PulseNet Latin America and the Caribbean. Towards a Regional Integration in Genome Analysis

Relavra 2019

Enrique Perez Gutierrez, Unit Chief Health Information and Risk Assessment. PHE

23rd of October 2019; Brasilia, Brasil

Pan American Health Organization
World Health Organization
Americas

PAHO

Contents

- Considerations regarding the epidemiology, surveillance, laboratory diagnosis and genomic epidemiology
- PulseNet Latin America and the Caribbean

Genomic Surveillance

- Track epidemic origins and transmission hotspots
- Characterize genetic diversity to aid molecular diagnostics,
- Detect mutations associated with disease severity, and supports the characterization of antimicrobial resistant patterns
- Exclude the possibility that human cases are caused by vaccine reversion

Genomic Surveillance

- The combination of genomic and epidemiological data from pathogen infections can give essential information:
  - Understanding the past and the future of an epidemic, its dynamics, making it possible to establish an effective surveillance framework
  - Tracking the spread of infections to other geographic regions
- PAHO has strategically strengthen the networking between
  - the national public health laboratories (NPHL),
  - the regional reference labs
  - PAHO/WHO Collaborating Centers (WHO-CC)
- To improve the epidemiological surveillance and response to outbreaks

Pan American Health Organization

World Health Organization
Americas

Arbovirus Diagnosis Laboratory Network of the Americas (RELDA)

30 Labs in 26 countries

4 WHO CC (MEX, ARG, CUB, USA)

All labs have **molecular platforms** for at least 4 arboviral diseases (DENV, CHIKV, ZIKV, YFV)

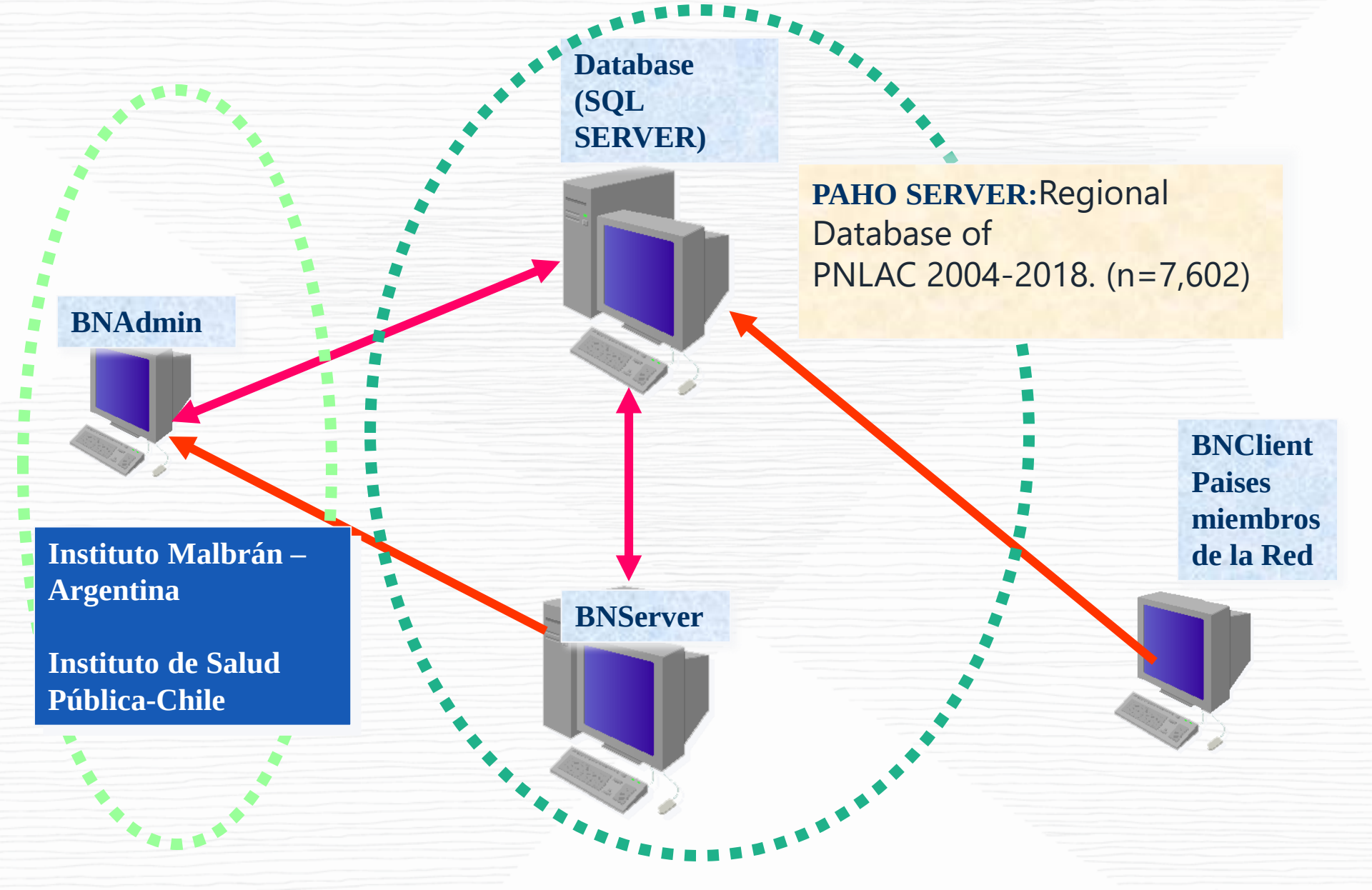
At least 10 Mayaro PCR

All labs have ELISA platforms for at least 3 arboviral diseases (DENV, CHIKV, ZIKV); YFV in endemic countries

