

**HIV Drug Resistance Technical Cooperation  
Network for Latin America and the Caribbean**

**2014 Activity Report**



## Table of Contents

<b>Introduction</b>	<b>3</b>
<b>Activities in 2014</b>	<b>4</b>
Virtual Sessions	4
Workshops and Technical Meetings	6
Working Groups	8
Additional Activities	9
<b>Appendix 1 - Transitioning HIV Genotyping from Trugene</b>	<b>10</b>
<b>Appendix 2 - Report from the Workshop on the methodology for the surveillance of HIV drug resistance in the Caribbean</b>	<b>16</b>
<b>Appendix 3 - Abstract from the meeting report: HIV Care and Treatment Retargeting and Improving Access and Quality of HIV-Related Point of Care Testing in the Caribbean</b>	<b>38</b>

## Introduction

The HIV Drug Resistance (HIVDR) Technical Cooperation Network (TCN) for Latin America and the Caribbean, or HIVDR TCN LAC is an international collaborative initiative coordinated by the Pan-American Health Organization (PAHO) that gathers technical expertise and mobilizes resources to support the implementation of HIVDR surveillance in Latin American and Caribbean countries. It was created in 2013 by a group of HIV experts from clinical and lab background, national program officers and technical cooperation agencies, with the main objective of supporting the implementation of HIVDR surveillance and strategic use of HIVDR data in the Region. <sup>1</sup>

The emergence and transmission of HIV drug resistance to antiretroviral drugs in the context of Universal Access to antiretroviral therapy (ART) is a major challenge for countries that could hinder the long term effectiveness and viral suppression at population level. Since 2004, the World Health Organization (WHO) and HIV-ResNet <sup>2</sup> partners have been developing a public health strategy to prevent and assess HIV Drug Resistance in resource-limited countries and in the context of accelerated ART scale up.<sup>3</sup> In 2012 WHO published the first Global HIVDR report <sup>4</sup> and the HIVDR strategy was revised and updated. <sup>5</sup>

This report, the second since the launch of the HIVDR Technical Cooperation Network, is a summary of the activities that took place in 2014 under the initiative of this technical group.

---

<sup>1</sup> HIV Drug Resistance Technical Cooperation Network for Latin America and the Caribbean 2013 Activity Report. Available in the PAHO web site:

[http://www.paho.org/hq/index.php?option=com\\_topics&view=rdmore&cid=7169&Itemid=40737&lang=en](http://www.paho.org/hq/index.php?option=com_topics&view=rdmore&cid=7169&Itemid=40737&lang=en)

<sup>2</sup> More information on the WHO HIV ResNet are available in the WHO web site:

<http://www.who.int/hiv/topics/drugresistance/hivresnet/en/>

<sup>3</sup> More information on the WHO HIVDR strategy are available in the WHO web site:

<http://www.who.int/hiv/topics/drugresistance/en/index.html>

<sup>4</sup> WHO HIV drug resistance report 2012. Document available at:

<http://www.who.int/hiv/pub/drugresistance/report2012/en/index.html>

<sup>5</sup> WHO global strategy for the surveillance and monitoring of HIV drug resistance 2012.

Document available at:

[http://www.who.int/hiv/pub/drugresistance/drug\\_resistance\\_strategy/en/index.html](http://www.who.int/hiv/pub/drugresistance/drug_resistance_strategy/en/index.html)

## Activities in 2014

### Virtual Sessions

- 12<sup>th</sup> of March 2014. <sup>6</sup>

Objectives:

- Presentation of the new WHO HIVDR strategy launched at CROI 2014 with highlights from the new pre-treatment drug resistance (PDR) and acquired drug resistance (ADR) surveys. (Giovanni Ravasi, PAHO)
- Presentation of the experience of HIVDR surveillance in France (George dos Santos, CHU Martinique).
- Presentation of the experience of Honduras in the monitoring of Early Warning Indicators (Sandra Nuñez, MOH Honduras).

- 9<sup>th</sup> of April 2014. <sup>7</sup>

Objective:

- Presentation and discussion on the new WHO protocol for the surveillance of pre-treatment drug resistance (PDR). (Giovanni Ravasi, PAHO)
- The final version of the protocol is available at: [http://www.who.int/hiv/pub/drugresistance/pretreatment\\_drugresistance/en/](http://www.who.int/hiv/pub/drugresistance/pretreatment_drugresistance/en/)

- 7<sup>th</sup> of May 2014. <sup>8</sup>

---

<sup>6</sup> The link to the recording of the session is: <https://sas.illuminate.com/site/external/installinfo/playback?sid=1110&psid=2014-03-12.0649.M.1BC839C524B0BA4B8BF53A3EC0770F.vcr>

<sup>7</sup> The link to the recording of the session is: <https://sas.illuminate.com/site/external/jwsdetect/nativeplayback.jnlp?sid=1110&psid=2014-04-16.1043.M.09A67A345CEE43D9D2F336830FB23B.vcr>

<sup>8</sup> The link to the recording of the session is: <https://sas.illuminate.com/site/external/jwsdetect/nativeplayback.jnlp?sid=1110&psid=2014-05-07.1110.M.09A67A345CEE43D9D2F336830FB23B.vcr>

Objective:

- Presentation and discussion on the new WHO protocol for the surveillance of acquired drug resistance (ADR). (Giovanni Ravasi, PAHO)
  - The final version of the protocol is available at: [http://www.who.int/hiv/pub/drugresistance/acquired\\_drugresistance/en/](http://www.who.int/hiv/pub/drugresistance/acquired_drugresistance/en/)
- 16<sup>th</sup> of October 2014.

Special session to discuss strategies and options for HIV genotyping transitioning from Siemens Trugene in 2015.

**See Annex 1 for the summary of the recommendations.**

- 31<sup>st</sup> October 2014.<sup>9</sup>

Objective:

Presentation on advances in the implementation of HIVDR surveillance in Latin America: the experience of Argentina (Emiliano Bissio, MOH Argentina), Brazil (Nazle Veras, MOH Brazil) and the Mesoamerican Project (Santiago Avila, CIENI/INER, México).

- 18<sup>th</sup> December 2014: TCN Coordinators meeting.

---

<sup>9</sup> The link to the recording of the session is: <https://sas.illuminate.com/site/external/installinfo/playback?sid=1110&psid=2014-10-31.0657.M.09A67A345CEE43D9D2F336830FB23B.vcr>

## Workshops and Technical Meetings

- ***“Workshop on the Methodology for the surveillance of HIVDR in the Caribbean”*** on 16-18<sup>th</sup> of June, 2014, in Port of Spain, Trinidad and Tobago.  
Organization and technical support: PAHO/WHO, CARPHA, PANCAP, UNAIDS, PHAC, CDC/PEPFAR.

### Meeting Objectives

- To introduce participants to the updated WHO HIVDR surveillance strategies utilizing a public health approach
- To support countries in the generation of the revised HIVDR Early Warning Indicators (EWIs) and to utilize the result for programmatic improvement
- To support countries in the development of harmonized protocols for surveillance of HIV pre-treatment resistance and acquired drug resistance in accordance with the recommendations of the PAHO/WHO
- To share challenges and strategies among countries for the adaptation of protocols and implementation logistics for the surveillance of the pre-treatment and acquired drug resistance.
- To discuss methods of harmonized analysis and use of programmatic data of viral load and acquired resistance for public health actions.

Representatives from national HIV programs and Ministries of Health of Caribbean countries attended the workshop: Trinidad and Tobago, Suriname, the Bahamas, Guyana, Jamaica, the Dominican Republic, Barbados, and OECS countries.

**See Annex 2 for the full report from the workshop.**

- Technical meeting: ***“HIV Care and Treatment Retargeting and Improving Access and Quality of HIV-Related Point of Care Testing in the Caribbean”*** on the 20-22<sup>nd</sup> October in Port of Spain, Trinidad and Tobago.  
Special session on HIV Drug Resistance:



- HIV Drug Resistance Prevention and Surveillance: Report from Sub-regional workshop on HIVDR Surveillance.
- Work group: Protecting 2020 treatment and care targets addressing the emergence and transmission of drug resistance

**See Annex 3 for the abstract from the full report of this meeting on this specific HIVDR focused session.**

## **Working Groups**

### **Caribbean HIV Drug Resistance Working group**

As a result of the HIVDR surveillance workshop held in Trinidad in June of 2014, a Caribbean HIV Drug Resistance Working group was formed with representatives from PAHO/PHCO, CDC Caribbean Office, UNAIDS RST Caribbean, CARPHA, PANCAP, PHAC, CHU Martinique, Ponce School of Medicine Puerto Rico, National Public Health Labs of Jamaica, Bahamas and Barbados.

The initial objective of this working group was to review the country planning exercise from the HIVDR Workshop held in Trinidad in June of 2014 and coordinate technical cooperation for an implementation roadmap.

