed that false positivity appeared to be essentially randomly distributed among the 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).

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. While several of the datasets submitted in 2021 were generated using assays that were used by 4 or fewer laboratories and thus, it was difficult to draw conclusions regarding the generalisability of the performance of these assays, some assays were used for generating quite several datasets. As an example, Anyplex II HPV 28 which was used to generate 17 data sets, provided 14/17 datasets which were fully proficient and 2/17 datasets which were not proficient with 1 to 2 false positive results. This is an example of the impact of the laboratory.

A major finding with robustness was detected with the assays by Hybribio. Datasets generated with these assays were fully proficiency in nearly all cases (79/80 datasets) from different laboratories, translating into being 51 % from the overall proficiency (86%) achieved by the 2022 proficiency study. The widespread use of these assays in laboratories in the WPRO region appears to be a major reason why the proficiency was highest in this region. Hybribio was used in 23/78 laboratories, with all of them belonging to the WPRO region.

All plasmids in the panel were detected at the required concentration for proficiency (at least 50 international units (IU) per 5 ul for HPV 16 and HPV 18, and at least 500 genome equivalents (GE) in 5 ul of the other HPV types) in minimum 93.7% datasets. Plasmids in the panel contained full-length genomes, except HPV 68a that only contained L1. All datasets generated using assays targeting other parts of HPV 68a or that used the PGMY primers were considered as not testing for

HPV 68a in this study. It is well reported in literature that all PGMY-based assays (directed against L1) cannot detect HPV68a, and therefore, we also added HPV 68b in the panel. HPV68b can be detected by PGMY-based primers and other common primer systems.

Three additional samples (A, B, C) in the PP were used to evaluate the DNA extraction step prior to HPV testing and typing. Two of the samples contained different amounts of the cervical cancer cell line SiHa mixed with the HPV negative cancer cell line C33A and one sample with only C33A cells served as negative control. There were at least 20 different extraction procedures used among the laboratories. The most commonly used was different extraction kits from Qiagen used to generate 17 data sets. Other utilised methods were MagNa Pure LC (Roche), Hybribio extraction kit, STARMag from Seegene and Maxwell from Promega. The HPV Direct flow-chip from Master Diagnostica is performed without DNA extraction, the cell suspensions are added directly to the PCR mix. We did not observe any obvious difference in performance between different extraction methods.

In sample C containing 2500 cells / 5 ul of the cervical cancer cell line SiHa, HPV 16 was correctly identified by 98 % of the datasets. Three data sets reported false positive HPV types in this sample. In sample A containing 25 SiHa cells / 5ul, HPV 16 was detected in 85 % of the data sets with three false positive result reported. The negative control containing only C33A cells was correctly reported as negative by 95 % of the laboratories.

Participating laboratories involved public health laboratories, research laboratories and diagnostic test manufacturers. There was a charge for laboratories to participate, although participants from low and lower middle-income countries could have their fees waived. It is thus possible that the improved performance observed in the 2022 proficiency study may reflect a bias with a preferential participation of laboratories who can afford the fee and who may preferentially come from high income countries and/or have HPV genotyping as a central priority for their activities. However, the analysis that was restricted to laboratories that have participated multiple times did also find a continued improvement in performance in 2022 (from 16/45 being 100% proficient in 2019 to 80/101 in 2021 and 81/105 in 2022, from 36% to 79%), indicating that there has indeed occurred a global improvement in the performance of HPV genotyping.

The PP is designed for the genotyping needs in HPV vaccine research and the proficiency criteria are not intended for clinical HPV screening purposes, where the requirements for analytical sensitivity may be different. Starting in 2022, we did issue a HPV screening panels (with screening-relevant concentrations of the HPV genotypes important for screening) to promote proficiency in

HPV screening services as well. Several laboratories that have previously participated in testing the genotyping panel have analyzed the screening panel, this might explain why there were fever laboratories that did perform testing on the 2022-year genotyping panel. The results from the screening panel will be presented in a separate technical report.

# 6. Conclusions and recommendations

This technical report summarizes the results obtained from the 9th HPV LabNet HPV DNA proficiency study that 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:
# Global HPV LabNet Proficiency Study for HPV DNA Typing 2022 (456)

Accurate and internationally comparable **HPV DNA detection and typing** methodology is an essential component in research on HPV vaccines and in effective implementation and monitoring. A WHO initiative established a Global HPV LabNet to support the worldwide implementation of HPV vaccines through improved laboratory standardization and quality assurance of HPV testing and typing methods to promote international comparability of results. The major methods for achieving progress towards this goal are developing international biological standards as well as preparing and validating proficiency panels to qualify methods.