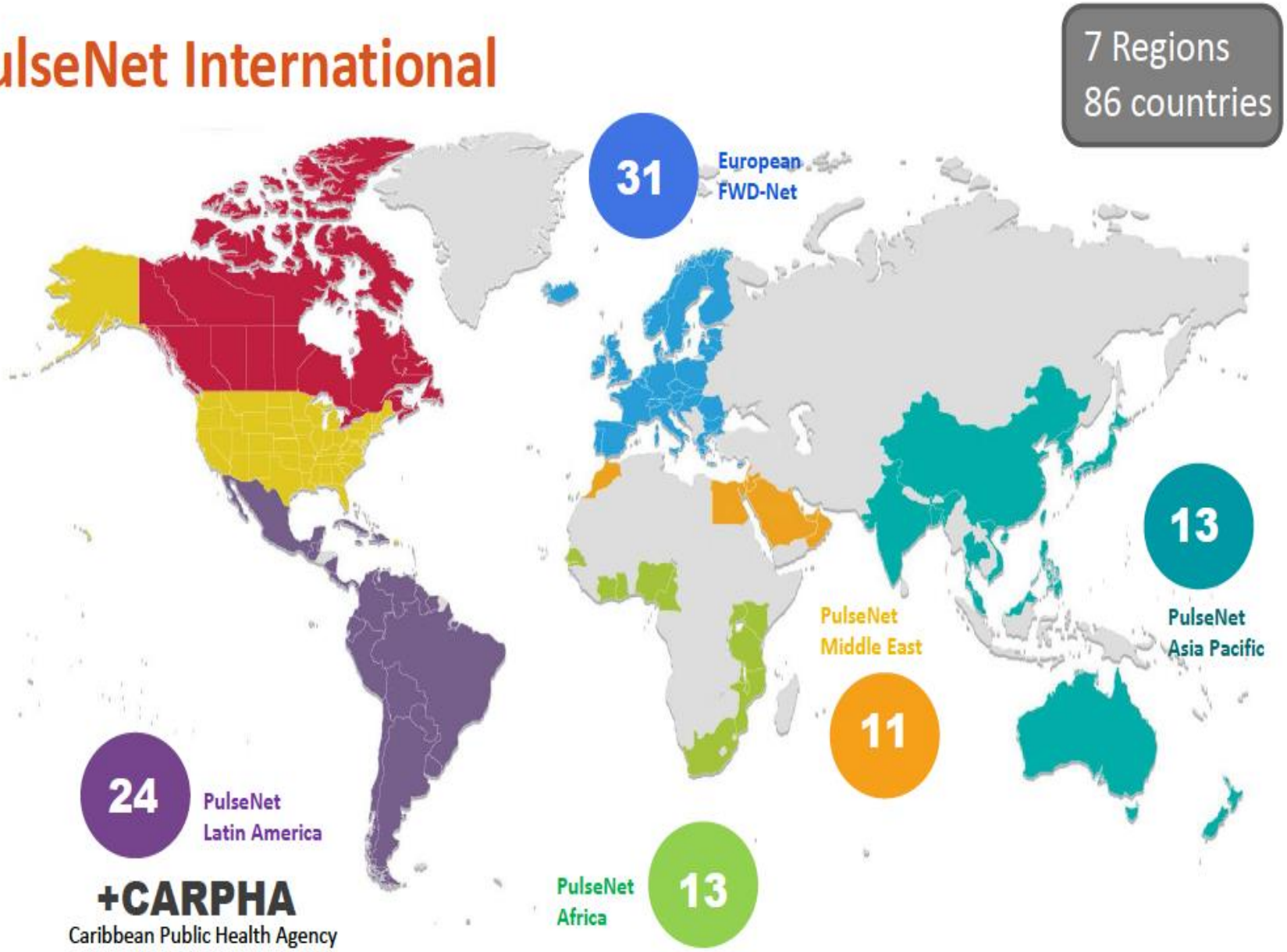
PulseNet Latin America and the Caribbean

- PulseNet Latin America and Caribbean (PNLAC) was established in 2003 and is one of seven Regional networks within PulseNet International.
- The main objectives of the network are to strengthen national and regional laboratory-based foodborne disease surveillance for early detection and investigation of outbreaks to setup control and prevention strategies in contribution to Public Health

PulseNet LA and Caribbean Flows of Information



PulseNet International



Vision of PN International

- To use WGS in all PHL in the world to identify, characterize, and subtype foodborne bacterial pathogens, replacing the existing phenotypic and molecular methods in support of foodborne diseases preparedness and response to save lives and reduce global social and economic loss

PulseNet™ International

USA, Canada, Europe, Asia Pacific, Africa, Middle East, Latin America and the Caribbean