Meetings were regularly held in June, October and December of 2014 and expanding the scope of the group to: develop a proposal of creating a Caribbean Reference Group for Laboratory Services; follow up on the implementation of HIVDR surveillance in the Caribbean; and develop a proposal for a HIV Genotyping Lab Network for drug resistance monitoring in patients on antiretroviral treatment.



## Additional Activities

- The following technical documents on the WHO HIVDR surveillance strategy are being translated to Spanish and will be available in January of 2015:
  - Surveillance of HIV drug resistance in adults receiving ART - [http://www.who.int/hiv/pub/drugresistance/acquired\\_drugresistance/en/](http://www.who.int/hiv/pub/drugresistance/acquired_drugresistance/en/)
  - Surveillance of HIV drug resistance in adults initiating antiretroviral therapy - [http://www.who.int/hiv/pub/drugresistance/pretreatment\\_drugresistance/en/](http://www.who.int/hiv/pub/drugresistance/pretreatment_drugresistance/en/)
  
- A specific web page on HIV Drug Resistance to be used for dissemination of technical documents on this topic, as well as for activities related to the Network, is currently under construction and will be hosted within PAHO's web site.

## Appendix 1 – Transitioning HIV Genotyping from Trugene

### Background

- By the end of 2014 Siemens will stop the production of Trugene kits for HIV genotyping, as well as other consumables and reagents.
- At least 3 labs from the Network (Uruguay, Chile, Guatemala) were performing HIV genotyping using Trugene in 2013 and have no capacity in place to perform *in house* HIV genotyping.
- In these countries, a transition plan should be developed to guarantee uninterrupted monitoring of resistance (clinical monitoring, surveillance, research).

### Options

1. **ATCC® HIV-1 Drug Resistance Genotyping Kit** (CDC HIV-1 Pan Group-M Drug Resistance Genotyping Assay) <http://www.atcc.org/hivkits>
  - The price of the sequencing module, that can process 96 samples, is \$3192 (\$66.50/sample). ATCC offers discount for high volume purchases of one free kit for every nine kits purchased (so the bulk order discount price is 59.85/sample).
  - **In Annex 1 - Materials Not Provided but Required for ATCC® HIV-1 Drug Resistance Genotyping**
  - Contacts at CDC for more information:  
Chunfu Yang [cxy0@cdc.gov](mailto:cxy0@cdc.gov) ; Zhang, Guoqing [uwz2@cdc.gov](mailto:uwz2@cdc.gov) ; Diallo, Karidia [edu9@cdc.gov](mailto:edu9@cdc.gov)
2. **Viroseq (ViroSeq® HIV-1 Genotyping System- Abbott)**
  - Also requires acquiring a new ABI sequencing machine, unless in-country provider/distributor provides it as part of an equipment lease agreement.
  - Recognized limitation of Viroseq of cut-off of 2000 viral load for amplification
3. **In House genotyping**
  - Requires transfer of capacity for In House genotyping from one of the WHO Accredited Labs with validated IH methods (CDC/USA; CHU/Martinique; Ponce/Puerto Rico; BCCE/PHAC/Canada; UFRJ/Fiocruz/Brazil and UNIFESP/Brazil – pending accreditation).
  - Next steps:
    - Share In House protocols currently in use in WHO accredited labs (ex. CHU Lab in Martinique)
    - Virtual sessions with individual labs to review lab equipment in place, assess capacity building needs for In House implementation and develop a plan to transfer the technology.
    - Workshop (hands-on lab based workshop) for transfer of technology on In House HIV genotyping to be organized in early 2015 (this will require identifying a suitable location and partners to finance the event).

- Establish EQA program (ex. twinning with WHO accredited lab; WHO accreditation program as National Reference Lab, if mandatory criteria are met: Ministry of Health designation; National plan for HIVDR surveillance and/or Monitoring implementation; At least one year experience in genotyping HIV or RNA viruses AND >100 specimens tested; Minimum infrastructure for HIVDR genotyping in place; Successful participation in the WHO HIV DR Proficiency Testing Program – see Annex 2 and 3).
4. Limited to the transition period, **sequencing of amplicons could be done by an external provider** (Ex. MACROGEN).
    - This requires shipment of amplified and purified products.
    - This requires building/transfer capacity for the preparation of amplicons.
    - All places capable of doing viral load assays could use a single round PCR amplification protocol, amplify PCR products at very low cost (using the leftover sample or even the leftover extracted RNA (if using the Abbott kit) and mail these non-hazardous PCR products at room temperature in the regular mail to a laboratory which would be willing to perform the remaining steps (BCCE offers this service at no cost). This would thus not require additional sample or cold-chain.
  5. **Next generation sequencing for HIV**
    - More sensitive (minority variants <20% of total viral populations)
    - Different assays currently available and being validated for clinical use
    - Valuable for low genetic barrier drugs (ex. NNRT used in 1st line)
    - Cheaper than traditional genotyping

A PHAC/PAHO project will introduce next generation sequencing in the region in 2015 – more details will be available shortly on this project.

## Opportunities

### BCCE (Canada)

- BCCE Lab (WHO Specialized) could make their methods and software available to any interested lab: for HIV protease/RT, integrase, V3, and gp-41 testing; access to "estimated phenotype" interpretations; software and Sanger sequencing approach. Local training available, but arrangements need to be discussed.

### Ponce School of Medicine Lab (Puerto Rico)

- A process has been validated with countries sending amplicons (after validating the PCR results using gel-electrophoresis) on filter papers (through identical process used for the DBS), followed by extraction and sequencing of amplicons (DNA sequencing and genotyping report preparation for \$35 per sample).

## Additional considerations

- The group considered that sending specimens to an external lab is not an option, in favor of building and strengthening lab capacity in the countries.



- Sequencing platforms and genotyping methods should be harmonized as much as possible among labs in the region – this may also have an impact in reducing prices in case of joint negotiation and purchase (ex. build on the experience of PAHO Strategic Fund).

**Contacts:**

Giovanni Ravasi - ([ravasigi@paho.org](mailto:ravasigi@paho.org))

George Dos Santos ([Georges.Dos-Santos@chu-fortdefrance.fr](mailto:Georges.Dos-Santos@chu-fortdefrance.fr))

**Recording of the session:**

<https://sas.illuminate.com/site/external/installinfo/playback?sid=1110&psid=2014-10-16.0610.M.09A67A345CEE43D9D2F336830FB23B.vcr>

## ***Annex 1 – Materials Not Provided but Required for ATCC® HIV-1 Drug Resistance Genotyping***

### **Equipment in Specimen Preparation Area**

- Biosafety Cabinet (BSC, level II)
- Bench top microcentrifuge, such as Eppendorf model 5417C or 5424 up to the speed of 10,000 g
- Bench top centrifuge, Jouan CR412 or equivalent
- Eppendorf Thermomixer, or equivalent
- Daigger Twist Shaker, TW3t or equivalent
- 37°C degree water bath
- Vortexer
- Dedicated adjustable P-10, P-20, P-200 and P-1000 pipettors
- Drummond Pipette Aid with Charger Stand, or equivalent
- Automate or manual RNA/TNA extractor
- Dedicated benchtop cooler
- -80°C freezer

### **Equipment in Pre-Amplification Area**

- Dead air PCR work station with UV light
- Dedicated adjustable P-10, P-20, P-200 and P-1000 pipettors
- UV Crosslinker
- Vortexer
- Bench top microcentrifuge
- -20°C freezer
- 4°C refrigerator
- Dedicated ice basket

### **Equipement in Amplification Area:**

- Thermocycler,
- Dead air PCR work station or BSC with UV light
- Vortexer
- Microfuge for PCR tubes/strips
- -20°C freezer
- Dedicated adjustable P-10, P-20, P-200 and P-1000 pipettors

### **Equipment in Post-Amplification Area**

- Thermocyclers
- ABI Sequence Analyzer (3130xl, 3500, or 3730)
- Dead air PCR work station or BSC with UV light
- Bench top microcentrifuge, such as Eppendorf model 5417C or 5424 up to the speed of 10,000 g
- Drummond Pipette Aid with Charger Stand, or equivalent
- Vortexer



- Microwave
- Bench top centrifuge with 96-well microwell plate rotor
- Dedicated adjustable P-10, P-20, P-200 and P-1000 pipettors
- -20°C freezer
- 4°C refrigerator
- Standard top-load balance
- Bioimage system or UV transilluminator
- Agarose gel separation apparatus and combs
- Power supply for gel systems

#### **Supplies for Specimen Preparation Area**

- Surgical scissors (DBS cutting)
- Aerosol barrier tips
- 1.5 sterile screw cap conical centrifuge tubes
- 15 and 50 ml sterile screw cap polypropylene tubes
- Bench top waste bag and holder
- Plastic beaker with 10% bleach
- 70% ethanol in spray bottle
- Biohazard bag with holder for tip and tube disposal
- Powder-free latex, vinyl or nitrile gloves
- Kimwipes
- Permanent markers
- Clean Blue laboratory coat
- Dedicated tube racks