We are now seeking international participation in an international HPV DNA testing and typing proficiency study. Laboratories that are or will be involved in HPV surveillance and/or vaccine development are particularly welcome.
Participant laboratories will be asked to perform HPV typing using one or more of their usual assays on the 44 challenges in this panel. This challenge is intended to evaluate assays that type HPV and is not appropriate for assays that detect HPV in general or grouped as high risk/low risk.

### Composition of sample material

- 41 tubes containing purified whole genomic plasmids of **HPV 6, 11, 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 single types or a mixture of HPV types at varying concentrations.
- 3 samples containing cell suspensions to allow evaluation of DNA extraction methods.

### Participation fee

Participation in the proficiency study is subject to a participation fee per panel consisting of 44 samples: 650 Euros for commercial entities and 275 Euros for academic entities. Participants from low and lower middle-income countries (World Bank classification with GNI (gross national income) per capita: <4045USD) 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**

15st 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 Typing Proficiency Study

| | |
|---|---|
| Fee for commercial entities: 1000 Euros, Fee for academic entities: 500 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 6, 11, 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 6 in pBR322 at position 4724 in the HPV genome, HPV 11 in pGEM4Z at position 4781, 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 6 nr X00203; HPV 11 nr M14119; 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 Typing, 2022

| Laboratory details |
|---|
| **AMR/PAHO – Regional Office for the Americas (8 labs)** |
| Maria Alejandra Picconi<br>Oncogenic Viruses Service<br>National Reference Laboratory for Papillomavirus<br>National Institute of Infectious Diseases- ANLIS "Dr. Malbran"<br>Av. Velez Sarsfield 563<br>C1282AFF- Buenos Aires<br>ARGENTINA<br>Email: mapicconi@anlis.gov.ar;<br>mapicconi@gmail.com |
| Diego Chouhy<br>Piso 3 de la Nave 4 del Campus Corporativo Cooperativo<br>Ruta Provincial N 16 km 5<br>Interseccion autopista Rosario-BsAs y AO12<br>Alvear<br>ARGENTINA<br>Email: dchouhy@detxmol.com.ar |
| Juliana Comerlato<br>Laboratório Epiclin - Hospital Moinhos de Vento<br>RuaRamiro Barcelos 630,sala817<br>BR-90035 -0<br>PORTO ALEGRE<br>BRAZIL<br>Email: juliana.comerlato@hmv.org.br |
| Keila Araujo Cruz de Olieviar<br>IBMP-Instituto de Biologia Molecular do Parana<br>Rua Prof. Algacyr Munhoz Mader 3775<br>Cidade Industrial De Curitiba<br>BR-81350-0<br>CURITIBA<br>BRAZIL<br>Email: marcel.tscha@ibmp.org.br |
| Alex Chauhan<br>Norgen Biotek Corp<br>3430 Schmon Parkway<br>CA-L2V4Y6<br>THORHOL |

| |
|---|
| CANADA<br>Email: alex.chauhan@norgenbiotek.com |
| Elizabeth R. Unger<br>Centers for Disease Control and Prevention<br>1600 Clifton Road<br>MS-G41, Atlanta, GA 30333<br>USA<br>Email: ERU0@cdc.gov |
| Casey Dagnall<br>Cancer Genomics Research Laboratory<br>National Cancer Institute<br>9615 Medical Drive<br>US-20850 Rockville<br>USA<br>Email: dagnallc@mail.nih.gov |
| Mercedes Piedad de León Bautista<br>Laboratorio Morelia<br>Juan B. Ceballos 872<br>Nueva Chapultepec<br>58280 Morelia,<br>MICHOACAN<br>MEXICO<br>Email: mercedes.deleon@centraladn.com |
| **EURO –European Region (31 labs)** |
| Gro Kummeneje Presthus<br>Akershus University Hospital<br>Department of Microbiology and Infection Control<br>Norwegian HPV Reference Laboratory<br>Sykehusveien 25<br>1478 Lørenskog<br>NORWAY<br>Email: gro.kummeneje.presthus@ahus.no |
| Inger-Lise Haakensen<br>Rom 08A04 Seksjon Genteknologi<br>Sykehuset Østfold Kalnes<br>Kalnesveien 320<br>NO-1714 GRÅLUM<br>NORWAY<br>Email: Inger.Lise.Hakensen@so-hf.no |
| Mona Hansen<br>Folkehelseinstituttet v/Jan Oksnes<br>Lovisenberggata 6<br>NO-0456 Oslo |