PAHO

Genomic Epidemiology

Pulsed Field Gel Electrophoresis

Challenge

- New paradigm
- Revolutionary

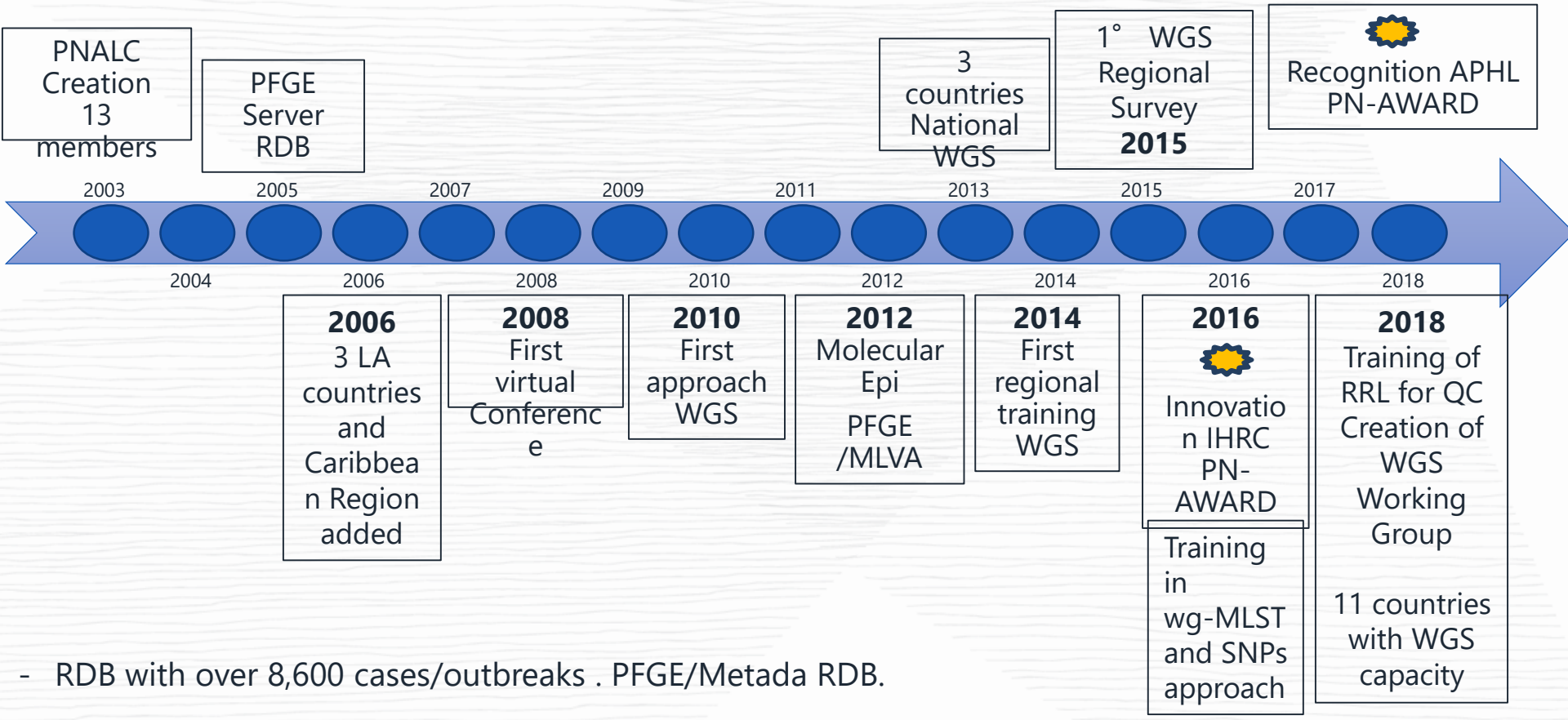
Political decision

- Resources
- Priorities Public Health

Whole Genome Sequencing (WGS)

Diagnosis, characterization and genomic epidemiology

Regional Network – 16 LA countries and Caribbean Region
PulseNet Latin America and The Caribbean (PNLAC)

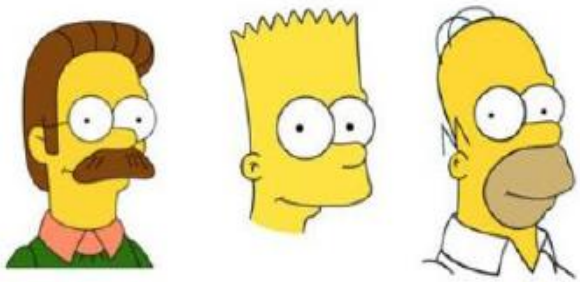


- RDB with over 8,600 cases/outbreaks . PFGE/Metada RDB.

To use WGS in a laboratory network: the tools must be …

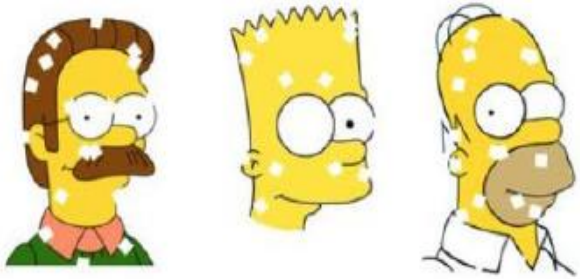
- Simple
- Universal standardized methods
- Public health laboratorians are NOT bioinformaticians
- Use existing software
- Comprehensive
- All characterization in one workflow
- Work in all laboratories
- Free sharing and comparison of data between laboratories
- Central AND local databases
- “IF IT WORKS, FOR PUBLIC HEALTH IT IS GOOD ENOUGH”

Genomes

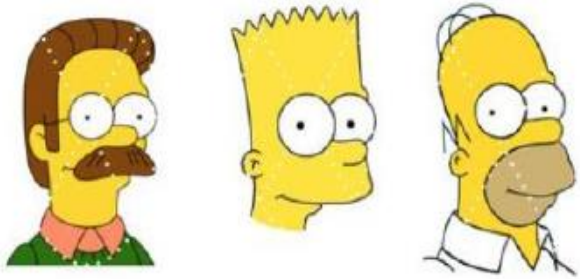


Multi Locus Sequence Typing

Core/Whole Genome MLST



Whole genome SNPs



Source: Torsten Seeman, University of Melbourne Australia.

2019 Update
WGS - Regional Status

	Seq Capacity	WGS analysis	Server
N° Countries	**12 (14 Lab)**	**9 BN 7.0-7.6 (10 Lab)**	**9 (10 Lab)**
Description	HiSeq Next Seq MiSeq MiniSeq Ion Torrent	BioNumerics 7.6 BioNumerics 7.0 Other institutional, commercial or public tools (NML-Canada pipelines; WTSI pipelines; CGE)	Cloud Server Server-access (NML-Canada ; WTSI)

Until 2017 - Mexico, Colombia, Chile, Argentina, Peru.

