Global HPV Reference LabNet Meeting – Minutes
Date: 4 November 2025
Location: Virtual (Microsoft Teams)

Participants

31 participants, 13 NRL laboratories

Participant	NRL/Institution
Dolores Fellner	Argentina
Mariel Correa	Argentina
Padalko Elizaveta	Belgium
Inge Roukaerts	Belgium
Marc Arbyn	Belgium
Jade Pattyn	Belgium
Christopher Gill	Gates Foundation
Jesper Hansen Bonde	Denmark
Jean-Luc Pretet	France
Alfred Mabika	Gabon
Steffi Silling	Germany
Marianna Martinelli	Italy
Clementina Cocuzza	Italy
Noé Escobar	Mexico
Milan Stosic	Norway
Gro Kummeneje Presthus	Norway
Kristiane Søreng	Norway
George Obregon	Peru
Pamela Rios	Peru
Lesly_Solis	Peru
Susan Espetia	Peru
Maribel Acuña	Peru
Poljak, Mario	Slovenia
Anja Oštrbenk	Slovenia
Sara Arroyo Mühr	Sweden
Joakim Dillner	Sweden
Camilla Lagheden	Sweden
Emel Yilmaz	Sweden
Carina Eklund	Sweden
Linzi Connor	Scotland
Maribel Almonte	WHO
Mariluz Hernandez	WHO

Note: Alejandra Piconi could not attend the meeting but notified the organizers beforehand.

Agenda

15:00 Introduction (Joakim Dillner)

15:15 IPVS Global HPV Reference Laboratory Meeting: Summary (Sara Arroyo)

15:25 International Collaborative Study on Limit of Detection of HPV virus types (Joakim Dillner)

15:45 Discussion on evaluation of new HPV tests (Joakim Dillner)

16:15 Laboratory Manual (Sara Arroyo)

- New chapters: Setting up laboratory, HPV Prof panels, Assay validation, WHO TPP for HPV Screening tests, NGS
- E-learning resources

Coffee Break

16:45 Working groups (5- 10 min each)

- International collaboration on HPV prevalences (Argentina, Sweden)
- Cancer Audit revision (discussion on adjunct WG members)
- Sample adequacy (Mario & Clementina)
- Manuscript on NGS consensus and quality assurance (UK, Norway, Sweden)
- HPV negative tumors (multi-omics) Norway, Sweden, Denmark
- Advisory task force for HPV testing in new countries (UK, Sweden)

17:30 LabNet collaboration with WHO (Maribel Almonte)

17:45 Other issues

1. Introduction – Joakim Dillner

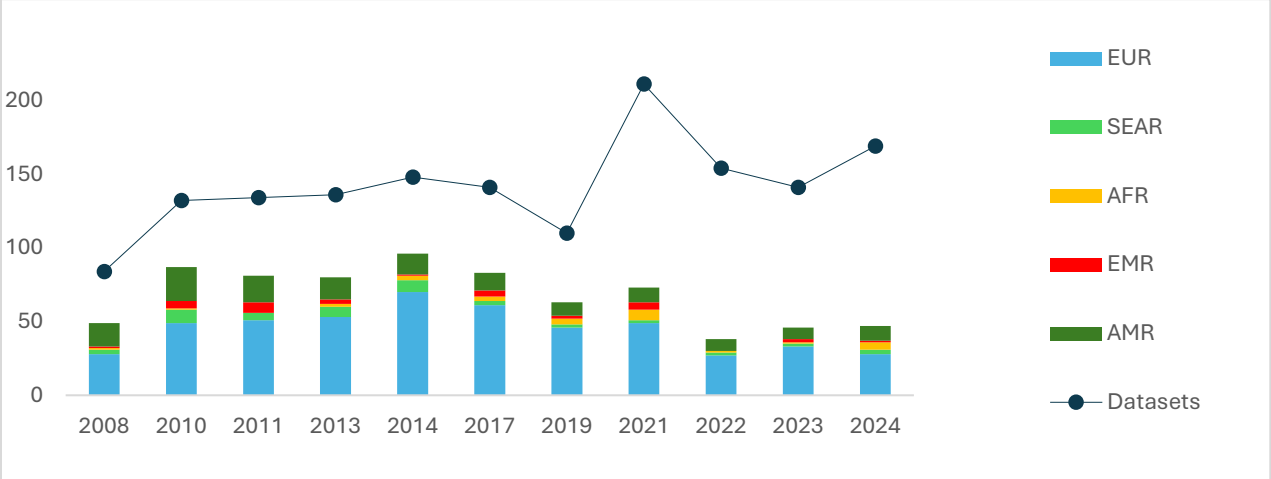
A) Welcome to participants and guests:

- WHO: Maribel Almonte and Mariluz Hernández
- Gates Foundation: Christopher Gill
- Invited laboratory expert: Jesper Bonde (Denmark)

B) Proficiency studies:

- The 2025 round includes 102 genotyping panels and 173 screening panels distributed globally. NRLs are now organizing national proficiency testing and receiving panels free of charge for regional distribution (Argentina, Peru, Norway, Rwanda, and Malawi). Perú published their quality assurance program using proficiency testing (https://pubmed.ncbi.nlm.nih.gov/40953692/)
- Peru visited the IHRC in May for hands-on training in panel design and preparation, supporting decentralization and capacity building.
- Continuous improvement has been observed in both laboratory proficiency and accuracy, with a clear decline in false positives since the program's start in 2008.

Participation in HPV genotyping proficiency panels, 2008–2024



Key takeaway message:

The proficiency program remains a cornerstone of global quality assurance of HPV testing, ensuring traceability to international standards and fostering national-level responsibility for quality monitoring in HPV testing.

C) Expansion of LabNet and international collaborations

Emphasis on strengthening global laboratory collaboration to accelerate cervical cancer elimination has focused on LMIC.

- Five new NRLs from LMICs have joined the network recently: Brazil, Gabon, Mexico, Peru, and Rwanda.

- Ongoing efforts to include additional countries such as Malawi, Ethiopia, Zimbabwe, Ukraine, and others in South America.

- A formal collaboration has been established with the International Cancer Screening Network (ICSN) and the United Nations Population Fund (UNFPA) to support global HPV-based screening implementation.

2. IPVS HPV Reference Laboratory Meeting: Summary

Sara Arroyo presented a summary of the LabNet symposium held during the 37th International Papillomavirus Society (IPVS) Conference in Bangkok. The session, titled "What does the international community really need from LabNet?", showcased examples of laboratory collaborations and capacity-building initiatives across different settings.

Presentations included:

1. *Support for the development and implementation of HPV testing in conflict settings* – Sara Arroyo-Muhr
2. *Collaboration and support for HPV testing between HIC and LMIC settings* – Elizaveta Padalko
3. *Establishing the Japanese HPV Reference Laboratory – opportunities for partnerships in Asia & beyond* – Iwao Kukimoto
4. *Validation of a locally produced HPV assay for cervical screening applications – the experience of Brazil* – Marcelo Alves Soares

The symposium concluded with a facilitated Q&A and open discussion on future directions for LabNet and how international partners can better support countries implementing HPV testing.

Presentations are attached for reference.

3. International Collaborative Study on Limit of Detection of HPV virus types and Evaluation of novel HPV assays

Joakim presented updates on the international collaborative study aimed at establishing meaningful limits of detection (LoD) for assays measuring oncogenic HPV types. The LoD thresholds define the viral levels that HPV assays should detect in order to be both sensitive and specific.

Table 1: Consensus on reference HPV type distribution by cases and controls determined from 13 datasets from 10 participating laboratories. LoD was not applied.