NORWAY
Email: mona.hansen@fhi.no

Kjersti Brusegard
OUS, Avdelning for patologi, Enhet for solide svulster
Enhet for solide svulster Molekylaer Patologi
OUS-Radiumhospitalet
Ullernshausseen 70
NO-0379 Oslo
NORWAY
Email: kbrenn@ous-hf.no

Liza Ho
Labo Pathologies moléculaire,
Clinical Pathology, 5th floor CMU, lab E05.2949
Geneva university hospital HUG
1 rue Michel-Servet
CH-1206 Geneva
SWITZERLAND
Email:liza.ho@hcuge.ch

Fredrik Pettersson
Eurofinc Clinical Testing Sweden AB
Rapsgatan 23
754 50 UPPSALA
SWEDEN
Email: FredrikPettersson@eurofins.se

Ola Forslund
Clinical Microbiology
Skåne University hospital
Sölvegatan 23 B
221 85 Lund
SWEDEN
Email: Ola.Forslund@skane.se

Annika Hellberg
Klinisk mikrobiologi
Virologi F68
Karolinska Universitetssjukhuset Huddinge
141 86 Stockholm
SWEDEN
Email: Annika.Hellberg@regionstockholm.se

Fanny Huynh Söderberg
ABC Labs/QC_QA Management
Tomtebodavägen 16
17165 Solna
SWEDEN
Email: fanny@abclabs.se

Christina Andersson
Virologiska laboratoriet
Sahlgrenska sjukhuset
Gulhedsgatan 10B
41346 Göteborg
SWEDEN
Email: christina.mar.andersson@vgregion.se

Jennie Malm
Klin mikrobiolog lab
Länssjukhuset
301 85 Halmstad
SWEDEN
Email: Jennie.Malm@regionhalland.se

Pernilla Tjernberg
Lab.medicin Västernorrland
Länssjukhuset S-vall/H-sand
851 86 Sundsvall
SWEDEN
Email: pernilla.tjernberg@rvn.se

Kate Cuschieri
Scottish HPV Reference Laboratory (SHPVRL)
Specialist Virology Centre
Dept of Laboratory medicine
Royal Infirmary of Edinburgh
51 Little France Crescent
Edinburgh EH16 4SA,
UK
Email: Kate.Cuschieri@nhslothian.scot.nhs.uk
Kirsty.E.Gray@nhslothian.scot.nhs.uk

Audrey King
National Institute for Public Health and the Environmen
RIVM Centre for Infectious Disease Control Netherlands
Laboratory for Infectious Disease and Screening (LIS)
Antonie van Leewenhoeklaan 9
3720 BA Bilthoven
The NETHERLANDS
Email: audrey.king@rivm.nl

Davy Vandenbroeck
Algemeen Medisch Laboratorium
Molecular Diagnostics
Emiel Vloorsstraat 9
2020 Antwerp
BELGIUM
Email: davy.vandenbroeck@aml-lab.be

Fanny Honshoven
Technologiepark 6
Fujirebio Europe NV
BE-9052 ZWIJNAARDE
BELGIUM
Email: fanny.honshoven@fujirebio.com

Nicola Paccagnella
AB ANALITICA SRL
Via Svizzera 16
351 27 PADOVA
ITALY
Email: paccagnella@abanalitica.it

Mario Cunha
Portuguese Institute of Oncology, Lisbon Francisco Gentil, EPE
Clinical Pathology
Laboratory Virology
Rua Prof. Lima Basto
1099-023 Lisbon
PORTUGAL
Email: mcunha@ipolisboa.min-saude.pt

Jesper Bonde, Helle Pedersen
Molecular Pathology Laboratory
Dept. Pathology, afs 134
Hvidovre Hospital
Kettegård Alle 30
26 50 Hvidovre
DENMARK
Email: Helle.Pedersen.03@regionh.dk