2017-2019 - Brazil AL (Sao Paulo), Brazil OC (Rio de Janeiro), Costa Rica, Panama, Ecuador, Paraguay, Venezuela, Uruguay.

2019-2020 – Bolivia, Cuba, CARPHA (en adquisicion)

TECHNICAL / ANALYSIS: Challenges during the implementation process

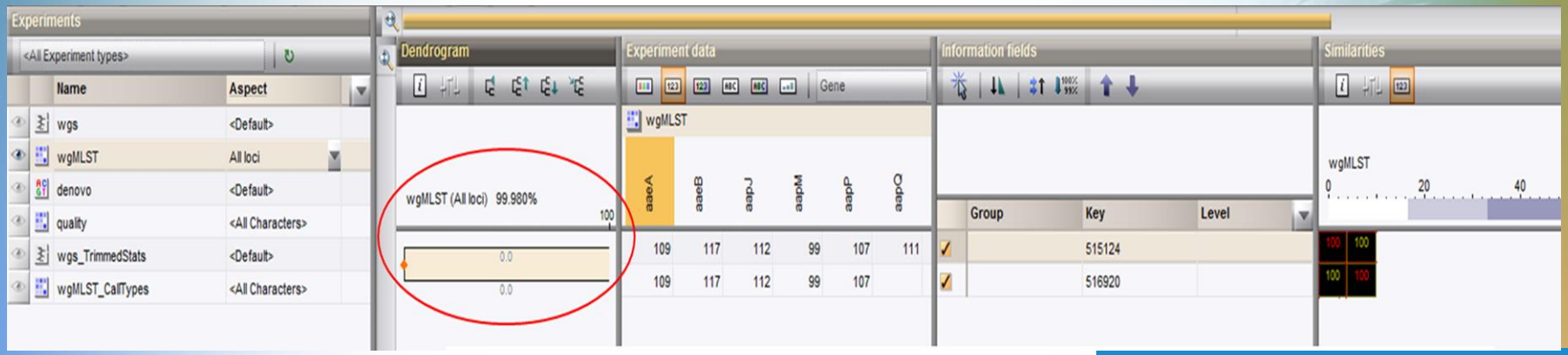
- Availability of the reagents / suppliers
- On job training and/or asistance were required for:
  - WGS capacity installation
  - First steps implementation
- Electric power supply / Internet connectivity
- Use of commercial / free softwares

Sequences in LA – updated to 2019

Country	N° sequences	Outbreaks
Argentina	163 *E. coli (*STEC; EAEC; EAEC-*stx*) 310 *Salmonella (S.* Enteritidis, *S.* Typhimurium, *S.* Typhi, other serotypes) 48 *Shigella;* 50 *V. cholerae; Streptococcus pyogenes*	7
Chile	100 *Salmonella, Shigella, V. parahaemolyticus, E. coli* y *Listeria*	1
Colombia	704 *Salmonella* (6 *S.* Infantis, 404 *S.* Enteritidis, 252 *S.* Typhimurium, 96 *S.* Typhi; 119 *S.* Derby, *S.* Dublin, *S.* Javiana, *S.* Muenchen, *S.* Muenster, *S.* Newport, *S.* Panama, *S.* 1,4,5,12:i:-, *S.* 4,5,12:i:-); 31 *Shigella sonnei,* 14 *V. cholerae; Campylobacter, Enterococcus*	1
México	946 *Salmonella, V. cholerae*	1
Costa Rica	46 *Salmonella* Parayphi B/Infantis /I 4,4,12:i:-/Typhi/Welbedere 14 Shigella flexneri /sonnei 22 *E. coli* 13 *Klebsiella pneumoniae /* 8 *S. liquefaciens /* 2 *Chronobacter Sakazakii*	10
Paraguay	14 *Salmonella*, *E. coli*	1
Perú	*24 Salmonella, Shigella, Vibrio*	--
Brazil AL	*Salmonella, Shigella, E. coli* y *Listeria* 96 (HiSeq); 24(IT)	1

Foodborne case of Cronobacter sakazakii - 2018

Costa Rica INCIENSA. Francisco Duarte
fduarte@inciensa.ca



WGS Advantages
- **Species confirmation**
- **Genetic similarity confirmation**
- **High resolution**

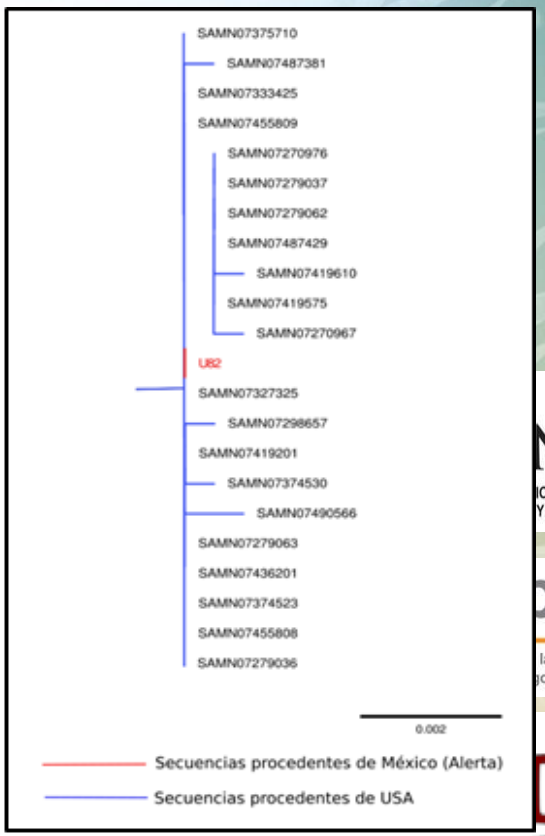
Results:

- Identical by PFGE and one allele difference by wg-MLST
- Sampling of infant formula by Ministery of health =➔ NEGATIVE
- Contamination by manipulation of infant formula at home

asm microbe 2019

S. Kiambu Investigation in Papayas – México

	SAMN07279036	SAMN07279037	SAMN07327325	SAMN07270967	SAMN07270976	SAMN07279062	SAMN07298657	SAMN07333425	SAMN07279063	SAMN07375710	SAMN07374523	SAMN07374530	SAMN07419575	SAMN07419610	SAMN07419201	SAMN07436201	SAMN07487381	SAMN07487429	SAMN07455809	SAMN07455808	SAMN07490566	U82
SAMN07279036	0	1	0	2	1	1	0	0	0	0	0	1	1	1	0	0	1	1	0	0	2	0
SAMN07279037	1	0	1	1	0	0	2	1	1	1	1	2	0	1	1	1	2	0	1	1	3	1
SAMN07327325	0	1	0	2	1	1	1	0	0	0	0	0	1	2	0	0	1	1	0	0	2	0
SAMN07270967	2	1	2	0	1	1	3	2	2	2	2	3	1	2	2	2	3	1	2	2	4	2
SAMN07270976	1	0	1	1	0	0	2	1	1	1	1	2	0	1	1	1	2	0	1	1	3	1
SAMN07279062	1	0	1	1	0	0	1	1	1	1	1	2	0	1	1	1	2	0	1	1	3	1
SAMN07298657	0	2	1	3	2	1	0	1	1	1	1	1	2	3	0	1	2	2	1	1	3	1
SAMN07333425	0	1	0	2	1	1	1	0	0	0	0	1	1	2	0	0	1	1	0	0	2	0
SAMN07279063	0	1	0	2	1	1	1	0	0	0	0	1	1	2	0	0	1	1	0	0	2	0
SAMN07375710	0	1	0	2	1	1	1	0	0	0	0	1	1	2	0	0	1	1	0	0	2	0
SAMN07374523	0	1	0	2	1	1	1	0	0	0	0	1	1	2	0	0	1	1	0	0	2	0
SAMN07374530	1	2	0	3	2	2	1	1	1	1	1	0	2	3	0	1	2	2	1	1	3	0
SAMN07419575	1	0	1	1	0	0	2	1	1	1	1	2	0	1	1	1	2	0	1	1	3	1
SAMN07419610	1	1	2	2	1	1	3	2	2	2	2	3	1	0	2	2	3	1	2	2	4	2
SAMN07419201	0	1	0	2	1	1	0	0	0	0	0	0	1	2	0	0	1	1	0	0	2	0
SAMN07436201	0	1	0	2	1	1	1	0	0	0	0	1	1	2	0	0	1	1	0	0	2	0
SAMN07487381	1	2	1	3	2	2	2	1	1	1	1	2	2	3	1	1	0	2	1	1	3	1
SAMN07487429	1	0	1	1	0	0	2	1	1	1	1	2	0	1	1	1	2	0	1	1	3	1
SAMN07455809	0	1	0	2	1	1	1	0	0	0	0	1	1	2	0	0	1	1	0	0	2	0
SAMN07455808	0	1	0	2	1	1	1	0	0	0	0	1	1	2	0	0	1	1	0	0	2	0
SAMN07490566	2	3	2	4	3	3	3	2	2	2	2	3	3	4	2	2	3	3	2	2	0	1
U82	0	1	0	2	1	1	1	0	0	0	0	0	1	2	0	0	1	1	0	0	1	0



PFGE – not conclusive data

0 a 2 hq-SNPs between Mexican Papayas (MARADOL) and USA cases/papayas

Red GenomeTrakr en 2018 ➔ NCBI

NASICA
IO NACIONAL DE SANIDAD,
Y CALIDAD AGROALIMENTARIA

oris
la Protección
gos Sanitarios

DRE
Instituto de Diagnóstico y Referencia Epidemiológicos
"Dr. Manuel Martínez Báez"

microbe
2019

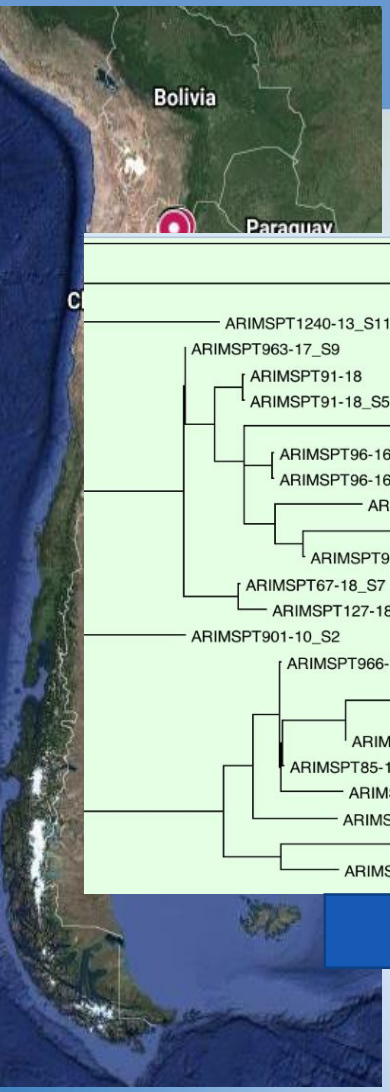
Foodborne outbreak of *Salmonella* Infantis Nariño, 2018. Colombia

