Preface: This newsletter aims to provide a brief and updated overview of the WHO HPV LabNet activities, this being the 8th edition of the 6-monthly newsletter.

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1. Overview

A WHO initiative: Development of an international reference system to support HPV vaccine introduction - An overview

Cervical cancer is the second most common type of cancer among women. Over 99% of cervical cancer cases are linked to HPV genital infection, which are the most common sexually-transmitted viruses worldwide infecting an estimated 660 million people. The availability of highly effective prophylactic vaccines that protect against the most common oncogenic HPV types has great potential to make a significant impact on cervical cancer prevention.

In 2005, at the time when two promising HPV candidate vaccines were on the horizon, WHO recognized the challenges that needed to be overcome before the vaccines could be successfully introduced into developing countries. In response, WHO developed a comprehensive strategy to address these challenges by collaborating with global partners involved in cervical cancer prevention to facilitate the development, accelerate the global introduction, and ensure future accessibility of HPV vaccines. WHO initiated these activities through a comprehensive project entitled Generating an Enabling Environment for HPV Vaccine Development and Global Introduction, which was funded by the Bill and Melinda Gates Foundation for a 5-year period from 2005-2010 (with no cost-extension until June 2011), and contributed by a group of collaborating institutions working in partnership.

The three main objectives of this project were to:

1. Support the international harmonization and standardization of laboratory procedures that measure vaccine effects in potential target populations through the creation of a global HPV Laboratory Network.

2. Generate an enabling environment for HPV vaccine introduction by creating an international multi-disciplinary policy platform and setting a global agenda for future HPV vaccine introduction in consultation with regions and countries.

3. Create a WHO Information Centre on HPV and Cervical Cancer to facilitate global, regional, and country-specific decisions on current and novel options for cervical cancer prevention.
Here we review the major activities and achievements towards Objective 1 above that was led by the team of Quality, Safety and Standards/IVB, WHO/HQ. Some of these were accomplished through the WHO HPV LabNet, which was established in 2006 with expert laboratories representing all WHO Regions.

Setting norms and standards, and promoting their implementation are core WHO activities. For over 50 years, WHO has played a key role in establishing the International Biological Reference Preparations to standardize biological materials, and in developing guidelines and recommendations on the production and control of biological products and technologies. These norms and standards, based on scientific consensus achieved through international consultations, assist WHO Member States in ensuring the quality and safety of biological medicines and related in vitro biological diagnostic tests worldwide. WHO accomplishes this work through its biological programme, WHO Collaborating Centres, and WHO Expert Committee on Biological Standardization (ECBS). This also requires close collaboration with the international scientific and professional communities, regional and national regulatory authorities, manufacturers and expert laboratories worldwide.

1. Development of international guidelines to assure safe and efficacious HPV vaccines

Global WHO technical specifications are used as the basis for the pre-qualification procedure for vaccines procured by UN agencies. The specifications are intended to:

- be scientific and advisory in nature
- provide guidance for National Regulatory Authorities (NRA) and manufacturers on assuring the quality, safety and efficacy of vaccines
- facilitate international harmonization of vaccine licensure

Due to the advanced development of HPV vaccines, and incorporating current experience and knowledge, WHO convened two informal consultations in 2006 that were attended by a broad range of international experts including academics, vaccine regulators and manufacturers and other stakeholders. The experts met to review current data on vaccine development, production and quality control (QC), clinical and non-clinical evaluations of HPV vaccines, as well as to develop international consensus. These meetings resulted in the development of WHO Guidelines to Assure the Quality, Safety and Efficacy of Recombinant Human Papillomavirus Virus-Like Particle (VLP) Vaccines that were adopted by the 57th meeting of the WHO ECBS in October 2006. These guidelines provide guidance for NRA and manufacturers on production, QC, clinical and non-clinical evaluation of HPV-VLP vaccines, and set up the basis for the WHO pre-qualification of HPV vaccines in 2009.

