Laboratory Diagnosis of SARS CoV-2 infection: impact of automation on the different steps

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U.O. MICROBIOLOGIA

Pievesestina

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale della Romagna

Financial Disclosure

- Speaker's Grants:
  - bioMerieux
  - Roche Diagnostics
  - ALIFAX
  - Cepheid
  - COPAN Italia
  - DiaSorin
  - Abbott Diagnostics

- Research Grants:
  - bioMerieux
  - DiaSorin
  - Diesse
  - Roche Diagnostics
  - Novartis Diagnostics
  - BioRad

Agenda

- COVID-19 Integrated Surveillance Data in Italy
- Specimens Collection: Type and Priority
- Emilia-Romagna Health Organization
- Covid-19 Diagnosis & Workflow in My Laboratory
- Can Automation Improve the flow?
- Current status of UniVerse in My Laboratory

International Press Review

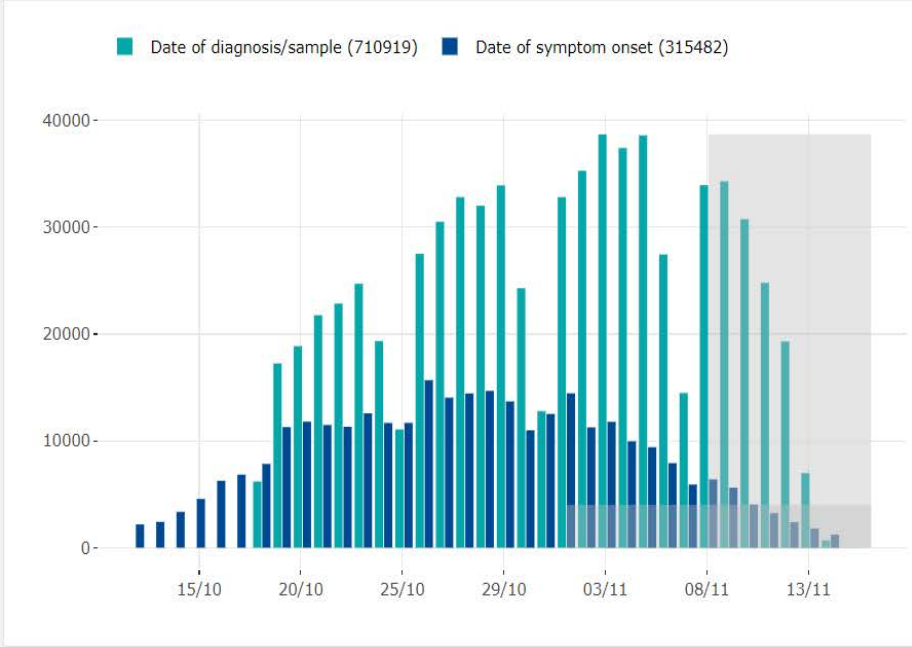
COVID-19 integrated surveillance data in Italy

(Last 30 Days)

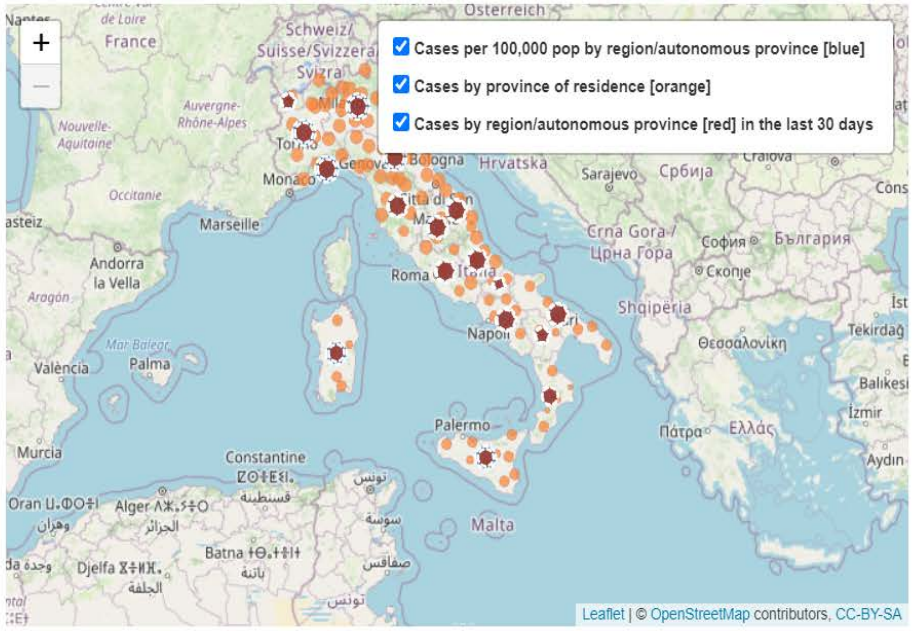
710,919	21,950	46 years	49.3% | 50.7%	7,359	137,727
Cases in the last 30 days	Cases among healthcare workers in the last 30 days*	Median age of cases in the last 30 days	Cases by sex: Males (%) | Females (%) in the last 30 days	Deaths in the last 30 days**	Recovered in the last 30 days

Cases of confirmed SARS-CoV-2 infection reported in Italy in the last 30 days

Note: more recent data (grey squares) should be interpreted with caution due to the possible reporting delay of more recently diagnosed cases and to the possibility that cases with date of onset within the reporting period may have not yet been diagnosed

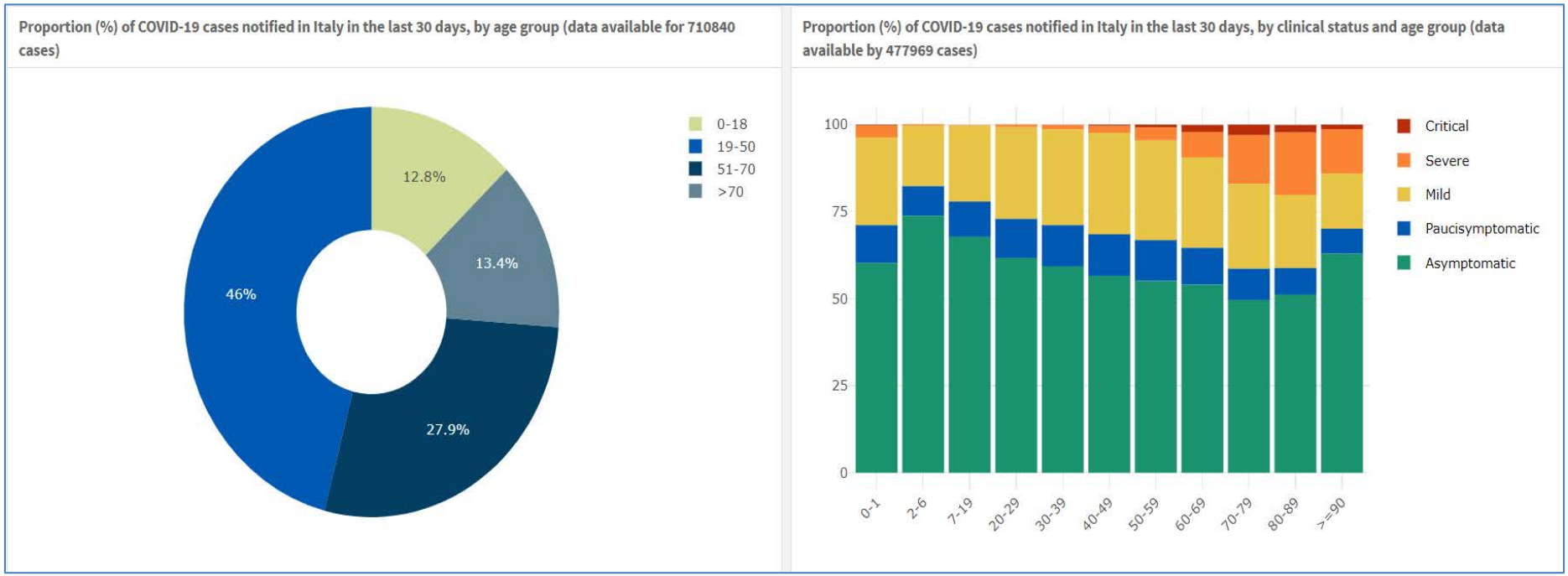


Cases of COVID-19:
-per 100.000 population per Region/Autonomous Province of diagnosis (blue)
-by province of residence (orange)
-in the last 30 days by region/autonomous province of diagnosis (red)



https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-dashboard

COVID-19 integrated surveillance data in Italy (Last 30 Days)



https://www.epicentro.iss.it/en/coronavirus/sars-cov-2-dashboard

INSTRUCTIONS FOR NASOPHARYNGEAL SAMPLE COLLECTION

USING FLOCKED MINI-TIP SWAB AND UTM™ UNIVERSAL TRANSPORT MEDIA

COLLECTION SUPPLIES

- Swab (1)
- Tube of medium (1)

This guide is for illustration Purposes Only. Always read the manufacturer's package insert for specific instructions regarding specimen collection and transport for the type of test kit being used.