#### **Supplies for Pre-Amplification Area**

- dH<sub>2</sub>O spray bottle
- Powder-free latex, vinyl or nitrile gloves
- Tube racks
- 1.5, 2.0 and 7.0 ml sterile RNase and DNase-free tubes
- Clean white laboratory coat
- Kimwipes
- Permanent markers
- Biohazard bag with holder for tip and tube disposal
- Aerosol barrier tips
- MicroAmp™ Optical 96-Well Reaction Plate/sealing membrane

#### **Supplies for Amplification Area**

- Powder-free latex, vinyl or nitrile gloves
- Clean white laboratory coat
- 70% ethanol in spray bottle
- dH<sub>2</sub>O spray bottle
- Kimwipes



- Permanent markers
- Biohazard bag with holder for tip and tube disposal
- Aerosol barrier tips

**Supplies for Post-Amplification Area**

- Powder-free latex, vinyl or nitrile gloves
- Clean white laboratory coat
- 70% ethanol in spray bottle
- 15 and 50 ml sterile screw cap polypropylene tubes
- 1.5 ml microfuge tubes
- Distilled water
- Weigh boats
- 250 and 500 ml Wheaton screw cap bottles
- 10X TBE
- UltraPure Agarose
- GelRed (10,000x stock in H<sub>2</sub>O) or Ethidium Bromide (10 mg/mL)

## Appendix 2 – Report from the Workshop on the methodology for the surveillance of HIV drug resistance in the Caribbean

JUNE 16-18, 2014

HILTON TRINIDAD HOTEL

### Background

The emergence and transmission of HIV drug resistance, in the context of universal access to antiretroviral therapy, is a major challenge, not only from the point of view of the effectiveness of the treatment in persons living with HIV, but also related to the effectiveness and sustainability of antiretroviral therapy within the context of the national programmes.

Since 2004, the World Health Organization (WHO) and partners of the global network of HIVDR (HIVResNet) have been developing a public health strategy to prevent and evaluate HIV drug resistance in countries with limited resources and within the context of the expansion of antiretroviral treatment. WHO Global Strategy for the Surveillance and Monitoring of HIV Drug Resistance was recently revised and is available on the WHO website<sup>10</sup>.

The implementation of studies for the surveillance of HIV resistance allows to generate strategic information that can be used to take public health action and control of resistance, such as the adaptation of regimens of first and second line to ensure its effectiveness in the long term; the intensification of the monitoring of viral load; the definition of the strategic use of the genotyping of HIV in countries that have this technology, among others. The information generated through surveillance of drug resistance studies can impact on policy for HIV services to improve the quality and sustainability of national programmes.

In March 2013 the Pan-American Health Organization (PAHO), with the support of other key partners, organized a Technical Consultation, in Brazil, on the HIV Drug Resistance Surveillance for Latin America and the Caribbean. The recommendations of this consultation are available on the PAHO website.<sup>2</sup> Among the other recommendations, surveillance of pre-treatment drug resistance (PDR) and acquired

---

<sup>10</sup> WHO Global Strategy for the Surveillance and Monitoring of HIV Drug Resistance: [www.who.int/hiv/pub/drugresistance/drug\\_resistance\\_strategy/](http://www.who.int/hiv/pub/drugresistance/drug_resistance_strategy/)

<sup>2</sup> Meeting report available at:

[http://www.paho.org/hq/index.php?option=com\\_content&view=article&id=8761%3Aconsulta-tecnica-sobre-la-vigilancia-de-la-resistencia-del-vih-en-la-region-de-america-latina-y-el-caribe&catid=4738%3Afch-events&Itemid=39650&lang=en](http://www.paho.org/hq/index.php?option=com_content&view=article&id=8761%3Aconsulta-tecnica-sobre-la-vigilancia-de-la-resistencia-del-vih-en-la-region-de-america-latina-y-el-caribe&catid=4738%3Afch-events&Itemid=39650&lang=en)

drug resistance (ADR) in people on antiretroviral therapy were highlighted as priority surveillance studies. The monitoring of HIVDR Early Warning Indicators still constitutes the pillar of the WHO strategy and should also be prioritized and integrated into national program monitoring and evaluation plans.

Several Caribbean countries are in the process of adaptation of the WHO generic protocols to implement surveys for surveillance of resistance at the national level. In order to promote a harmonized process of adaptation of national protocols, a workshop is being organized on the methodology of surveillance and monitoring of HIV drug resistance with the participation of representatives of the National HIV Programmes and national laboratories responsible for monitoring HIV resistance.

### **Meeting Objectives**

- To introduce participants to the updated WHO HIVDR surveillance strategies utilizing a public health approach
- To support countries in the generation of the revised HIVDR Early Warning Indicators (EWIs) and to utilize the result for programmatic improvement
- To support countries in the development of harmonized protocols for surveillance of HIV pre-treatment resistance and acquired drug resistance in accordance with the recommendations of the PAHO/WHO
- To share challenges and strategies among countries for the adaptation of protocols and implementation logistics for the surveillance of the pre-treatment and acquired drug resistance.
- To discuss methods of harmonized analysis and use of programmatic data of viral load and acquired resistance for public health actions.

### **Expected Results**

- Methodology for the defined or updated national protocols, adapted to the Caribbean, for surveillance of HIV pre-treatment and acquired drug resistance
- Recommendations developed for harmonized analytical framework and programmatic use of PDR and ADR data.
- Recommendations developed for methods of analysis of existing viral load suppression and acquired resistance data.

### **Meeting Summary**

Participants were welcomed to the meeting and the PAHO/WHO Representative (PWR) for Trinidad and Tobago, Dr. Bernadette Theodore-Ghandi brought greetings

and made opening remarks. The objectives and expected results were reviewed by Dr. Paul Edwards and participants were invited to introduce themselves.

**Session I: Introduction: HIVDR Surveillance in the Caribbean and WHO Global Strategy for Surveillance and Monitoring of HIV Drug Resistance**

***HIVDR Surveillance Experience in the Caribbean***

There were three presenters in this session, Dr. Noreen Jack, Dr. George Alemnji, Dr. George Dos Santos. They provided a summary of the background, achievements and challenges in the implementation of HIV Drug Resistance strategies and laboratory support in the Caribbean

Dr. Jack presentation focused on the history of the implementation of the 2004 WHO HIV Drug Resistance Strategy in Caribbean beginning in 2006 utilizing a public health approach. The strategies were introduced through a Caribbean sub-regional meeting in Fort de France, Martinique in May 2006. This followed by annually meetings between 2007 to 2010 to continue to increase awareness of the strategy and to support the implementation in the Caribbean. Major accomplishments during the period 2006-2012 included implementation of HIVR Early warning indicators in a number of Caribbean countries resulting in the availability of data from 58 sites in 10 countries representing 20,794 in patients on ARVs in 2008 and by 2009, 15 countries produced HIVDR reports. The HIV DR monitoring survey and the threshold study for the identification of transmitted resistance was not feasible in many Caribbean countries, however the HIVDR monitoring protocol was implemented in Haiti and Guyana.

Dr. Alemnji presented on the support provided and the progress made in the implementation of HIVDR genotyping in Caribbean countries to increase the laboratory capacity for genotyping in the Caribbean. CDC conducted a Laboratory Needs Assessment (2008-09) and identified the molecular testing challenges and the findings of this Assessment fostered the development of Caribbean HIV Regional and Sub-regional Laboratory Referral System for the Caribbean supported by CDC. This included support for the increasing molecular testing capability in Barbados and Jamaica as well as HIVDR genotyping in Barbados, Jamaica, The Bahamas.

Dr. Dos Santos presented the findings of the HIVDR monitoring survey conducted in Haiti indicating that 70% of viral load suppression was achieved at 12 months. It underscored the need to reinforce HIVDR prevention strategies, and to increase availability of viral load (VL) testing. He also provided information on the goals of the WHO/HIVResNet Laboratory Network which includes maximizing the transfer of knowledge and expertise from WHO accredited laboratories to those that have not achieved WHO accreditation.



