HIV VIRAL LOAD TESTING OPERATIONAL GUIDE

→ 60 LESSONS LEARNED FROM THE OPP-ERA PROJECT

SUMMARY

FOREWORD

From its inception, the OPP-ERA project was part of the global strategy to respond to HIV / AIDS, especially to help achieve the 3rd goal of the "90-90-90", i.e. 90% of all people receiving antiretroviral treatment have viral suppression. An undetectable viral load is a guarantee of effective treatment and non-transmission of the virus and is therefore crucial.

Unitaid played a pioneering role from 2012 in introducing viral load measurement in Africa by funding several innovative projects, including OPP-ERA which has been implemented in four countries of Francophone Africa, namely the Republics of Burundi, Cameroon, Côte d'Ivoire and Guinea. The project was led by a French consortium, in collaboration with the health authorities and partner associations of the four countries.

Increasing access to viral load measurement and raising laboratories' standards to the minimum standards of quality of Molecular Biology, both in terms of health staff training and the organization of sites, was a lengthy process. These 4 countries are now ready to roll out viral load testing on a large scale. For people living with HIV, it means increased access to viral load testing and treatment follow-up.

In this context, it seemed necessary to make this Guide available for viral load testing implementation, as well as a comprehensive toolkit available in French on viral load testing implementation.

Unitaid is very proud to have supported the development of these materials, the result of six years of project and field experience in Francophone Africa. These materials are essential for all players trying to improve access to viral load measurement in their country.

Lelio Marmora,
Executive Director, Unitaid - which supported the project from 2013 to 2019

"In order to implement HIV viral load testing, the only choice of a technical solution is not sufficient. The conditions needed for its realisation in resource-limited countries also need to be created. This is what we wished to highlight in this Guide. We are proud to bring you our 60 lessons learned, for all the viral load testing stakeholders."

Louis Pizarro,
CEO, Solthis – which implemented the project in Guinea and led the project from 2016 to 2019

"The OPP-ERA project is a model of success of a translational research project: initiated by virologists and economists based on the results of their research, it helped build an innovative routine HIV viral load testing strategy and demonstrated its feasibility in resources-limited settings."

François Dabis,
Director, ANRS – in charge of the project's scientific coordination

"The deployment of the OPP platforms in our countries of operation not only contributed to the decentralization of HIV viral load testing but also helped to get closer to reaching scaling-up objectives. The coexistence of open and integrated platforms in these countries, even in some sites, proved that they were complementary."

Antoine Peigney,
Director, Health Department, Expertise France – which implemented the project in Cameroon and in Côte d'Ivoire and led the project from 2013 to 2016

"This project has shown how relevant the commitment of civil society and community players, alongside the national authorities, was in the fight against HIV. The transition of the OPP-ERA project in the countries ensures a continuum of the viral load measurement activities, now included in national strategies."

Florence Thune,
Executive Director, Sidaction – which implemented the project in Burundi

EXECUTIVE SUMMARY

The situation has changed since HIV viral load testing was recommended in 2013 by WHO as the tool of choice for evaluating the efficacy of antiretroviral treatment, then selected by UNAIDS as the 3rd key indicator of the "90-90-90" strategy to end the HIV / AIDS epidemic. The test is now on the agenda of HIV / AIDS programs, but its effective access to West and Central Africa is still a challenge.

The purpose of this Guide is to share the richness of the experience gained over six years of implementation of the OPP-ERA project in four Francophone countries. This document is the result of collective reflection between the project's coordination teams and the teams mobilized in the field, cross-examination between several disciplines and extensive synthesis work.
Based on both successful and sometimes mixed experiences, and assuming that some achievements remain fragile, this Guide is intended both as a bridging tool after the transition in the project's four partner countries, and as a constructive testimony for all the other players involved in HIV viral load testing operationalization.

The **OPP-ERA project** supported partners from the Republics of Burundi, Cameroon, Côte d'Ivoire and Guinea in the deployment of HIV viral load testing offer. This Guide starts with the presentation of the results of the OPP-ERA project in each of these countries.
Eleven laboratories were opened in these countries, all equipped with OPP (open and polyvalent viral load platform, combining equipment and reagents that can be provided by several manufacturers, to perform viral load tests and diagnoses of various infectious agents).

Beyond the technical solution, viral load operationalization is based on a systemic approach including complementary links, presented in the five thematic chapters of this Guide.

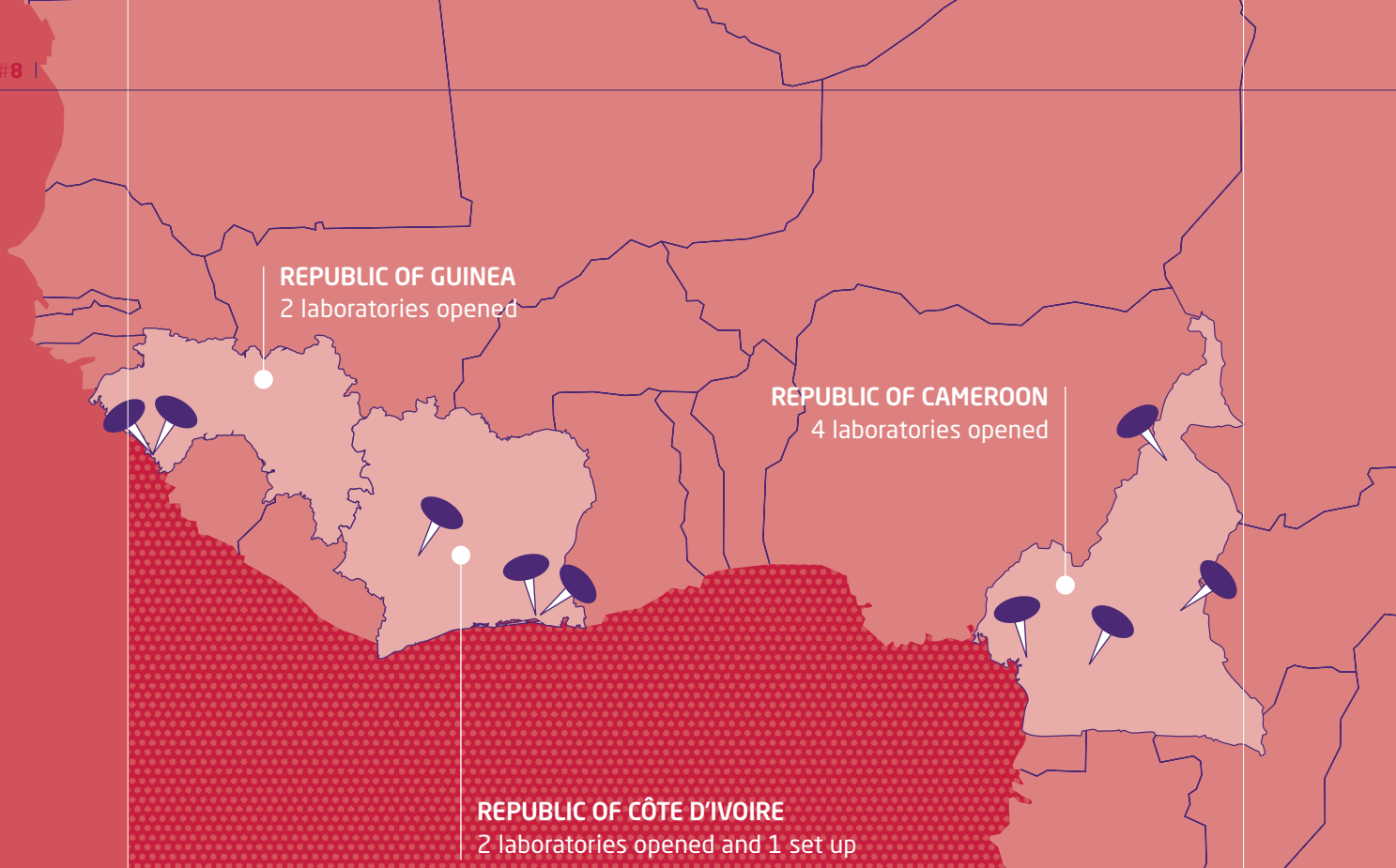
- **The national strategy** addresses issues of governance, stakeholder coordination, the creation and consolidation of viral load testing offer and demand, and the production of data informing the programmatic and clinical levels.
- In the **laboratory**, the quality requirement is high as the results can influence patient care. To achieve this, the focus must be on training and coaching staff, organizing the activities in the laboratories and achieving quality standards through the implementation of Good Laboratory Practices.

How to read the thematic pages of this Guide?

03	shows lessons learnt and illustrated focus of attention
	provides tips and solutions for operational implementation
	highlights considerations for National HIV / AIDS programs and financial partners
OPP	points out aspects specific to the OPP platforms; the rest of the Guide is common regardless of the technique used
	refers to the Online toolkit in French by mentioning the name of the tool corresponding to the issue considered; access this Toolkit, available in French, by using the QR code provided at the beginning of the chapter

- The **procurement and supply** includes needs estimation as well as procurement and inventory management for each laboratory product to ensure continued availability. It presents logistical challenges, including cold chain and maintenance management, all issues that are aggravated in weakened health systems. The skills required are also very specific.
- In terms of **patient care**, after focusing on the prescription of HIV viral load testing, which is an essential first step, it is now urgent to strengthen the use of the results. In the case of virological success, it ensures regular monitoring of treatment effectiveness. In the case of virological failure, the use of the results makes it possible to adjust management of each patient and to slow the development of resistance.
- Finally, the **economy** sheds additional light. The observation of the widening and diversification of technical solutions gives hope for access to viral load testing for a larger number of patients. The full cost analyses that we conducted for viral load testing and waste management help inform programmatic decisions.

Today, the challenges of operationalization and perpetuation of viral load testing lies in the setting to music of this complex and multidisciplinary score. Everyone has a role to play. Strong leadership from the Ministries of Health, in line with national and international technical partners, and with adequate funding, will ensure that quality care becomes a reality for all people living with HIV.



REPUBLIC OF GUINEA
2 laboratories opened

REPUBLIC OF CAMEROON
4 laboratories opened

REPUBLIC OF CÔTE D'IVOIRE
2 laboratories opened and 1 set up

PROJECT SUCCESSES FROM 2013 TO 2019:

→ **11**
laboratories rehabilitated, equipped and operational

→ **2**
laboratories rehabilitated, equipped and prepared for opening

→ **+ 300**
health professionals trained (clinicians, PSM experts, laboratory staff)

→ **25**
laboratory staff certified to perform HIV viral load testing on OPP

→ **more than 230,000**
viral load tests performed

→ **+ 81 %**
of patients with suppressed viral load and up to 89% in some sites

THE OPP-ERA PROJECT

REPUBLIC OF BURUNDI
3 laboratories opened and 1 set up

The OPP-ERA project has been part of the global HIV / AIDS strategy from its inception, including the UNAIDS' 90-90-90 target, and especially the "3rd 90": reaching by 2020 the target of 90% of all people receiving antiretroviral treatment and having viral suppression.
Launched in 2013, the OPP-ERA project has thus helped to expand access to this key test in four countries in West and Central Africa.

This project was supported and funded by Unitaid, implemented by a consortium led by Solthis, in charge of operational coordination and implementation in the Republic of Guinea; the ANRS, as co-funder and in charge of the scientific direction; Expertise France, in charge of the implementation of the project in the Republics of Cameroon and Côte d'Ivoire; and Sidaction in the Republic of Burundi.

In each country, the project was carried out in close collaboration with the Ministries of Health and the National HIV / AIDS Programs, the HIV care units, the laboratories and the partners from the civil society.