Rosemarie Preyer
GenID GmbH
Ebinger Strasse 4
DE-72479 Strassberg
GERMANY
Email: preyer@aid-diagnostika.com

Thomas Iftner
Institute for Virology
Universityhospital Tuebingen
Elfriede-Aulhorn-Strasse 6
DE-72074 Tübingen
GERMANY
Email: angelika.iftner@med.uni-tuebingen.de

Steffi Silling, Ulrike Wieland
Institute of Virology, University of Cologne
Fuerst-Pueckler-Strasse 56
50935 Koeln

| |
|---|
| GERMANY<br>Email: steffi.silling@uk-koeln.de |
| Sven Hauke<br>ZytoVision GmbH, QC and Clinical Trials Services<br>Fischkai 1<br>275 72 BREMERHAVEN<br>GERMANY<br>Email: hauke@zytovision.com |
| Sandra Ehser<br>42 life sciences GmbH & co. KG/QC and Clinical Trials Servic<br>Fischkai 1<br>275 72 BREMERHAVEN<br>GERMANY<br>Email: ehser@42ls.com |
| Mario Poljak<br>Institute of Microbiology and Immunology Medical Faculty,<br>Laboratory for Molecular Microbiology and Slovenian HIV/AIDS<br>University of Ljubljana Zaloska 4,<br>1000 Ljubljana<br>SLOVENIA<br>Email: mario.poljak@mf.uni-lj.si<br>kristina.fujs@mf.uni-lj.si |
| Sonia Perez Castro<br>Servizo Microbioloxia<br>Hospital Meixoeiro, CHUVI<br>36214 Vigo<br>SPAIN<br>Email: sonia.maria.perez.castro@sergas.es |
| Asuncion Olma-Sevilla<br>Vitro S.L<br>P. T. Ciencias Salud<br>Avda Conocimiento 100<br>18016 Granada<br>SPAIN<br>Email: asuncion.olmo@vitro.bio; belen.espigares@vitro.bio |
| Antonio Moreno Docon<br>Hospital Clinico Universitario Virgen de la Arrixaca<br>Virology / Microbiology Service<br>Ctra Madrid-Cartagena<br>ES-30120 Murcia<br>SPAIN<br>Email: antomodo@yahoo.es |
| Sabine Legner<br>Labor Dr. Mustafa Dr. Richter OG |

| |
|---|
| Strubergasse 20<br>AT-5020 Salzburg<br>AUSTRIA<br>Email: qm@medilab.at |
| Jean-Luc Prétet<br>CHRU Besancon<br>J. Minjoz Niv 2<br>Magasin Cancero Biologi<br>Rue Charles Bried<br>Fr-25030 Besancon<br>FRANCE<br>Email: lpepin@chu-besancon.fr |
| Yalin Kilic<br>Izmir University of Economics<br>Faculty of Engineering<br>Department of Biomedical Engineering<br>TR-35330 Izmir<br>TURKEY<br>Email: kilic.yalin@ieu.edu.tr |
| **SEARO –South-East Asia Region (2 labs)** |
| Sompong Vongpunsawad<br>Dept. Pediatrics, Faculty of Medicine<br>Chulalongkorn University<br>1873 Rama 4 Road<br>Pathumwan, BANGKOK 10330<br>THAILAND<br>Email: sompong.vo@chula.ac.th |
| Neeraj Jain<br>Room No 111, Research Laboratory IV (Biological Sciences)<br>CHARUSAT, Changa<br>Charotar Univ. of Scines&Techno<br>P D Patel Inst of appl.science<br>IN-388421 ANAND<br>INDIA<br>Email: neerajjain.as@charusat.ac.in |
| **WPRO –Western Pacific Region (41 labs)** |
| Joohee Lee<br>Genematrix<br>700 Daewangpangyo-ro Bundang<br>Korea Bio Park B Bldg. 8F<br>KR-13488 Seongnam-si<br>SOUTH KOREA |