Other studies conducted were the Mesoamerican study involving Belize and Dominican Republic as well as Central American countries and Suriname study on HIVDR transmission in antiretroviral naïve patients in 2009. There were two publications, one in the Pan-American Journal of Public Health: HIVDR Strategy in LAC: Progress Report and the second in the Clinical Infectious Diseases: Supplement on WHO HIVDR Strategy: Global, Regional and Country Progress on the implementation of HIVDR EWIs in the Caribbean

### ***WHO Global Strategy for the Surveillance and Monitoring of HIVDR and Recommendations for LAC***

Dr. Ravasi's presentation focused on the revised WHO HIVDR Strategies 2014 which included the updated HIVDR EWIs and the new surveys. These new protocols include nationally representative surveillance surveys of acquired and pre-treatment resistance. The presentation provided a summary of the scale up of people on ART in LAC (2013 update) with an estimated 765,000 eligible PLWH on ART at the end of 2013. With the new WHO 2013 treatment guidelines (i.e. tx indicated at CD4 count of 500), The coverage of ART in LAC has been reduced from 71% (eligibility based on 2010 WHO guidelines) to 48% treatment coverage (eligibility based on 2013 WHO guidelines). There was a median of 80% retention on ART at 12 and 24 months after initiation of ART, however many Caribbean countries are below 80% indicating most lost to follow-up occurs before 12 months of initiating ART. A median of 66% of patients on ART have achieved viral suppression.

The new WHO HIVDR Strategy (2014) was published in 2014 following review of the previous strategy by WHO and partners. In addition to the pre-treatment and the acquired HIVDR surveys it included the transmitted Drug Resistance (TDR) and the Pediatric (or initial) HIVDR survey. Instead of surveillance aiming just to identify the presence of resistance it was updated to quantify the magnitude of resistance using point prevalence within confidence interval limits. The new surveys reflect a change from area-specific or even clinic specific surveys to truly nationally representative surveys that can provide information on national programme functioning. With respect to EWIs, the change is from an assessment of EWIs as a vertical effort towards integration of EWIs into the broader M&E framework of the national programme. In the past, the surveys were only feasible in generalized epidemic and the new surveys are more applicable to all types of epidemics. In addition, whereas the previous surveys took a long time for implementation with results being realized up to 3 years, the new surveys generate results within 12 months. The new WHO HIVDR strategy (2014) is reflected in the 2013 WHO clinical guidelines in Chapter 11 *Monitoring and evaluation of universal access to treatment*, which has several components, including: Indicators for programmatic performance; Cascade of the

continuum of care; HIVDR surveillance; Pharmaco-vigilance; and operational research.

The recommendations arising from the LAC regional meeting held in Brasilia, Brazil in March 2013 were also presented. At this meeting the priority surveys identified for adoption in LAC were pre-ART or pre-treatment drug resistance (PDR) and acquired drug resistance (ADR) surveillance (including viral load suppression analysis). Lower priority was given to the transmitted drug resistance (TDR) surveillance and initial drug resistance in children less than 18 months. It was agreed that there should be standardize analysis of data for comparability; the use of programmatic data, if available and complete and reliable as in the case of determining acquired HIVDR. The recommendations included maintain HIVDR EWI monitoring as pillar of the strategy.

### **Discussion, Recommendations and Conclusions**

#### Scale- up of HIVDR Strategy

- Advocacy with CMOs and Ministers of Health and donors is required on the importance of HIVDR surveillance. This includes the allocation of national and technical cooperation funds for HIVDR surveillance and ensuring sustainably beyond donor funding. Strengthening communication and collaboration between programs and experts/universities for enhanced horizontal cooperation.
- Optimize strategic use of ART (Treatment 2.0) and improve long term effectiveness of treatment is key to prevent HIVDR emergence and transmission. Creation of National Working Groups (can be sub-committee of existing working group) at country level and which should include donors to support internal and external mobilizations of funds.

Countries should implement HIVDR surveillance and use data to support the process of ART guidelines update. Of countries present, the following are currently producing HIVDR EWI Report include Jamaica, Barbados, Guyana, Dominica and Grenada. HIVDR surveillance protocol methodologies should be harmonized among countries.

- Training of clinicians on interpretation and use of HIV genotyping results and programme managers/epidemiologist on Epi analysis, interpretation and use of HIVDR surveillance data for public health actions.

### Laboratory capacity

- Strengthening of national laboratory capacity for viral load (VL) and HIV genotyping is important in the Caribbean. Promote initiatives of horizontal technical cooperation among countries to support transfer of technology and capacity. Technical cooperation opportunities are available (WHO network, regional TCN Network) to support implementation in countries with limited capacity and resources
- Establish HIVDR genotyping facilities to perform testing at competitive prices or reduced cost. Where possible, save financial resources through the utilization of dried blood spots. Cost reduction of commercial kits is required to make HIVDR genotyping more affordable in the Caribbean. HIVDR clinical testing of patients' samples to commence in Barbados and Jamaica. Engage discussion with CARPHA (in charge of Regional Lab Network) on strategies to ensure access to HIVDR services for other countries in the region
- Participation in external quality assurance programs is a key component of efforts to ensure the quality of genotyping results and a common approach for quality assurance for genotype testing is needed. The Caribbean region has technical and financial capacity for HIVDR surveillance, but with disparities among countries.

### **Session 2: HIVDR Early Warning Indicators and Cascade Analysis for Programmatic Monitoring**

#### ***HIVDR Early Warning Indicators and Cascade Monitoring Framework***

Dr. Ravasi presented details on the HIVDR EWIs, the continuum of case cascade and monitoring framework: PAHO/WHO has released a new (2014) publication "HIV Continuum of Care Monitoring Framework 2014" with standardized definitions for cascade indicators and prioritized monitoring indicators. For the continuum of care, all countries should be able to build their national cascade analyse to guide programmatic improvement. Once specific gaps are identified, there are additional indicators that may be utilized to explain the gaps, as indicators of access, treatment coverage, quality of care, and other additional indicators. These additional indicators fit under each pillar of the cascade. The six pillars of the cascade are:

- Pillar 1: Estimated # of people living with HIV. (Data source: Spectrum or other estimation process.)



- Pillar 2: # of people diagnosed and **alive** in the analysis year. (Data source: HIV case-based surveillance systems or integrated systems). This indicator links to two important Global 2020 goals: (1) Expand testing such that 90% of PLHIV are diagnosed and (2) Reduce the number of people diagnosed at CD4 <200.
- Pillar 3: PLHIV linked to HIV care where the numerator can be based on CD4 count, VL test or ARV pick-up at least once in the reporting year. (Data source: Health facility registers or PMS, or lab/pharmacy/ARV logistics information system). Calculation of this indicator will depend on the most reliable and complete information system in each country, and reports should include a technical note explaining how the indicator was calculated.
- Pillar 4: PLHIV retained in HIV care: Numerator defined as # of PLHIV in treatment services with 2 or more consultations/CD4 counts/VL measurements/ARV pickups in the last 12 months.
- Pillar 5: PLHIV on ART, defined as # of eligible PLHIV currently receiving ART at the end of the reporting period. Source: (Facility-based antiretroviral therapy registers drug supply management systems.) This indicator aligns with Global 2020 goal 3 (increasing persons on ART to 90%), however we must note that the treatment cascade and the indicator for the goal use different denominators, e.g. the 90% for eligible people on ART will equal about 80% of total PLHIV.
- Pillar 6: PLHIV with undetectable viral load, where the numerator is # of patients with a viral load under 1000 copies/ml in the last test in the reporting year. (Data source: Health facility registers or PMS or lab info system). This indicator aligns with Global 2020 goal 4 (to have 90% of persons on treatment with undetectable viral load), however we must note that the treatment cascade and the indicator for the goal use different denominators, e.g. the 90% for people on ART virally suppressed will equal about 70% of total PLHIV.

The new EWI guidance was published in 2012; these were revised based on challenges observed with reporting for the older set of indicators, and were evaluated using the GRADE methodology. Score card using a colour coding indicate where there are areas for concern: Red, yellow, green and gray. Sample sizes for indicator calculation (at each clinic site) are based on the number of people starting ART at the clinic site in the previous year. The new EWIs are

- EWI 1: On-time pill pick-up
- EWI 2: Retention in care: # or adults and children who are still alive and on ART 12 months after initiating treatment
- EWI 3: Pharmacy stock-outs
- EWI 4: ARV dispensing practices, defined on % of patients on HAART who pick up from the pharmacy a regimen consisting of one or two ARVs.

- EWI 5: Viral suppression at 12 months, defined as % of patients receiving ART at the site after the first 12 months or ART whose viral load is <1000 copies/ml.

The approach towards implementation of the new HIVDR EWIs is through the integration into national M&E frameworks.