In response to WHO recommendations on HPV vaccination, it is anticipated that HPV vaccine introduction will be implemented in countries worldwide. However, a crucial part of the process of vaccine licensure and regulation is the capacity of the National Control Laboratories (NCLs) to test HPV vaccines. A WHO survey identified that there were difficulties in performing the testing and a need for technical support was identified, particularly from developing countries. In response to these needs, and in order to strengthen the capacity of the NCLs in developing countries, WHO organized a technical training workshop at the International Laboratory for Biological Standards, National Institute for Biological Standards and Control (NIBSC) in the United Kingdom in 2009. The workshop provided practical knowledge for performing QC and lot release for HPV vaccines, and promoted the implementation of WHO Guidelines, harmonized HPV vaccine QC testing and facilitated international harmonization of vaccine licensure.

2. Establishment of a global WHO HPV laboratory network

HPV surveillance and vaccination impact monitoring are critical elements of HPV vaccine introduction. Accurate HPV DNA and antibody detection have proved crucial in epidemiological studies, both for measurement of disease burden and vaccination outcomes. WHO has previous experience in organizing global networks of laboratories to provide standardized quality laboratory
testing to facilitate vaccine implementation worldwide. Therefore at a WHO meeting held in
Geneva from 15-17 August 2005, a group of experts recommended the establishment of a global
HPV laboratory network (LabNet). The HPV LabNet would contribute to improving the quality of
laboratory services for effective HPV surveillance and vaccination impact monitoring, as well as
conduct training. It was envisaged that the HPV LabNet would accelerate the introduction of HPV
vaccination by:

- facilitating the implementation of validated, standardized laboratory
  procedures
- developing quality assurance (QA) system and proficiency testing
- training personnel
- providing a network for surveillance

The HPV LabNet would facilitate the worldwide availability of competent laboratory services for the
evaluation of HPV DNA and antibody detection in biological specimens, through capacity-building
and by providing 1) up-to-date technical information; 2) technical advice and guidance; and 3)
training on laboratory practice and quality assurance.

In 2006, following an open call for applications to participate in a WHO global HPV LabNet, an
external expert review of the proposals with comprehensive site visits was conducted and resulted
in the designation of two Global Reference Laboratories (GRLs) and eight Regional Reference
Laboratories (RRLs) in the six WHO worldwide regions. The mission of the WHO HPV LabNet was
"to contribute to improving quality of laboratory services for effective surveillance and monitoring
of HPV vaccination impact, through enhanced, state-of-the-art laboratory support."

International collaborative studies indicated that in order to produce HPV data that could be
compared and interpreted worldwide, international standards (IS) and standardized procedures for
HPV test performance were required. Evaluating vaccine quality, efficacy, consistency and
impact using internationally comparable assays based on IS would facilitate developing countries’
initiatives to formulate new HPV vaccines at reduced cost. Inter-laboratory comparability of
epidemiological, clinical and vaccine-related data gathered in various studies throughout the world
would also be assured.

The work of the HPV LabNet has been focused on 1) development and implementation of IS for
HPV DNA and serology; 2) harmonization and standardization of HPV assays for use in surveillance
and vaccine evaluation; 3) develop QA/QC program (Proficiency Study, Confirmatory testing); 4)
capacity building and providing technical support to worldwide laboratories.

3. Development of international measurement standards for use in HPV DNA and
serology assays

The development of international measurement standards, which include IS and WHO Reference
Reagents, are used:

- by regulatory authorities
- in the development, evaluation, standardization and control of products in industry
- in clinical trials in immune response assays
- in QC testing of vaccines
- in biological research in academic and scientific organizations

International measurement standards provide a global standard against which experimental values
can be compared. This allows direct comparisons between products and measurements obtained
by different methodologies and different laboratories around the world. IS for type-specific HPV
DNA and anti-HPV sera are essential for standardizing and harmonizing assays used in HPV
vaccine clinical trials, surveillance and vaccination impact monitoring to allow data comparisons
between laboratories worldwide.
WHO convened a series of international expert consultations to discuss and identify the need for HPV standards\(^9\) (meeting reports available online), and the subsequent project proposals were endorsed by the WHO ECBS. The projects, which were co-ordinated by NIBSC with support from WHO, were conducted by the HPV LabNet and other expert labs worldwide. Final establishment of IS must be adopted by ECBS. So far, IS have been established for HPV type 16 and 18 DNA\(^{10}\) and for anti-HPV type 16 serum\(^{\text{in press}}\). Qualified VLPs are critical to ensure the specificity and sensitivity of HPV serology assays, but have been difficult for most labs to produce and evaluate. Providing a supply of qualified VLPs was strongly recommended by the HPV LabNet labs as a prerequisite for performing HPV serology studies. Following a call for donation of VLP and extensive characterization studies, WHO HPV LabNet established a supply of qualified HPV 16 and 18 VLPs for the intended use of HPV vaccine monitoring. A well validated serum panel is also essential for organizing a proficiency study of HPV serology. In 2008, WHO opened a call to the public to donate serum samples, and as a result of this effort, a panel of 90 serum samples was established and used in the HPV LabNet serology studies.