HPV type	Total	Controls	Case	Cum.sensitivity%	Cum. Specificity (%)
16	40	6	34	33,66	97,03
18	9	2	7	40,59	96,04
45	6	2	4	44,55	95,05
33	12	3	9	53,47	93,56
58	13	7	6	59,41	90,10
31	20	5	15	74,26	87,62
52	10	2	8	82,18	86,63
35	6	1	5	87,13	86,14
59	3	1	2	89,11	85,64
39	6	3	3	92,08	84,16
51	3	2	1	93,07	83,17
56	6	3	3	96,04	81,68
Other HPV*	17	15	2	98,02	74,26
Not detectable/No consensus	152	150	2	100,00	0,00
Total	303	202	101		

***HPV6, 40, 42, 44, 54, 61, 66, 68, 70 and 82**

Key findings:

- Preliminary consensus LoD values:
  - **3 IU/µL** for HPV16 and HPV18
  - **25 IU/µL (or GE/µL)** for vaccine types and HPV35
  - **100 GE/µL** for HPV39, 51, 56, and 59

Table 2: Consensus HPV type distribution among 7 participating laboratories by cases and controls with applied cut offs at 3 IU/ ul of DNA extract for HPV16 and 18; 25 IU/ ul of DNA extract for HPV31, 33, 35, 45, 52 and 58; 25 GE/ ul of DNA extract for HPV35, 100 GE/ ul of DNA extract for HPV39, 51, 56 and 59. Sensitivity for detecting ICC attributable to HPV type was shown using IARC HPV type specific attributable fraction of ICC.

HPV type	Controls - Reference	Controls (determined with detection limits)	Cases - reference	Cases (determined with detection limits)	Sensitivity	Cum.sensitivity CIN2+ %	Cum Spec. %	Population Attributable Fraction of ICC % **	Sens with cutoff %	Cum Sens. ICC weighted %
16	6	4	34	33	0,97	37,08	97,60	62,40	60,56	60,56
18	2	2	7	6	0,86	43,82	96,41	15,30	13,11	73,68
45	2	1	4	4	1,00	48,31	95,81	4,80	4,80	78,48
33	3	1	9	8	0,89	57,30	95,21	3,90	3,47	81,95
58	7	3	6	5	0,83	62,92	93,41	3,70	3,08	85,03
31	5	3	15	14	0,93	78,65	91,62	2,90	2,71	87,74
52	2	0	8	5	0,63	84,27	91,62	2,60	1,63	89,36
35	1	0	5	5	1,00	89,89	91,62	1,40	1,40	90,76
59	1	1	2	2	1,00	92,13	91,02	0,90	0,90	91,66
39	3	1	3	2	0,67	94,38	90,42	0,80	0,53	92,19
51	2	0	1	0	0,00	94,38	90,42	0,20	0,00	92,19
56	3	1	3	3	1,00	97,75	89,82	0,20	0,20	92,39
Other HPV	15	na*	2	na*	na*	97,75	89,82	na*	na*	na*
Neg/Not detectable/No consensus	150	150	2	2		100,00	0,00			

*: not available
**: % PAF according to IARC

5 new HPV tests have asked for evaluation using these thresholds.

The quantification proposed by Italy (C. Cocuzza) & M. Poljak, uses viral load per 10^4 cells, producing similar LoD levels (9, 75, and 300 IU-GE/µL, respectively) and comparable sensitivity/specificity (>89% and >91%).

Table 3: HPV distribution among cases and controls with estimation of HPV virus amounts per 10^4 cells using results received from laboratory from Italy. Applied detection limits were 9 IU/ 10^4 cells for HPV16 and 18; 75 IU/ 10^4 cells for HPV31, 33, 35, 45, 52 and 58; 75 GE/ 10^4 cells for HPV35, 300 GE/ 10^4 cells for HPV39, 51, 56 and 59. Sensitivity for detecting ICC attributable to HPV type was shown using IARC HPV type specific attributable fraction of ICC.