*Country experiences were documented through presentations from Barbados, Jamaica and Suriname.*

**Barbados:** Dr. Anton Best, Senior Med Officer of Health (CD), MoH Barbados presentation focused HIVDR EWIs and on the continuum of care looking at both a cohort approach (new cases in a given period) and a prevalent group. Based on people diagnosed in 2012: 133 people diagnosed with HIV; 81% linked to care within 6 months; 82% linked to care; 68% eligible for ART (based on CD4 count of 500); 59% prescribed ART; 43% virally suppressed. When looking at the entire cohort diagnosed with HIV in Barbados: 2200 estimated to be living with HIV; 2024 diagnosed; 67% linked to care (defined as those registered at the HIV care clinic); 55% retained in care; 46% on ART (as per HIS data); 39% virally suppressed (at threshold <1000 copies/ml). Review of Barbados data against the LAC 90-90-90 targets: Barbados does not meet the target 2 or 3: of 90% of eligible people on ART (based on CD4 count of 350) or the target of 90% of people on treatment virally suppressed. However, given that the targets are set for 2020, Barbados is already close as both indicators are high 80%. The analysis performed focus on the previous WHO indicators. Challenges noted: Indicator on stock-outs was very intolerant and did not allow for substitution practices used in Barbados with particular drugs were not available. Barbados published an article entitled “Ten year trends in community HIV viral load in Barbados: Implications for treatment as prevention” by Landis RC et al, PloS On 8(3):e58590. Doi”10.1371/journal..Pone.0058590. Planned next steps include:

- Incorporating the cascade of care data into annual HIV survey reports.
- Complete HIVDR survey monitoring
- Implement HIVDR lab testing by Dec 2014.
- Incorporate the EWI into annual HIV survey reports.

**Jamaica:** Dr. Sasha Martin, MoH Jamaica presentation began with the epidemiology of HIV in Jamaica indicating a generalised epidemic, less than 2% prevalence in the general population, but much higher in key populations (e.g. 32% in MSM; 4.1% for FSW). Vertical transmission has decreased from 22% in 2004 to 2.4% in 2012 (based

on public sector data). HIV prevalence among public antenatal clinic (ANC) attendees has declined to less than 1%. HIV remains one of the 10 leading causes of death in Jamaica. Epidemic driver remain multiple partnerships, early sexual debut and other behavioural factors. Since 2004, the number of deaths have reduced to less than half of the number of cases, however an increase has been observed in AIDS cases. Continuum of care was presented with an estimated 30,265 PLHIV; 72% diagnosed; 58% linked to care; 30% retained in care; 26% on ART; 14% virally suppressed. Key findings are a gap in people who know their status; low retention in care; viral suppression is low – adherence levels are questionable as they are based on pill counting and self-reporting. A pilot (cross-sectional) study conducted provided some preliminary evidence of 12.6% of treatment naïve patient with transmitted DR. Findings were published in Antiviral Therapy 2013 (Author: Barrow, Hylton-Kong, Figueroa). Early warning indicators: Calculated using the 2013 WHO guidance. Data was not available for one indicator (on-time pick-up), however there are opportunities to start reporting on this indicator using treatment site database data on prescriptions. This will require linkage to pharmacy pick-up data to properly report on this indicator. For the stock-out indicator: There was one stock-out, however this was handled with routing of meds from other clinics.

**Suriname** Dr. Ward Schrooten presented on behalf of J.Roosblad, MoH, Suriname

Dr. Schrooten provided an overview of available HIV data in Suriname. Initially existing data sources were compared to separate “data islands”, ie they have been collected independently for many years. To report on the cascade, the data islands needed to be linked; this was possible because all data islands use the same data codes. Some challenges were:- There was no patient master index (i.e. no one island contained a comprehensive list of all patients) and this had to be created in order to measure cascade indicators; over time, the patient identifier method was changed; there were some data errors in the unique code; there was no gold standard to use to resolve code errors. Results (2007 to 2013): 83% linked to care within 6 months; 44% retained in care (or 60% if measures other than CD4 counts were used for this indicator); 45% of those eligible were on ART; 24% virally suppressed.

### ***Information Systems for HIVDR EWI and Treatment Cascade Analysis***

Dr Schrooten presentation provided a background into surveillance in the Caribbean. In the early 2000s, most countries in Caribbean region were using 1<sup>st</sup> generation HIV surveillance. In 2007, patient monitoring was launched, which included the use of HIV case-based surveillance. Currently, more and more countries are working

towards or implementing health information systems (HIS). For countries with HIV case-based surveillance and/or patient monitoring systems in place, the key data elements needed for cascade generation are available (although some improvements may still be required).

The necessary data elements are: Patient characteristics; date of diagnosis; VL results and dates; visit dates in care, CD4 dates and results, VL dates and results, ART treatment history, date and reason (deceased, transfer out, LTFU) of drop-out. Each data element must have the following components: Unique ID-Date-Attribute-Value, e.g. for CD4 data: 576-8/June/2014-CD4-432. With such info, info can be transferred to different/new database systems. Unique IDs are ideal and should be instituted as part of a systematic approach (not just a code) with standardized formats and attributes. Analyses can be conducted in any platform however the key is to have analysis code available to allow for automated analyses. Reporting: Multiple reports are used by countries to inform their programs e.g. Epi profiles, HIVDR EWI, Treatment cascades. In addition, it's important to remember to provide feedback to data providers and to patients, and to participate in benchmark initiatives (i.e. comparisons to neighbouring countries).

Country Experiences--Dominica and Antigua & Barbuda,

**Dominica:** The experience in implementation of health information systems in Dominica were presented by Dr. Paul Ricketts, MOH, Dominica. The rationale for information system strengthening is to improve efficiency in collecting and collating data and the automation of databases should mitigate the impact of human resource challenges. An experience in implementation of unique identifier was presented with its implications for linking data and generating reports. Unique ID for OECS countries will include country specific codes to accommodate patients moving between countries. Legislation has to be passed for this system. Revision of case based surveillance manuals has been conducted for OECS countries, reviewed by key partners (95% finished), but now need to include updates coming out of this meeting. A Caribbean sub-regional approach to informational systems development has been in process since 2006. A TWG is in place and road map developed. Legal framework needs to be addressed and harmonised. Challenges: Legal framework needs strengthening and the private sector providers do not report; competing priorities; limited financial and human resources. The HIV module is the next step to be implemented in Dominica HIS and the PM1.3 database will be incorporated into medical record systems. Change management will be critical to encourage use new system.

**Antigua:** Dr. Makinde, MOH, Antigua and Barbuda made the presentation indicating there were challenges with retrieving the data due to elections on the island. She reported there was no integration of the various databases and the system does not automatically collect all data elements to generate the EWIs or Treatment Cascade. Hope to have better information in the future. Stats presented identified gaps in available data. It was noted that more data available in country for Antigua and the analysis can be re-run to generate the treatment cascade.

**Jamaica Quality improvement collaborative project (JAQIC)- Dr. Clive Anderson , CHART, RCU, Jamaica:** CHART is working on collaborative quality improvement model, which involves shared learning to achieve significant improvements. It included learning by doing and from each other. The project utilizes data at front line and changes implemented based on the findings. The methodology includes creating a group of health care workers (HCW) with capacity and interest in improving quality of care. Use of data to recognise deficit in CD4 testing and aimed to improve CD4 testing in a short space of time as levels were low. Teams formed including persons who were important to improving the process of CD4 testing and included patients, drivers, etc. Process analysed from moment when test should have been ordered until the point when a result is returned to the patient. The data analysis has so far demonstrated the biggest gap is persons being lost to care. The findings included improved team-work in HIV treatment and care, Empowerment of front line staff and giving them ownership of their data and interest in it; Ensuring Quality of Care is maintained or improved as decentralisation takes place. The initiative required time and team effort, but not lots of external resources. The study is being expanded to other islands and will utilize reporting on reporting on EWIs.

## **Discussion, Recommendations and Conclusions**

### **Continuum of care/Treatment Cascade and HIVDR EWIs**

- The full monitoring framework and EWIs give more details regarding access, coverage, quality and prevention of drug resistance. The construction and annual update of the “cascade” gives a full picture of the continuum of HIV care at national level, highlights and measures existing gaps.
- How to manage the issue of difference in eligibility for treatment between countries and the ensuing gap that will be represented within cascade data? As per WHO, this gap is an acceptable and explainable one as it is influenced by country treatment



protocols/guidelines. The gap of concern is the gap between pillar 3 (linked to care) and 4 (retained in care); in the region, the countries with cascade data have shown that this is where the big gap occurs, which indicates a problem with the care programs for those not yet eligible for treatment.

- In-country analysis should be conducted by the local team. Ownership of data by team is important. The hope is that participants of the workshop will review their data as a team when they return back in country. Participants attend meetings; develop plans; but practicalities of situation render work done at these meetings less than useful. Implementation deficits
- Monitoring of indicators at national level, as well as at each ART site will provide evidence for prioritization of interventions (“what and where”). There is a poor job of analysing data and getting reports frontline workers.

#### Information systems

- Information systems should be strengthened to support data analysis both at local and national level. An important issue to recall is the issue of data security and privacy, to ensure no confidentiality breaks.
- How to we move forward with integrated health info systems and away from vertical HIV systems? Developing integrated systems is not easy. Different health practitioners have very different information requirements. As such, it is difficult to find one system that collects all information that is useful to different practitioners. There is currently no simple answer or system that works for all; there is no perfect system out there. One simple strategy used in Norway and Denmark is that different info systems are linkable, i.e. data can be transferred/shared between different systems due to existence of unique id and standardized/defined data elements.

