

Workshop on international regulatory capacity enhancement for influenza vaccines, 8-10 June 2011, São Paulo, Brazil

Meeting Report

Executive Summary

Robust vaccine regulatory capacity is essential to the achievement of global health and millennium development goals as well as to a number of vaccine-specific initiatives. The Workshop on International Regulatory Capacity Enhancement for Influenza Vaccines¹ (WIRCEIV) brought together regulators and policymakers from across the world to envision ways to build regulatory capacity in developing countries. The workshop served as a catalyst to initiate and strengthen partnerships and coordination between governments, Ministries of Health, National Regulatory Authorities (NRAs), regulatory networks, and international organizations. Workshop participants expressed satisfaction with face-to-face meetings between regulators and policymakers such as the WIRCEIV and the WHO NRA Strategic Forum of Regulatory Agencies for Vaccines (3-5 May 2011, Thailand).

Capacity for vaccine regulation, available expertise, and resources vary amongst NRAs in developing countries. No regulatory model can fit-all or be directly imported into a recipient NRA because of differences in the political, legal, public health, techno-scientific, and socio-cultural-economic contexts. Progress in regulatory capacity building requires mutual understanding and appreciation for each stakeholder's roles and responsibilities, political and resource commitment to coordinate efforts as well as maintaining effective lines of communication between all stakeholders.

The workshop occurred at an opportune time, just as international focus was drawn anew to increasing vaccine delivery to the world's poorest countries by the recently launched Bill & Melinda Gates initiative 'Decade of Vaccines'.

Sustainable influenza vaccine production capacity worldwide requires continued support of capacity building of the entire regulatory system. Influenza vaccine use and vaccination policy can also aid in ensuring sustainability. Suggestions arising from the workshop include support to:

- Regulatory preparedness for influenza vaccines by ear-marking a percentage of grants provided to a country to build manufacturing capacity to be dedicated to NRA capacity building;
- Strengthen regulatory regional partnerships, approaches, and networks; particularly, models that address specific regulatory needs of developing countries;
- Enhance post-marketing surveillance and monitoring adverse events following immunization in countries with and without influenza vaccine manufacturing capacity;
- Strengthen evaluation of clinical trial data for regulatory registration;

¹ The WIRCEIV organizing committee defined 'international regulatory capacity enhancement' as any efforts related to the development, utilization and enforcement of international scientific regulatory standards that help assure the efficacy, safety and quality of a regulated product.

- Regulatory capacity building initiatives and recommendations of the World Health Organization (WHO) including the NRA Strengthening Programme, the Vaccine Prequalification Programme, NRA Strategic Forum of Regulatory Agencies for Vaccines, the Global Learning Opportunities (GLO) for Vaccine Quality, and the Global Action Plan for Influenza Vaccines (GAP).

These suggestions were brought forward to inform the review and refinement of the implementation of the WHO Global Action Plan for Influenza Vaccines (GAP II) in July 2011 in Geneva, Switzerland.

Introduction

The U.S. Department of Health and Human Services (DHHS), WHO, and other like-minded organizations and governments are committed to support regionally-based, independent, and sustainable vaccine production in developing countries through capacity building and technology transfer². A coordinated discussion among the international community on this shared goal was initiated at the Sustainable Influenza Vaccine Production Capacity Stakeholders' Workshop of 2010 in Washington D.C. An emerging discussion theme was the fact that sustainable vaccine production capacity is unachievable in the absence of robust national regulatory systems, defined as those that exhibit capabilities to perform specific functions with consistency under a wide range of conditions.

The vaccine development and production landscape is moving from vaccine manufacturing consolidated in a few countries, to emerging economies. A growing proportion of United-Nations-procured vaccines, representing access to 60% of the world's population, are produced by vaccine manufacturers in emerging-economy countries. Despite current production levels, vaccines are insufficient to meet growing public health needs, particularly in times of an influenza pandemic. This shift highlights the need for enhanced global regulatory capacity and cooperation in assuring equitable access to quality, safe, and effective vaccines globally.