| |
|---|
| Email: mangoid@genematrix.net |
| Yaeseul Suh<br>Seegene Inc<br>91 Ogeum-ro, Songpa-gu<br>KR-05548 Seoul<br>SOUTH KOREA<br>Email: yssuh@seegene.com |
| Suzanne Garland, Monica Molan<br>Centre for Women's Infectious Diseases, Level 7<br>The Royal Women's Hospital<br>Locked Bag 300<br>3052 Parkville, Victoria<br>AUSTRALIA<br>Email: Monica.MolanoLuque@thewomens.org.au |
| Jenna Carlisle<br>PathWest Laboratory Medicine<br>PP Block, QEII Medical Centre<br>Room 5.13.2 Hospital Ave<br>6009 NEDLANDS<br>AUSTRALIA<br>Email: jenna.carlisle@health.wa.gov.au |
| Iwao Kukimoto<br>Center for Pathogen Genomics,<br>National Institute of Infectious Diseases,<br>4-7-1 Gakuen, Musashi-Murayama,<br>Tokyo 208-0011,<br>JAPAN<br>Email: ikuki@nih.go.jp |
| Khishigsuren Narmandakh<br>Molecular Biology Laboratory<br>"Gyals" medical center<br>Peace avenue 61A, 4th khoroo<br>13345 Ulaanbaatar<br>MONGOLIA<br>Email: amarmend@gyals.mn |
| Wenjing Hu<br>Jinan Hybribio Medical laboratory<br>999077 Hong kong<br>CHINA<br>Email: wjhu@hybribio.cn |
| Liejun Li<br>Molecular Biology Laboratory<br>27/F Bonham TradeCenter<br>Hongkong |

| |
|---|
| 50 Bonham Strand, Sheung Wan<br>521000 Chaozhou<br>CHINA<br>Email: ljli@hybribio.cn |
| Ting Wang<br>Shenzhen Hybribio Medicla Laboratory<br>No.1301-76 Guanguang Road<br>Room A401, Building 1, Yinxing Zhijie Phase II<br>Xinlan Community, Guanlan Street<br>518110 Shenzhen<br>CHINA<br>Email: tingwang@hybribio.cn |
| Xu Feng<br>Guangzhou Hybribio Medical Laboratory<br>No 3 Sheung Yue RoadKowloonBay<br>35/F Enterprise Square Two<br>CN-510555 GUANGZHOU<br>CHINA<br>Email: fengxu@hybribio.cn |
| Walter Zhang<br>Shanghai ZJ Bio-Tech Co., Ltd. Lab<br>Building 26, 588 Xinjunhuan Road<br>2011 14 Shanghai<br>CHINA<br>Email: walter_zhang@liferiver.com.cn |
| Lala Du<br>Hangzhou Hybribio Medical Laboratory<br>No.448-1, North Donghu Road<br>Room 301, Building 32<br>311100 Hangzhou<br>CHINA<br>Email: lldu@hybribio.cn |
| Ken Kwok<br>Pangenia Lifesciences Ltd<br>1 Trademart Drive<br>Unit 1380, 13/F, KITEC<br>Kowloon Bay<br>HONG KONG<br>CHINA<br>Email: ken.kwok@pangenia.com |
| Xianxu Zeng<br>The Third Affiliated Hospital of Zhengzhou University<br>No. 7, Kangfu front street<br>Erqi district, Zhengshou city<br>450008 Zhengzhou |

| |
|---|
| CHINA<br>Email: xianxu77@163.com |
| Weiying Liu<br>Foshan Nanhai Hybribio Medical Laboratory<br>No. 14-2 Guihe Road, Lishui T<br>Nanhai District, Guangdong<br>528200 Foshan<br>CHINA<br>Email: wyliu@hybribio.cn |
| Tao Zou<br>Nanchang Hybribio Medical Laboratory<br>No. 188 Longtan Road<br>Qingshanhu District, Jiangxi Province<br>330000 Nachang<br>CHINA<br>Email: tzou@hybribio.cn |
| Hengtao Ji<br>The second Affiliated Hospital of Zhengzhou University<br>No.2, Jingba Road<br>Jinshui district, Henan province<br>450000 Zhengzhou<br>CHINA<br>Email: ttb8232@163.com |
| Xiang Liu<br>No 9. Weidi Road Qixia District<br>Nanjing Hybribio Medical Laboratory<br>CN-210000 Nanjing<br>CHINA<br>Email: xliu@hybribio.cn |
| Bing Wei<br>Henan Cancer Hospital<br>No.127, Dongming road<br>Jinshui district, Henan province<br>450003 Zhengzhou<br>CHINA<br>Email: weibing1999@hotmail.com |
| Jinhui Shao<br>Xian Hybribio Medical Laboratory, Room 10101-10106<br>Building B7, caotan 10th Road<br>China Electronics Xian Industry<br>710000 Xian<br>CHINA<br>Email: yydou@hybribio.cn |
| LiPing Zhang |