HPV type	Controls - Reference	Controls (determined with detection limits)	Cases - reference	Cases (determined with detection limits)	Sensitivity	Cum.sensitivity%	Cum Spec. %	Population Attributable Fraction of ICC % **	Sens with cutoff %	Cum Sens. ICC weighted %
16	7	5	35	34	0,97	36,56	97,22	62,40	60,62	60,62
18	2	2	7	6	0,86	43,01	96,11	15,30	13,11	73,73
45	2	1	4	4	1,00	47,31	95,56	4,80	4,80	78,53
33	3	2	8	7	0,88	54,84	94,44	3,90	3,41	81,94
58	12	6	10	6	0,60	61,29	91,11	3,70	2,22	84,16
31	6	3	13	13	1,00	75,27	89,44	2,90	2,90	87,06
52	2	0	7	6	0,86	81,72	89,44	2,60	2,23	89,29
35	1	1	5	5	1,00	87,10	88,89	1,40	1,40	90,69
59	1	1	2	2	1,00	89,25	88,33	0,90	0,90	91,59
39	5	1	3	3	1,00	92,47	87,78	0,80	0,80	92,39
51	2	0	1	1	1,00	93,55	87,78	0,20	0,20	92,59
56	2	1	3	3	1,00	96,77	87,22	0,20	0,20	92,79
Neg/Not detectable/No consensus	138	138	3	3						
Invalid	19	19	0	0						

Discussion highlighted that CIN can no longer be used for evaluation of HPV assays as vaccination has resulted in that the more progressive HPV types are increasingly uncommon in CINas and certain non-vaccine types (e.g., HPV51) are now common in CIN, but rarely cause invasive cancer.

Adaptation of these thresholds to various testing contexts (e.g., ThinPrep vs. self-collected samples, different assays, and collection volumes) is underway.

Comparative data with a comparator commercial assay, BD Onclarity, showed that the comparator assay has high sensitivity (~97%) but low specificity (~76%).

Table 4: Consensus on reference HPV type distribution vs BD results

HPV type	Control - Reference	Controls - BD	Case - reference	Case- BD	HPV type-specific sensitivity among CIN2+	Cumulative sensitivity all CIN2+ %	Cumulative Specificity %	Population Attributable Fraction of ICC % **	Type-specific sensitivity, ICC weighted %	Cumulative sensitivity, ICC weighted %
16	5	5	34	34	1,00	34,69	96,09	62,40	62,40	62,40
18	2	2	7	6	0,86	40,82	94,53	15,30	13,11	75,51
45	2	1	4	4	1,00	44,90	93,75	4,80	4,80	80,31
P1	10	8	15	14	0,93	59,18	87,50	7,60	7,09	87,41
31	5	4	15	15	1,00	74,49	84,38	2,90	2,90	90,31
52	2	1	8	8	1,00	82,65	83,59	2,60	2,60	92,91
P3	6	4	10	9	0,90	91,84	80,47	2,40	2,16	95,07
P2	6	5	5	5	1,00	96,94	76,56	1,10	1,10	96,17
51	1	0	1	1	1,00	97,96	76,56	0,20	0,20	96,37
Other HPV*	8	na**	0	na**	na**	na**	na**	na**	na**	na**
Neg/Not detectable/No consensus	100	98	2	2	1,00	97,03	12,93			