Building upon the Stakeholders' Workshop, WHO and DHHS worked collaboratively with the Developing Countries' Vaccine Regulators Network (DCVRN), the Brazilian National Health Surveillance Agency (ANVISA), the Pan American Health Organization (PAHO), Health Canada, the European Medicines Agency (EMA), and other key stakeholders, to develop the WIRCEIV³. The workshop brought together representatives from 34 countries on behalf of NRAs, regional regulatory networks, policy-making bodies, government agencies, ministries of health, academic institutions, and non-governmental organizations. The group worked to identify needs and gaps in vaccine regulatory oversight in developing countries; generate ideas for leveraging resources; define the roles and responsibilities of stakeholders; and delineate policy issues and options.

This Meeting Report summarizes the major discussion themes and outcomes of the WIRCEIV as well as the proposed next steps to further enhance regulatory capacity for influenza vaccines in

² Friede M, Palkonyay L, Alfonso C, Pervikov Y, Torelli G, Wood D, Kieny MP. WHO initiative to increase to increase global and equitable access to influenza vaccine in the event of a pandemic: supporting developing country production capacity through technology transfer. *Vaccine* 2011; 29S:A2- A7

³ <http://www.globalhealth.gov/global-health-topics/communicable-diseases/influenza/vaccine-workshops/june2011/index.html>

developing countries.

The suggestions arising from WIRCEIV were brought forward to inform the review and refinement of the implementation of the WHO Global Action Plan for Influenza Vaccines (GAP II)⁴ in July 2011 in Geneva, Switzerland. The new implementation plan will align a timeline to stakeholder roles and responsibilities in the creation of sustainable influenza vaccine production capacity worldwide.

Enhancing Regulatory Capacity: Challenges and Lessons Learned

The workshop breakout sessions provided structured opportunities for small group discussions of issues relevant to a particular stakeholder group and/or region. Challenges identified during the breakout sessions are summarized in Table 1.

Table 1. Challenges to enhancing regulatory capacity

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| Common challenges faced by technical partners and recipient NRAs |
| <ul style="list-style-type: none"> • Lack of clear legislative framework • Limited clarity, definition and respect for regulatory authority • Inadequate surge capacity to handle emergency situations • Undefined specific guidelines and standard data criteria for manufacturers • Insufficient standard operating procedures for regulatory staff |
| Common challenges faced by policymakers |
| <ul style="list-style-type: none"> • Politics • Lack of routinely used channels for communicating and coordinating between the Ministry of Health and the NRA • Communication with the public and the media • Perceived rigor of regulatory standard setting • Breakdown in communications between policymakers and NRAs in the post pandemic period • Insufficient surveillance data on influenza incidence, mortality, burden of disease with economic analyses, and product adverse events reporting |
| Common challenges faced by both NRAs and policymakers |
| <ul style="list-style-type: none"> • Lack of political support and resources • Differences between the policymaking and regulatory cultures with different mandates, language, and expectations |
| Common challenges faced by NRAs across geographic regions |
| <ul style="list-style-type: none"> • Communication • Language barriers |

⁴ http://www.who.int/influenza_vaccines_plan/resources/5report_gap_ag_5may11.pdf; http://www.who.int/influenza_vaccines_plan/news/agenda.pdf

- Absence of regional regulatory standards
- Lack of harmonization with other NRAs (e.g. to use International Conference on Harmonization ICH) Common Technical Document (CTD) formats
- Recruiting, training, and retaining qualified staff

Challenges for the Regulatory Oversight of Influenza Vaccines

Unique challenges for influenza vaccines also exist. Regulatory pathways applicable to seasonal influenza vaccines are well established in several countries and are largely applicable to pandemic influenza vaccines. Many production and regulatory challenges include provisions for influenza virus strain change, unpredictable yields and growth properties, complexity of manufacturing processes, and heterogeneous safety and efficacy profiles which must be addressed on a case by case basis. To aid in regulatory decision making, written WHO recommendations exist to assure the quality, safety and efficacy of seasonal and pandemic influenza vaccines⁵.

While it is important to routinely pursue the seasonal influenza vaccine approval pathway, mechanisms to provide regulatory flexibility in the context of pandemic or health emergencies are needed to respond appropriately to the health threat while maintaining the integrity of the regulatory system and confidence in it. Vaccine regulatory approval involves not only demonstration of safety and immunogenicity via preclinical and clinical evaluation but also well-controlled clinical efficacy studies in which influenza illness is assessed as the primary endpoint. In order to provide regulatory flexibility in pandemic or health emergencies, manufacturers would commit to conduct well-controlled clinical trials establishing that their product has an effect on a surrogate endpoint to predict clinical benefit. The manufacturer also commits to conduct appropriate post-marketing studies that verify vaccine safety.