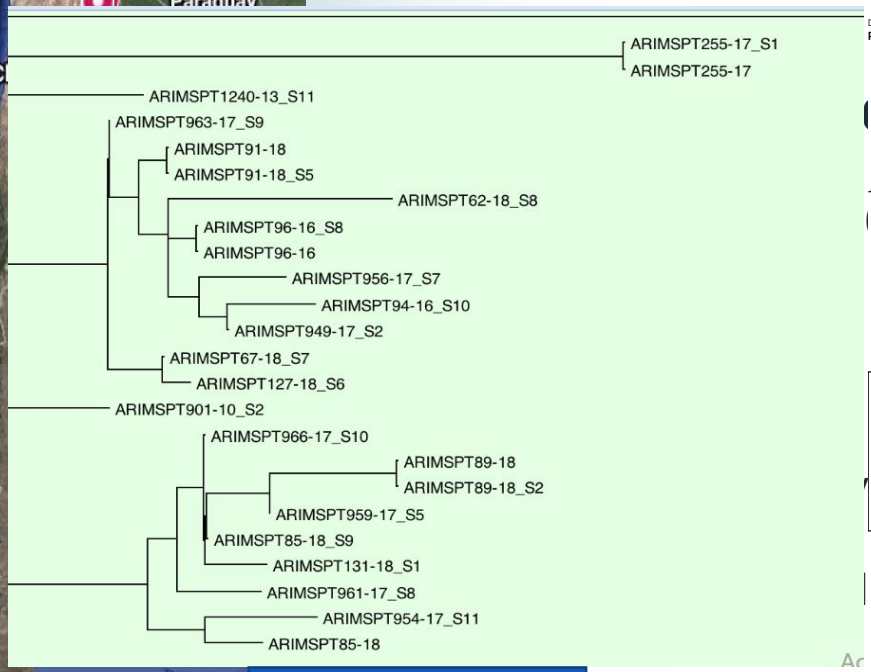
WGS

- Serotype and AMR confirmation
- *bla*TEM-family, sul2, floR, tetA, aac(6')-laa and *par*C and *gyr*B
- Plasmid families Inc1 and IncX4

ɔurces not detected

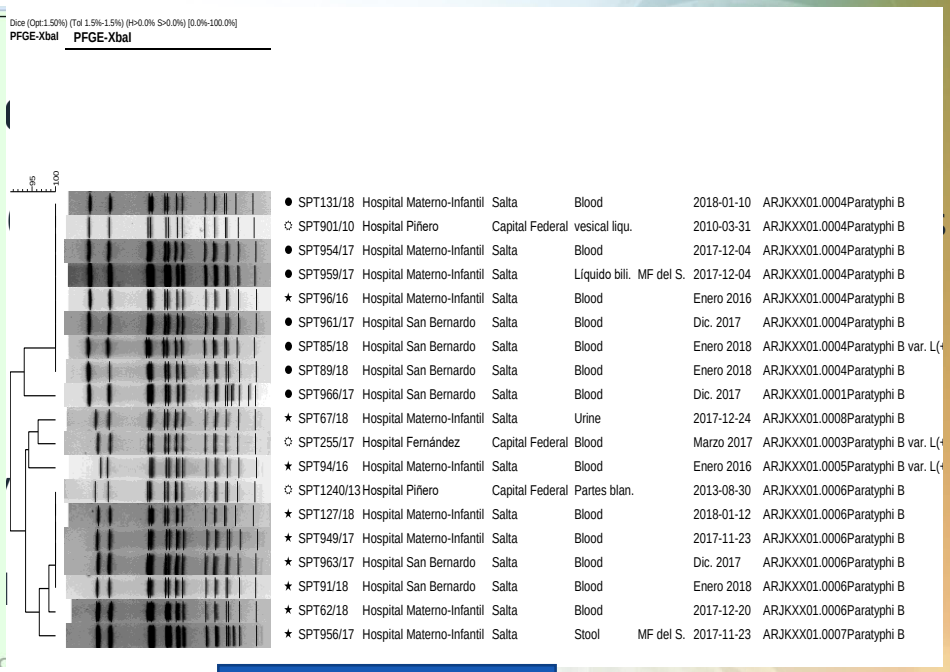
Salmonella Paratyphi B Outbreak 2018-2019. Argentina





WGS

t detected.