→ Discover results by country

REPUBLIC OF BURUNDI

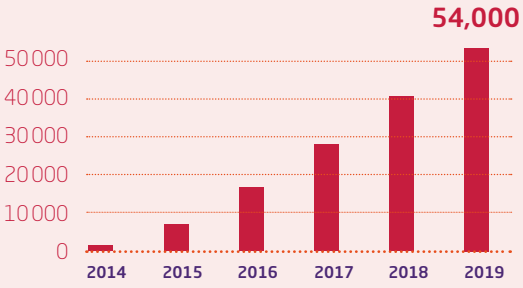
3 LABORATORIES OPENED AND 1 SET UP:

1. ANSS - National Association for the Support of HIV-positive and AIDS patients, Bujumbura / opened in 2014.
2. Muyinga Hospital / opened in July 2018.
3. CHUK - Kamenge University Hospital Bujumbura / opened in September 2018.
4. Gitega Hospital / opening scheduled for late 2019.

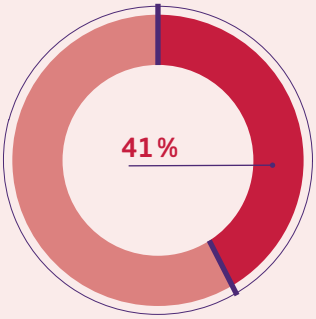
Number of people living with HIV on antiretroviral treatment: **68,012**

Source: National AIDS and IST control program (PNLS/IST), June 2019

Number of HIV-1 viral load tests performed as part of the OPP-ERA project
(cumulative data from 2014 to 2019)



Ratio of viral load tests performed on OPP on all viral loads at national level between 2016 and 2019



Average virological success rate between 2016 and 2019: **89%**

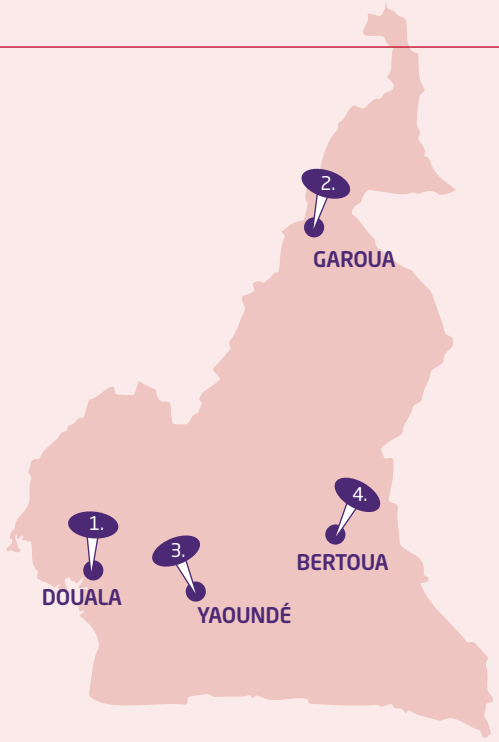
THE TRANSITION OF THE OPP-ERA PROJECT IN THE REPUBLIC OF BURUNDI

After more than five years of operation, Sidaction concluded the OPP-ERA project in July 2019, giving way to a national strategy for scaling up viral load testing, which is currently being developed.
The transition from the OPP-ERA project to the PNLS/IST (National AIDS and IST control program), in collaboration with the Global Fund, ensures a continuum of activities on the OPP platforms and contributes to the achievement of the "3rd 90" target set by UNAIDS.

"ANSS, the leading community association in the care of PLHIV, has become the first associative laboratory to perform viral load testing in Burundi and, thanks to its professionalism, has opened the way to the establishment of 3 other laboratories in hospitals. Thanks to the OPP-ERA project, the staff and patients, the quality of the increasing offer of viral load testing is high."

Angéline Inamahoro,
OPP-ERA project supervisor in the Republic of Burundi

REPUBLIC OF CAMEROON



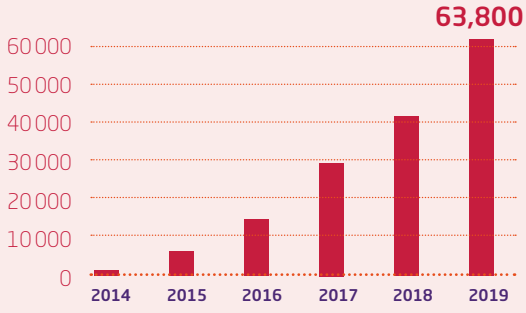
4 LABORATORIES OPENED:

1. Laquintinie hospital of Douala / opened in 2014.
2. Centre Pasteur of Cameroon, Annex of Garoua / opened in 2014.
3. Central Hospital of Yaoundé / opened in February 2019.
4. Regional Hospital of Bertoua / opened in February 2019.

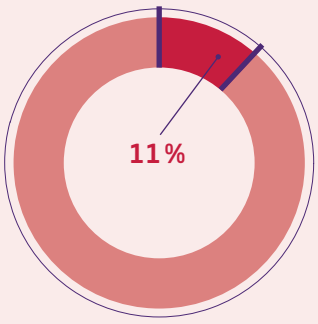
Number of people living with HIV on antiretroviral treatment: **302,822**

Source: National Committee to Fight AIDS (CNLS), June 2019

Number of HIV-1 viral load tests performed as part of the OPP-ERA project
(cumulative data from 2014 to 2019)



Ratio of viral load tests performed on OPP on all viral loads at national level between 2016 and 2019



Average virological success rate between 2016 and 2019: **81%**

THE TRANSITION OF THE OPP-ERA PROJECT IN THE REPUBLIC OF CAMEROON

The transition of the OPP-ERA project will be led by the CNLS, with the support of Expertise France. It is the subject of a specific plan, written in close collaboration with the Ministry of Health and its various directorates as part of participatory workshops. Procurement, demand consolidation and generation, as well as laboratory activities are all included in this plan. The procurement of OPP products will be done through the CNLS via the Global Fund HIV grant.

"The OPP-ERA project was introduced in Cameroon at the right time: it laid the foundations and contributed to decision-making about setting up the viral load testing as a test of choice for routine monitoring of treatment effectiveness. It also helped create demand by training physicians, investing in the sample circuit, and reducing the turn-around time to the patients."

Dr Marinette C. Ngo Nemb Epse Tchato,

Public Health Doctor,
Head of the Support Section for the Health Sector,
CNLS, Republic of Cameroon

REPUBLIC OF CÔTE D'IVOIRE

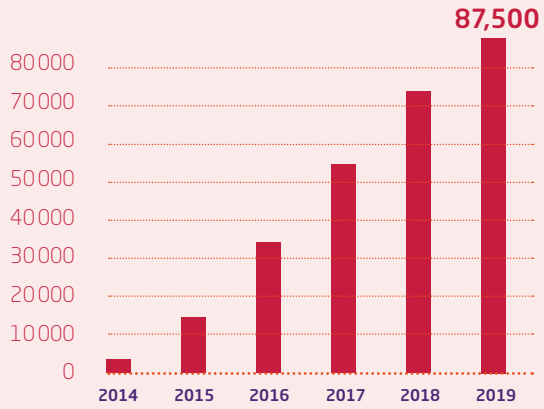
2 LABORATORIES OPENED AND 1 SET UP:

1. CeDReS - Diagnosis and Research Centre on AIDS and other opportunistic diseases, / opened in 2010, OPP-ERA support since 2014.
2. CePReF - Treatment Research and Training Centre, Abidjan / opened in 2014.
3. Regional Hospital Center of Daloa / preparation for opening at the end of 2019.

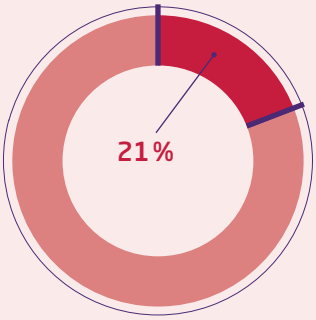
Number of people living with HIV on antiretroviral treatment: **268,894**

Source: National AIDS Control Program (PNLS), June 2019

Number of HIV-1 viral load tests performed as part of the OPP-ERA project
(cumulative data from 2014 to 2019)



Ratio of viral load tests performed on OPP on all viral loads at national level between 2016 and 2019



Average virological success rate between 2016 and 2019: **78%**

THE TRANSITION OF THE OPP-ERA PROJECT IN THE REPUBLIC OF COTE D'IVOIRE

The OPP-ERA project is being carried out under the leadership of the National AIDS Control Program (PNLS), supported by the various structures of the Ministry of Health and Public Hygiene. In practice, the priorities of this transition, discussed with Expertise France, are to pursue staff reinforcement (laboratory, clinical, community staff) and supply of products required to operate on OPP platforms, by the national stakeholder via the Global Fund.

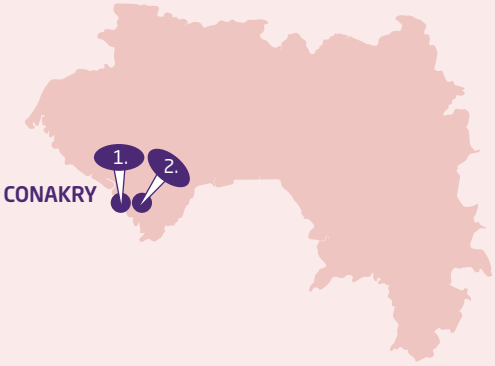
"Today, the routine free viral load testing is a reality in Côte d'Ivoire, and the country is fully committed to eliminating AIDS by 2030.
The OPP-ERA Project is firmly set in this approach and its implementation by Expertise France in Côte d'Ivoire, especially through human resource training, construction and equipment of laboratories, undoubtedly contributed to achieving our common goal."

Pr Bakary Soro Kountele Gona,
Director of Cabinet of the Minister of Health and Public Hygiene, Republic of Côte d'Ivoire

REPUBLIC OF GUINEA

2 LABORATORIES OPENED

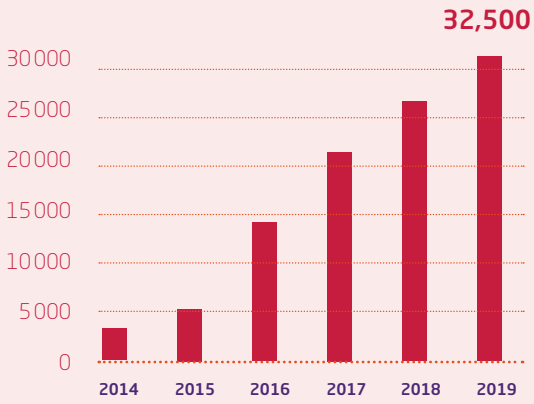
1. INSP - National Institute of Public Health, Conakry / opened in 2014.
2. Donka Hospital, Conakry / opened in 2014.



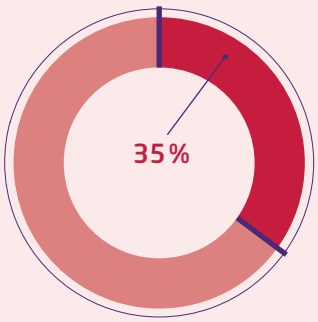
Number of people living with HIV on antiretroviral treatment: **50,664**

Source: National AIDS and hepatitis Control Program (PNLSH), June 2019

Number of HIV-1 viral load tests performed as part of the OPP-ERA project
(cumulative data from 2014 to 2019)



Ratio of viral load tests performed on OPP on all viral loads at national level between 2016 and 2019



Average virological success rate between 2016 and 2019: **79%**

THE TRANSITION OF THE OPP-ERA PROJECT IN THE REPUBLIC OF GUINEA

Most of the activities of the OPP-ERA project have already been taken over by the main partner, PNLSH, especially the supply of the necessary products via the Global Fund grant.
The implementation of the transition plan at the end of 2017, with Solthis' support, led to the creation of a Working Group on the 3rd 90, gathering all the viral load stakeholders, and the production of a 4-year operational plan of action for scaling-up HIV viral load testing.