Several other ongoing projects related to development of HPV standards include:

- IS for anti-HPV 18 serum
- Reference panel of HPV type 16 and 18 specific monoclonal antibodies for QC of HPV VLPs used in immunoassays
- IS for high-risk HPV types 31, 33, 45, 52, 58 DNA and low-risk HPV types 6 and 11 DNA. DNA standards for these additional HPV types are important for use in monitoring cross-protection of HPV vaccines, the potential occurrence of type replacement, and in evaluating the next generation of HPV vaccines that target additional high-risk HPV types

Development of international measurement standards is a long process, with multiple scientific and legal factors contributing to the time required for completion. The main challenges encountered in this area were difficulties in sourcing candidate material and Intellectual Property (IP) and related Material Transfer Agreements (MTA).

Once IS are established, an important component of WHO biological standardization programme will be to facilitate their implementation. Extensive efforts were made to disseminate knowledge and information about these IS and to promote their use through HPV LabNet meetings, WHO website, HPV LabNet newsletters, and in presentations at meetings in WHO/HQ, regions and countries. Education on IS and their use has been part of the HPV LabNet training curriculum provided to other labs in workshops attended by individuals from clinical and academic HPV testing labs, NCLs, national reference labs, diagnostic manufacturers, to name a few. All IS have “Instructions For Use” that were developed at the time of their establishment, and further modified in light of feedback from users. These instructions include advice on storage, use of the standards and safety information. These standards are available from NIBSC upon request (http://www.nibsc.ac.uk/products/biological_reference_materials.aspx). More detailed information and guidance on preparation and use of IS and calibration of secondary standards are provided in the HPV Laboratory Manual\(^2\).

### 4. Harmonization and standardization of HPV DNA and serology assays; development of QA/QC scheme for HPV laboratory testing

HPV DNA (genotyping) assays and serology assays are used to design HPV vaccination programs and monitor vaccine impact by providing estimates on HPV prevalence pre- and post-vaccine introduction. These assays are also used in clinical trials of HPV vaccine efficacy. In addition to the timely development of international standard reagents, harmonization and standardization of HPV assays, together with the previously described IS, to generate qualified and comparable data in vaccine development and epidemiology studies.

There are a variety of HPV assays in use worldwide, including “in-house” and commercial assays, which have different performance characteristics\(^{6,7,10}\). Multiple HPV types complicate the assays in...
terms of sensitivity and type-specificity and make inter-assay comparisons difficult. The WHO HPV LabNet recommended that HPV DNA assays: 1) have good sensitivity and specificity as evaluated in international proficiency testing; 2) have ease of transfer to laboratories with varying levels of experience and resources; 3) be affordable to allow use in low-resource settings; and 4) specifically detect and identify the 4 types currently targeted by vaccines and other high risk HPV types. At the WHO meeting on standardization of HPV assays and the role of HPV LabNet in supporting HPV vaccine introduction held in Geneva in 2008\(^2\), it was recommended that HPV LabNet evaluate the HPV DNA genotyping and serology assays currently used in laboratories worldwide, and that “both in-house assays and commercial assay kits may be evaluated by the WHO HPV LabNet in proficiency or collaborative studies.” The LabNet then worked on two aspects 1) organization of proficiency study to assess the performance of laboratories and different assays to identify laboratories in need of improvement and to identify promising assays; 2) organization of collaborative studies to validate selected assay protocols, optimize standard operating procedures (SOP) and develop guidance for the HPV laboratory manual\(^5\).