The 2009 H1N1 influenza pandemic demonstrated that international collaboration was particularly critical in post-marketing safety monitoring due to limited clinical trials data to capture all possible adverse events following immunization (AEFI) with pandemic influenza vaccine in mass campaigns. This internationally coordinated effort allowed for signal validation and confirmation of potentially-associated AEFI with influenza vaccines. Countries with limited capacity that rely on passive surveillance for post-marketing safety were assured by safety monitored in countries with more sophisticated post-marketing surveillance systems. The challenges to enhancing regulatory capacity to respond to the 2009 H1N1 pandemic are summarized in Table 2.

⁵ <http://www.who.int/biologicals/vaccines/influenza/en/index.html>

Table 2. Challenges to enhancing regulatory capacity to respond to the 2009 H1N1 pandemic

- Lack of definition of the distinct roles and responsibilities of NRA staff and policymakers
- Limited preparedness to accept responsibility for decision making
- Internal and external pressure to authorize vaccines quickly, often with the lack of the regulatory mechanism to do so
- Responsibility for vaccine marketing authorization in the absence of data for registration and/or with only limited information provided (especially in cases of donated vaccines)
- Managing expectations and demands of senior (government) officials, the media, and the public, including the view that vaccine should be available to the entire national population at the same time that it is available in other jurisdictions
- Adapting pandemic influenza preparedness plans to the H1N1 scenario based on H5N1 experience
- Absence of guidance on vaccine licensure, including expedited process
- Having to regulate multiple vaccines concurrently (for countries with large domestic production capacity)
- Securing supply for countries with relatively small markets
- Establishing adverse drug reaction (ADR) and surveillance systems for donated vaccine
- Less than optimal communications from government to the public
- Pressure from policy makers to approve vaccines quickly and make regulatory decisions in the absence of data or in a manner that was inconsistent with regulatory practice in their respective jurisdiction

Resources and Opportunities for Enhancing Regulatory Capacity

The WHO NRA Strengthening Programme

After more than a decade of assessing regulatory functionality, the WHO NRA Strengthening Programme has built an extensive database with detailed qualitative and quantitative information on the status of regulatory agencies of more than 100 countries. This information helps tailor Institutional Development Plans (IDPs) and timelines suited to the specific needs of the countries' NRA.

The WHO NRA Strengthening Programme⁶ developed a five-step NRA capacity building model which includes i) benchmarking / assessment tools method; ii) the NRA assessment; iii) elaboration of IDP; iv) implementation of the IDP including technical input from WHO; and, v) progress monitoring via follow up assessments. The Programme provides a system to assess functionality of vaccine regulation according to performance indicators in six regulatory functions i) licensing and marketing authorization; ii) post-market surveillance (PMS) including monitoring of adverse events following immunization (AEFI); iii) lot release; iv) access to testing laboratories; v) good manufacturing practice (GMP) inspections; and, vi) regulatory oversight of clinical trials.

All vaccines distributed by United Nations (UN) agencies are WHO-prequalified⁷. The WHO

⁶ http://www.who.int/immunization_standards/national_regulatory_authorities%20strengthening/en/index.html

⁷ http://www.who.int/immunization_standards/vaccine_quality/pq_system/en/

prequalification programme is product-specific and linked to the requirement that the NRA overseeing the specific product is functional according to the WHO NRA assessment system. Regulatory strengthening aspects of the WHO influenza vaccine production capacity building programme have been integrated into the WHO NRA Strengthening Programme.

Mentoring Partnerships between Regulators

WHO plays a pivotal role in enhancing in-country and regional regulatory capacity by engaging experts and facilitating collaborations between NRAs from different countries and regions and between NRAs and manufacturers. Regulatory capacity has been successfully strengthened through mentoring partnerships between NRAs seeking to enhance capacity and NRAs assessed by WHO as functional. Three different mentoring models were highlighted in the workshop via case studies.