COLLECT THE SAMPLE

Wash hands with soap and water and don personal protective equipment.

1 Remove the swab from its packaging, holding by the end of the applicator and identify the breaking point.

2 Position head slightly back.

3
- Gently insert the swab into the nostril. Keep the swab near the septum floor of the nose while gently pushing the swab into the post nasopharynx.
- As a visual reference, the swab should be inserted about half the distance from the opening of the patient's nostril and the ear.

4 When the swab is in place, rotate in a circular motion gently against the nasopharyngeal mucosa for 10 – 15 seconds then gently remove swab.

PACKAGE THE SAMPLE

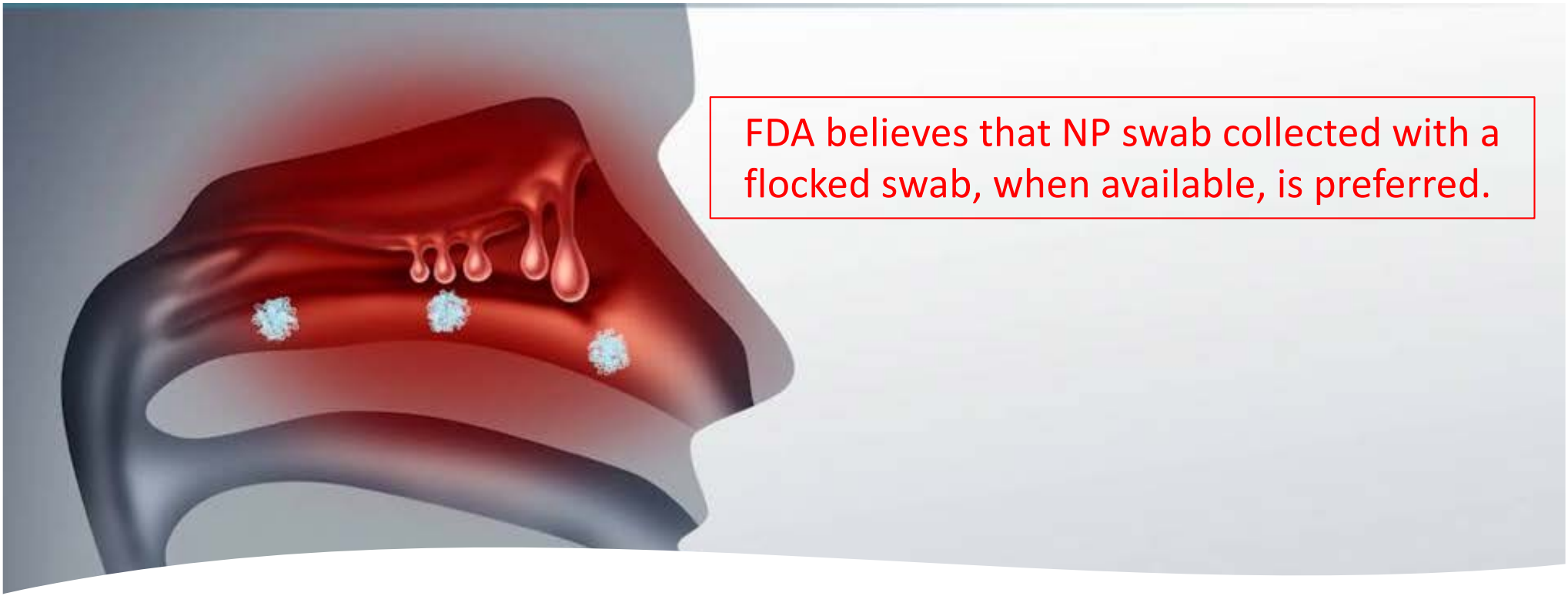
5 While holding the swab, remove the cap from the tube.
- Insert the swab into the tube until the breakpoint is level with the tube opening.
- Bend the swab shaft at a 180 degrees angle to break it off at the breaking point. You may need to gently rotate the swab shaft to complete the breakage.

6 Discard the broken part of the applicator into an approved waste disposal container.

7 Screw the cap back onto the tube and apply patient identification label or write patient information on the tube label.

Wash hands with soap and water.

Collecting the NP swab. Insert flexible wire shaft swab through the nares parallel to the palate (not upwards) until resistance is encountered or the distance is equivalent to that from the ear to the nostril of the patient indicating contact with the nasopharynx. Gently, rub and roll the swab. Leave the swab in place for several seconds to absorb secretions before removing.



FDA believes that NP swab collected with a flocked swab, when available, is preferred.

Sample Collection COVID-19: upper respiratory tract

The following are acceptable specimens collected by a healthcare provider :

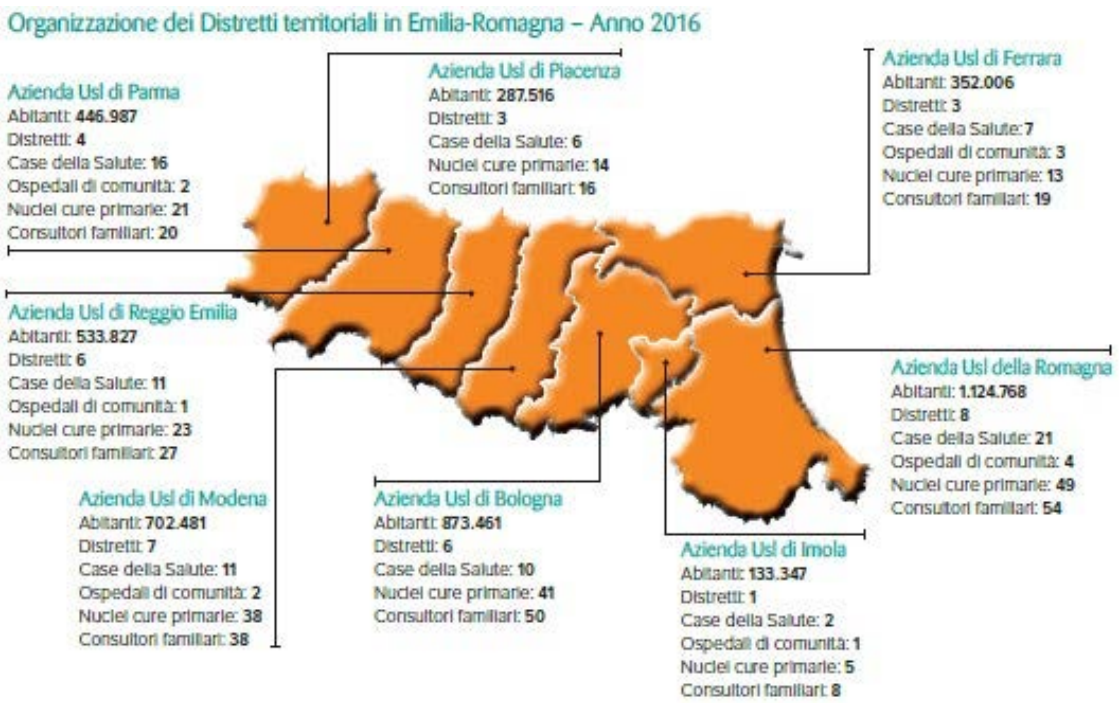
- **A nasopharyngeal (NP) specimen**
- **An oropharyngeal (OP) specimen**
- **A nasal mid-turbinate swab**

- Swabs should be placed immediately into a sterile transport tube containing 2-3mL of either viral transport medium (UTM), Amies transport medium (eSwab), or sterile saline.