### **Session 3: Introduction: Pre-treatment HIVDR Surveillance**

#### **Pre Treatment HIV DR surveillance -Survey overview and design**

Dr. Ravasi presented an overview of the pre-treatment HIVDR survey. The aim of this survey is to determine the prevalence of HIV DR in persons starting treatment to guide choices of first line therapy. Eligible participants include naïve patients and those re-starting therapy (those who discontinued treatment for > 3 months and restarted first line). Results are calculated within a 95%CI point prevalence. Majority of countries in the Caribbean considering implementation of this study have less than 15 sites.

**Trinidad and Tobago:** Dr. Ayanna Sebro presented the preliminary calculations and issues for implementing the pre-treatment protocol in Trinidad and Tobago. There were challenges with data to generate treatment cascade and case based surveillance is in the process of being strengthened to improve linkage to care. Questions for consideration in the protocol adaptation included “Should immigrants who may or may not admit previous treatment be included? The hospital is to be considered to be one of the sites for sampling as some eligible patients may be first identified there. Queries were raised on proportion of patients diagnosed that make it into treatment and proportion missed if clinic alone sampled was noted. It was suggested that patients eligible for treatment should be sampled prior to starting care despite the query on whether to consider them pre-treatment or not, since they didn’t start treatment. It was further suggested to analyse this sub-group that did not start treatment separately.

**Jamaica:** Dr. Michelle Hamilton presented for Jamaica indicating that Jamaica does in-house HIV DR testing using the CDC in-house protocol and they are working toward validation. A preliminary study conducted in Jamaica identified transmitted drug resistance discovered to be ~12.6%. Jamaica has developed a protocol with CDC to measure pre-treatment and acquired HIVDR. The study has a cross-sectional and longitudinal component and the exclusion criterion was HIV infected pregnant women many of whom are having a repeated pregnancy. The study includes 9 sites that represent what 80-90 % of the patients on treatment.

### **Working Session on the Development of National Protocols for Pre-treatment HIVDR Surveillance**

There was a working group session with countries for preparation for implementation of the re-treatment surveys utilizing prepared tools and country data to calculate the sample size required and the distribution of potential study patient in the various treatment sites in country. Countries then summarized the key findings in plenary and the key issues are highlighted below:

- 
- Most countries (except Dominican Republic) have less than 15 sites nationally.
  - What happens in countries with one site or very small populations?
  - PPS can still be used if island populations are pooled. Country level makes more sense for programmatic interventions, unless countries share programmatic planning when combined sampling etc. could be used.
-

- Pooling of data does not allow site-specific analysis, so it may not be feasible to get accurate individual estimates for a given country if you pool sites in the OECS countries?
  - Does DBS versus Plasma testing provide the same results on HIVDR genotyping
  - What is the budget for the study? Important to note how region can benefit from existing infrastructure for HIVDR genotyping in Jamaica and Barbados
  - Ideal source of info for calculation is # of initiators at each clinic. Less optimal is number of persons on treatment
- 

#### **Session 4: Acquired HIVDR Surveillance**

**Session Presenters:** Dr. Natalie Exner, Dr. Giovanni Ravasi;

##### **Acquired HIVDR Surveillance: Survey overview and design**

The overview of the acquired HIVDR survey was presented by Dr. Exner and the aim is to calculate nationally representative prevalence estimates of viral load suppression and of HIVDR in populations receiving ART for two time points - 12 and for 48 months or more. The outcomes for the survey include viral load suppression (Outcomes 1a, b, c), retention measures (outcomes 2a, b, c) and prevalence of HIV DR among patients who have been on ART (outcomes 3a, b, c, and outcome 4). It is important to account for people who are not retained (i.e. die or are lost to follow-up) in order to properly assess the level of viral load suppression. This allows for comparisons between countries and over time. Two possible sources of data for outcome 2a: Census (all patients) or survey. Key characteristics of the survey approach: Randomly sample clinics from a list of ART clinics in country; clinics selected proportionally to the number of people accessing ART; select patients and have sample tested for DR (based on eligibility). The survey calculator is provided by WHO, with parameters adjustable for country context. WHO recommends repeating the survey every three years.

##### **Use of programmatic data for ADR surveillance**

Dr. Ravasi presented an alternative approach to determine acquired drug resistance utilizing programmatic data where there is routine viral load testing. Outcomes 1 a, b, and c are indicators that should be feasible to calculate using program data, given that VL testing is now done routinely. Key questions to assess feasibility of using



programmatic VL data: Is VL testing available to all treatment sites? How complete is the data on VL, i.e. is the information system national in scope or just based on selected treatment sites? What is the quality of the available VL data?

Key questions to assess feasibility of using programmatic genotyping data: Is genotyping testing available to all treatment sites? What proportion of people with virologic failure have genotyping tests performed? How complete is the data on genotype results i.e. is the information system national in scope or just based on selected treatment sites? What is the quality of the available data?

### **Working Session on the Development of National Protocols for Acquired HIVDR Surveillance**

Group work by countries allowed countries to consider the feasibility of implementing the ADR surveillance utilizing the survey approach or the programmatic data. Countries then presented their findings in a plenary session that followed. The following were the key discussion points and issues: ns:

- WHO change the methodology from the longitudinal survey to this cross-sectional design based on feedback from implementing countries on challenges experienced and the modified protocol is seen to be more feasible while still providing sufficient information for action in a timely manner.
- If viral load is performed at least annually as part of clinical care with a high coverage of patients (with VL and genotyping testing) and high quality data, then programmatic data can be used rather than survey.
- Many Caribbean countries have small number of treatment sites which would necessitate them doing a census of patients as opposed to sampling
- Can this ADR survey be used to look at DR for specific populations? A: While it would be possible to look at the data stratified by population, the current tool for sample size calculation is not geared for that purpose, and so the sample size for national estimates would not be sufficient for population-specific outcome estimates.
- Participants were asked to what extent is genotyping influencing care for PLHIV?
  - TT: Genotyping is done for special cases, e.g. medico-legal cases, cases from outside of country which limited available info on their infection, and cases put on ART where limited response occurs.
  - Barbados: Samples are taken for surveillance purposes, but genotyping is done only for cases that are failing (i.e. for clinical purposes) either to influence choice of medications or to validate regimen already prescribed.
  - Currently, WHO does not recommend routine genotyping for all patients suspected of failing therapy . The recommendation is to start patients on



first line therapy, and if that fails, to move to 2<sup>nd</sup> line. Genotyping is indicated is patients failing 2<sup>nd</sup> line therapy.

- How comprehensively is VL testing done for patients and what are the issues that influence VL testing? A: In country examples given, there are logistical issues that influence how frequently VL testing is done for patients. In the Jamaica example, the quality improvement project conducted by CHART showed improvement from 30% to almost 60% of patients with VLs being done. Logistical issues that hinder testing range from lab related issues (e.g. running out of reagents), to facility issues (e.g. physicians forgetting or otherwise deciding not to order VL tests), to patient issues (e.g. challenges getting time off work for test; costs for transportation from remote areas; frustration from previous tests for which samples were not successfully tested or fear of needles (so skipped tests)).
- What are the arrangements for genotyping data ownership? A: In the Jamaica DR protocol, it is stipulated that the lab data (from the CDC lab) are the property of the MoH Jamaica, and the CDC will not publish or report on the findings without agreement/collaboration with the MoH Jamaica.
  - How will countries support ADR which is done every three years for public health purposes? And how will countries support DR testing done for clinical purposes (presumably using the regional labs in Barbados and Jamaica, when they achieve accreditation)? A: This discussion must be included in future discussions of the Caribbean Laboratory network

## **Session 5: HIVDR Surveillance implementation and technical cooperation and support**

### **HIVDR surveillance implementation and technical cooperation and support**

Drs Alemnji and Dos Santos presented complementary sessions on the laboratory logistics or implementation of these surveys. Dr. Alemnji highlighted the operational preparations for national laboratories supporting these surveys. They are as follows:

- Need to set up a functional laboratory referral and backup system (i.e. a functional lab network)
- Ensure clearly defined SoPs and other working documents are in place
- Ensure maintenance of the cold chain, especially at the airport
- Train staff on:
  - Biosafety and biosecurity
  - Shipment of infectious substances
  - Molecular testing

- HIV DR protocol development and implementation
- Quality assurance
- Formalize discussion on sample transportation with airlines and courier companies (LIAT, Caribbean Airlines, DHL, etc)

Dr. Dos Santos highlighted the sample collection through to testing logistics indicating that all steps should include quality assurance with an organised way to record, store and retrieve data associated with pre-testing, processing and post-testing info