PFGE

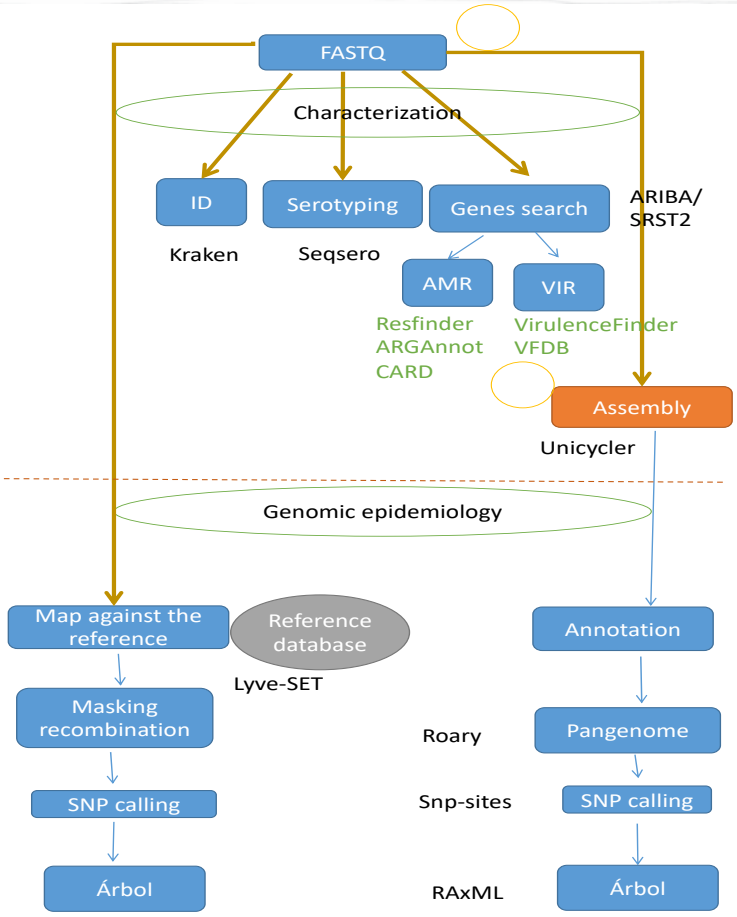
asm microbe 2019

Shigella sonnei – Outbreaks 2010-2011 Argentina

WGS	USES	PATHOGENS
- Species confirmation - Virulence genes detection - AMR genes detection	- Diagnostic (genus /species) - Virulence Genes profile - Resistance Genes profile	*Chronobacter sakazakii* *E. coli* /*S. sonnei* / *S.* Infantis/ *S.* Paratyphi B / S. Kiambu
- Phylogenetic relationship • Genetic similarity • High resolution	- Outbreak /cluster	*S.* Infantis/*S.* Paratyphi B/ *S. sonnei* / *E. coli*
	- Foodborne cases	*Chronobacter sakazakii* / *E. coli*
	- Food safety	*S.* Kiambu
	- Population studies	*E. coli* / *S.* Paratyphi B

PAHO

REGIONAL WORFLOW
Diagnosis and outbreak investigation



WGS for Public Health in LA

WGS for Public Health

National & International collaboration

WSG specific events/projects

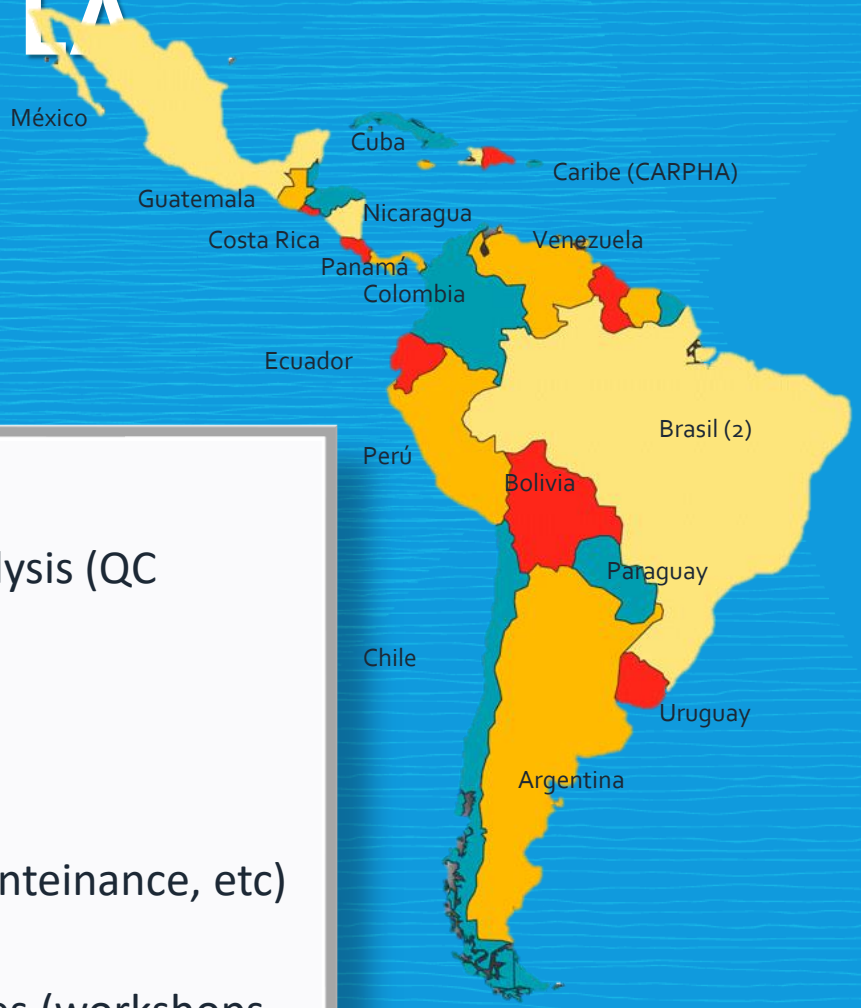
- ✓ Visits
- ✓ Training on job
- ✓ Meetings
- ✓ Courses
- ✓ Technical Support
- ✓ Financial Support
- ✓ Informatic / Bioinformatic supp