CDC

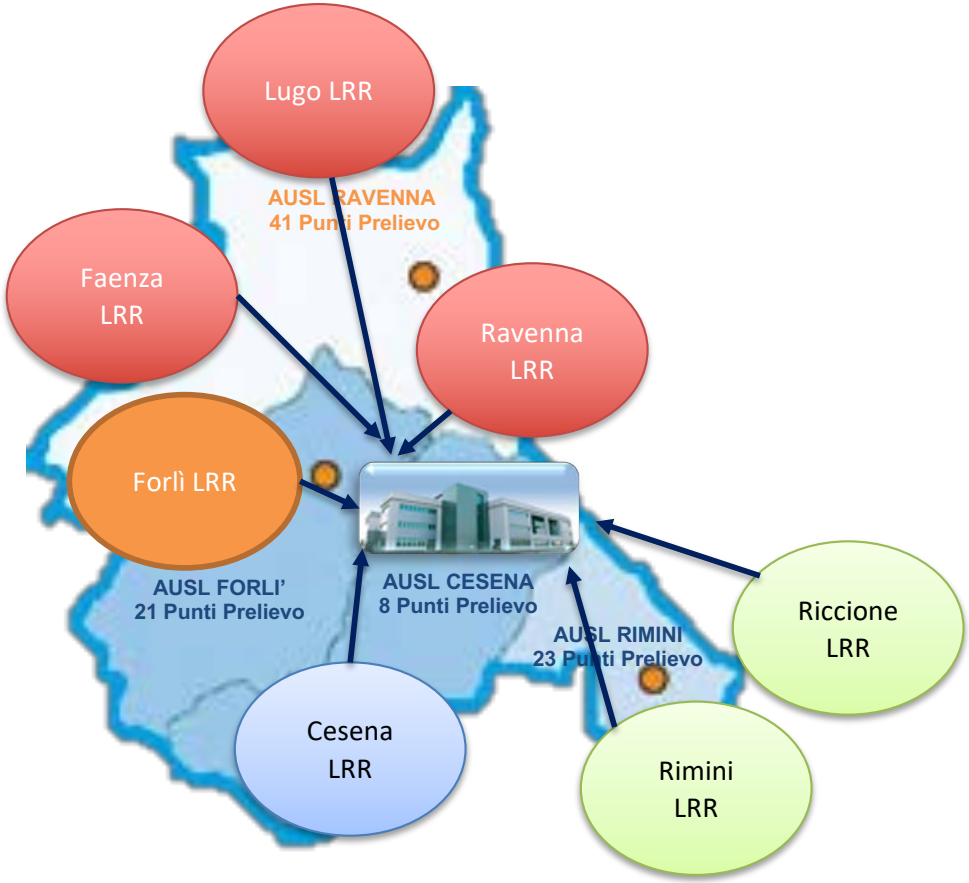
FDA

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA



Emilia Romagna Health-Care Organization

The Greater Romagna Area: organization of *Hub and spoke laboratory model*



ROMAGNA: organization of labs	
AUSL (Ravenna, Rimini, Forlì, Cesena)	4
Laboratories on site	7
Tests performed/year	21.000.000 /1.050.000 Micro)
Population	1.200.000

Daily Routine in Area Vasta Romagna	
N° of Samples Collection Sites	93
Out patients	4500
Access Sites	400
In Patients	1500
Hospitals in Area Vasta Romagna	15

The samples trip outside the lab

Where our specimens are travelling every day?

VAGINAL
URETHRAL
RESP. TRACT
OTHER
MATERIALS
STOOL

HOSPITALS - ED

15 Hospitals + outpatients
Area Vasta Romagna

1

Sample collection in patient with suspected symptoms

Nasopharyngeal Swab
2500 samples/day

Transfer the flocked swab into a test tube containing UTM transport medium. Release of the virus into the media