*: HPV6, 42, 44, 54, 61,

**: not available

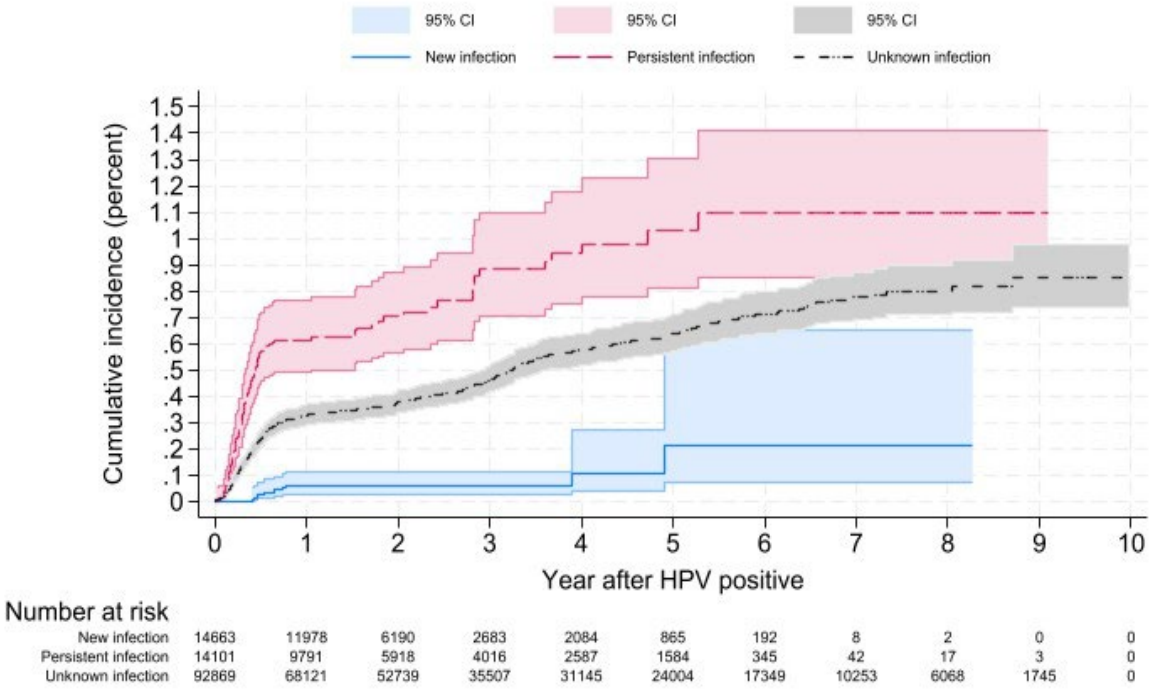
**: % PAF adapted from IARC

Jesper Bonde presented Danish screening data, showing differences among the key target HPV types. For example, only HPV33 but not HPV58 strongly correlates with CIN3+. He also illustrated the impact of persistent HPV infection on long-term ICC incidence, underscoring the value of HPV-based screening over cytology.

Conclusion:
The collaborative study provides an evidence-based framework for defining which Limit of Detection that should be demanded from HPV tests. The results are in line with the WHO Target Product Profiles (TPPs) definition and will enable evaluation of new HPV assays that are conforming to the TPP, using international standards.

Joakim showed the following figure on cancer risk after persistent HPV and incident HPV.

Cumulative incidence (%) of Invasive Cervical Cancer by infection pattern: new, persistent or unknown (prevalent) infection