### 4.1 Proficiency studies

One of the tasks of the WHO HPV LabNet is to support the worldwide implementation of HPV vaccines. This is achieved through improved laboratory standardization and QA/QC of HPV testing and typing methods used for evaluating HPV vaccines, population surveillance and monitoring HPV vaccination programmes.

The number of HPV detection and typing assays using target amplification that are being developed and introduced are increasing. Laboratories must validate the sensitivity and specificity of each assay they use, whether it is an “in-house” or commercial assay, to ensure that the assay is performing as intended. Proficiency testing is a crucial element in the QA/QC of HPV laboratory performance, and is an efficient tool to assure the quality performance of HPV assays used in HPV epidemiological studies. The WHO HPV LabNet proficiency testing scheme offers a unique opportunity for laboratories to verify their assays and performance.

Since 2007, the WHO HPV LabNet has organized annual proficiency studies to assess the proficiency of HPV assays used routinely in laboratories worldwide, and identify potential problems with the assays and/or laboratory performance. Following an open announcement, the 2008 and 2010 WHO HPV LabNet HPV DNA typing proficiency panel was made available upon request to laboratories worldwide. The study involved worldwide laboratories active in vaccine development, HPV surveillance and vaccination impact monitoring, as well as companies involved in manufacturing HPV tests and HPV vaccines. The panel tested assay specificity and sensitivity for the identification of 14 high-risk HPV types and 2 low-risk HPV types that are the most important for HPV vaccine characterization as well as for HPV surveillance and monitoring. The results were published and the information is publically available\(^12\).

The HPV LabNet also conducted an inter-laboratory comparison of the HPV 16 VLP ELISA assay proposed for the HPV laboratory manual. Each laboratory was provided with HPV 16 L1-VLP coated plates and a panel of coded sera, and assay results were recorded as positive or negative. On the basis of the successful outcome of this testing, the direct VLP ELISA with parallel-line method of analysis was included in the HPV laboratory manual\(^7\).

These studies identified assays with good performance in order to direct further work towards laboratory standardization. Based on a review of the data and considering the criteria for “ideal assays”, the HPV LabNet further evaluated a VLP-ELISA and a non-commercial HPV genotyping assay, the PCR reverse blotting hybridization (RBH) (PGMY-RBH) assay with aims to 1) evaluate basic laboratory-based SOP; 2) improve, generalize and optimize the SOP following experience in the study; 3) identify any training needs in the HPV LabNet in establishing the testing methods; 4) help needed labs set up reliable assays for both HPV genotyping and antibody testing to be
4.2 HPV DNA genotyping assays

4.2.1 Evaluation and validation of a non-commercial HPV genotyping assay

HPV DNA genotyping is required to determine HPV type-specific prevalence and distribution for epidemiological studies. The presence of multiple HPV types complicates assays and demands high sensitivity, specificity and reproducibility. For this reason a variety of HPV DNA detection and genotyping assay formats have been used in laboratories worldwide. Inter-laboratory and inter-assay comparisons have not been performed, and no assay can be considered to be the “gold” standard. Although commercial assays may improve standardization, they are more expensive than in-house assays. On the other hand, in-house assays may lack validation and require addition efforts to standardize. To assist in validating a reliable non-commercial HPV DNA genotyping assay that would be more affordable than commercial assays, the WHO HPV LabNet selected the non-commercial PGMY-RBH assay and organized the transfer of this technology to each HPV LabNet laboratory in 2008. The assay protocol was evaluated in a collaborative inter-laboratory comparison study. This study demonstrated that the assay was sensitive, transferrable and acceptable for HPV detection and typing at a cost of $3-4/per sample. Further study has shown good comparability between this assay and commercial assays in terms of robustness, sensitivity and specificity. Based on the experience from these studies, the SOP was further optimized and included in the HPV Laboratory Manual. The proficiency of this assay and the successful set-up in LabNet labs has further been proven in the 4th HPV LabNet proficiency study in 2010.

4.2.2 Evaluation of commercial HPV genotyping assays

While in-house assays have a significant cost advantage, they require extensive training and investment of resources in reagent preparation and QC. Commercial kits are optimized to simplify set-up and training and provide standardized quality assured reagents. As a result, the cost is significantly higher than in-house assays. Commercial kits can contribute to stability of testing results over time and facilitate inter-laboratory standardization.