2

3

TRANSFER TO THE LABORATORY

LABORATORY
AREA VASTA ROMAGNA

5

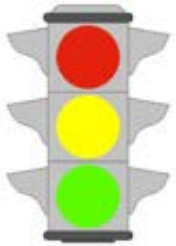
Sample preparation

4

NAATs processing

- RNA extraction
- RNA retro-transcription
- cDNA amplification
- Detection

Clinical samples sorting



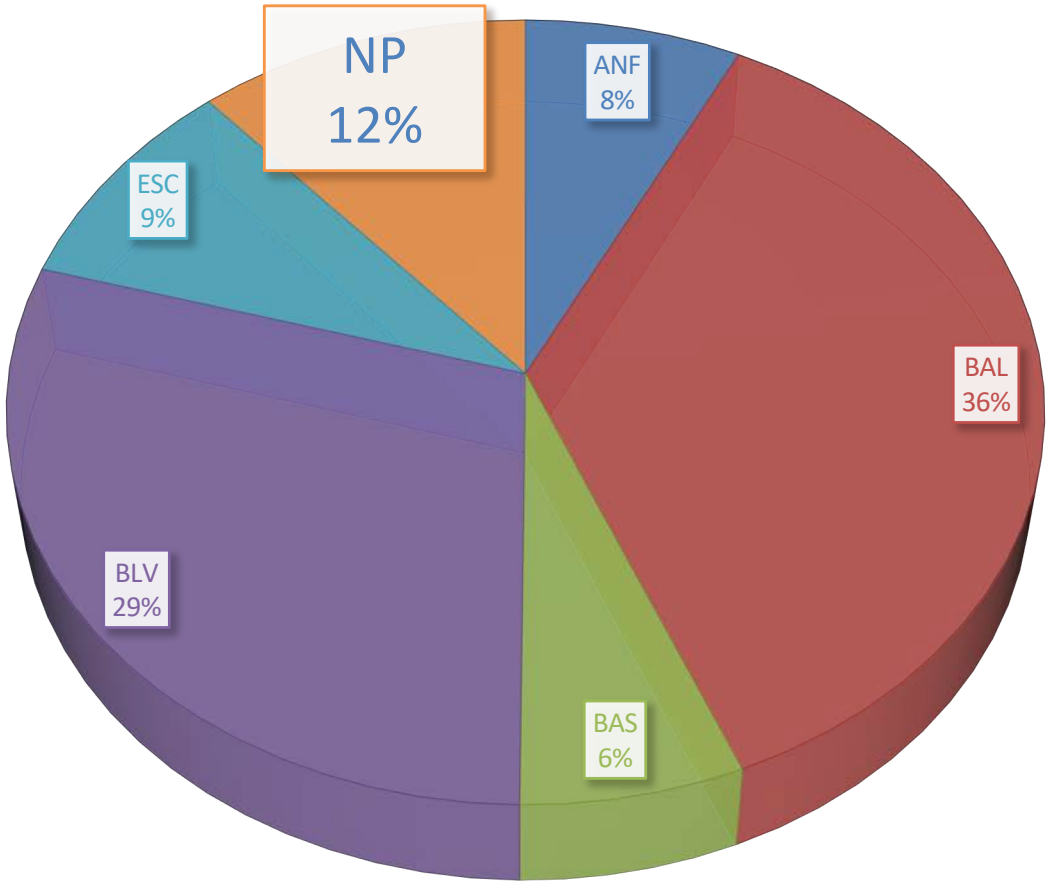
2h sample to result

6h sample to result

24h sample to result

COVID-19 IMPACT IN MY LAB

RESPIRATORY SAMPLES DISTRIBUTION LAST WEEK DECEMBER 2019



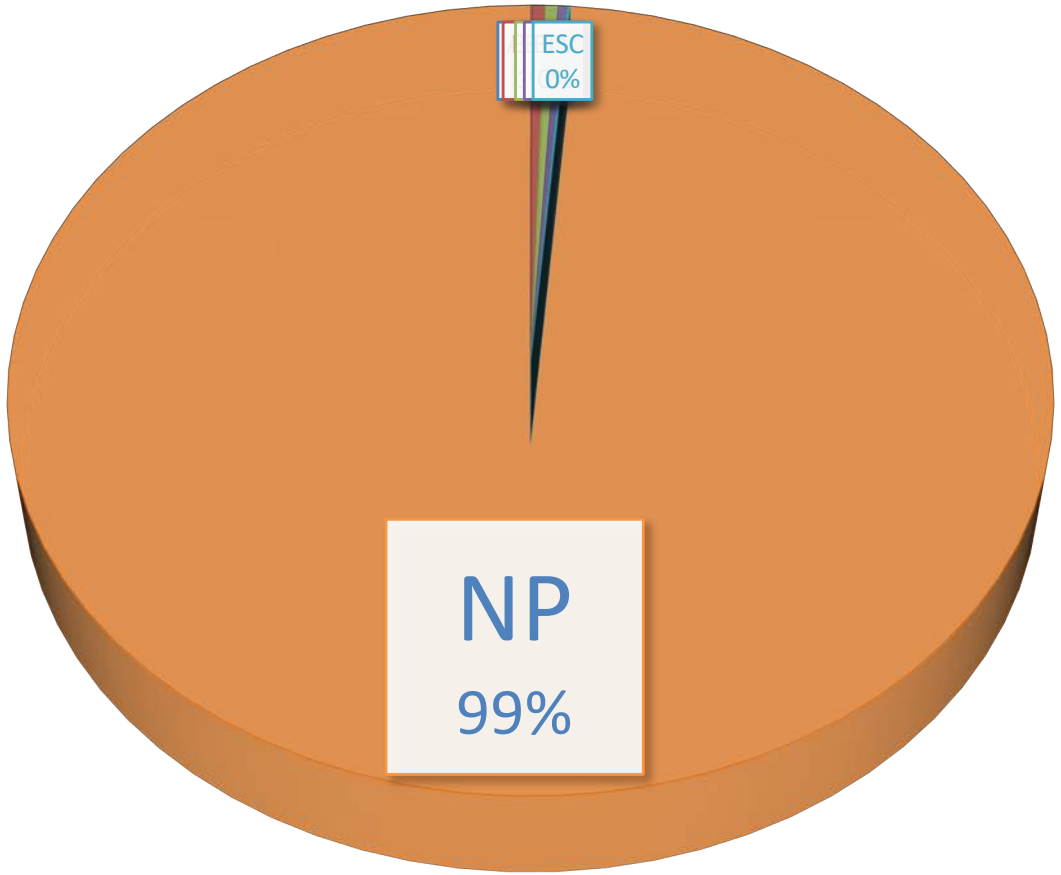
NP: Nasopharingeal Swab
ANF: Nasopharingeal Aspirate
BAL: BronchoAlveolar Lavage
BAS: Bronchial Aspirate
BLV: Bronchial Lavage
ESC: Sputum

Daily Total Number of Samples: **41**

Data Source: LIS extraction from October 2019 to October 2020

COVID-19 IMPACT IN MY LAB

RESPIRATORY SAMPLES DISTRIBUTION LAST WEEK OCTOBER 2020

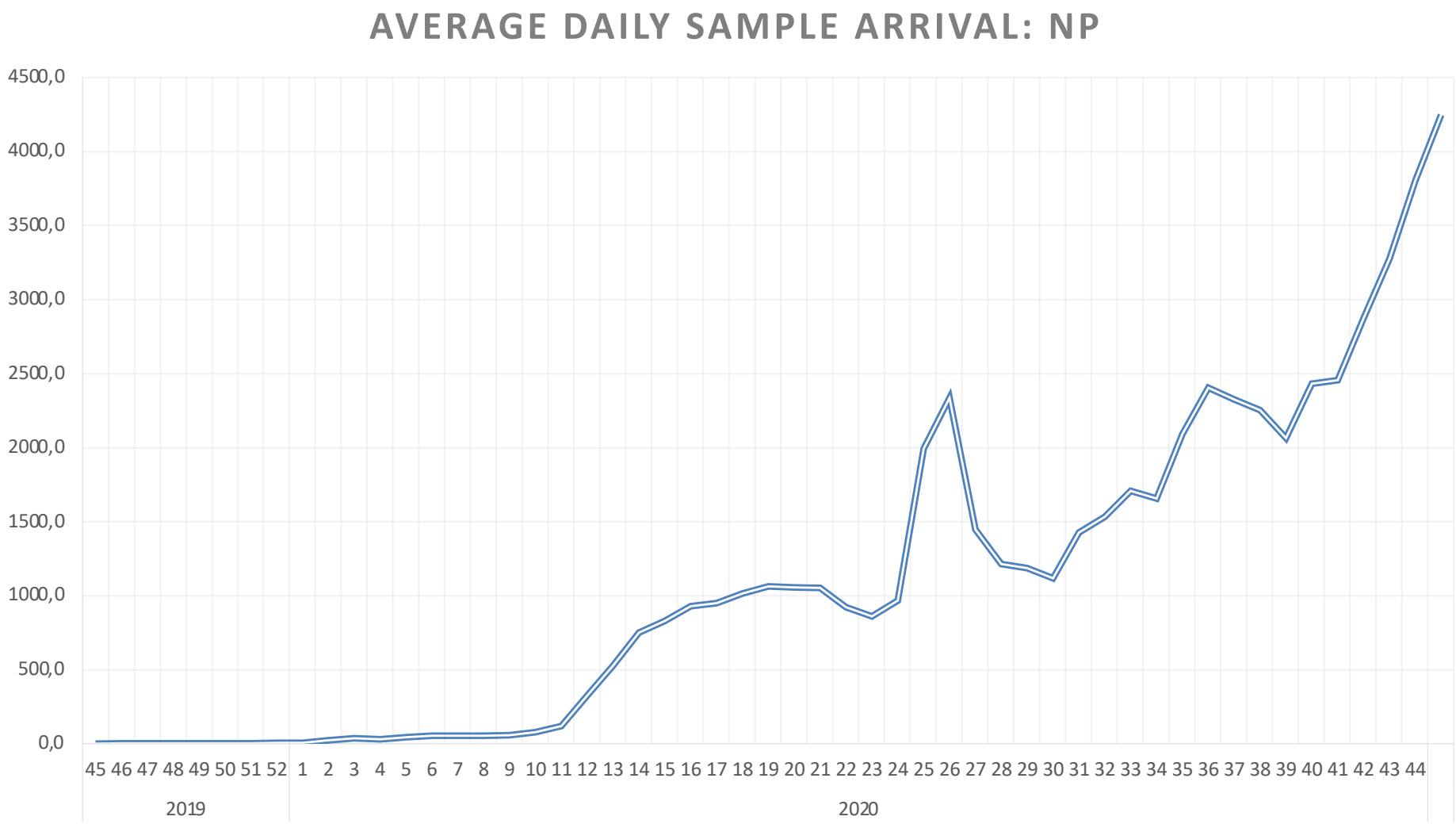


NP: Nasopharingeal Swab
ANF: Nasopharingeal Aspirate
BAL: BronchoAlveolar Lavage
BAS: Bronchial Aspirate
BLV: Bronchial Lavage
ESC: Sputum

Daily Total Number of Samples: **4248**

Data Source: LIS extraction from October 2019 to October 2020

COVID-19 IMPACT IN MY LAB

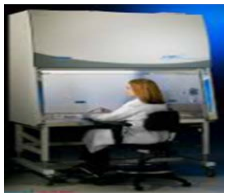


Data Source: LIS extraction from October 2019 to October 2020

Main Workflows in MY LAB

Clinical Sample Sorting

Primary Sample Prep



Manual Prep

Manual Prep

Manual Prep

Freedom EVO, Tecan

Starlet, Hamilton

Manual Prep

Panther, Hologic

CFX 96, Biorad, Seegene

Liaison, Diasorin

The **level of integration** between the primary samples and the downstream analyzers is too low:

IT IS MANUAL
REQUIRES TIME
REQUIRES RESOURCES
IT IS DANGEROUS

BOTTLE NECK OF THE TESTING CAPACITY?

The samples trip inside the lab

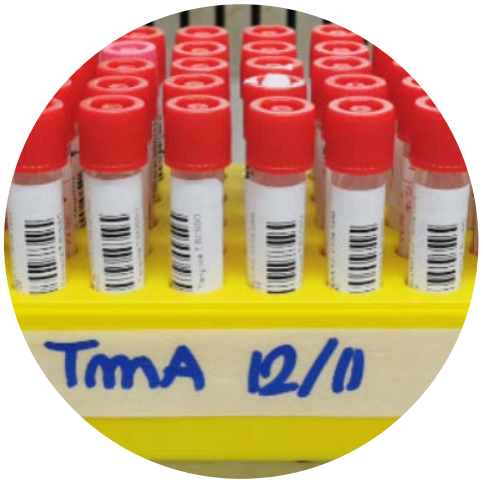
Focus on the Sample Preparation

- Sample Arrival: Removal from Biohazard Bags
- Sample Classification
- Sorting Into Generic Racks
- Sample Check-In
- Preparation of UTM: Decapping and Swab Removal (if needed)
- Preparation of Secondary Tubes (labelling and decapping)
- Aliquoting
- Closure and storage

- Sample Arrival: Removal from Biohazard Bags
- Sample Classification
- Sorting Into Generic Racks