"We have been careful to list activities that will ensure the sustainability of the OPP-ERA project as part of the Global Fund grant. This will allow us to establish all the mechanisms required to ensure continued viral load measurement activity in the country, but also to pursue decentralization and scale up as much as possible."

Dr Youssouf Koïta,
National Coordinator, PNLSH, Republic of Guinea

1

HIV VIRAL LOAD
STRATEGY

Online toolkit in French

toolkit-chargevirale-oppera.solthis.org/strategie-nationale

toolkit-chargevirale-oppera.solthis.org/collecte-des-echantillons

toolkit-chargevirale-opperasolthis.org/gestion-des-donnees

The issue of access to HIV viral load testing and the actions to be implemented far outweigh the choice of laboratory equipment. Access to viral load testing must be considered through an ambitious and rewarding approach of capacity building and quality requirements.
Coordinated by the various stakeholders, such as governance bodies, laboratories, HIV care units, procurement and supply departments, as well as by patients and the civil society, this approach contributes to the success of operationalization of HIV viral load testing program.

DEVELOP A NATIONAL HIV VIRAL LOAD TESTING STRATEGY

Lesson learnt No 01

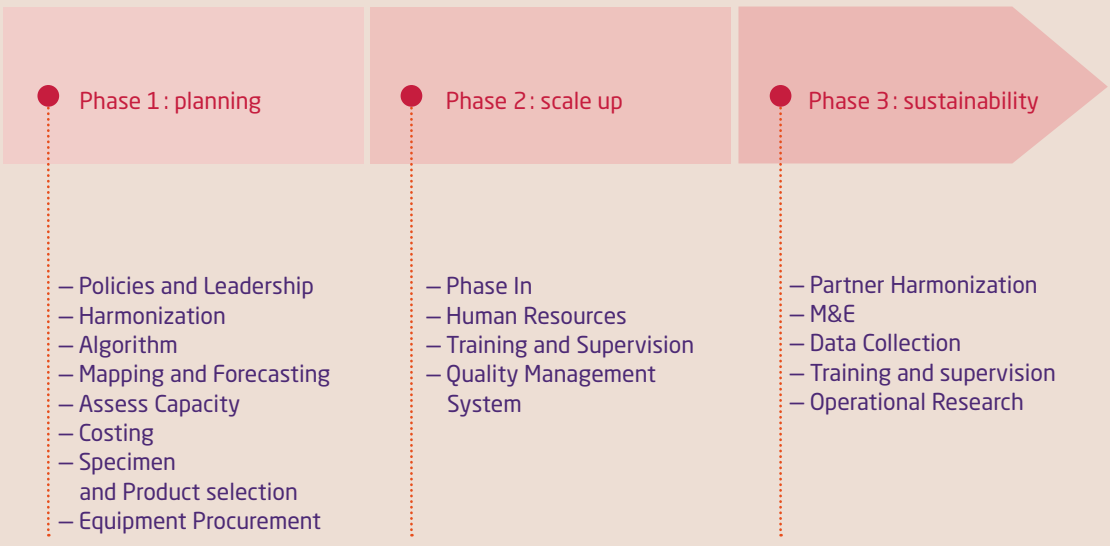
The development of a national strategy for accessing and scaling up viral load testing, with a sequential operational plan, helps to define a common vision and targeted objectives with all stakeholders. Close activity monitoring and setting up of indicators for programmatic monitoring then stem from this national strategy. (Fig. No 1)

Programmatic consideration

→ Anticipate that the introduction of the HIV viral load testing necessarily implies the adoption of national recommendations, the training of laboratory and staff from the HIV care units (especially in the management of virological failures), the reorganization of health care channels (especially to reinforce the provision of adherence support) and the provision of laboratory products and new therapeutic lines.

Figure No 1 : **Technical and operational considerations for the implementation of HIV viral load testing**

(From WHO -Technical and Operational Considerations for Implementing HIV Viral Load Testing - Interim Technical – Update July 2014)



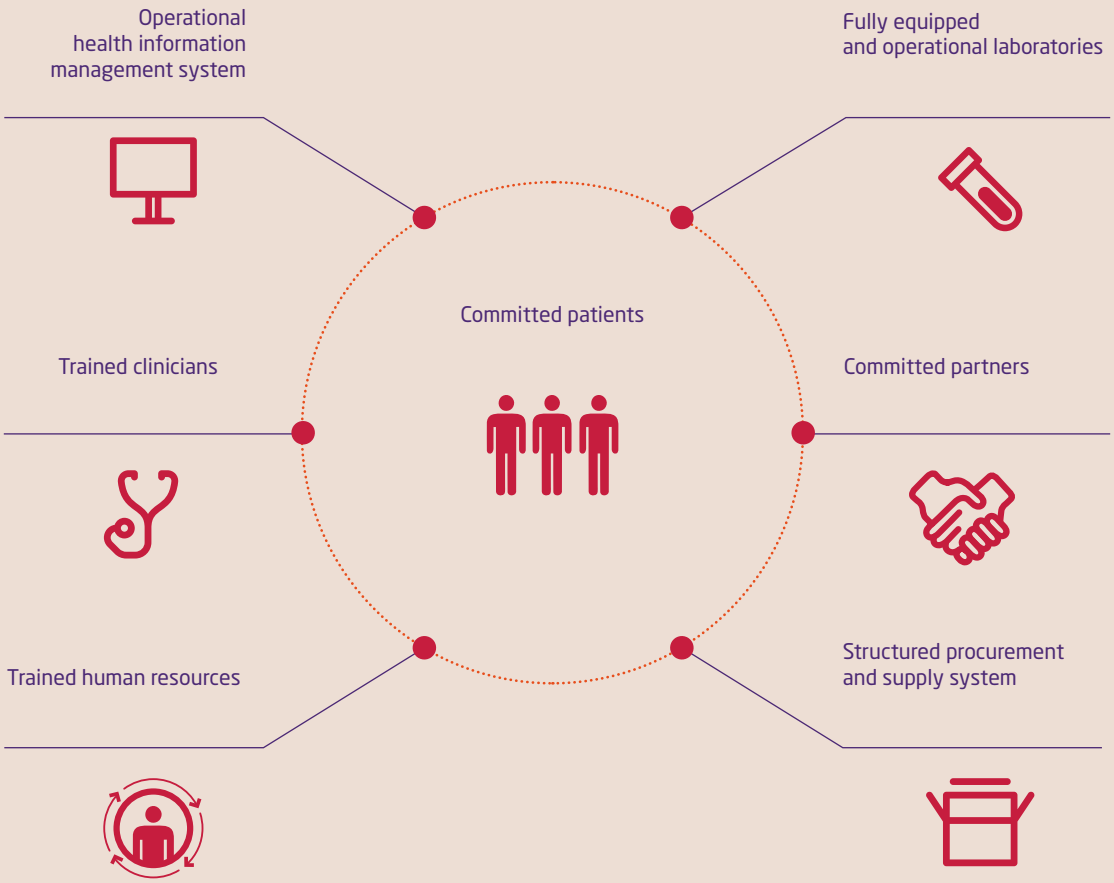
Lesson learnt No 02

The national strategy integrates both a mapping of the existing supply at national level and a reflection on demand creation or consolidation, including within the framework of the decentralization. The focus is often more on supply through ambitious quantitative targets (number of HIV viral load tests), while a more global approach allows for better consideration of all dimensions to improve access to viral load testing. (Fig. No 2)

Programmatic consideration

→ Proceed in stages in terms of operationalization of the national strategy and resist the temptation to respond to the access issue by simply deploying viral load measurement equipment, useless if the other conditions are not met. Access to viral load is a necessary tool to improve patient care and is not a goal in itself.

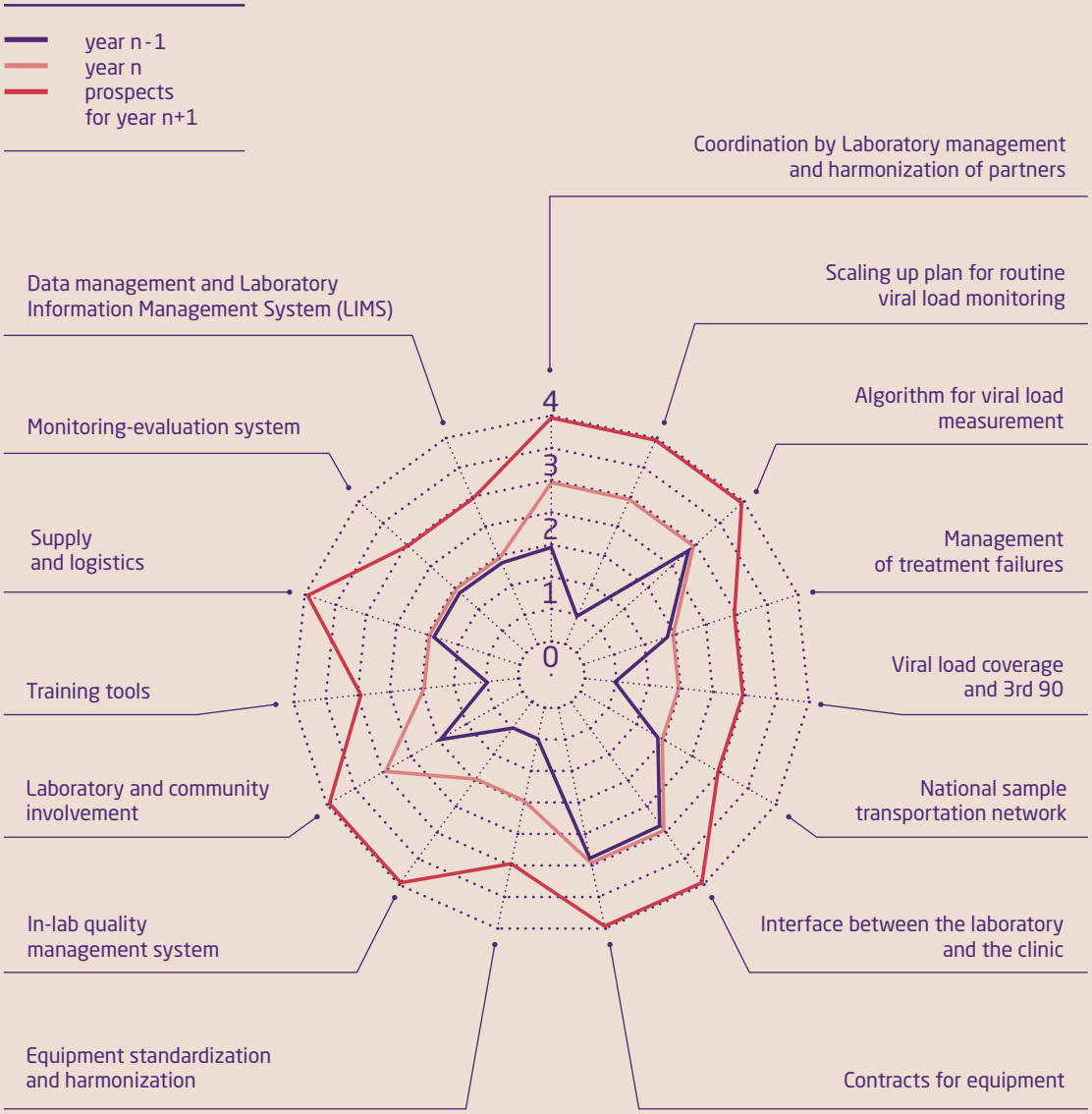
Figure No 2: **Global approach used in the OPP-ERA project to establish favorable conditions for HIV viral load testing in health systems**



Tip

→ Use the WHO Viral Load Scorecard tool (based on 15 criteria, rated from 1 to 4, 4 being the Gold Standard) for an overall analysis of viral load scaling up status. (Fig. No 3)

Figure No 3: **Example of use of the WHO Viral Load Scorecard**



Online toolkit in French

→ **Stratégie Nationale de mise à l'échelle de l'examen de charge virale en Guinée**

ESTABLISH A ROBUST NATIONAL LEADERSHIP AND COORDINATE PARTNERS

Lesson learnt No 03

Strong national leadership is essential to optimize available resources, steer the multiple actions needed to consolidate and expand access to HIV viral load testing country-wide and find solutions to challenges encountered.
The steering of a national viral load testing program requires the involvement of the various stakeholders (governance bodies, laboratories, HIV care units, procurement and supply departments, patients and civil society), but also the country's technical and financial partners.
Regular interactions facilitate the resolution of certain issues in a field which is finally very "technical" and allows to foster the commitment of all parties.