Pan American Health Organization
World Health Organization
PAHO

Moving Forward

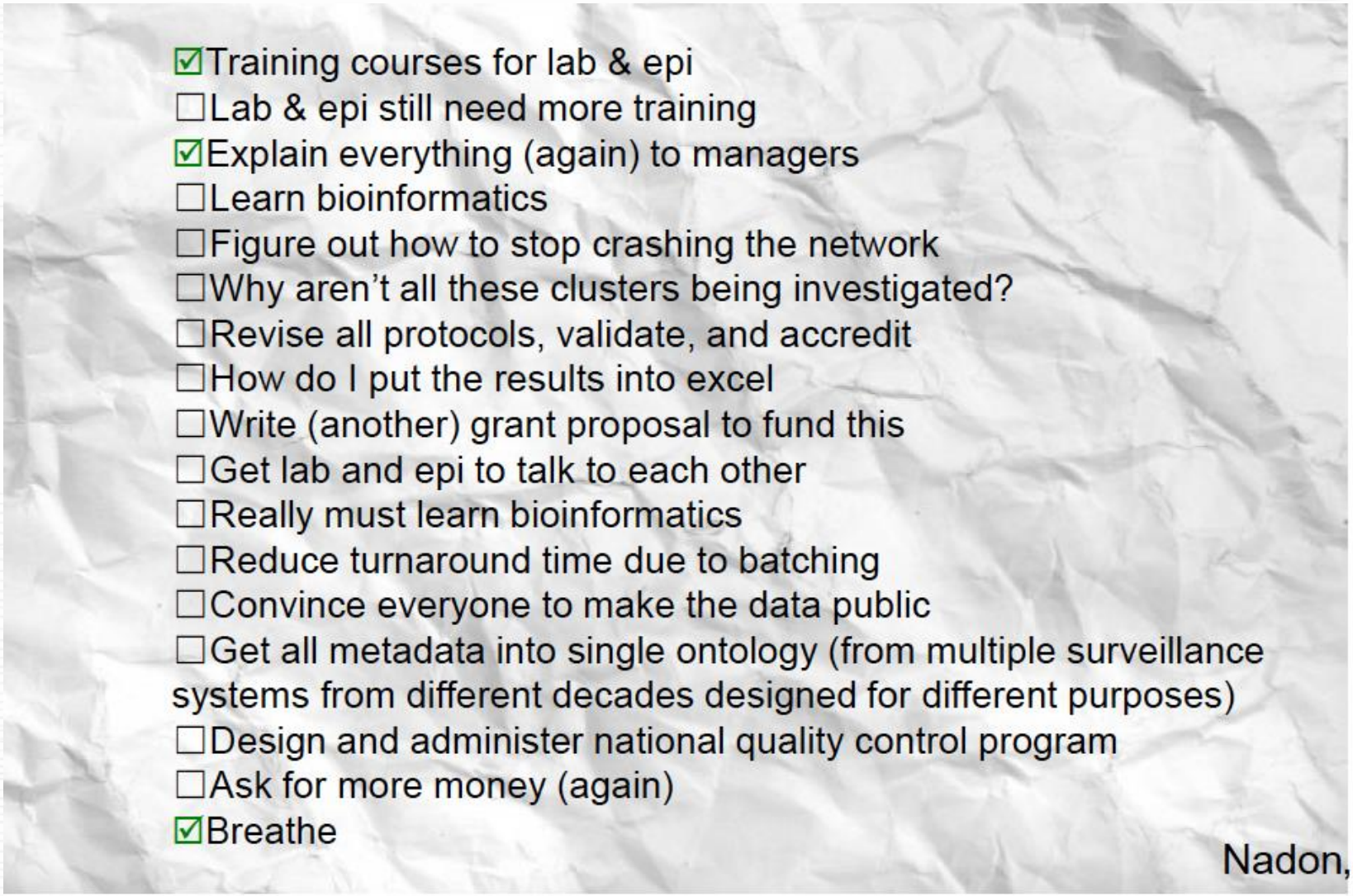
- Raise awareness at higher levels
- Acquire resources to fund its implementation
- Prove that WGS works for national real-time surveillance
- Identify/develop, test, and validate the pipelines
- Develop a QA/certification/proficiency testing system
- Insure availability of sequencers and IT-infrastructure at country level
- Train implementers and future users (lab AND epi)
- Implementing all network laboratories (RELDA and PulseNet)

WGS Future Steps - LA



- Regional workflow
- Standardized protocols for Lab and analysis (QC metrics)
- Regional SERVER
- Regional Database
- WGS Certification/Proficiency Test
- Sustainability (reagents, installation manteinance, etc)
- Sharing of best practices
- Training/assistance to different countries (workshops, visits, virtual conferences)

PAHO



Source: Celine Nadon, Public Health Agency of Canada, National Microbiology Laboratory, Canada

Acknowledgment

PulseNet™ América Latina y Caribe
Red Regional de Subtipificacion Molecular para la Vigilancia de las Enfermedades Transmitidas por Alimentos

INEI-ANLIS MALBRÁN - Argentina

Isabel Chinen
Josefina Campos

INLASA - Bolivia

Giovanni Rodrigo García Rada
Vesna Boric

ADOLFO LUTZ - Brazil

Carlos Henrique Camargo
Monique Tiba

FIOCRUZ - Brazil

Dalia dos Prazeres Rodrigues
André Felipe
Bruno Roges Pribul

CARPHA – The Caribbean
Caribbean Public Health Agency CARPHA
Lisa Indar
Gabriel Gonzalez Escobar

ISP - Chile

Jorge Fernández
Soledad Ulloa

UCREVE/LNS - Guatemala

Ericka Pérez

COIN - Colombia

Paula Lucía Díaz Guevara
Jaime Moreno

CORPOICA - Colombia

Johan F. Bernal Morales
Pilar Donado

INVIMA - Colombia

Miguel Díaz
Mabel Gartner

INCIENSA – Costa Rica

Francisco Duarte Martínez

INST. MED. TROP. P. KOURÍ - Cuba

Adalberto Águila Sánchez

INST. IZQUIETA PÉREZ - Ecuador

Victor Rafael Tamayo Trujillo
Dra. Yolanda Narvaez San Martín

C. NAC. DIÁG. REF – Nicaragua

Julissa Ávila

INST. C. Gorgas - Panamá

Rubén
Ramos

InDRE - México

Elizabeth González Durán
Edgar Mendieta

SENASICA - México

Cindy Fabiola Hernandez Pérez
Otoniel Maya Lucas
Linda Coatlicue García López
Mayrén Cristina Zamora Nava

COFEPRIS - México

Dianelly Yazmin Colli Magaña

LCSP - Paraguay

Natalie Weiler Gustafson

INS - Perú

María Luz Zamudio Rojas
Ronnie Gustavo Gavilán Chávez

Lab. Salud Pública - Uruguay

Teresa Camou
Alfredo Sirok

INST. Rafael Rangel - Venezuela

Carmen Isaura Ugarte
Anabel Bandes

OPS-OMS
Organización Panamericana de la Salud
Organización Mundial de la Salud
Américas
Enrique Pérez Gutiérrez

RELAVRA 2019. Genomic Epidemiology in the Region of the Americas Genomic Epidemiology

Pan American Health Organization
World Health Organization
Americas
PAHO