Sample Check-In to the Laboratory Information System

Preparation of UTM



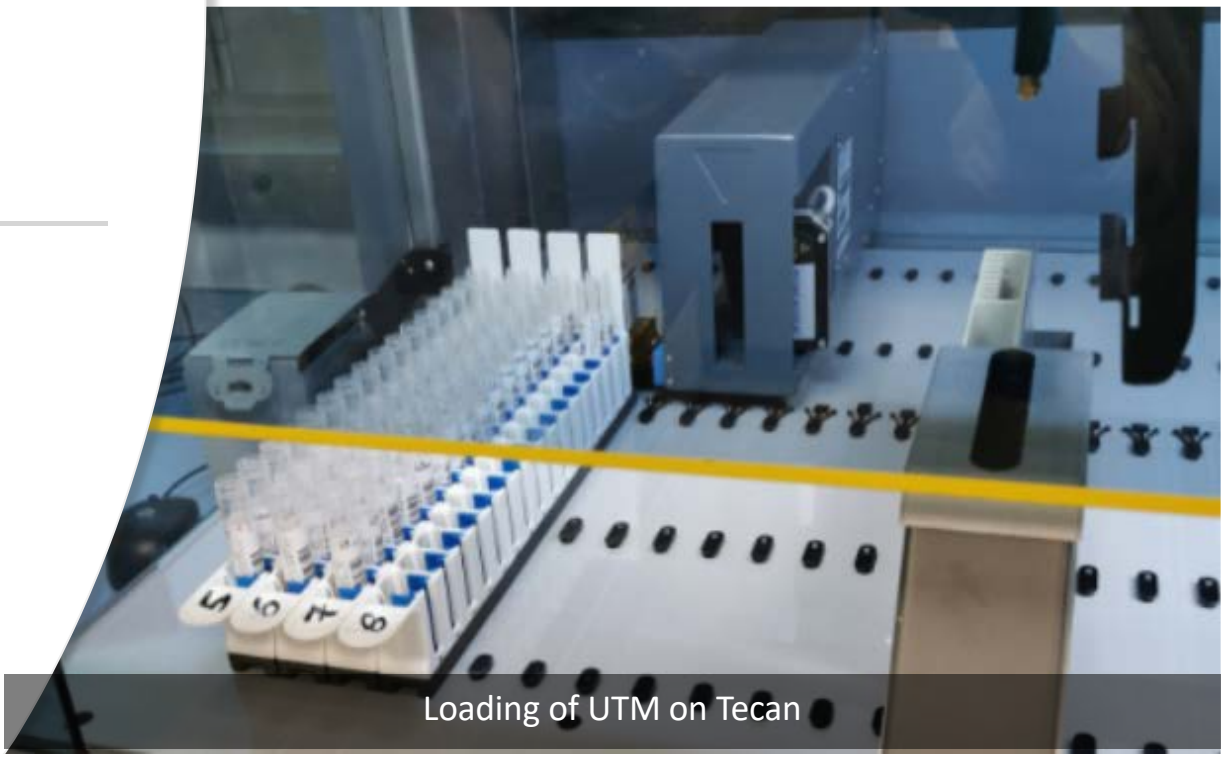
UTM Rack under Laminar Flow

UTM Decapping

O/P Swab Removal

Preparation of UTM Tubes

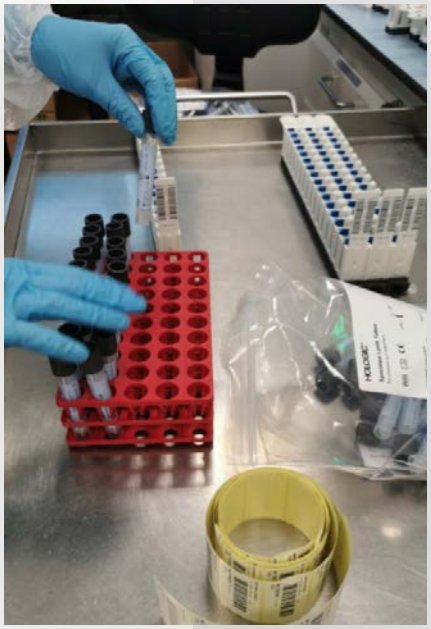
UTM is moved to Tecan Rack

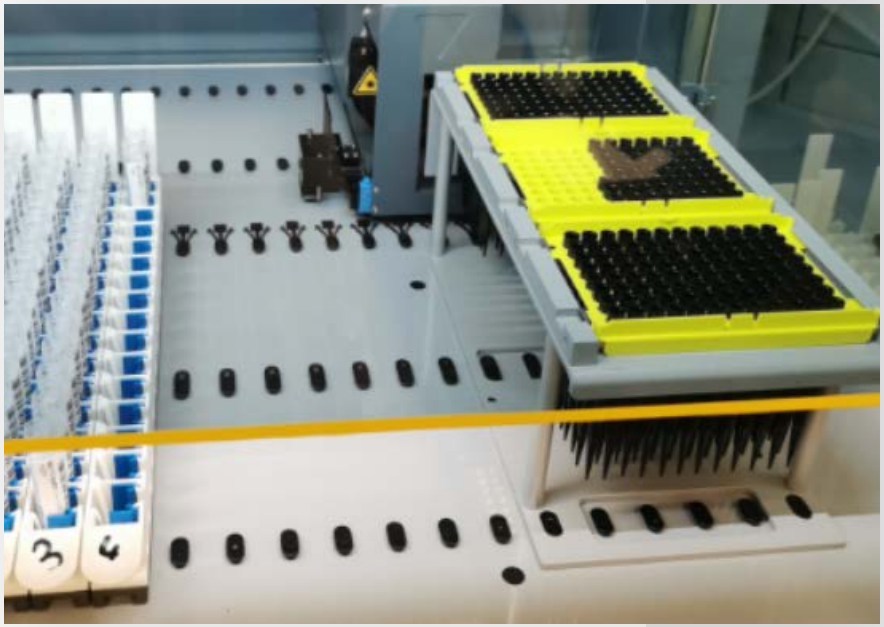


Loading of UTM on Tecan

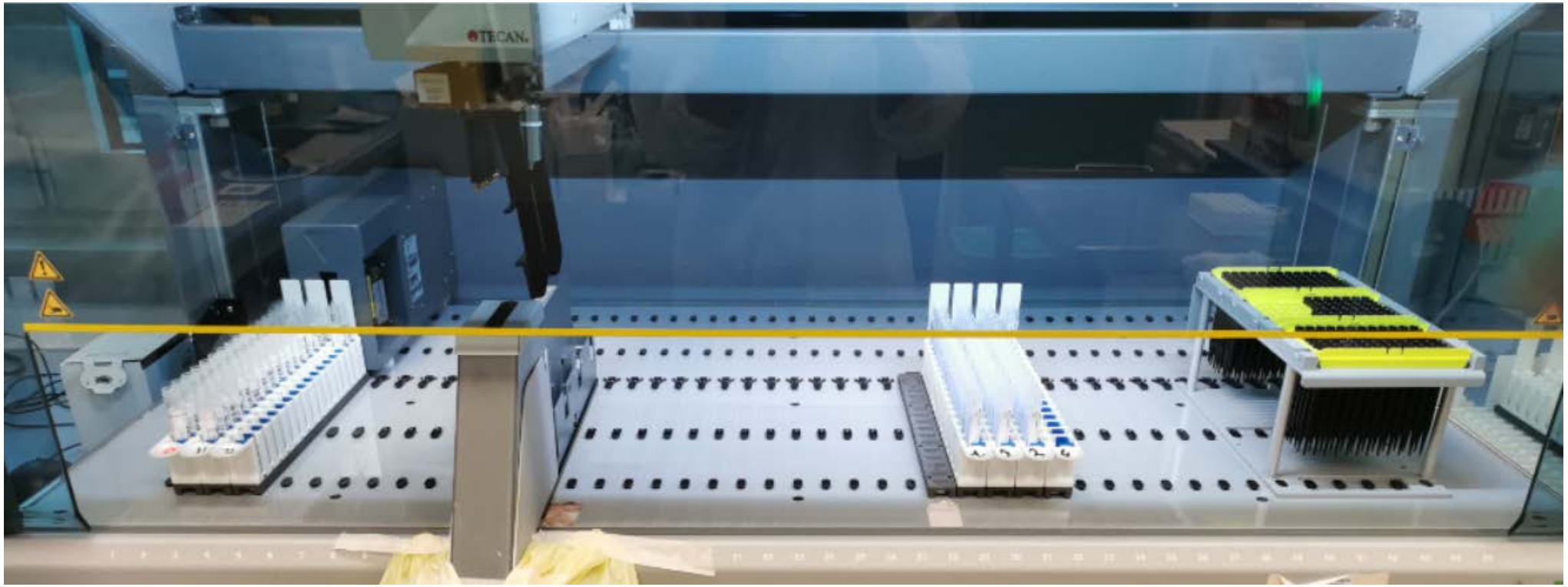
Preparation of Panther Tubes:

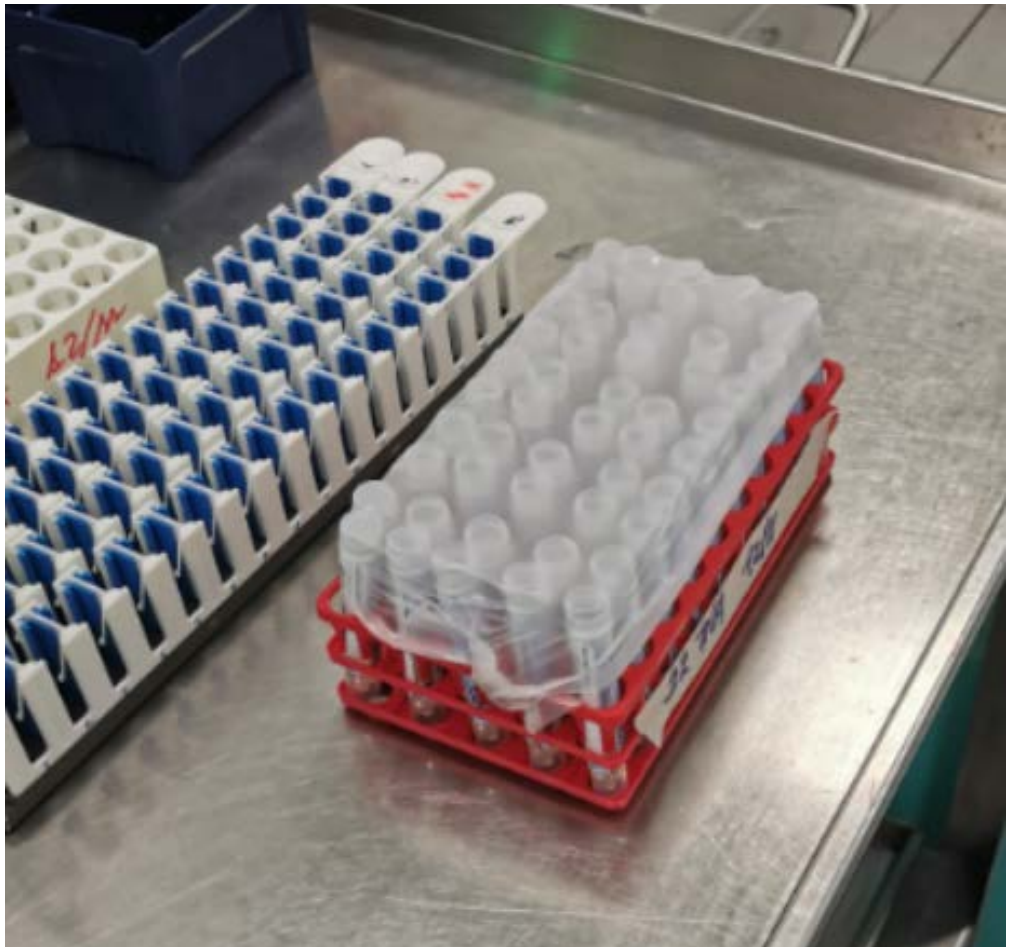
- ❑ Panther Tubes in Generic Rack
- ❑ Labelling
- ❑ Loading in Tecan Racks

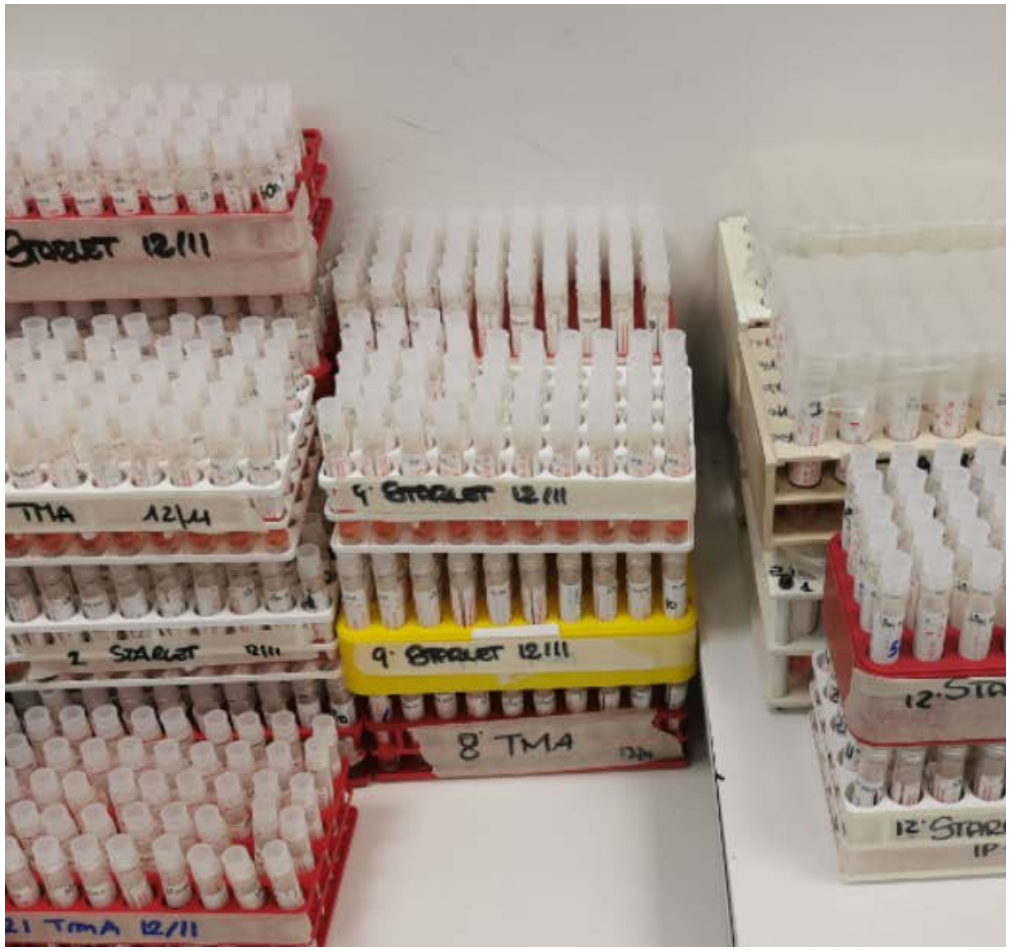




Aliquoting of UTM in Panther Tubes:





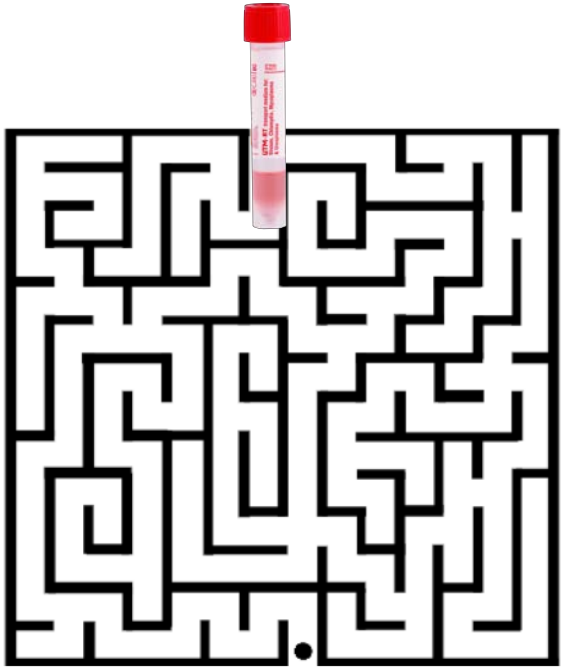


UnLoading of Instrument and Storage of Samples:

Goal Reached!