Programmatic consideration

→ Involve the National Directorates of Laboratories of the Ministry of Health in coordinating the scaling up of HIV viral load testing.
→ Establish a technical group that regularly brings together all players involved in activities related to viral load testing under the auspices of the Ministry of Health, intended to play a central role in the governance of the "HIV viral load testing" or "3rd 90" program.

Lesson learnt No 04

During annual programming (or as part of the Global Fund grant applications), realistic and achievable targets should to be defined. Scaling up of HIV viral load testing programs is still a real challenge and can only be considered step by step.

Programmatic consideration

→ Coordinate projects funded by various donors and implemented by various operators to ensure complementarity in support of national strategy implementation.

Lesson learnt No 05

Targets for access to HIV viral load should take into account the capacity of the laboratories (equipment and trained staff).

Lesson learnt No 06

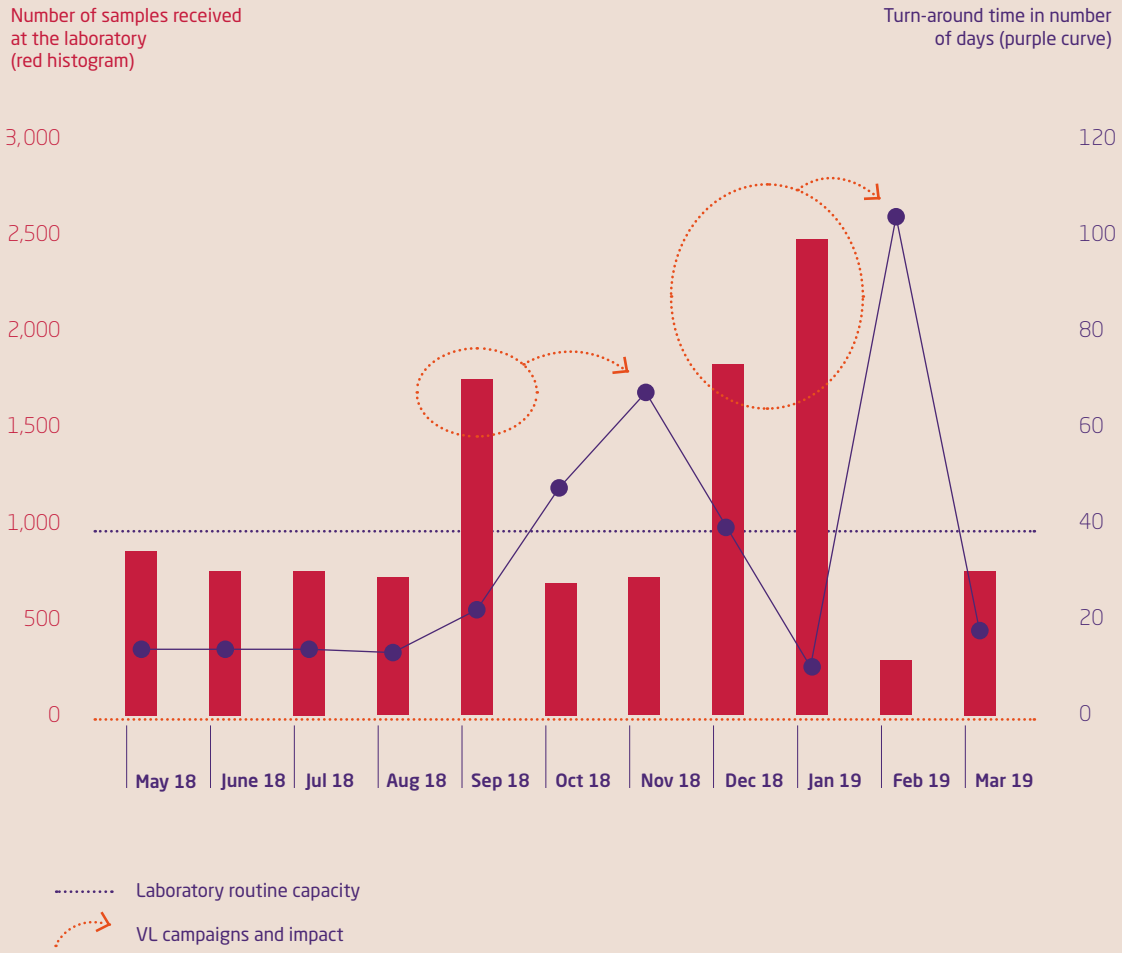
The organization of HIV viral load testing campaigns is often considered as a simple solution to perform a large number of viral load tests. However, it leads to significant workload variation in laboratories that disrupts their operations and generally significantly slows down the turn-around time. (Fig. No 4)

Programmatic consideration

→ Schedule viral load testing monitoring within 3 to 6 months for patients facing virological failure, when organizing viral load testing campaigns in areas where access is non-existent.

→ Foster an approach focused on the quality indicators of viral load testing (especially turn-around time) on the one hand, and on the clinical use of the viral load tests, on the other.

Figure No 4: **Illustration of the impact of viral load testing campaigns on a laboratory's turn-around time, based on the experience of the OPP-ERA project**



PROVIDE PROGRAMMATIC AND CLINICAL DATA WITH THE ESTABLISHMENT OF AN HEALTH INFORMATION SYSTEM

Lesson learnt No 07

Databases installed in viral load testing laboratories could be used to provide the desired programmatic data (number of patients who benefited from viral load testing during the year, ratio of patients with suppressed viral load) as well as to inform the HIV care units, as it facilitates access to each patient's full medical history.
Completeness of laboratory databases is an issue : too little data is generally usable.

Tip

→ The information to be collected through the HIV viral load testing application forms should be limited in number.
→ Laboratory databases are not intended to replace clinical databases.

Programmatic consideration

→ Coordinate the various players involved in defining the data to be collected, in providing the necessary tools for this collection, as well as for the exploitation of this data.
→ Recruit staff with advanced computer skills to ensure database maintenance.
→ Ensure that there is enough time for data entry, if possible with dedicated data clerks, and that the laboratory is supported by a data manager.
→ Educate the staff in charge of filling in the collection tools about the importance of quality data (for patients and prescribers, and to improve programmatic decisions).
→ Ensure that the data entry is carried out simultaneously with testing, so as not create delay the turn-around time.
→ Integrate viral load testing data collection into pre-existing laboratory information management systems (LIMS).

Online toolkit in French

→ **Base de données laboratoire du projet OPP - ERA**
→ **Manuel d'utilisation de la Base de données laboratoire du projet OPP - ERA**

STRUCTURE HIV VIRAL LOAD OFFER

Lesson learnt No 08

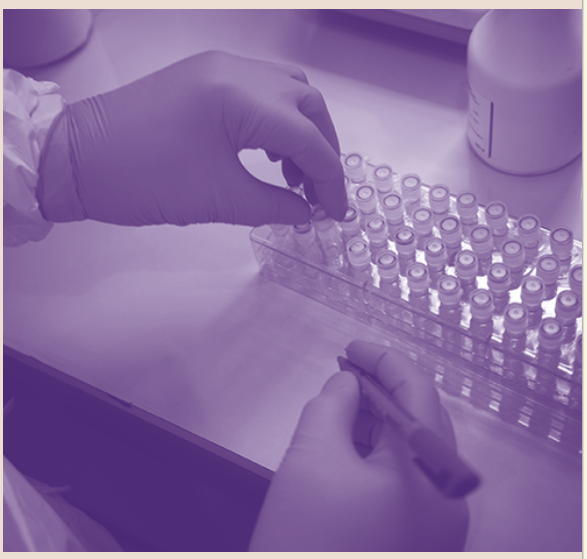
An effective viral load test offer means that operational laboratories should be available (adequate infrastructure, operational equipment, continuous availability of laboratory products, trained laboratory staff, etc. *(Cf. Laboratory section)* and that appropriate and effective patient sample (blood samples) collection channels are defined and set up.

Lesson learnt No 09

It may be useful to have several types of equipment without complicating too much the equipment management.
Indeed, this makes it possible to meet different types of needs (in particular from a quantitative point of view), but also to have an alternative in case of immobilization of equipment, an unfortunately common situation.

Figure No 5 : **Examples of delivery of samples to the laboratory based on the sampling location, experimented in the OPP-ERA project**
(HIV viral load test on plasma)

	Case No1	Case No2	Case No3
Sampling location	**Clinic or laboratory**	**Clinic or laboratory of the HIV care unit**	**Relay clinic or laboratory**
Pretreatment of samples	No	Yes (plasma separation)	Yes (plasma separation)
Samples intermediate storage location	–	Clinic or laboratory of the HIV care unit	Relay laboratory
Intermediate shelf life before transfer to the laboratory	Blood sample: 24h at room temperature	Plasma: 5 days at 4°C	Plasma: 5 days at 4°C or higher duration if samples are frozen
Frequency of sample transfer to the laboratory	Daily	Once a week	Once a week or less if frozen
Indication	Laboratory and clinic on the same site	Remote laboratory and clinic	Remote laboratory and clinic



Lesson learnt No 10

The essential link that is sample transportation from HIV care units to the laboratory is still underestimated, sometimes relegated to the patients themselves, or entrusted to associations or NGOs, even though this activity is key to scale up and its cost remains low. (Fig. No 5)

Tip

- → Train the caregivers in good sampling practices to ensure the samples can be analyzed later in the laboratory.
- → Identify and use the circuits to avoid duplicates.
- → Provide alternative circuits to other laboratories to maintain HIV viral load testing activity when a laboratory is temporarily non-operational or if the demand significantly exceeds the laboratory capacity.
- → Provide consumables and equipment required for sampling, sample storage on site, and transport to the laboratory.

Programmatic consideration

- → Whenever possible, pool the sample collection circuits for better cost-effectiveness between national programs (especially between HIV/AIDS and Tuberculosis programs for example) and/or the various HIV viral load testing projects.
- → Coordinate the various circuits to ensure complementarity and avoid the recovery of some of them, by counterparts willing to quickly achieve high quantitative objectives.
- → Integrate the costs associated with the collection/transportation sample circuits, essential for the activities, as eligible for funding.
- → Where possible, structure the sample collection and transportation circuits in parallel with the circuits for results delivery (in order to use the same circuits in the opposite direction).
- → Ensure that the people responsible for the different steps are identified and trained (collection, storage, transportation, reception) so that the patient sample collection circuits operate.

Online toolkit in French

- → **Options pour le choix des prestataires de services pour les circuits de collecte des échantillons**
- → **Modèles de circuits de collecte des échantillons et de rendu de résultats**

CONSOLIDATE HIV VIRAL LOAD DEMAND

Lesson learnt No 11

Prescribers, patients and patient associations / community based organizations are the drivers of demand.

Information and education of patients on the benefits of viral load test follow up, through health education measures and mobilization of PLHIV associations, seem key.
Such education facilitates a better understanding by patients of their care and better adherence to antiretroviral treatment.

On the one hand, clinicians must be trained to prescribe the HIV viral load exam and to use the viral load results *(cf. Patient care section)* and, on the other hand, be informed of exam availability and of laboratory sample collection and delivery procedures.