Case Study 1: Health Canada and the Central Drugs Standard Control Organization of India In 2007, WHO conducted an assessment of the Central Drugs Standard Control Organization⁸ (CDSCO) of India, which revealed gaps in vaccine regulation. The assessment led to the closure of three public sector vaccine manufacturers due to non-compliance with GMP. Because of the key role Indian vaccine manufacturers play as suppliers of essential vaccines to UN agencies and approximately 150 countries, immediate action was required to help CDSCO meet WHO standards of regulatory functionality. With WHO support, Health Canada⁹ agreed to a mentoring partnership with CDSCO. Following in-depth assessments and comprehensive trainings over the course of a year, CDSCO met critical indicators and regained regulatory functionality under WHO standards. In May 2009, Health Canada and CDSCO agreed on further capacity building support and arranged to conduct parallel review of one vaccine submission which is in the process of completion.

Case Study 2: South-South Cooperation between the Brazilian National Health Surveillance Agency and the Centro para el Control Estatal de la Calidad de los Medicamentos of Cuba for Technology Transfer

In order to facilitate technology transfer in the Americas, the Brazilian National Health Surveillance Agency¹⁰ (ANVISA) of Brazil and the Centro para el Control Estatal de la Calidad de los Medicamentos¹¹ (CECMED) of Cuba set up a technical regulatory committee for technology transfer. The committee was comprised of CECMED as the NRA of the technology-transferring country, ANVISA as the NRA of the technology-receiving country, the Centro de Immunología Molecular¹² (CIM) and the Centro de Ingeniería Genética y Biotecnología¹³ (CIGB) of Cuba as the producers from the technology-transferring country, and Biomanguinhos¹⁴ Brazil as the producer in the technology-receiving country. The committee held two general meetings per year with follow

⁸ <http://cdsco.nic.in/>

⁹ <http://www.hc-sc.gc.ca>

¹⁰ <http://anvisa.gov.br/eng/index.htm>

¹¹ <http://www.cecmec.sld.cu/>

¹² <http://www.cim.co.cu/>

¹³ <http://www.cigb.edu.cu/>

¹⁴ http://www.fiocruz.br/bio_eng/cgi/cgilua.exe/sys/start.htm?tpl=home

up meetings to address critical points in the technology transfer process. Products for technology transfer included erythropoietin, interferon alpha, meningococcal AC vaccine (WHO, ANVISA and CECMED joint work), and pegylated interferon.

Challenges faced by ANVISA and CECMED included the specificities in each country's laws, regulations and guidelines for each NRA, and differences in internal NRA processes. They overcame these challenges through information exchange (regulations, guidelines, working procedures), training and site visits. Because of this cooperation, ANVISA and CECMED avoided duplication of efforts e.g. pegylated interferon clinical trials authorization and GCP inspections. Cooperation also led to the sharing of information and knowledge.

Case Study 3: Thai Food and Drug Administration and the Australian Therapeutic Goods Administration Formal Training Initiative

In 2008, WHO reassessed the Thai Food and Drug Administration¹⁵ (TFDA) for vaccine prequalification purposes. Following the assessment, WHO recommended a capacity building programme to strengthen TFDA's vaccine evaluation process and technical skills. A tri-partite cooperation training initiative involving the Therapeutic Goods Administration¹⁶ (TGA) of Australia as the leading NRA, the TFDA as the recipient NRA and WHO as the facilitator/coordinator body was developed and implemented. The foundation of the capacity building initiative was the parallel review of the Japanese Encephalitis Vaccine. The review process entailed a preliminary assessment, scientific problem-solving, in-depth assessment, and a final assessment report.

Ultimately, TFDA became more knowledgeable in the scientific aspects of reviewing the vaccine dossier and more confident in selecting international guidelines as appropriate references in reviewing the vaccine dossier. In consequence, Thai FDA was able to implement and review the full common technical document (CTD). The parallel review process increased credibility and confidence in making scientific justifications and improved knowledge and skill in writing full assessment reports that met international standards. Thai FDA has subsequently been able to sustain good cooperation and technical consultation with immediate response from international experts.

Mentoring partnerships constitute win-win situations. Through mutual commitment to training and investment of resources by WHO and partner countries, the recipient NRA gains valuable scientific knowledge and experience with greater credibility as the vaccine national regulatory authority. The recipient NRA also gains confidence in its ability to review applications, provide guidance to manufacturers, and make regulatory decisions based on international standards and sound science. In turn, the leading NRA derives understanding of implications and impact of regulatory decisions at the global level.