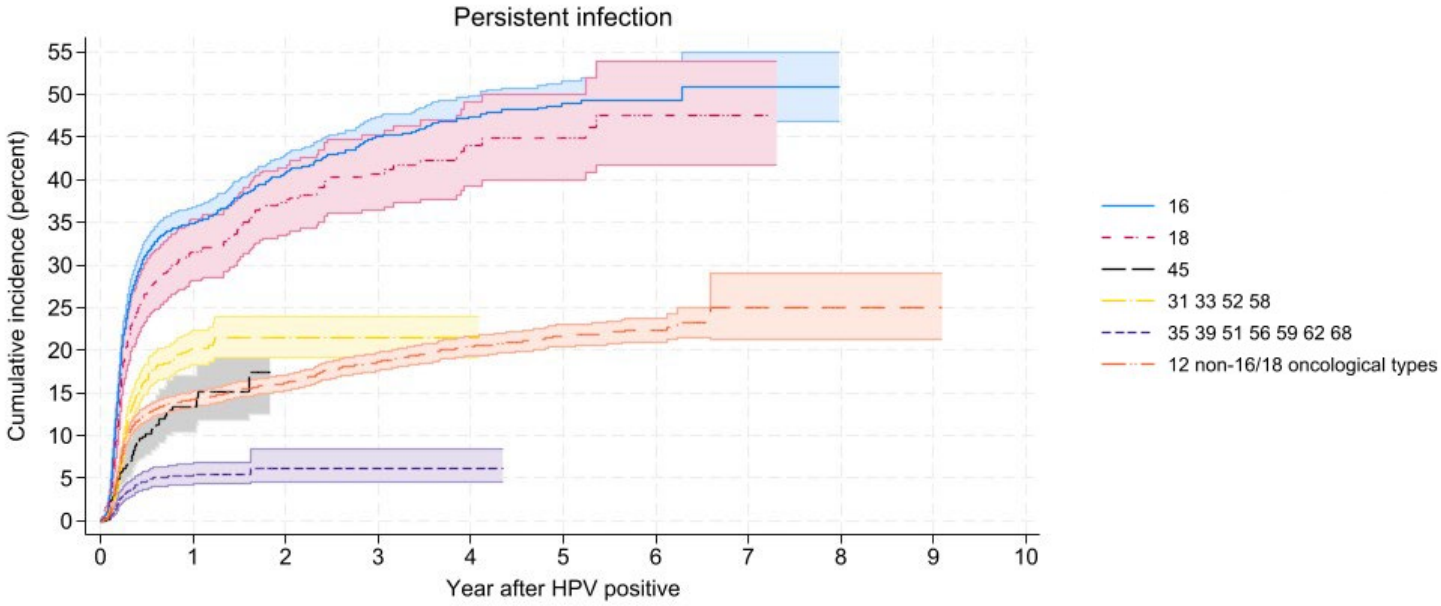


- Persistent infection defined as 2 tests with HPV positivity→ high ICC cumulative incidence
- Negative test during the previous screening round and HPV positive test now→ very small ICC risk for about 4 years,
- Prior unknown (first time HPV test) is almost as bad as persistent infection

Question on screening age from Maribel and the analysis on other oncogenic types. The data comes from an HPV screening program that targeted all women in the age range is 30-64 years.

Other oncogenic types: We currently use BD for screening and can follow the cancer risk after different HPV types (figure below). However, 4 years ago, and earlier, we used Cobas that reports HPV 16 and 18 but other oncogenic types as "Other HPV".

Cumulative incidence (%) of CIN2+ in persistent infection by HPV genotype



Discussion

- WHO wonders if additional data collection is needed to increase sample size. We expect that several countries that have ongoing screening programs can provide very large datasets from that country (based on Ct values converted to viral load).

The present international collaborative study is intended to provide an international comparability when many countries test exactly the same specimens.

- Results showed that LoD expressed either as IU/µl or as IU per 10,000 human cells in the sample provided consistent outcomes, enabling transfer of the LoD definitions to a variety of different settings.
- Clementina Cocuzza (Italy) emphasized the importance of normalizing virus amounts to cellularity to reduce false negatives and to account for different sampling methods. She noted that current data cannot yet be directly applied to self-collected samples, underscoring the need for a dedicated study on this topic.
- France shared experience with virus quantification, stating that while normalization by viral quantity is less critical, standardizing the sampling method is essential to ensure comparability.

4. Laboratory Manual

Sara Arroyo presented the progress on the HPV Laboratory e-Manual, now available online at https://www.hpvcenter.se/hpv-laboratory-manual/. The manual currently includes 10 chapters, each written and peer-reviewed by 2–3 National Reference Laboratories (NRLs), with additional external reviewers ensuring scientific rigor and harmonization.

New and upcoming chapters cover:

- Setting up an HPV laboratory
- HPV proficiency panels and quality assurance
- Assay validation
- WHO Target Product Profile (TPP) for HPV screening tests
- Next-Generation Sequencing (NGS)
- Cervical screening registry linkage

WHO has reviewed all chapters, to ensure alignment with elimination strategies.

e-Learning initiatives:

- The NRL in Scotland is developing an online Quality Assurance course to complement the manual.
- Other chapters will also be developed as e-learning resources; the IHRC will lead their creation if the contributing NRLs are unable to do so.
- NRL laboratories are encouraged to propose new topics for future chapters, which will be developed collaboratively and reviewed within the LabNet network.

Key aim:

To provide accessible, standardized, and continuously updated guidance for HPV laboratory operations, validation, and quality assurance worldwide.

5. Working groups

5.1 International collaboration on HPV prevalences (Argentina, Sweden)

Joakim presented work on HPV prevalence surveillance using data from the Swedish national cervical screening program. The analysis includes HPV type–specific prevalence by calendar year with 95% confidence intervals and distinguishes between never-vaccinated, catch-up vaccinated, and school-based vaccinated birth cohorts.