- Minimum data to be collected include:
  - Informed consent; clinic ID, patient ID, prior ARV exposure, type of ARV exposure; age, gender, CD4 count before ART initiation; regimen prescribed
  - A questionnaire to apply to summarize patients information at the time of study enrolment to collect data as Clinic ID, Patient ID , Prior ARV exposure (yes/no/unknown; and if yes Type(s) of prior ARV exposure: PMTCT, prior ART for one's health, PrEP, PEP, unspecified, more than one type of previous exposure), Age, Gender (female/male/other), CD4 count before ART initiation (if results are already available and are from a test performed less than six months prior to survey enrolment), Regimen prescribed: list drugs prescribed.
  - Laboratory information: Specimen ID, Reverse transcriptase (RT) region of pol gene successfully sequenced? (yes/no), Protease (PR) region of pol gene successfully sequenced? (yes/no/NA), Drug resistance results according to the Stanford database algorithm interpretation.
  - Clinic-level information: Clinic name, Clinic ID, Date when specimen collection started (DD/MM/YYYY), Date when specimen collection ended (DD/MM/YYYY), Date when patient screening ends (DD/MM/YYYY), Number of ART initiators between date when specimen collection started and patient screening ended (if specimen collection ends earlier than three months), Estimated number of ART initiators during the six- month period, Clinic size as contained in the table used for systematic sampling, Type of clinic: urban/rural
  - WHO recommended survey ID should include: ISO standard country abbreviation; survey type (ADR or PDR); year survey started; site abbreviation; 4-digit unique patient number e.g. TRT-PDR-2014-POS-0001
- There should always be a back-up of the data



- Specimen management (at the lab) involves eight steps: collecting samples, receiving, evaluating quality, labelling, pre-testing storage and generating pending list, communication and turn-around time, inventory and post-testing storage, disposal. DBS or plasma can be used for genotyping (see WHO guidance). DBS can be made from venipuncture samples collected in an EDTA tube, or from a finger (or heel) prick; It is recommended to keep a duplicate sample be kept in the home laboratory in case something happens to the specimen being shipped. The movement of samples through to lab processing should be tracked using a lab tracking form (see slide with example from Haiti)
- When preparing the SoP for specimen shipment, the entire path should be traced. Ask the questions: What happens to the specimen during shipment? What could happen to the specimen to compromise lab safety or testing quality? When preparing SoPs it is helpful to develop flowcharts that describe all stages of the process, from inclusion of the patient through to genotyping, outlining the SoP, tools, equipment, etc needed for each step.
- Plan evaluation of the implementation (e.g. half way through the study) to have a chance to implement corrective actions as identified.

#### Questions from participants:

- Besides VL testing, the only additional lab technology necessary will be genotyping? What capacity is there in the region for genotyping?
- For VL testing, wouldn't it be better to support routine VL monitoring for patient management, rather than conducting special surveys? Where should emphasis be placed? More viral load tests and genotyping per patient, versus fewer VL tests and moving on to genotyping?
- Some participants were happy that HIVDR surveys are now applicable to smaller countries.
- Question regarding discussion between partners and countries regarding fund raising for HIVDR surveys.
- Dr. Dos Santos reminded participants of the continuing offer to the OECS countries to send samples for HIVDR genotyping. CHU Martinique is still able to continue providing genotyping support to the OECS.
- Continuity of service is a problem: Laboratory training (e.g. for VL) usually involves one representative per country. As such, all testing stops when the people leave, either on vacation or permanently.

<b>Country</b>	<u>Outcomes of Working session on next steps towards implementation</u>	<u>In –country follow-up action and specific TC request</u>
<b>OECS</b>	<p>OECS participants have determined that the protocols for PDR and ADR surveys are feasible, and that the OECS will proceed together with one cooperative endeavour. Each country has a small sample size and challenges in access funds for laboratory testing.</p> <p>Partners identified: OECS MoH (lab and Epi) as the leads, PHAC and Service Virologie, Centre Hospitalier Universitaire de Martinique as co-investigators</p> <p>After approval has been obtained, each of the meeting participants will determine key in-country focal points as co-investigators. In particular, it will be important to ensure identification of a laboratory-based focal point, and if appropriate/necessary, a clinician from key HIV private practice.</p>	<p>PHAC will provide technical assistance for development of a protocol to encompass PDR and ADR surveys for the OECS</p> <p>OECS participants to establish if there is approval in-country (from the PS) for implementation of the DR studies (by July 4); Paul Ricketts to liaise with James St. Catherine (OECS HAPU) to obtain letter of support for outcome of this workshop.</p> <p>Martinique is able to support ongoing genotyping testing (in general and for the PDR survey, A decision was made to prepare an OECS-wide protocol (for external funding, possibly from Martinique) which will cover the implementation of pre-treatment DR and ADR.</p>
<b>Bahamas</b>	<p>Discussions focused on ensuring that data collected in country is suitable for reporting on EWIs.</p> <p>The Ministry of Health supports the implementation of HIV DR surveillance, and as such, are setting up a platform for DR testing</p> <p>Bahamas lab will embrace the opportunity to increase collaboration with other laboratories in the region</p>	<p>Internal discussions are needed to determine whether the ADR surveys are a priority, are feasible and will be implemented. There is a need to determine if the WHO protocols are a good fit and will provide the needed information for the Bahamas.</p> <p>No specific TC identified.</p>
<b>Guyana</b>	<p>DR studies using the previous WHO protocol have been completed recently, and there is now a need to conduct data</p>	<p>Technical assistance is needed for data analysis, and has been requested from Giovanni (PAHO).</p>

	<p>analysis. Results from the analysis will inform prioritization of future DR monitoring studies needed.</p> <p>In the future, for conduct of the DR surveys as outlined in the revised protocol, funding will be required; financial assistance will be needed for shipment of samples in future studies.</p>	<p>Will need to take up discussions in-country with the HIV technical working group to obtain directions on conduct of these surveys, and then approach PAHO counterparts to obtain funding</p> <p>Used the tool to developed sample size estimates for both the 12 and 48 month PDR, however will need to improve available data to have reliable estimates for some of the sample size parameters (e.g. patients on first line treatment).</p>
<p><b>Jamaica</b></p>	<p>Jamaica is poised and ready for implementation of HIV DR studies and will proceed as planned. Upon completion, results will be reviewed against the objectives of the revised guidelines, in order to identify any gaps to be addressed in the future with different surveys.</p>	<p>During the discussion session, some consideration was given to expanding the current site sample plan for the threshold survey to incorporate an additional sub-sample for the pre-treatment DR.</p> <p>After feedback the decision was to develop a new study for PDR (approximately 500 patients for the 12 and 48 month time periods), if funding is available to support it. If there are no external funds available, then the approach for decision making will be based on in-country decision on the priority for this activity over other on-going work.</p>
<p><b>Barbados</b></p>	<p>Samples have been taken from patients (in public sector) and archived since 2008; there are currently almost 500 archived samples; patients from private sector (&lt;5% of patients) do not have specimen taken for DR.</p> <p>Currently, samples are sent to BC Centre of Excellence for DR testing, for clinical purposes, when patients are failing treatment</p>	<p>The WHO protocol is seen as being feasible, however the surveys as prescribed may not be necessary. A protocol already exist in-country for collection of DR samples, and assistance may be needed for engagement of private practices in adoption of these protocols.</p> <p>Cooperation will be needed for the</p>

	<p>In the meantime, may consider use of archived samples for a cross-sectional retrospective survey using the WHO protocol</p> <p>Review of the WHO protocol revealed that there is a need to use the census approach applied to samples already collected from all patients.</p>	<p>laboratory and surveillance aspects</p> <p>May need to secure external funding for sustainability of these programs</p> <p><b>Need to sensitize policy makers on the need for HIVDR monitoring. External partners can assist with advocacy with ministers of health and chief medical officers of health.</b></p>
<b>Trinidad and Tobago</b>	<p>There is an interest in conducting these surveys, however there are gaps in the data needed to inform protocol development.</p> <p>PDR survey is feasible. ADR analysis could be attempted using existing data (genotyping performed at treatment failure).</p>	<p>Advocacy at MOH level is required to guarantee political support and strengthen collaboration of ART sites.</p> <p>Technical support from PAHO and genotyping performed at WHO Lab in Ponce.</p>
<b>Dominican Republic</b>	<p>The data on DR is needed given that treatment started eleven years ago and so far no nationally-representative DR studies have been done. In a special (academic study) done, some HIV DR was detected in ART naïve patients.</p>	<p>The exercise for sample size calculation was successfully completed, based on 20 treatment sites. Will need to go back in-country to get input from the national HIV working group on whether this exercise will be prioritized for implementation.</p> <p>Support is needed for genotyping testing as VL testing is already done in-country. Support from US-CDC, PEPFAR, PAHO or any other agency would be welcomed.</p>
<b>Suriname</b>	<p>A draft protocol exists for pre-treatment DR monitoring; study is being funded by US-CDC. Samples will be sent to Puerto Rico.</p>	<p>No specific TC identified</p>

--	--	--

**Conclusion:**

- The exercises demonstrated that the protocols are feasible for use by the Caribbean countries
- One major issue is the financial support necessary for these surveys, which will impact the feasibility of implementation of the surveys.
- Important to answer the questions: Who is this data for? Who will use these data? If high prevalence of HIV DR is observed in a country, what will be the response of the government? Will there be programmatic impact?