¹⁵ <http://www.fda.moph.go.th/eng/index.stm>

¹⁶ <http://tga.gov.au/>

Regulatory Capacity Building Networks in Vaccine Clinical Trials in Developing Countries

Global and regional regulators' networks have enabled advancement in vaccine regulatory oversight via information sharing, development of common application documents, interagency joint review, legal and structural regulatory reform, and enforcement actions. Regulators' networks that were described during the WIRCEIV include:

The Developing Countries' Vaccine Regulators Network¹⁷ (DCVRN) which was established to promote strengthening capacity and procedures for the regulatory oversight of clinical trial protocols and clinical trial data for registration. Membership eligibility criteria include countries with vaccines and manufacturers to be WHO pre-qualified, NRAs with WHO functional status, and domestic expertise in clinical research of new vaccines. The DCVRN has helped increase support from Ministries of Health and introduced national legal and structural reform. They have also encouraged consistency in review of clinical trial applications through the use of standard criteria for protocol assessment. Scientific knowledge from DCVRN discussions has been applied directly to the evaluation of submissions, and clinical trials have been initiated with stronger regulatory systems in place.

The African Vaccine Regulators Forum¹⁸ (AVAREF) was established to address gaps in ethical and regulatory oversight of clinical trials in Africa. AVAREF has developed the African Common Clinical Trial (ACCT) guidelines and helped develop a legal framework for regulation of clinical trials via training modules. The Pan-African Clinical Trials Alliance¹⁹ (PACTA) under AVAREF offers a strategy for integration among ethical and regulatory oversight and registration of vaccine clinical trials in Africa and strengthening of these components. It has also created a common platform for Ethical Committees, NRAs and a clinical trials registry. Through AVAREF many countries have worked together on joint reviews of clinical trial applications and GCP inspections. This model has set the foundation for stronger collaboration and harmonization of procedures.

The European Medicines Agency: A Model for the Coordination of Networking National Agencies

The European Medicines Agency (EMA) was another model explored during the WIRCEIV. The historical, geographical and legislative setting of the European Union (EU) provided the drivers on regulatory framework for the creation of the EMA as a decentralized Agency of Commission. EMA issues EU Scientific Opinions and the Commission issues Pan-European Marketing Authorizations. EMA is a network of more than 45 national authorities dealing with human and veterinary medicines comprised of over 4,900 European experts.

The Medicines Control Laboratories Network²⁰ (OMCLS) is comprised of national authorities in Europe. Scientific competence is guaranteed by their nominating authority, independence and

¹⁷ http://www.who.int/immunization_standards/vaccine_regulation/devrn/en/

¹⁸ http://www.who.int/immunization_standards/vaccine_regulation/africa_network/en/index.html

¹⁹ <http://www.panafrican-med-journal.com/content/article/9/42/full/>

²⁰ <http://www.edqm.eu/en/General-European-OMCL-Network-46.html>

integrity assured by public declaration of interests. They provide services to EMA on the basis of contracts with the member states. In turn, EMA provides consistent approaches through development of training programmes, tools to increase communication, guideline development that keep standard level, and improve processes on a continuous basis.

In order to prepare candidate Member States to join EU Pharma²¹ activities, the EU provides assistance programmes. The Instrument for Pre-accession Assistance²² (IPA) programme provides support through preparatory measures for participation in the EU by new Member State. The IPA aims to foster links between EMA and the beneficiaries to ensure future cooperation in the Agency's networks.