Programmatic consideration

- → From the moment when the test is available to patients, adapt the usual awareness messages and tools to incorporate the use of viral load testing, and train the caregivers / partners to promote viral load testing.
- → Within the national HIV / AIDS program, identify the contact person in charge of the HIV care units monitoring, who is capable of supporting the prescription of viral load testing and facilitating issue resolution by regular site visits.
- → Support clinicians to use HIV viral load testing (training and tutoring) to improve patient care quality.
- → Use databases to identify sites and prescribers to prioritize in terms of support needed.

Lesson learnt No 12

The delivery of results from the laboratory to the HIV care units and their different clinical services can be organized in various ways: information can be sent directly to the clinician; patients may be asked to get their results from the laboratory; an SMS delivery system could also be considered. In any case, it is essential that the results reach both the clinician and the patient.

When the test results arrive at the HIV care units, they must each be integrated into the corresponding patient records. The laboratory can then be sent a reminder in case of missing results, which then allows for the use and notification of the results to the patient at their next consultation, and finally clinical decision-making. (Fig. No 6)

While the OPP-ERA project has not always managed to make turn-around time optimal, it seems at least essential that high viral loads (> 1000 copies / mL) can be easily identified, and that patient care adapted to this situation can be arranged as early as possible.

Tip

- → When defining indicators, bear in mind that the turn-around time at the laboratory differs from the turn-around time to the prescriber and then to the patient.
- → Set up computerized databases in laboratories, useful because it allows one to publish the list of patients with virological failure and to regularly transmit it to the clinical site.

Figure No 6 : **The different steps to take into account in the calculation of the results' turn-around time.**
(Source : ASLM)

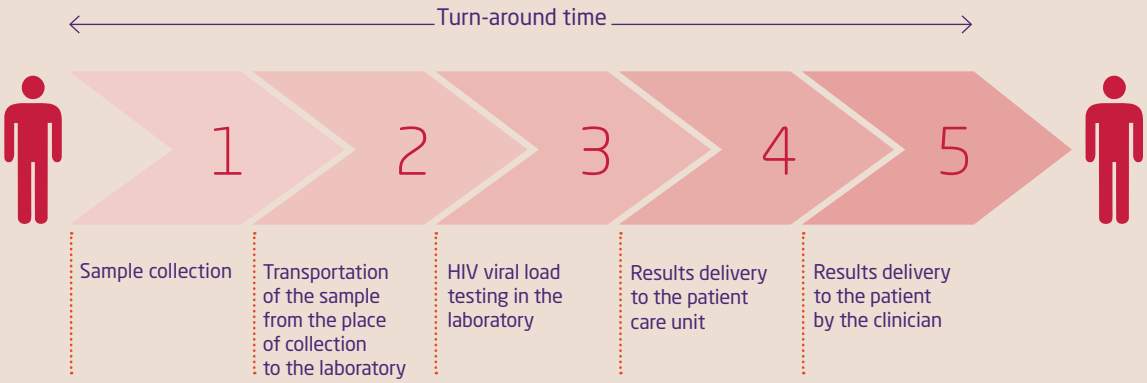
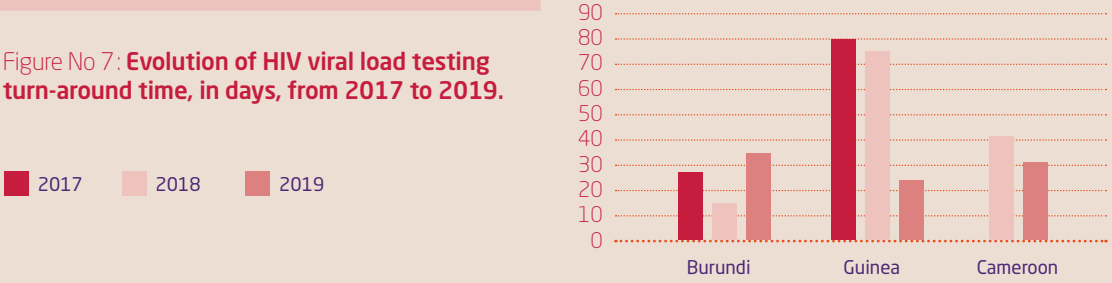


Figure No 7 : **Evolution of HIV viral load testing turn-around time, in days, from 2017 to 2019.**



Programmatic consideration

→ Delivering the results within an acceptable timeframe should be one of the quality targets of the laboratory: the prescriber can then have the results at the consultation following viral load testing prescription, especially when a follow-up viral load testing is expected. (Fig. No 7)

→ Set up warning systems to quickly identify patients whose HIV viral load results have been received and those requiring adequate care (use of a registry to identify patients with virological failure).

Online toolkit in French

→ **Outil de mobilisation pour les patients pour la charge virale en Guinée**
→ **Formulaire de demande de test de charge virale VIH-1**
→ **Modèle de rendu de résultat indétectable**
→ **Modèle de rendu de résultat détectable inférieur à 1000 copies / mL**
→ **Modèle de rendu de résultat détectable supérieur ou égal à 1000 copies / mL**
→ **Modèle de rendu de résultat invalide**

2

LABORATORY

A number of prerequisites is necessary for HIV viral load testing laboratories to be operational, regardless of the technique used.
The establishment of a dedicated laboratory, built according to the standards of Molecular Biology, continuous training and empowerment of laboratory technicians, organization of activities and implementation of Good Laboratory Practices (GLP) guarantee the quality of the results delivered to the patient.
In the scaling up, the success of the HIV viral load testing activity at national level depends on the integration of the laboratories and their staff at all decision-making levels.

Online toolkit in French

toolkit-chargevirale-oppera.solthis.org/laboratoire

COORDINATE EXPERTISE TO SET UP A LABORATORY OF MOLECULAR BIOLOGY

Lesson learnt No 13

The establishment of a Laboratory of Molecular Biology (LMB) is based on a complete preliminary assessment of its environment:

— At the level of the existing structure or laboratory:

Equipment maintenance and repair
Products and cold chain management
Sampling management
Data and information management
Quality assurance, hygiene and biosafety

— At the level of the new LMB to set up:

Permanent availability of water and electricity
Premises layout and overall condition
Inventory of existing laboratory equipment
Expected volume of activity
Human resources assigned to the laboratory and their availability for this new activity

Lesson learnt No 14

Laboratory design and close monitoring of installations require various competencies:

— a laboratory expert, specialized in LMB, to propose suitable layout of the premises (e.g. separation of the pre- and post-amplification areas, respect of the "forward flow" principle),
— an engineer specialized in health / laboratory structure to ensure the conformity of the installations (e.g. hermetically insulated rooms, covering of the walls, specificities of the benches),
— an electrician to ensure that the electrical installation will meet the needs of the laboratory *(Cf. Procurement section)*. (Fig. No 8)

OPP

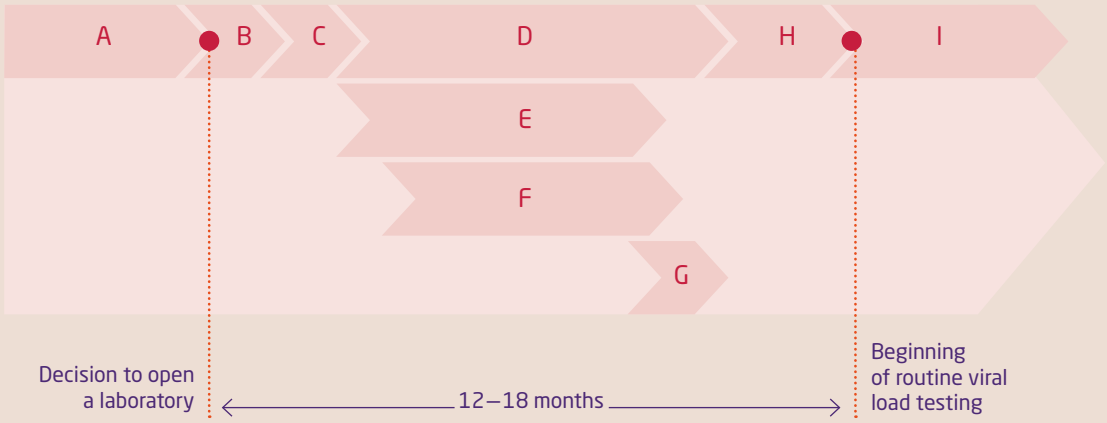
Tip

→ Provide a total surface area of at least 60 m2 to set up a laboratory performing HIV viral load testing on OPP.

Programmatic consideration

→ Use the competencies already existing in the country (at the level of the reference centers for example).
→ Provide major investment for infrastructure upgrades ahead of the opening of the laboratory, then for their maintenance, in order to ensure activities' sustainability. Integrate this key budget into the financing plans.

Figure No 8: **The different stages of a Laboratory of Molecular Biology establishment based on the experience of the OPP-ERA project**



Steps	Approximate duration	Entities in charge
A Site Selection	N/A	Ministry of Health and partners
B LMB's environmental assessment	15 days - 1 month	Expert in Laboratory of Molecular Biology (LMB)
C LMB design	1 month	LMB expert, health structure / laboratory engineer and electrician
D Selection, purchase and installation of equipment	3 - 6 months	LMB expert, health structure / laboratory engineer
E Facilities	4 - 7 months	LMB expert, supply expert and suppliers
F Quantification, purchase and delivery of products	5 months	LMB expert, supply expert
G *Ex situ* staff training	15 days - 1 month	Reference center
H *In situ* staff training	2 months	Reference center and / or LMB expert
I Staff continuous training	Continuous	Reference center and / or LMB expert

Online toolkit in French

→ **Grille d'évaluation et plan d'action : mise en place de laboratoires de biologie moléculaire réalisant des tests de charge virale VIH**
→ **Exemples - Plans de laboratoire de biologie moléculaire**

TRAIN AND SUPPORT LABORATORY STAFF

Lesson learnt No 15

The identification of the laboratory team dedicated to the HIV viral load testing activity (biologists, technicians, data clerks) and of its actual availability makes it possible to set realistic activity objectives and ensures the quality of the tests within acceptable turn-around times.

Tip

- → Ensure that the structure's management develops an organizational chart that clearly defines the functional, organizational and hierarchical links within the HIV viral load testing laboratory.
- → Consider the time dedicated to external activities (e.g. teaching, participation in training and/or workshops) in the calculation of actual staff availability.
- → Provide a data clerk as soon as the volume of laboratory activity exceeds 300 viral load tests per week.
- → Define the weekly activity volume of the laboratory according to the accredited staff, and not trainees who are not a sustainable resource.

Programmatic consideration

- → Establish a strategy for the retention of staff trained and certified to perform HIV viral load testing on the platform used in the laboratory, with regard to skills that are often highly specific compared to those of other laboratory services.

Lesson learnt No 16

The presence of a biologist is highly recommended to guide and carry out HIV viral load testing activities: not only for results validation and interpretation (taking into account their clinical impact) but also for the organization and the management of the laboratory.
This position is even more essential in a laboratory with a volume of activity greater than 200 viral load tests per week. (Fig. No 9 and 10)

Tip

- → When it isn't possible to recruit a biologist, set up a double technical validation system as well as laboratory supervision by a network of national, regional or international experts.

Programmatic consideration

- → Recruit biologists for each laboratory, especially as part of the scaling up of HIV viral load testing activity.