There is a strong impact of vaccination:

- HPV16 prevalence: 0.36% among women born in 2001
- HPV18 prevalence: 0.08% among women born in 2001

- Evidence of cross-protection for HPV31 with Gardasil 4, but no cross-protection for HPV45

Other participating NRLs also shared updates:

- Scotland (Linzi Connor): Ongoing genotyping-based surveillance (2024–2030) to monitor the impact of the quadrivalent vaccine; type-specific results are forthcoming.
- Denmark (Jesper Bonde): Genotyping data available from population-based screening since 2021 and self-sampling from non-responders since 2017; several scientific publications in preparation.
- Argentina: Conducting national surveillance integrating vaccination and screening data.

Joakim emphasized the importance of creating an internationally available database to compare HPV prevalence results across countries. Access to harmonized, up-to-date data rather than requiring consultation of multiple individual reports would be very useful for elimination efforts.

5.2 Cancer Audit revision

Jesper Bonde (Denmark) and David Hawkes (Australia) presented a proposal to revise and harmonize cancer audit procedures for invasive cervical cancer (ICC) within the LabNet framework.

The discussion highlighted significant variation across European (and worldwide) countries in how audits are currently conducted, with no existing consensus or standardized guidance. Traditionally, audits have relied on cytology slides to evaluate missed cases, but with the transition to primary HPV screening, there is a need to redefine procedures and reference materials.

Key discussion points included:

- The potential use of primary HPV screening samples instead of cytology slides for audit purposes.
- The lack of biobanking services for retaining HPV screening samples in some countries.
- The need to establish minimum and preferred requirements for ICC audit setups.
- Suggestions to use assay raw data (e.g., BD system files) to verify viral amplification even in cases reported as HPV negative.
- The importance of evaluating sample cellularity to distinguish between truly HPV-negative results and inadequate samples.

The group agreed that the current HPV LabNet guidance publication could be elaborated on for ensuring reliability, comparability, and quality assurance across programs.

5.3 Sample adequacy *(Mario & Clementina)*

Mario Poljak and Clementina Cocuzza presented ongoing discussions on sample adequacy and quality assurance, which will also be the focus of an upcoming Eurogin session. The discussion addressed the need for future quality panels to assess factors such as sample inhibition, cellularity, and false negatives due to inadequate sample quality.

Key points included:

- The importance of understanding how many commercial HPV assays include internal controls, and what cut-off values they apply.
- A proposal that cut-off thresholds for internal controls should be equal to or lower than those of the target, but never higher, to avoid misclassification of inadequate samples as HPV negative.
- The relationship between internal control performance and cell content, including cases with blood, epithelial cells, and lymphocytes.
- The recommendation that samples with insufficient epithelial cells must be reported as invalid due to lack of cellularity, rather than as HPV negative, to ensure quality and minimize false-negative results.

The meeting agreed that defining standardized criteria for sample adequacy and inhibition testing will be crucial for maintaining the reliability of HPV screening across laboratories.

5.4 Manuscript on NGS consensus and quality assurance (UK, Norway, Sweden)

The group emphasized that there is currently no formal quality assurance system in place for NGS-based HPV detection, making this effort essential for ensuring comparability and reliability of sequencing results across laboratories. The initiative originated from the recognition that different laboratories were applying variable NGS methods, underscoring the need for a standardized approach and shared quality framework.

Key points discussed:

- Earlier collaborative work highlighted inconsistencies in NGS protocols across laboratories.
- Since the initial attempt and published article (https://pubmed.ncbi.nlm.nih.gov/34372528/), substantial methodological advances have been made, prompting renewed efforts to establish consensus standards.
- Current collaborations to support bioinformatics analysis include multiple NRLs, notably NRL Peru (focused on HPV sublineages, https://pubmed.ncbi.nlm.nih.gov/40954219/), and non-NRLs (Eduardo francos Group, https://pubmed.ncbi.nlm.nih.gov/41147664/)

The working group is established and drafting will be presented at Eurogin.