Data from the HPV LabNet proficiency study provided preliminary information on the worldwide performance of various commercial assays for HPV genotyping used by participating laboratories. In order to further investigate the performance, in 2010 the WHO HPV LabNet conducted a study to evaluate currently available commercial assays for HPV genotyping. The assays that met the following criteria were evaluated 1) will detect and individually identify all or the majority of the thirteen high risk types as well as the two low risk types currently targeted by one vaccine formulation; 2) do not require purchase of expensive instrumentation for assay performance and interpretation; and 3) have been used by participants in the WHO HPV proficiency testing program. The study was designed to compare performance of these assays with the potential needs of a global network in mind. Specifically, assay sensitivity, specificity and reproducibility were assessed. In addition, attention was given to ease of use, suitability for the most common specimen types and cost per sample. The data from this study is providing useful information to HPV labs who consider use of commercial assays when resources are available. The manuscript is in preparation in order to make the results published.

4.3 HPV serology assays

4.3.1 Evaluation and validation of a VLP-based ELISA

The direct L1 VLP-ELISA is the most basic assay to measure type-specific HPV antibodies. While production and validation of VLPs is difficult, the ELISA platform itself is common in laboratories and easy to adopt. Assuming availability of the key VLP reagents, VLP-ELISAs are the most likely serology assays to be used worldwide. The WHO HPV LabNet organized two collaborative studies using a standard, well-characterized supply of VLPs and a validated HPV sera proficiency panel, to evaluate and optimize a basic ELISA protocol and SOP for inclusion in the
WHO HPV Laboratory Manual. This process ensured that a validated serology assay that could be used for large scale monitoring of vaccination would be available to all LabNet laboratories.

### 4.3.2 Neutralization assay
Most antibodies against conformational epitopes on HPV VLPs will show neutralizing activity in experimental systems. These experimental systems use pseudovirion; HPV VLPs with reporter DNA that generate a signal after a pseudovirion (PsV) binds to the cell and releases DNA. Not all WHO LabNet laboratories need to have the capacity to conduct neutralization assays, but to have the capacity to verify VLP-assay results with neutralization assay results is required in assessing the immune response to HPV vaccines in clinical trials, dosing studies, and in searching for correlates of protection and cross-protection. The protocol and constructs for a PsV-based neutralization assay using secreted alkaline phosphatase reporter DNA were developed by Dr John Schiller but it is still a relatively complex assay. WHO HPV LabNet members who were using this assay evaluated the reproducibility of this protocol using inter-laboratory comparison on sera used to validate the VLP-ELISA. Based on successful results of this study, the SOP was included in the HPV Laboratory Manual. A manuscript describing the results of the inter-laboratory comparison is in preparation.

### 4.4 Confirmatory testing
An important part of a QA program is sample-exchange between laboratories to confirm HPV assay results (namely confirmatory testing). Confirmatory testing determines the extent of agreement between laboratories sharing samples that have been previously tested. A discrepancy in results may identify problems and suggest ways to resolve these problems. Two WHO HPV LabNet GRLs perform confirmatory typing of selected samples from RRLs and "problematic" samples submitted from any laboratory in the world. Between 2009-2010, the RRLs sent samples to one of the GRLs, after completing their testing the GRLs then exchanged these samples. In all cases, the samples were DNA extracts or cell lysates ready for PCR testing. Therefore the comparison testing could not address variations or problems in extraction. Each RRL received a database of their results, along with the results of the two GRLs. The extent of agreement was clearly influenced by assay platform. As there is no "gold standard", the extent of agreement of the two GRLs, presumed to have validated expertise in HPV DNA testing, was the most that could be expected of the RRL.

In order to standardize the exchange of data within the WHO HPV LabNet and eventually in global monitoring, the HPV LabNet developed a standardized format for reporting results of HPV typing assays. This format will be used in future inter-laboratory comparison studies.