OPP

Figure No 9: **Ideal composition of the laboratory team according to the target volume of activity for optimal equipment use, based on the experience of the OPP-ERA project**

Capacities are expressed in number of HIV viral load tests per week (1 plate = 82 VL tests)

* requires two different daily shifts for technicians

Staff	Full-time equivalent dedicated to the VL activity	Maximum activity volume based on HR	Number of extractors	Theoretical maximum activity volume (according to the supplier) based on the number of extractors
Biologists Technicians Data clerks	50% 200% 0%	246	2	410
Biologists Technicians Data clerks	50% 200% 50%	328		
Biologists Technicians Data clerks	50% 200% 100%	410	3	615
Biologists Technicians Data clerks	100% 300% 150%	615*		

OPP

Figure No 10: **Examples of laboratory team compositions with adjustment recommendations to increase volumes of activities, based on the experience of the OPP-ERA project**

* requires two different daily shifts for technicians

	Laboratory 1	Laboratory 2	Laboratory 3	Laboratory 4
Staff and full-time equivalent dedicated to the VL activity	Biologists: 60% Technicians: 0% Data clerks: 0%	Biologists: 10% Technicians: 300% Data clerks: 50%	Biologists: 0% Technicians: 200% Data clerks: 100% trainee	Biologists: 25% Technicians: 100% *+ 300% trainees* Data clerks: 100%
Number of extractors	2	2	3	3
Maximum activity volume based on existing HR	82	246	328	369
HR adjustment recommendations	Recruit at least one full-time technician for routine activity, the biologist can then dedicate herself / himself to the validation and management of the laboratory	Increase to 50% the time of the biologist dedicated to the laboratory, have one of the technicians supporting the data clerk	Recruit a biologist (at least part-time) to maintain quality; appoint the trainee on a permanent basis or recruit a full-time data clerk instead	Increase to 100% the time of the biologist dedicated to the laboratory, recruit 2 technicians (or appoint 2 trainees on a permanent basis),recruit a data clerk on a part-time basis
Maximum activity volume if recommendations are followed	164	328	410	615*

Lesson learnt No 17

A sequential, comprehensive and tailored staff training plan (defined after assessment of staff knowledge/skills) is to be planned prior to the opening of an LMB. The process is long-term (continuous training guaranteeing the sustainability of a quality routine activity).

Putting this plan into action led to the certification of 25 staff from the 11 laboratories supported by the project. The third-party organization that conducted the skills assessment assigned "referent" (12 individuals) or "competent and independent" (13 individuals) levels in performing HIV viral load testing on OPPs. At least two people were certified as "competent and independent" in each supported laboratory.

Tip

- → Anticipate that nearly 80% of the training time is dedicated to activities that "surround" the technical aspects of viral load testing and allow the routine operation of the laboratory, regardless of the HIV viral load testing equipment used: pre and post-testing phases, laboratory organization and management, quality assurance and sample traceability, GLP, hygiene and biosafety.
- → Avoid being limited to the training offered by the suppliers, who solely focus on equipment use.

Online toolkit in French

- → **Mise en place de laboratoire de biologie moléculaire dans les pays à ressource limitée**
- → **Extrait OMS - Considérations techniques et opérationnelles pour la mise en œuvre de la mesure de la charge virale du VIH**
- → **Habilitation du personnel: 13 documents**
- → **Outil de calcul des besoins en intrants pour la mesure de la charge virale du VIH sur plateformes ouvertes**

Programmatic consideration

- → Identify a national reference center for HIV viral load testing on OPP: this center is a laboratory where this technique is performed routinely, which may be different from the national reference laboratory, and which has a group of experts capable of conducting or supervising the training activities of other laboratories.
- → Promote sub-regional collaboration between laboratories to create a community of practice.
- → Provide a budget for all Figure 11 trainings, including national, regional or international travel as needed.

Lesson learnt No 18

As soon as a LMB is opened, regular assessment of the biologists and technicians' skills ensures their ability to carry out the activity or identify additional training needs.
This assessment takes into account all the steps involved in viral load testing, from reception, recording and preparation of samples, sample analysis, to the recording and submission of results. Certification of biologists and technicians for HIV viral load testing happens at the end of the assessment process. (Fig. No 11)

Programmatic consideration

- → Encourage the reference center to periodically support the skills assessment and staff certification process.

OPP

Figure No 11 : **Training of laboratory staff in carrying out HIV viral load testing on OPP: the OPP-ERA model**

PREPARATION FOR THE OPENING OF THE LABORATORY (2 months)

- 4 weeks — **Initial training - *ex situ* by the Reference Center**
  Training on Good Laboratory Practices (GLP), reception and pre-testing sample processing, extraction
- 1 week — **Training on platform equipment - *in situ* by the suppliers**
  Take advantage of the 1 week visit from the supplier of the amplification reagents for platform qualification (extractor + thermocycler) - in situ (requirement of ISO15189)
- 1–2 weeks — **Database training - *in situ* by the database expert**
  Installation of the database in the laboratory and database training
- 2–4 weeks — **Comprehensive training in routine VL testing and GLP - *in situ* by a laboratory expert**
  Training on VL testing on OPP from sample reception to results submission
  + Establishment of GLP and tools to ensure traceability of samples
- 1 week — **Skills assessment and certification - *in situ* by an external evaluator (then internal process)**
  Skills assessment throughout the process and certification of competent staff

CLOSE MONITORING (the first 6 months)

- 1 week / quarter — **Formative supervision - *in situ* by the laboratory expert**
- 0,5 days / week — **Remote mentoring by the laboratory expert**

CONTINUOUS TRAINING (every year)

- 1–2 weeks / quarter — **Formative supervision - *in situ***
- 1 week — **Refresher trainings and annual capacity building (workshops)**
- as needed — **Remote Mentoring**

*The training of technicians in situ (in their laboratory) provides for better ownership of the activity, taking into account the challenges and specificities of the laboratory, and thus adapting the content of the training accordingly.

ORGANIZE AND COORDINATE HIV VIRAL LOAD TESTING ACTIVITIES

Lesson learnt No 19

The success of routine HIV viral load testing is based on optimal management and organization of activities at the laboratory, at the hosting facility and at country level. The organization of viral load testing at the laboratory level results in:

- Human resources management, including the distribution of tasks and the assignment of transversal roles (with identified focal points for inventory management, quality assurance, biosafety, database and communication with HIV care units),
- Weekly planning of activities for laboratory staff, taking into account activity volumes and organizational requirements related to the management of priority samples, compliance with the timeframe for HIV viral load testing in the laboratory, and the implementation of a quality approach,
- Close monitoring of inventory and equipment functionality, management of the premises (maintenance of air conditioners) and monitoring of the cold chain,
- Seamless communication with the HIV care units, including, inter alia, the biologist's participation in clinical meetings to anticipate variations in the number of samples to be received, and, if necessary, to discuss the quality of samples and support clinicians in the interpretation of results. (Fig. No 12, 13 and 14)

Tip

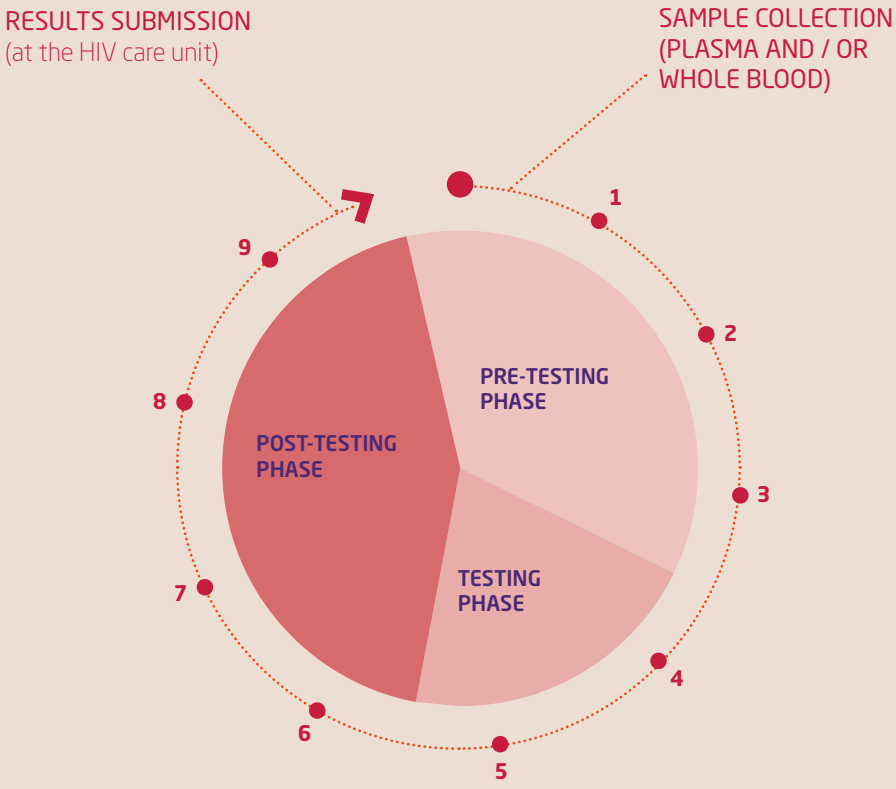
→ Regarding reference centers, plan their involvement in the training and supervision of other viral load testing laboratories at the time of planning activities.

Programmatic consideration

→ Define and set up a priority sample management system (e.g. pregnant and/or breastfeeding women).

OPP

Figure No 12: **Viral load testing process - from reception of samples to results submission, based on the experience of the OPP-ERA project**



PRE-TESTING PHASE

1 Reception of samples at the laboratory

- Rejection / acceptance of samples
- Filling in of the non-compliance form in case of rejection
- Identification of priority samples

2 Sample record

- Allocation of the sample code
- Recording in the paper register
- Recording in the database

3 Pre-testing sample processing and freezing

- Plasma aliquoting from whole blood
- Filling in of the freezing form

TESTING PHASE

4 Extraction

- Preparation of worksheets using the HIV Generic VL roadmap
- Extraction from plasma

5 Amplification

- Preparation of the amplification mix
- Amplification of HIV RNA by RT - qPCR

POST-TESTING PHASE

6 Analysis and technical validation

- Analysis and validation of the entire plate
- Analysis and validation of each sample
- Identification of the samples to be retested
- Filling in of follow-up form and validation of HIV VL tests

7 Analysis and biological validation

- Verification of the follow-up form and validation of HIV VL tests (double validation)
- Consideration of the clinical impact at 1 000 copies / mL

8 Results recording and printing

- Recording in the database and printing
- Recording on the paper register

9 Final biological validation of the results and signature

- Interpretation of the result at 1000 copies / mL
- Possible analysis of the results history already obtained in the laboratory for each patient
- Verification of compliance of the result report sheet and signature

Figure No 13: **Example of a typical weekly schedule for a laboratory that routinely handles 3 plates (246 viral load patient tests) per week with two full-time technicians and a part-time biologist, based on the experience of the OPP-ERA project**

* corresponds to the activities for which the focal points are responsible (e.g. inventory management, calls to HIVcare units, revision of protocols or internal laboratory audit)

		Technician A	Technician B	Biologist (50%)
Monday	AM	VL testing on 82 patient samples: preparation, extraction, amplification (plate 1)	Other activities * + preparation for Tuesday	
	PM		Receipt, pre-testing sample processing and entry into the database	
Tuesday	AM	Interpretation and technical validation of plate 1, then entry, printing and verification of the results if double validation accepted + preparation for Wednesday	VL testing on 82 patient samples: preparation, extraction, amplification (plate 2)	Double-validation, check and signature
	PM	Receipt, pre-testing sample processing and entry into the database		
Wednesday	AM	VL testing on 82 patient samples: preparation, extraction, amplification (plate 3)	Interpretation and technical validation of plate 2, then entry, printing and verification of the results if double validation accepted	Double-validation, check and signature
	PM		Receipt, pre-testing sample processing and entry into the database	
Thursday	AM	Interpretation and technical validation of plate 3, then entry, printing and verification of the results if double validation accepted	Other activities *	Double-validation, check and signature
	PM	Other activities *	Receipt, pre-testing sample processing and entry into the database	
Friday	AM	Weekly activity monitoring meeting between the biologist and the technicians		
	PM	Other activities * preparation for Monday	Receipt, pre- testing sample processing and entry into the database + laboratory clean up	Laboratory organization and management
Weekend			Standby for freezers' temperature monitoring	

Lesson learnt No 20

The organization of HIV viral load testing at the level of the structure hosting the laboratory results in:

- The involvement of its management team in the pre-opening stages of the laboratory, followed by monitoring and support of routine HIV viral load testing activities (e.g. HR management, electricity supply to ensure cold chain continuity),
- The participation of laboratory staff in the structure's meetings,
- The integration of the HIV viral load testing laboratory in all the laboratory services of the structure to pool or centralize the systems for receiving samples, managing laboratory information and reporting results to the HIV care units. harge. (Fig No 14)

Tip

→ Have the laboratory expressing its requirements clearly and early, and ensure that the management of the structure does take it into consideration.
→ Foster communication between the laboratory and the clinicians, to provide for a common understanding of expectations and raise awareness of laboratory staff on the impact of their work on patient care; in order to guarantee a quality service to patients.