Enhancing Interactions between NRAs and Decision/Policy-Making Government Bodies

One of the critical themes addressed during the WIRCEIV was how to enhance interactions between NRAs and decision-making/policy-making government bodies. National Immunization Technical Advisory Groups²³ (NITAGs) were presented as an important model for this type of interaction. The primary aim of NITAGs is to enhance the use of evidence-based decision-making processes in the development of immunization programmes and policies at national level. With assistance from NITAGs, national governments can address matters of immunization and vaccines linked to policies and strategies, introduction of new vaccines and immunization technologies, vaccine quality and safety, and public health needs for new and reemerging vaccine-preventable diseases, and others. In particular, NITAGs help adopt policies based on national priorities, resist pressure from interest groups, reinforce the credibility of national vaccine and immunization policies, enhance the ability to secure government and/or donor funding, and encourage comprehensive approaches that consider the health of vulnerable populations. The Agence de Médecine Préventive (AMP) implements the Supporting National Independent Immunization and Vaccine Advisory Committees²⁴ (SIVAC) Initiative which aims to support the development of sustainable NITAGs in Global Alliance for Vaccines and Immunisation (GAVI)-eligible and middle-income countries worldwide.

Countries differ in their approaches to vaccination decision-making. Ghana has an Inter-Agency Coordinating Committee (ICC) with similar advisory functions and less comprehensive membership than a NITAG. The Expanded Programme on Immunization (EPI) acts as the secretariat to the ICC. However, Ghana plans to establish NITAGs to address the growing need for new vaccine introduction with proper prioritization framework. Vietnam, a vaccine producing country, has had a National Committee for Vaccine Utilization since 1998. With membership from the General Department of Preventive Medicine, the Department of Medical Treatment and Management, the Department of Science and Training, the National Institute of Health and Epidemics (NIHE), Pasteur Institutes, hospitals, and relevant experts, the committee provides advice on EPI and non-EPI vaccines, evaluation of vaccine use, and new vaccine introduction.

²¹ <http://www.pharma-eu.com/french.htm>

²² http://europa.eu/legislation_summaries/agriculture/enlargement/e50020_en.htm

²³ <http://www.sivacinitiative.org/node/4>

²⁴ <http://www.sivacinitiative.org/>

National approaches to following NITAG recommendations also vary. A NRA can request additional documentation from manufacturer following a NITAG recommendation in cases of change on package insert, post-pandemic vaccine use, vaccine use in age group not covered under licensure, and others. In the United States, a pandemic influenza vaccine-producing country, the US-FDA²⁵ maintains close collaboration with its Advisory Committee on Immunization Practices²⁶ (ACIP) and the U.S. Centers for Disease Control and Prevention²⁷ (US-CDC). Sometimes the US-FDA makes decisions on licensing and the CDC on package insert without the manufacturer's involvement.

The 2009 influenza pandemic constituted a wake-up call for most countries and lessons should be used as education platform for the future. Advisory bodies such as NITAG should be set up in advance with proper membership, a charter and clear standard operating procedures to advise the Ministry of Health and NRAs in decision-making during pandemic emergencies.

Capacity Building Models to Address Needs and Gaps

As part of its global strategic framework for vaccines and immunization capacity building, WHO provides assistance to countries in developing strategic plans that strengthen their regulatory systems. Through this initiative, WHO facilitates the provision of regulatory expertise from functional NRAs to other functional and/or non-functional NRAs, NCLs, pharmaco vigilance centres, ethics committees, and/or immunization programmes. In support of regulatory functions, WHO also facilitates developing and sustaining regulators networks, maintaining rosters of skilled resource persons, vaccine quality and regulation experts as well as planning, organizing and conducting institutional and/or in-country learning activities. Several WHO's initiatives were highlighted during the WIRCEIV:

Vaccine Working Group: Pan American Network on Drug Harmonization

A Vaccine Working Party (VWG) was established by the Pan American Network on Drug Harmonization²⁸ (PANDHR) in response to the need to develop harmonized documents in the vaccines field in the Americas. The VWG mission is to promote the harmonization of pharmaceutical requirements for vaccines to ensure their quality, safety and efficacy thereby creating efficient mechanisms to enhance vaccine availability to all countries in the region. A guidance document on 'Harmonized requirements for the licensing of vaccines in the Americas and guidelines for preparation of application' was developed by the PANDRH/VWG via a consultation process that started in 2005 ending in document approval by the PANDRH Conference in 2008 and publication in 2010. Based on the ICH CTD and WHO Technical Report Series (TRS) documents, this PANDRH document addresses recommendations on vaccine regulation, administration, law, QC, non-clinical and clinical evaluations, and licensing conditions, in particular vaccine requirements from NRAs in the Americas. The recommendations in the document are currently under implementation and document is available in Spanish, French and English.²⁹