**Closure remarks**

**CARPHA:** With ongoing transition, discussions are still ongoing to establish roles and responsibilities in HIV DR monitoring and for other diseases in general.

**CHU Martinique:** Happy to see the outcomes of this meeting and will continue to provide support for genotyping, as per previous arrangements.

**UNAIDS:** The representatives were happy to be involved in the meeting and saw the meeting as catalytic for HIV DR monitoring further implementation in the Caribbean. They look forward to working with PAHO and CARPHA in the area of laboratory strengthening as the cornerstone for quality of care for HIV patients. They will also will continue to work with regional partners in the area of information management.

**CHART:** Starting a regional collaborative on that are of early warning indicators, and look forward to sharing some results in the future.

**PAHO:** Will continue to provide technical support for the implementation of the revised WHO strategies assisting countries with protocol adaptation and support for in country implementation.

## Appendix 3 – Abstract from the meeting report: HIV Care and Treatment Retargeting and Improving Access and Quality of HIV-Related Point of Care Testing in the Caribbean

### Session 3: HIV Drug Resistance

#### **Presentation - HIV Drug Resistance Prevention and Surveillance: Report from Sub-regional workshop on HIVDR Surveillance.** Presenter – Avery Hinds, CARPHA

CARPHA provided a summary of the HIVDR meeting which was held in June 2014. Below is a summary of some key points presented:

#### **General recommendations on HIVDR surveillance**

- Advocacy with CMOs, Ministers of Health and donors is required on the importance of HIVDR surveillance, especially for the allocation of national and technical cooperation funds for HIVDR surveillance and ensuring sustainably beyond donor funding.
- Creation of National Working Groups (can be sub-committee of existing working group) at country level, which should include donors to support internal and external mobilizations of funds. Strengthening communication and collaboration between programs and experts/universities.
- Countries should implement HIVDR surveillance and use data to support the process of updating the ART guidelines. HIVDR surveillance protocol methodologies should be harmonized among countries.
- Optimize strategic use of ART (Treatment 2.0) and improving the long term effectiveness of treatment is key to prevent HIVDR emergence and transmission.

#### **HIVDR Surveillance in the Caribbean and WHO Global Strategy for Surveillance and Monitoring of HIV Drug Resistance**

#### **Key recommendations on laboratory capacity**

- Strengthening of national laboratory capacity for viral load (VL) and HIV genotyping.
- Promote initiatives of horizontal technical cooperation among countries to support transfer of technology and capacity. Technical cooperation opportunities are available (WHO network, regional TCN Network) to support implementation in countries with limited capacity and resources.
- Establish HIVDR genotyping facilities to perform testing at competitive prices or reduced cost. Where possible, save financial resources through the utilization of dried blood spots. Engage discussion with CARPHA (in charge of Regional Lab Network) on strategies to ensure access to HIVDR services for other countries in the region.
- Participation in external quality assurance programs is a key component of efforts to ensure the quality of genotyping results. A common approach to quality assurance for genotype testing is needed.

#### **HIVDR Early Warning Indicators and Cascade Analysis for Programmatic Monitoring**

#### **Key recommendation on the Continuum of care/Treatment Cascade and HIVDR EWIs**

- The PAHO monitoring framework and early warning indicators (EWIs) give details regarding access, coverage, quality and prevention of drug resistance.

- The construction and annual update of the “cascade” gives a full picture of the continuum of HIV care at national level, highlights and measures existing gaps.
- In-country analysis should be conducted by the local teams. Ownership of data by team is important.
- Monitoring of indicators at national level, as well as at each ART site will provide evidence for prioritization of interventions (“what and where”).

## **HIVDR Early Warning Indicators and Cascade Analysis for Programmatic Monitoring**

### **Key recommendations on information systems**

- Information systems should be strengthened to support data analysis both at local and national level. An important issue to recall is the issue of data security and privacy, to ensure no confidentiality breaks.
- Linkage between information systems enhances the capacity to generate strategic information. The use of unique identifiers and standardized/defined data elements is desirable to link different databases.

### **Pre-treatment and Acquired HIVDR Surveillance**

- The new WHO surveys for pre-ART resistance surveillance are feasible even in countries with few ART sites or very small populations (the sampling design - PPS - can still be used if populations from small islands are pooled, although it does not allow site-specific analysis).
- The new WHO cross-sectional design for acquired resistance surveillance is considered more feasible while still providing sufficient information for action in a timely manner.
- If viral load is performed at least annually as part of clinical care with a high coverage of patients (with VL and genotyping testing) and high quality data, then programmatic data can be used rather than survey.

### **Conclusions from the HIV DR Workshop**

- WHO protocols are feasible for use by the Caribbean countries (country planning exercise available)
- The main challenge is financial support for HIVDR surveillance, which will impact the feasibility of implementation of the surveys.
- HIVDR surveillance data may generate new questions: if high prevalence of HIVDR is observed in a country, what will be the response of the government? Will there be programmatic impact?
- HIVDR Working Group was formed after the workshop with participation of WHO HIVDR labs and Public Health multilateral and bilateral agencies to coordinate technical cooperation to countries for the implementation of HIVDR surveys.

### **Key points emanating from the discussion following the presentation:**

- Significant challenges for countries to collect data, especially small countries. One area identified is to focus on the “low hanging fruits” in order to start the surveillance process.

- The emergence and transmission of drug resistance may hinder the achievement of the target of 90% viral suppression by 2020.
- Preventing acquired drug resistance in persons on ART is key to improve the long term effectiveness of ART, as well as to reduce the risk of transmission of resistance. Transmitted resistance may also impact the early response to first line ART.
- Monitoring HIVDR is necessary to provide reliable information for decision making on optimal use of ARV drugs (1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> line) and drug resistance prevention efforts.

### Protecting 2020 treatment and care targets addressing the emergence and transmission of drug resistance – Group work

Following a brief discussion, the groups discussed key issues related to two key questions which are provided in the table below. Box X highlights the discussions which resulted from the groups.

#### GROUP 1

*How could HIV drug resistance be best prevented in Caribbean countries to improve viral suppression? Discuss priorities and challenges.*

- Increased adherence through education of the patient and general population
- Targeted program for defaulters (missed appointments & missed treatment pick-ups etc.)
- Increased monitoring of Early Warning Indicators (through training etc.)
- Increased outreach to the more difficult groups (e.g. substance abusers) through increased:
  - Participation of Civil Society
  - Social work activities
  - Involvement of non-traditional healers & faith-based organization
  - Implementation of Buddy Systems
  - Careful control of prescribing practices
  - Treatment Preparedness Protocol (training & implementation)
  - Good & efficient supply chain
  - Good Prevention with Positives

#### Challenges

- Human Resources
- Development of specific training programmes to address gaps e.g. thorough patient evaluation
- Need for Increased training of:
  - Clinical teams
  - Pharmacy staff
  - PLHIV
  - Civil Society

*Considering the recommendations from the HIVDR workshop and WHO recommended tools (Early Warning Indicators - indirect monitoring of HIVDR related factors and quality of care; Pre-ART HIVDR surveillance; Acquired HIVDR surveillance), what are the next necessary step for the implementation of HIVDR surveillance in Caribbean countries?*

Documentation of best practices within LAC

- Strengthen data collection and M&E
- Development of protocols for drug resistance testing
- Investigations/Pilot programmes to determine baseline resistance
- Development of reference laboratories within the region
- Access to regional reference laboratories

#### GROUP 2

*How could HIV drug resistance be best prevented in Caribbean countries to improve viral suppression? Discuss priorities and challenges.*



### **Priorities**

- Training for Clinicians on proper prescribing practices
- Adherence Education
- Access to HIVDR testing (Money)
- Expand second line and third line treatment (Salvage Therapy)
- (pool procurement)
- collaboration/communication
- Functioning multidiscipline team HIV DR Protocols

### **Challenges**

- Bureaucracy
- Availability of Salvage Therapy
- Adherence

*Considering the recommendations from the HIVDR workshop and WHO recommended tools (Early Warning Indicators - indirect monitoring of HIVDR related factors and quality of care; Pre-ART HIVDR surveillance; Acquired HIVDR surveillance), what are the next necessary step for the implementation of HIVDR surveillance in Caribbean countries?*

- Strengthen Patient Monitoring System
- Implementing Surveillance system
- Conduct Study among OECS Countries (Personal Delivery of Samples to Martinique/Guadeloupe for some territories.
  - Identify focal Point for the study
  - Identify appropriate committee to coordinate the implementation of study(Multidisciplinary Team)