"The viral load laboratory has been very well received at the Bertoua Regional Hospital where we have to manage a large number of people living with HIV.
Before its opening, my role as head of the structure was to take ownership of the project and to activate everything that was possible to accelerate the effective establishment of the laboratory.
Today, now that this one runs routinely, as far as possible, my role is to facilitate its operation, by involving myself whenever necessary to solve the problems met daily."

Dr Hugette Claire Nguélé Méké,
Director, Regional Hospital of Bertoua,
Republic of Cameroon

"In Guinea, viral load testing emerged in the public sector thanks to the OPP-ERA project. At this point, almost all physicians could start prescribing viral load testing.
At the beginning, they had difficulties understanding the tests' results.
My participation in the various meetings helped them to understand for example the difference between the results presentation modes (log and copies) or the requirements for filling in the test application forms.
Today, my cross-cutting involvement in all viral load activities makes me a resource person, capable to use this expertise in the meetings of the Technical Medical Committee and laboratory technical meetings of the National HIV / AIDS Program."

Penda Maladho Diallo,
Head of the Molecular Biology Unit,
National Institute of Public Health,
Republic of Guinea

Lesson learnt No 21

The organization of viral load testing at the national laboratory level results in:

- The integration of the Laboratory of Molecular Biology (LMB) in the national network of laboratories
- The involvement of the laboratory staff in the technical committees' decisions related to the HIV viral load activities, including:

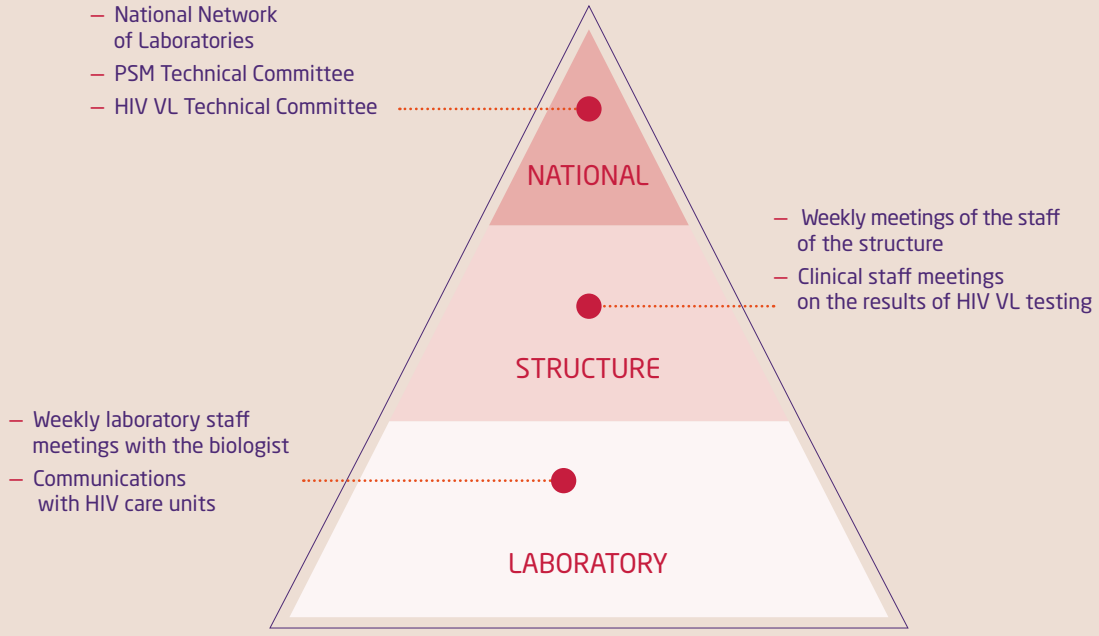
— Supply and inventory management, especially when defining activity targets for laboratories, selecting and quantifying products and monitoring equipment functionality,

— Operational coordination of the HIV viral load activity, especially in the definition of sampling circuits and the organization of sampling campaigns.
(Fig. No 14)

Programmatic consideration

→ Involve the National Directorate of Laboratories as well as the reference center in the organization and monitoring of HIV viral load activity at national level.
→ Ensure that HIV viral load laboratories are linked to the National HIV / AIDS Program, while being integrated into the national laboratory strategy (in order to limit the verticalization of activity) and into national technical groups such as PSM (Procurement and Supply chain Management) and HIV viral load testing groups.

Figure No 14: **Integration of the laboratory and its staff to organize the activity at all decision-making levels, based on the OPP - ERA project experience**



STRENGTHEN GOOD LABORATORY PRACTICES AND ENSURE TESTING QUALITY

Lesson learnt No 22

The strengthening of the Good Laboratory Practices (GLP) and the implementation of a quality assurance process make it possible to guarantee the quality of the tests in the Laboratory of Molecular Biology (LMB). Several tools and initiatives were thus set up under the OPP-ERA project, including:

- Traceability of the patient samples, at all stages, from receipt to results submission,
- Establishment of standard operating procedures and incident notification forms (essential for setting up a warning system),
- Weekly monitoring of laboratory activity indicators (e.g. number of samples received, number of valid tests performed),
- Weekly monitoring of the quality indicators (e.g.: sample rejection rate, invalid results rate, no stock shortage or equipment failure, respect of turn-around times, results of internal quality control in tests),
- Competency assessment for the certification of biologists and technicians to perform HIV viral load testing,
- Quarterly formative supervision and regular mentoring by a laboratory expert,
- Participation in external quality audit (EQAs) through programs managed by the Center for Disease Control and Prevention (CDC), free in Africa (with a success rate of 100% for the OPP-ERA laboratories in 2019), Quality Control for Molecular Diagnostics (QCMD) and / or Oneworld Accuracy (1WA) (with a success rate of 73% in 2019),
- Implementation of the routine use of a Quality Control independent from the supplier. A proof of concept was conducted as part of the OPP-ERA project with NRL (a non-profit organization) to anticipate the future requirement of monitoring the quality of tests in biomedical laboratories.
- Conducting internal audits using the HIV viral load laboratory evaluation scorecard developed jointly by the World Health Organization (WHO), the African Society for Laboratory Medicine (ASLM) and the CDC. (Fig. No 15 and 16)

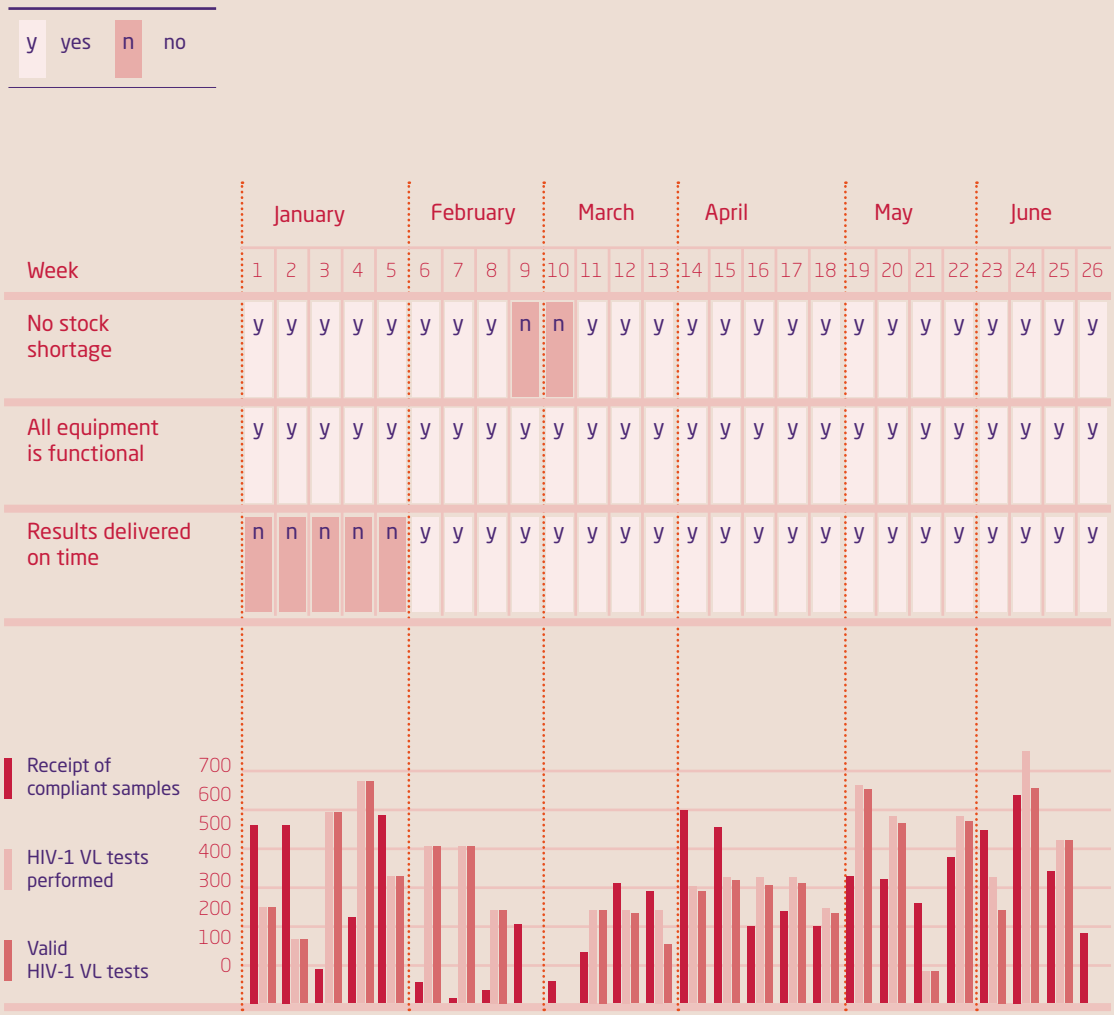
Tip

→ Roll out a rigorous sample traceability system within the laboratory to limit the risk of false results.

→ Establish optimal coordination of activities at the level of the laboratory, of the structure and of the laboratory networks carrying HIV viral load testing through monitoring of activity and quality indicators.

→ Consider retesting invalid samples or plates as a guarantee of reliability, all the more important in a context of increasing quality requirements within laboratories.

Figure No 15: **Example of weekly use of the HIV-1 viral load testing validation tool and monitoring of activity and quality indicators**



Programmatic consideration

→ Provide a budget for participation in an external quality audit (EQA) program for all laboratories performing HIV viral load testing.

→ Ensure that all laboratories performing viral load testing are enrolled in a continuous quality improvement program such as SLIPTA (Stepwise Laboratory Improvement Processes Towards Accreditation).

→ Identify a quality assurance manager in each structure (full-time activity, requiring specific skills and training) and a quality focal point in each laboratory department.

→ Ensure that quality indicators related to business interruptions and equipment failures are properly monitored through the implementation of warming systems.