### 5. Development of HPV laboratory manual
Based on the knowledge and experience that the WHO HPV LabNet has obtained through its international collaborative studies over the past several years, the first HPV Laboratory Manual was developed and published by WHO. This manual aims to assist in establishing the laboratory support required for implementation and monitoring HPV vaccination programmes. The manual also provides useful information to all audiences involved in development and implementation of HPV vaccines, particularly those involved in generating or using HPV laboratory data. The manual was shared and "tested" on several HPV LabNet training occasions, and was found to be helpful and informative.

### 6. Capacity building and training
The laboratory testing capacity of HPV LabNet labs has been built upon and strengthened by transferring technology, providing training at courses and workshops, and conducting collaborative inter-laboratory comparisons and proficiency testing of both HPV genotyping and serology assays. This ensured the HPV LabNet laboratories had both the capacity and competence to provide technical support to national labs, and prepare for the anticipated support of vaccine implementation and monitoring. Requests for technical support with HPV testing were received from some countries; in particular those setting up HPV laboratory testing activities to define national HPV vaccination programmes. In response to these requests WHO HPV LabNet, in
collaboration with WHO regional offices, organized a series of trainings at global, regional and
country level. The workshops provided theoretical and practical knowledge to laboratories,
particularly those from developing countries, on all aspects of HPV laboratory testing. Participants
were from HPV LabNet labs, national reference labs and other interested labs who have been
involved in national HPV vaccination programmes. The workshops also provided a good
opportunity to exchange information, promote communication and networking among HPV LabNet
and national labs in the area of laboratory HPV surveillance and vaccination monitoring.

7. Contribution and support to international/regional/national HPV activities
HPV LabNet labs have been involved with, and contributed to, technical consultations at global,
regional, and country levels by conducting HPV epidemiological studies; providing
scientific/technical advice; providing training, technical support and collaboration to other labs
(particularly developing countries); and initiating networking between labs within countries or
regions. This greatly helped those countries who were initiating national studies determine the
type-specific prevalence and sero-epidemiology of HPV, prior or post HPV vaccination, design HPV
vaccination programmes.

8. International consultations to guide the work of HPV LabNet; presence of HPV
LabNet in global/regional/national forum
The WHO biological standardization programme involves close collaboration with the international
scientific and professional communities, regional and national regulatory authorities,
maintainers and expert laboratories worldwide. WHO organized a series of meetings attended
by international experts and partners to consult on the role of an HPV LabNet. These meetings
were a platform to discuss scientific issues, identify standardization required
to support HPV surveillance, exchange experience, share information and
knowledge, seek collaboration and to develop the LabNet work plan by
addressing the needs from the field. The outcomes from those meetings set
up the rationale for the LabNet work.

To inform the broader public on HPV LabNet activities, share knowledge and
explore collaboration in future HPV surveillance and vaccination monitoring, the HPV LabNet has
participated in important forums at global/regional/country level attended by researchers and
laboratory technicians, regulators, industries, and other relevant stakeholders; WHO launched the
WHO HPV LabNet website; developed semi-yearly newsletters; and created the HPV LabNet
workstation. Efforts have also been made to publish HPV LabNet studies. All this provides a
platform to share the HPV LabNet activities, knowledge and experience, promote communication
and explore collaboration in the area worldwide.

Since its establishment in 2006, the WHO HPV LabNet has made tremendous progress towards
harmonization and standardization of HPV laboratory testing. Based on their scientific excellence
and strong volunteerism, the LabNet laboratories have developed a consensus on criteria for HPV
laboratory testing and are pioneers in building an international reference system to support
qualified HPV surveillance and vaccination monitoring. The HPV LabNet is able to:

- assist in evaluating and validating assay methodologies used in vaccine evaluation,
surveillance and monitoring
- provide standards and standardized assay protocols for use in HPV surveillance and
monitoring, to promote data comparability between laboratories and over time in one
laboratory
- provide QA/QC programs, e.g. Proficiency Panel, Confirmatory testing, to ensure reliable
and proficient assay performance in HPV epidemiology studies;
- provide specialized laboratory expertise, technical transfer, advice, support and training to
needed labs
- provide service for testing surveillance samples.
The HPV LabNet offers a unique resource for supporting HPV surveillance and vaccination impact monitoring and facilitating assessment of HPV vaccine efficacy, subject to available logistical and budgetary considerations.