²⁵ <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm>

²⁶ <http://www.cdc.gov/vaccines/recs/acip/downloads/article-2010-role-procedures-ACIP-508.pdf>

²⁷ <http://www.cdc.gov/>

²⁸ <http://www.paho.org/spanish/ad/ths/ev/GTVacunas.htm>

²⁹ http://new.paho.org/hq/index.php?option=com_content&task=view&id=5342&Itemid=513

Regional Network of Quality Control of Vaccine Laboratories

The Regional Network of National Laboratories for Quality Control of Vaccines (RRLNCCV) was initiated by the Regional System for Vaccines³⁰ (SIREVA) in the Special Programme for Vaccines and Immunization (SVI) of the Pan American Health Organization³¹ (PAHO). A strategy for the development, production, control and access to quality vaccines in Latin America and the Caribbean was developed. The RRLNCCV aims to harmonize protocols and methodologies in vaccine licensing, reference vaccine and standard development, and conducting collaborative studies on new techniques and validation methods. In addition, the network facilitates accreditation for producers, exchange and training programmes for NCLs, evaluating production protocols, establishing post-marketing surveillance systems, and controlling vaccines for used in clinical research. The network maintains active links with control laboratories across the world.

³⁰ <http://www.paho.org/Project.asp?SEL=TP&LNG=ENG&ID=115>

³¹ <http://new.paho.org/hq/index.php?lang=en>

Conclusion

The key elements in creating an environment conducive to regulatory capacity enhancement are summarized in Table 3.

Table 3. Key elements in creating an environment conducive to regulatory capacity enhancement

- Political commitment
- Education and outreach to enhance understanding of and appreciation for the importance of regulatory capacity
- Commitment to training
- Endorsement of a bottom-up approach of alerting leadership to key issues
- Capitalizing on international engagement and leveraging support through regional activities
- Understanding NRA-specific needs at all levels (i.e. technical, regulatory, political, cultural, social, financial, others)
- Commitment to improving communications between the Ministry of Health, policymakers, regulators, surveillance agencies, regional networks, advisory bodies, and others. This can be done through international exchanges via inter-country workshops, vaccine/clinical trial discussions and conferences
- Formal written agreements (i.e. memorandum of understanding, confidentiality agreements, letter of exchange) that ensure information flow between regulators and policy makers and assist in clarifying scopes, mandates and general relationships governing information sharing between organizations
- Improvement of surveillance on influenza incidence, mortality, economic analysis of disease burden, and product adverse events reporting
- Additional consideration of regional regulatory models and approaches to NRA capacity building and functionality

Proposed priorities and next steps are summarized in Table 4.

Table 4. Proposed priorities and next steps on enhancing regulatory capacity for influenza vaccines

- Commitment to support regulatory preparedness for influenza vaccines by ear-marking a percentage of grants provided to a country to build manufacturing capacity to be dedicated for NRA capacity building
- Support the recommendations from the 1st WHO NRA Strategic forum of regulatory agencies for vaccines convened on 3-5 May 2011 in Bangkok, Thailand
- Strong support to strengthen and develop regulatory regional partnerships, models, approaches, and networks
- Support to develop and strengthen models that address specific regulatory needs of developing countries as no regulatory model can fit-all
- Enhanced support to post-marketing surveillance and monitoring adverse events following immunization in countries with and without influenza vaccine manufacturing capacity
- Enhanced support to the evaluation of clinical trial data for regulatory registration
- Enhanced support to the WHO NRA Strengthening and Vaccine Prequalification Programmes
- Support to the WHO Global Learning Opportunities to develop influenza vaccine regulatory training modules catered to NRAs, NCLs, EPI, Pharmacovigilance institutions, Ministry of Health and policy makers in newly producing countries
- Support training programmes such as the one developed at the Netherlands Vaccine Institute on influenza vaccine technologies, manufacturing processes and quality control specifically catered to regulators
- Support for the development of WHO written guidance on regulatory preparedness for seasonal and pandemic influenza vaccines catered to countries without influenza vaccine manufacturing capacity. This would facilitate the WHO efforts of pandemic influenza vaccine deployment and influenza vaccine use worldwide

WHO and DHHS plan to develop several more international workshops to address specific themes on enhancing influenza vaccine manufacturing capacity in developing countries.