5.5 HPV negative tumors (multi-omics) Norway, Sweden, Denmark

An update was provided on the collaborative project investigating HPV-negative cervical cancers using a multi-omics approach. The project aims to better understand the molecular characteristics and potential biomarkers associated with tumors that test negative for HPV DNA.

Key points discussed:

- The study will leverage biobank samples from participating countries.
- A stepwise approach is being applied: HPV genotyping will first confirm HPV negativity, after which multi-omics analyses (including genomics, transcriptomics, and methylation profiling) will be performed to identify possible biomarkers of HPV-independent carcinogenesis.
- The project is currently supported by existing funding (Sweden, Norway) and will be expanded through a joint grant application with Iceland and Denmark. This collaboration aims to harmonize methodologies and ensure high-quality, comparable data across sites.

5.6 Advisory task force for HPV testing in new countries (UK, Sweden)

A proposal from UK was discussed to establish an Advisory Task Force to support countries introducing HPV testing. The goal is to provide practical guidance, answer frequently asked questions, and share best practices from experienced National Reference Laboratories (NRLs).

Key points:

- The task force would serve as a support mechanism for laboratories and health authorities implementing HPV testing for the first time.
- Common topics expected to be addressed include assay selection, validation, quality assurance, and integration into national screening programs.
- The meeting considered that effective support requires substantial long-term commitment and proposed that the initiative could preferably be launched as a “twinning” system within LabNet. The idea would be that one designated experienced NRLs would regularly mentor and support new or developing laboratories throughout their implementation and development process. Sweden proposed to become such a Twinning laboratory for Gabon.

6. LabNet collaboration with WHO

The discussion focused on strengthening collaboration between LabNet and WHO to promote global standards, visibility, and quality assurance in HPV testing and screening.

Key points:

- Joining LabNet and required activities:
    - Laboratories can join LabNet if they have official support from their national authorities (a letter from the government is required).
    - Participation in proficiency testing (PP) studies and attendance at meetings are strongly encouraged.
    - LabNet remains active through conferences and collaboration with the WHO International Screening Team.
- Standardization and quality assurance:
    - Participants discussed the need for improved standardization of sensitivity and specificity across HPV tests.
    - LabNet could support WHO in developing strategies to address test performance issues and harmonize evaluations globally.
- Lab Manual collaboration:
    - The WHO was invited to consider ways to promote the LabNet Laboratory Manual, such as featuring it on the WHO website (with a disclaimer) or listing it as a useful external resource.
    - WHO cannot be listed as endorsing the current version as it was not approved by WHO prior to publication, but WHO can provide comments on future drafts prior to publication.
    - The new TPP (Target Product Profile) chapter will be included in the upcoming update of the manual and this chapter could be endorsed.
- Joint initiatives:
    - Proposal to organize two joint WHO–LabNet seminars per year, focusing on topics such as laboratory quality assurance, cancer audit, setting up HPV laboratories, and sample adequacy.
    - Collaboration opportunities identified with countries such as China and India to help integrate them into the LabNet network.
- Cervical Cancer Elimination Day of Action (17 November):
    - Members were encouraged to submit photos or short videos showing LabNet's contributions to elimination efforts for increased visibility.

- Future directions:
    - Suggestion to hold a consensus meeting for updated technical guidelines to replace the Meijer criteria, covering: a) New technical specifications for HPV tests, including point-of-care methods; b) Inclusion of self-collection approaches, and c) Sample adequacy criteria.

7. Other issues

Biobanking of samples

- The NRL in Norway is applying for research grants from the Norwegian Research Council to strengthen biobanking capacity.
- Norway currently uses SurePath samples and sought guidance on best practices for biobanking this sample type.
- It was recommended that they contact Jesper Bonde (Denmark) for technical advice and collaboration.

Guidance documents

- A need was identified for international guidance documents on biobanking and other technical processes to promote harmonization across NRLs.

Gabon (NRL Representative: Alfred Mabika)

- Gabon has implemented HPV screening among women living with HIV, using a validated HPV genotyping assay covering 21 HPV types, with positive, negative, and internal controls. Sweden offered to provide support on further developments.