BUT

Almost 65 samples
Per Hour per FTE



DECEMBER 2019

OCTOBER 2020

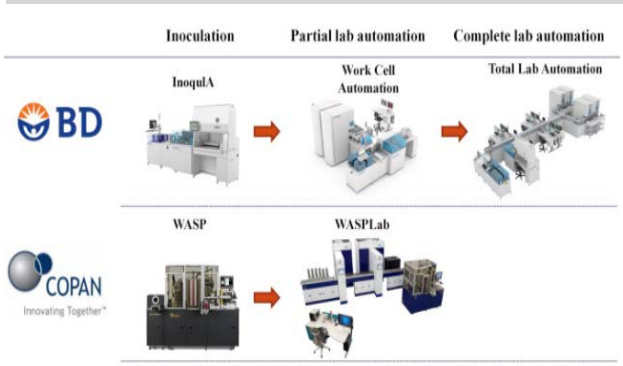
40 Samples a day

4500 Samples a day

How Much is Missing from Collapse?

- Frustration
- Biological Risk
- Staff Turn-Over
- Increase of Testing Numbers?

The Possible Role of Automation: a revolution occurred in bacteriology



Review

Laboratory Automation in Clinical Microbiology

Irene Burckhardt

Department for Infectious Diseases, Microbiology and Hygiene, Heidelberg University Hospital, Im Neuenheimer Feld 324, 69120 Heidelberg, Germany; irene.burckhardt@med.uni-heidelberg.de; Tel.: +49-6221-56-37795; Fax: +49-6221-56-4343

Received: 17 October 2018; Accepted: 19 November 2018; Published: 22 November 2018

check for updates

Review > Clin Lab Med. 2013 Sep;33(3):567-88. doi: 10.1016/j.cll.2013.03.002.

Automation in the clinical microbiology laboratory

Susan M Novak [1], Elizabeth M Marlowe

Affiliations + expand

PMID: 23931839 DOI: 10.1016/j.cll.2013.03.002

Review > Clin Lab Med. 2019 Sep;39(3):371-389. doi: 10.1016/j.cll.2019.05.002.

Total Laboratory Automation: What Is Gained, What Is Lost, and Who Can Afford It?

Richard B Thomson Jr [1], Erin McElvania [2]

Is Molecular Biology **FULLY** Automated?

Review

The cobas® 6800/8800 System: a new era of automation in molecular diagnostics

Bryan Cobb, Christian O. Simon, Susan L. Stramer, Barbara Body, P. Shawn Mitchell, Natasa Reisch, ...show all

Pages 167-180 | Received 25 Aug 2016, Accepted 20 Dec 2016, Accepted author version posted online: 03 Jan 2017, Published online:12 Jan 2017

Download citation https://doi.org/10.1080/14737159.2017.1275962 Check for updates

cobas®
Rx Only

cobas® SARS-CoV-2

Qualitative assay for use on the cobas® 6800/8800 Systems

For use under the Emergency Use Authorization (EUA) only

For in vitro diagnostic use

HOLOGIC®

Panther Fusion® SARS-CoV-2

SARS-CoV-2 Assay (Panther Fusion® System)

For Emergency Use Authorization (EUA) only

For *in vitro* diagnostic use only

Rx only

Instructions for use

Procedural notes

- Do not use **cobas®** SARS-CoV-2 reagents, **cobas®** SARS-CoV-2 Control Kit, **cobas®** Buffer Negative Control Kit, or **cobas omni** reagents after their expiry dates.
- Do not reuse consumables. They are for one-time use only.
- Refer to the **cobas®** 6800/8800 Systems – User Assistance and/or User Guide for proper maintenance of instruments.

Running cobas® SARS-CoV-2

cobas® SARS-CoV-2 can be run with a minimum required sample volume of 0.6 mL.

Always use caution when transferring specimens from primary containers to secondary tube.

Use pipettes with aerosol-barrier or positive-displacement tips to handle specimens.

Always use a new pipette tip for each specimen.

Ensure samples are equilibrated to room temperature prior to transfer into a cobas omni Secondary Tube.

Follow the steps below to transfer patient sample from a UTM-RT or UVT tube into a **cobas omni** Secondary Tube:

- Unscrew the primary sample tube cap.
- Lift the cap and any attached swab to allow a pipette to be inserted into the sample tube. Avoid lifting the swab completely out of the sample tube.
- Transfer 0.6 mL into the prepared barcoded secondary tube.
- Transfer secondary tube to a rack. Close the primary sample tube cap.

A. Swab specimen collection

Collect NP swab, nasal swab, and OP swab specimens according to standard technique using a polyester-, rayon-, or nylon-tipped swab. Immediately place the swab specimen into 3 mL of VTM or UTM. Swab specimens may alternatively be added to saline, Liquid Amies or STM. The Aptima Multitest Swab Specimen Collection Kit may be used for the collection of OP and nasal swab samples.

The following types of VTM/UTM were verified for use.

- Remel MicroTest M4, M4RT, M5 or M6 formulations
- Copan Universal Transport Medium
- BD Universal Viral Transport Medium

Note: *Do not use medium that may contain Guanidium thiocyanate or any guanidinecontaining material.*

B. Nasopharyngeal Wash/aspirate and Nasal Aspirate Specimen Collection

Collect nasopharyngeal wash/aspirate and nasal aspirate specimens according to standard techniques.

C. LRT specimen collection

Collect bronchoalveolar lavage fluid and bronchial wash specimens according to standard techniques.

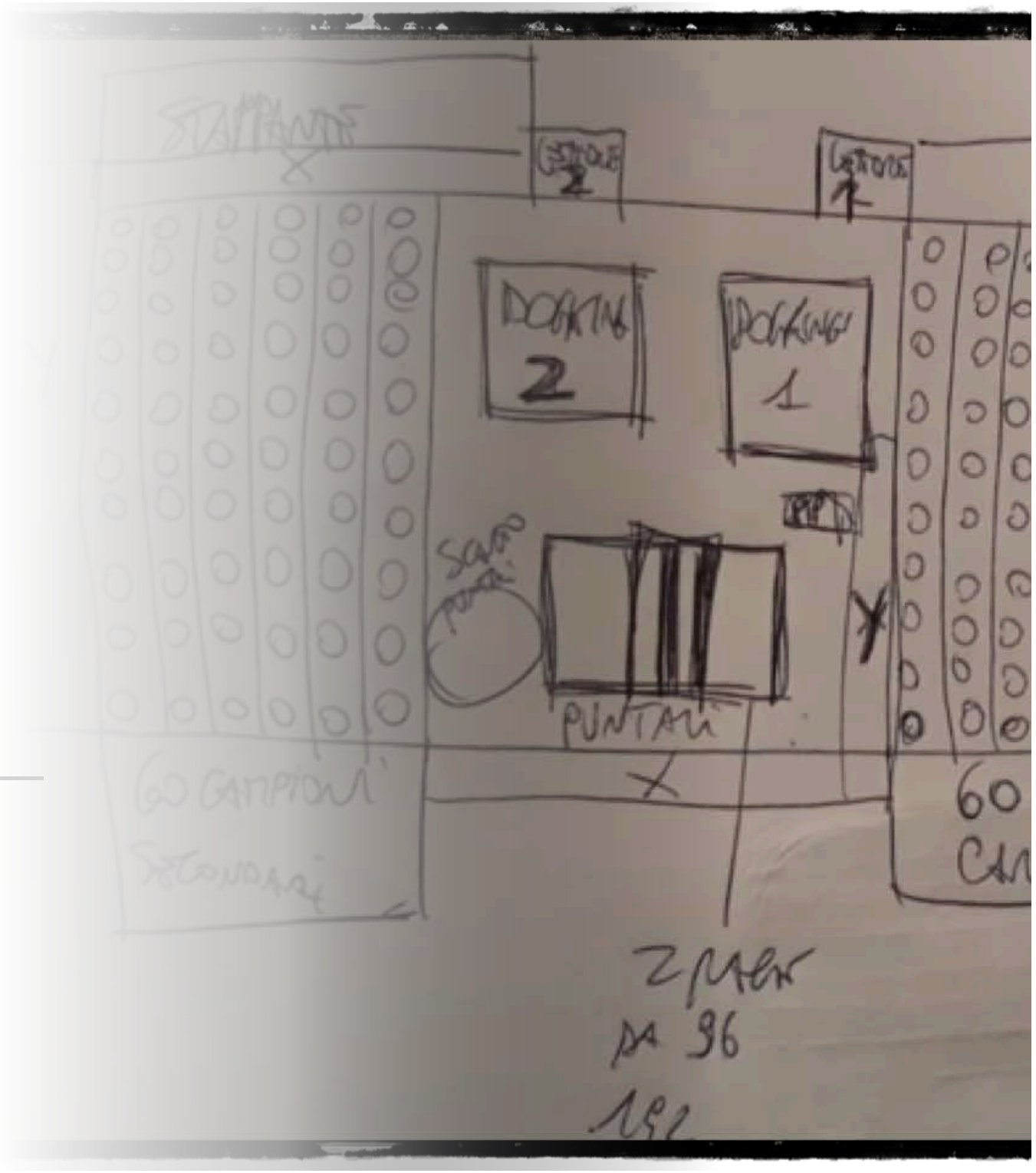
D. Specimen processing using the Panther Fusion Specimen Lysis Tube