**References**


2. Announcement

The current WHO HPV LabNet was established by WHO in 2006, as part of a project funded by the Bill and Melinda Gates Foundation for a 5-year period, until June 2011. The main task undertaken by the HPV LabNet defined in this project, was to harmonize and standardize HPV laboratory testing procedures to support consistent laboratory evaluation of regional disease burden and monitor the performance of HPV vaccines. This project would further permit the build-up of laboratory capacity for HPV testing in each WHO region and provide technical support to other laboratories worldwide. The reference laboratories were selected based on their technical expertise in the area of HPV laboratory testing and epidemiological study, and their strong willingness to contribute to the WHO project.

As summarized in the above "Overview", over the past several years the WHO HPV LabNet has endeavoured to make great achievements in the international harmonization and standardization of HPV laboratory testing practice and has provided technical support to other laboratories around the world to support implementation of HPV vaccination. The strong willingness and enthusiasm of the HPV LabNet laboratories to contribute to the worldwide improvement of quality of HPV laboratory testing are highly appreciated.

In conclusion, the WHO HPV LabNet has successfully completed the tasks outlined in the current project, which was led by the Quality, Safety and Standards team at WHO and funded by the Bill and Melinda Gates Foundation. The HPV LabNet reference laboratories have agreed to lead the ongoing work towards developing harmonized and standardized HPV surveillance. WHO will continue to support outputs from the HPV LabNet that support biological standardization.

We believe that the expertise built-up in the laboratories, and the availability of established international standards will contribute to supporting future harmonized and standardized HPV surveillance and vaccination impact monitoring work worldwide. Once again, we acknowledge all the HPV LabNet laboratories for their effort and constant support to this WHO project.

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Conclusion: The participants all showed great interest and good molecular biology techniques; most of them were already members of the Argentine HPV LabNet with varying levels of knowledge on HPV and experience with HPV assays. However, some participants were new to this field, so the theoretical training helped to harmonize these aspects.

At the end of the Workshop, participants stated that they felt very motivated to incorporate new methods of genotyping and greatly appreciated the hand-on approach of the practical course. Participants found the course interesting, well-organized, helpful and user-friendly. Trainers were considered well-prepared and responsive to the participants’ learning needs.

Argentina is a large country with region-specific health concerns. The Workshop provided an opportunity to gather professionals from academic and public health institutions from various Argentine provinces interested in investigating HPV infection and cervical cancer from a population surveillance perspective. Experience exchange was very rich from the scientific, technical and logistic perspective, demonstrating the benefits of interacting face-to-face and integrating scientific knowledge with each province’s health related issues. Participants also indicated the possibility of interacting with the HPV LabNet once they return to their provinces.

The Workshop was particularly timely this year as it was held two months before the Argentine National Authorities announced the introduction of the HPV vaccine to the National Vaccination Schedule. This is an important step towards cervical cancer prevention in Argentina; and an adequate virological surveillance program will be crucial for evaluating the vaccine impact.

4. Recent Publications of WHO HPV LabNet Work

5. Upcoming Meetings

27th International Papillomavirus Conference & Clinical Workshop
Berlin, Germany
17-22 September, 2011

More information can be obtained on the link:
http://www.hpv2011.org

WHO HPV LabNet Satellite Symposium
Berlin, Germany
20 September, 2011

- Co-organized by Prof. Joakim Dillner and Dr. Elizabeth Unger, GRLs of WHO HPV LabNet

"Based on the success of the WHO HPV LabNet symposium organized at the 2010 International Papillomavirus Conference, the two global reference laboratories (GRL) are proposing a similar session at the 2011 meeting. As before, this will be an informal meeting allowing those representing reference laboratories who are attending the 2011 IPV to meet and exchange information with each other."

The goals of the session will be to:
1. Review activities of GRLs, regional reference laboratories (RRLs) and official National HPV Reference Laboratories (NRLs) appointed by their respective countries
2. Review accomplishments of the WHO LabNet
3. Discuss future of HPV LabNet and identify methods to maintain communication and continue standardization and harmonization of testing.

6. Useful Web Links

- http://www.who.int/hpvcentre/en
- http://www.who.int/immunization/en
- http://www.who.int/biologicals/en
- http://www.ipvsoc.org/index.html
- http://www.uicc.org