| |
|---|
| Zhengzhou Hybribio medical Laboratory<br>CN-450000 Zhengzhou<br>CHINA<br>Email: lpzhang@hybribio.cn |
| Jingfen Sun<br>Shanxi Bethune Hospital<br>No. 99 Longsheng street<br>030032 Taiyuan city<br>CHINA<br>Email: fenfen_sun@163.com |
| Ying Yin Zhang<br>Wuhan Hybribio Medical Laboratory Co. Ltd<br>CN-430000 Wuhan<br>CHINA<br>Email: yyzhang@hybribio.cn |
| Juanjuan Zhu<br>Shanghai Hybribio Medical Laboratory<br>CN-201318 Shanghai<br>CHINA<br>Email: jjzhu@hybribio.cn |
| Yuying Lv<br>Beijing Hybribio Medical Laboratory Ltd.<br>CN-102206 Beijing<br>CHINA<br>Email: yylv@hybribio.cn |
| Minfang Li<br>Changsha Hybribio Medical Laboratory Ltd.<br>CN-410000 Changsha<br>CHINA<br>Email: minfangli@hybribio.cn |
| Lu Yuchen<br>Yaneng Bioscience Co ltd<br>Gaoxingqi Industrial Park, 10th Floor, Building 1, Phase 2<br>Liuxian 1st Road, Baoan District<br>518000 Shenzhen<br>CHINA<br>Email: chenziyu@yanengbio.com |
| Canbin Zhuo<br>Shantou Kaipu medical laboratory Co Ltd<br>CN-515041 Shantou<br>CHINA<br>Email: cbzhuo@hybribio.cn |
| Jun Xiong Wen |

Guang Zhou Kingmed Center for Clinical Laboratory
CHINA
Email: happywjx@kingmed.com.cn

Xinle Feng
Chaozhou Hybribio medical Laboratory Co Ltd
CN-521000 Chaozhou
CHINA
Email: fengxl@hybribio.cn

Taiyangsheng Yin
Shenyang Hybribio Medical Laboratory Co Ltd
CN-110000 Shenyang
CHINA
Email: ytys@hybribio.cn

Binhua Dong
Laboratory of Gynecology,
Fujian Maternity and Child Health Hospital
College of Clinical Medicine for Obstetrics & Gynecology and Pediatrics
Fujian Medical University
CHINA
Email: dbh18-jy@126.com

Shixian Geng
Kunming Hybribio Medical Laboratory Ltd
CN-650217 Kunming
CHINA
Email: sxgeng@hybribio.cn

Yijing Zeng
Chengdu Hybribio Medical Laboratory Ltd
Chengdu
CHINA
Email: yijingzeng@hybribio.cn

Yihui Yang
Wuhan Ping An Medical Laboratories
CHINA
Email: yang.yihui@zs-hospital.sh.cn

Xiaoyan Zhou
Diagnostic Molecular Pathology
Department of Pathology
Fudan University Shanghai Cancer Center
Shanghai
CHINA
Email: 545898973@qq.com

Ling Ji
Peking University Shenzhen Hospital

| |
|---|
| CHINA<br>Email: lijie_bio@126.com |
| Ping Zhang<br>Wang Jing Hospital of CACMS<br>CHINA<br>Email: |
| QiDing Mei<br>Zhongda Hospital Southeast University<br>CN-210000 Nanjing<br>CHINA<br>Email: qdmei@hybribio.cn |
| Jing Liu<br>Wuhan Ping An Medical Laboratories<br>CHINA<br>Email: liujing282@pingan.com.cn |
| Peicheng Huang<br>Shenzhen Jinshi Medical Laboratory<br>CHINA<br>Email: hpc1987qq@163.com |
| **AFRO –African Region (1 labs)** |
| Anna-Lise Williamson, Cremildo Maueia<br>WHO LabNet reference laboratory for Africa region<br>Div of Medical Vir., Inst for Infedt Dis and Molecular med<br>Anzio Road, Observatory<br>7925 Cape Town<br>SOUTH AFRICA<br>Email: anna-lise.williamson@uct.ac.za;<br>cremildogo@gmail.com |