1. Prior to testing on the Panther Fusion system, transfer swab or LRT specimen* to a Panther Fusion Specimen Lysis Tube.
   - For swab specimens, transfer 500 µL of the collected specimen to a Panther Fusion Specimen Lysis Tube. Affix the provided penetrable cap.
   - For LRT specimens, transfer 250 uL of the LRT specimen (avoid transferring mucus) and 250 uL of VTM/UTM to a Panther Fusion Specimen Lysis Tube. Affix the provided penetrable cap.

   Note: *When testing frozen specimen, allow specimen to reach room temperature prior to processing.*

Project UniVerse

April 2020



Copan UniVerse

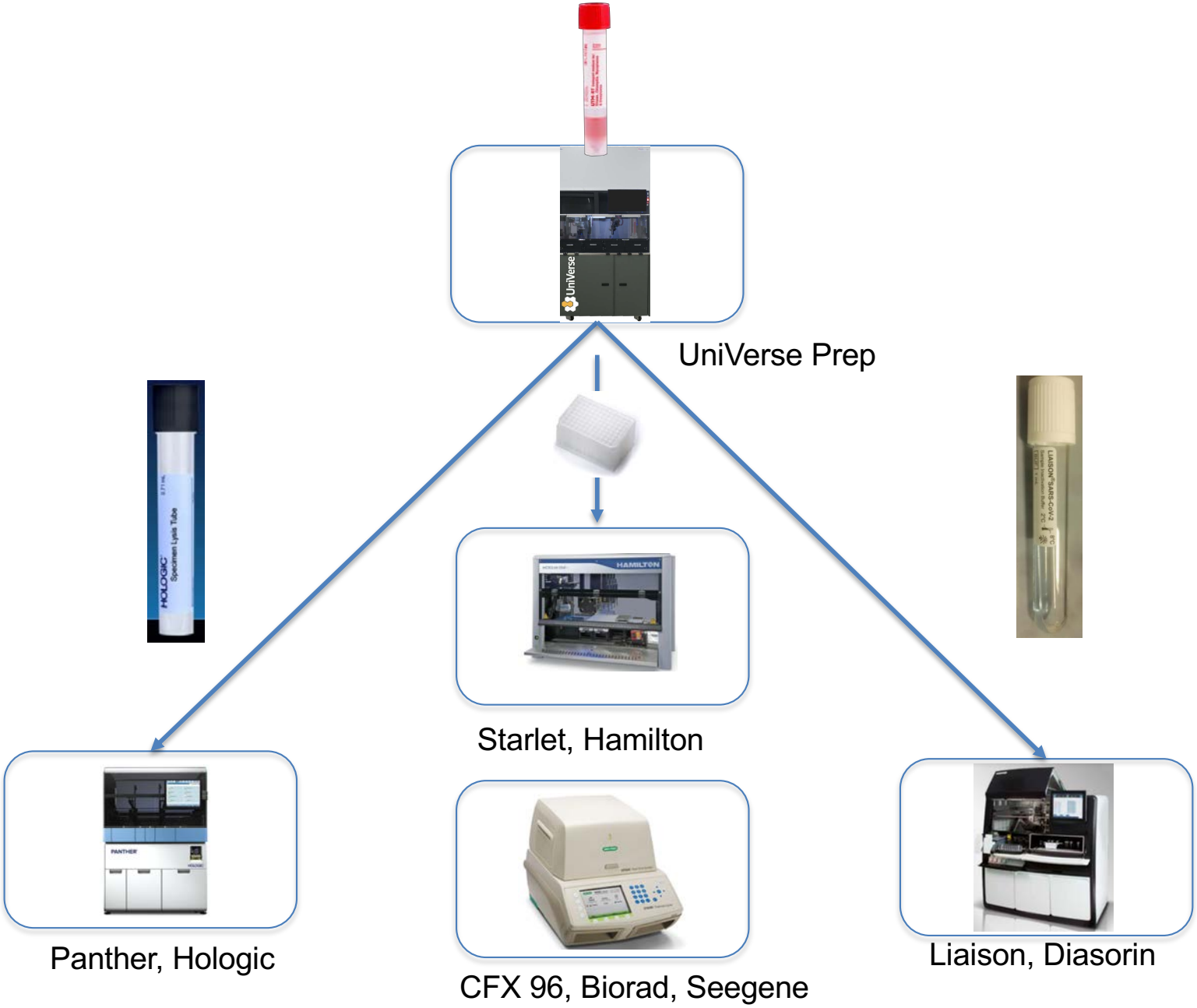
- Installed the 15° of October
- Validated, the 20° of October
- Training Sessions, the 2° of November
- Currently running UTM with Hologic & Liaison tubes

Copan UniVerse

Front End System designed for the Sample Preparation in Molecular Biology & …

- BSL 2 Laminar Flow
- Vortex
- Decap– Recap
- Liquid Handling
- Label Printer

The New Workflow in MY LAB



INPUT SAMPLES:

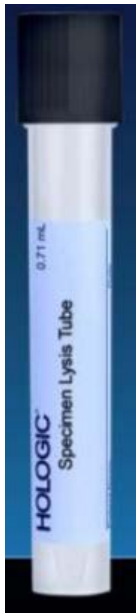
UniVerse works with a variety of containers

Works with the swab inside!

OUTPUT SAMPLES:

- Inoculate Secondary Tubes
- Deep Well-Plates

individual or pooling modality are possible



Clinical Evaluation

The evaluation was performed in my Lab during the validation of the instrument.

Data collection: 19th -20th October

Sample Size: **150** UTM samples from routine:

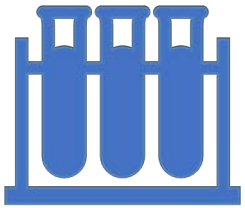
- 66 negative
- 84 positive

Testing Protocol

- All the samples were tested **1-2 days before** as per **manual** internal workflow using the Hologic Panther Assay.

- Samples were **frozen and thawed** the day of the re-processing with Copan UniVerse.

- TMA results obtained from samples processed automatically were compared to those obtained manually.

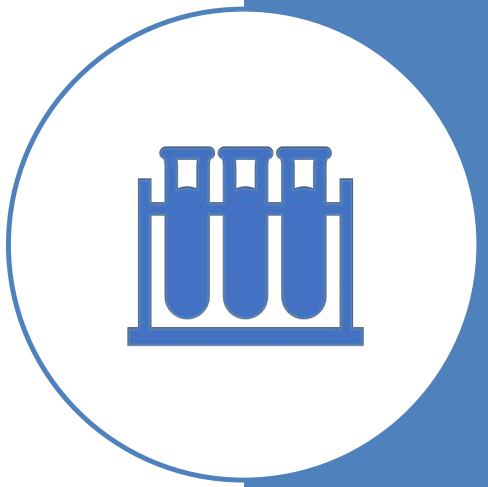


		Manual		
		Positive	Negative	Total
UniVerse	Positive	81	2	83
	Negative	3	64	67
	Total	84	66	150
Overall agreement		96.7 (95% C.I. 92.4% - 98.6%)		
PPA		96.4 (95% C.I. 90% - 98.8%)		
NPA		97 (95% C.I. 89.6% - 99.2%)		

Results

Discrepant Results Analysis

- The original UTM specimens providing discrepant results (n=5) were **retested**
- **In parallel** with the 2 procedures (manual & automatically) the same day providing **concordant results**.



Next Steps…

- LIS connection in order to obtain a secure Check – In
- Further connection with the downstream platform
- Change Management: implementation into the current Chaos is not that easy…

Thank you for your attention

https://focus.copangroup.com/universe/

U.O. MICROBIOLOGIA
Pievesestina