Figure No 16: **Participation of OPP-ERA Laboratories in the EQA programs in 2018 and 2019**

* new laboratories not subject to the EQA
** replacement of the QCMD EQA with the 1WA EQA in 2019 for the following reasons: higher number of EQA panels per year, lower cost and more appropriate format of the reports returned to the laboratory
*** laboratory in the process of being registered for 2020

		2018		2019	
		CDC EQA (twice a year)	QCMD EQA (once a year)	CDC EQA (twice a year)	1WA EQA (3 times a year)**
Burundi	ANSS	no	yes	ongoing***	yes
	CHUK	na*	na*	ongoing***	yes
	Muyinga	na*	na*	ongoing***	yes
Cameroon	Douala	oui	yes	yes	yes
	CPAG	oui	yes	yes	yes
	Bertoua	na*	na*	ongoing***	yes
	HCY	na*	na*	ongoing***	yes
Côte d'Ivoire	CeDReS	oui	yes	yes	yes
	CePReF	oui	yes	yes	yes
Guinea	INSP	oui	yes	yes	yes
	Donka	oui	yes	yes	yes

Lesson learnt No 23

HIV viral load testing requires handling potentially infectious samples. The training of all staff in biosafety is therefore essential from the opening of the laboratory.
The implementation of biosafety management rules and of secured equipment remains a major issue and needs to be the focus of continuous / renewed efforts, especially in terms of staff training, risk management and emergencies, and the implementation of documentation / regulations. (Fig. No 17)

Lesson learnt No 24

Biomedical waste management is a challenge in resource-limited countries.
Uncollected and / or poorly treated waste can have serious consequences for the health of laboratory staff and the general population, as well as for the environment.
In the context of the OPP-ERA project, this topic was not taken into account from the time of establishment of the HIV viral load testing laboratories.
Infectious and chemical waste management involves a specific organization, with the implementation of standards and protocols, and the training of the staff involved.
In addition, the structure hosting the laboratory must organize and take charge of the waste disposal, especially through the installation and maintenance of incinerator-type equipment.

Figure No 17: **Examples of Biosafety assessment results (before Biosafety training) of 4 OPP-ERA laboratories in very different contexts**

	Reference laboratory, in a context of very limited resources, opened in 2014	Laboratory in a community center, opened in 2014	Laboratory of a university hospital in a capital city, opened in 2018	Decentralized laboratory with involved management team, opened in 2019	Average of all OPP-ERA laboratories
General score	39%	34%	58%	47%	37%
1 Building and workflow	40%	45%	68%	58%	46%
2 Staff management and training	26%	30%	62%	36%	33%
3 Good Laboratory Practices	68%	35%	57%	85%	61%
4 Cleaning, disinfection, sterilization, waste management	64%	43%	61%	71%	48%
5 Emergencies	6%	29%	62%	33%	21%
6 Risk management	0%	0%	60%	13%	5%
7 Documentation and regulations	24%	29%	45%	12%	8%
8 Biosafety	73%	49%	58%	60%	67%
9 Other risks	51%	47%	47%	54%	42%

Programmatic consideration

→ Carry out an inventory of waste management conditions in the structure before establishing a new Laboratory of Molecular Biology (LMB).

→ Provide a budget for the management of laboratory waste, taking into account:

- before opening: the initial investment needed in infrastructure and equipment,
- in the long term: the costs related to infrastructure and equipment maintenance, and the organization of the waste collection and disposal activity.

Online toolkit in French

→ **Habilitation du personnel: 13 documents**
→ **Outil de validation des tests de charge virale VIH-1 et de suivi des indicateurs d'activité et de qualité**
→ **Audit interne des laboratoires: 5 documents**
→ **Biosécurité: 3 documents**
→ **Outil d'évaluation des coûts de la gestion des déchets des tests de charge virale**

STRENGTHS AND LIMITATIONS OF THE OPP PLATFORM: OPP-ERA'S EXPERIENCE WITH BIOCENTRIC REAGENTS

Strengths

- **Application:** the technique is adapted to WHO recommendations in the Central and West African contexts: detection limit (390 copies / mL) and very good quantification of HIV viruses - 1 B, non-B and complex recombinants circulating in this region (Rouet F et al. 2007; Rouet F et al. 2011; Kerschberger B et al. 2018; Avettand - Fénoël V et al, 2019)
- **Flexibility:** an OPP can perform from 1 to more than 650 viral load tests per week, and is therefore suitable for different volumes of HIV-1 viral load testing activities and low to medium HIV prevalence settings
- **Facility:** 250µL plasma is sufficient to quantify the HIV-1 viral load
- **Activity continuity:** the installation of several compact extractors makes it possible to maintain basic activity in the event of the failure of one of them
- **Robustness:** Semi-automatic extractors are more robust than highly mechanized fully automated systems that require more training, infrastructure, equipment and maintenance
- **Capacity building:** the training of technicians in a Molecular Biology technique allows them to develop their skills and, in the long term, the establishment of a Molecular Biology expertise group in environments where it is rarely or never taught
- **Manual validation of plates:** this allows laboratories to understand and analyze the results produced
- **Polyvalence:** can be considered:
  - hepatitis B virus (HBV) viral load (Kania D, 2014; Castéra - Guy J et al, 2017),
  - HIV-2 viral load (Avettand - Fenoel V et al, 2014; Ekouévi DK et al, 2015; Bertine M et al, 2017),
  - HIV-1 viral load on DBS (Kerschberger B et al, 2019),
  - tuberculosis detection (Obasanya J et al, 2017) and any other tests based on real-time PCR

  The effective implementation of routine polyvalence depends on the capacity of generic reagent suppliers to meet international quality requirements (e. g. CE marking, WHO prequalification).

Limitations

- **Intensive training:** the technique requires more training and skills from technicians and biologists due to manual plates validation
- **Manual pipetting:** the test consists of several manual steps, requiring good pipetting skills and the use of calibrated equipment to limit the risk of error
- **Negative temperature storage:** the storage of amplification reagents between -18°C and -30°C is a constraint
- **Laboratory layout:** pre- and post-amplification zones must be separated, and the mix preparation zone isolated
- **Variant detection:** HIV-1 viruses of the rarer groups N, O and P are not correctly detected and amplified
- **Multiplicity of suppliers:** procurement from various reagent and equipment suppliers makes purchasing and maintenance more complex

> What I particularly appreciate about the OPP platform is that it gives fewer error messages than our integrated platform, generating fewer technical failures and fewer repetitions, and leaves the technician in charge and therefore able to rectify a mistake as far as possible.
> In a resource-limited setting, this is an advantage because saving a handling saves reagents and their cost.
> In addition, it allows the technician in charge to better understand the different steps of viral load testing and the associated Molecular Biology principles.
> Finally, we can test a large number of samples at a time and, by not depending on a single supplier, we can benefit from competition, for example in the choice of thermocyclers or consumables.
> However, it is important to take into account that this platform requires significant training and follow-up.

Dr. KONE Fatoumata, Pharmacist Biologist
CeDReS (Molecular Biology Unit), OPP-ERA Technical Advisor,
Republic of Côte d'Ivoire

For the references of the publications mentioned on this page, please refer to the section "Aller plus loin" in the online Toolkit : https://toolkit - chargevirale - oppera. solthis.org/


The Medical Export group BV
www.meg.nl
CATHOLIC RELIEF SERVICES – USCCB
RUE DI 024, CORNICHE NORD CAMAYENNE,
COMMUNE DE DIXIN
CONAKRY
Attn : Jean Marie Bhizi
Phone : + 224 664 20 20 26
E-mail : Jean-Marie.bihizi@crs.org
PO : VPP- 50451- 0

3 PROCUREMENT AND SUPPLY

Procurement and supply chain management (PSM) of laboratory products (health products and equipment) requires collaboration between PSM and laboratory specialists.
Indeed, the technical specifications of the products needed to carry out HIV viral load testing (extraction reagents, amplification reagents, laboratory equipment such as centrifuges, equipment and consumables) must be taken into account throughout the PSM cycle.

Other challenges must also be addressed with regard to equipment management, in order to guarantee continuous functionality, especially the securing of power supply for cold chain maintenance for temperature dependent reagents.

Online toolkit in French

toolkit-chargevirale-oppera.solthis.org/approvisionnement

STRENGTHEN THE SKILLS OF PSM SPECIALISTS IN LABORATORY PRODUCTS MANAGEMENT

Lesson learnt No 25

Laboratory products management is specific, particularly for Molecular Biology. Here are some examples:

- The reagents are stored at a negative temperature (-20°C)
- The micropipettes are adapted to the desired volumes and the tips are adapted to the micropipettes used
- Freezers meet laboratory standards and not food standards
- Personal protective equipment makes it possible to handle samples presenting a risk of infection

Laboratory products procurement and equipment management is facilitated by the identification of PSM focal points for laboratory activities within national authorities (National HIV / AIDS Programs, National Directorates of Laboratories, Equipment Directorate, central purchasing office, etc.) and within each of the HIV viral load testing laboratories.

Programmatic consideration

→ Identify PSM focal points responsible for laboratory products management at both national authority and laboratory level.

Lesson learnt No 26

PSM specialists from national authorities are expected to strengthen their knowledge and skills on laboratory activities and, in particular, to develop specific know-how in cold chain management (including the following stakeholders: international freight forwarder, customs, national carrier, supply chain manager at laboratory level).

Programmatic consideration

→ Strengthen the skills of all parties involved in the PSM of laboratory products.

Lesson learnt No 27

A smooth and regular flow of information between PSM specialists and those in the laboratory facilitates the continuity of HIV viral load testing activities.

Programmatic consideration

→ Create coordination mechanisms between PSM specialists and those in the laboratory (sharing of actual consumption, collective assessment of needs and order planning, alert system in the event of equipment failures or inventory shortages).

MANAGE PROCUREMENT AND SUPPLY CHAIN OF LABORATORY PRODUCTS

Lesson learnt No 28

The selection and quantification of laboratory products require a joint effort by PSM and laboratory specialists.
Several categories of items are required to perform HIV viral load testing (consumables, reagents and laboratory equipment). Items missing or unsuitable for each technique and laboratory can compromise HIV viral load testing activities.
Reagent suppliers can facilitate the ordering process by offering to supply the associated consumables.

Tip

→ Consider that the equipment necessary to achieve viral load testing but not used within the Molecular Biology laboratory (consumables and equipment for sampling and storage: EDTA tubes, needles, cool boxes, etc.).
→ Bring together virology skills when selecting laboratory equipment.

Lesson learnt No 29

Similarly, quantification work requires the combination of PSM and laboratory skills.
National quantification of patient viral load testing must take into account both the patient's needs to be covered and the laboratory capacity (average number of tests performed per week, depending on the equipment and the number and availability of trained human resources).
National quantification of the requirements of tests to be supplied must take into account the controls / standards necessary for the validation of patient viral load testing (14 controls / standards for each plate).
National quantification of the requirements of tests to be supplied must also take into account a retesting ratio for the laboratory activity (an average retesting rate of 15% was considered during the OPP-ERA project). (Fig. No 18 and 19)

Programmatic consideration

→ Systematically involve laboratory specialists in laboratory products selection and quantification exercises.
→ Take into account the capacity of laboratories during quantification exercises.

Figure No 18: **Calculation of the number of patient viral load tests that can be performed per kit of 220 tests or 440 tests of Generic HIV Charge Virale Biocentric based on the experience of the OPP-ERA project**

- **Kit of 220 tests**

With a kit of 220 tests, it is possible to test 164 patient samples with half plates and 178 patient samples with full plates.

	Number of patient VL tests	Number of controls / standards
half-plate 1	41	14
half-plate 2	41	14
half-plate 3	41	14
half-plate 4	41	14
Total	164	56

	Number of patient VL tests	Number of controls / standards
plate 1	82	14
plate 2	82	14
plate 3	14	14
Total	178	42

- **Kit of 440 tests**

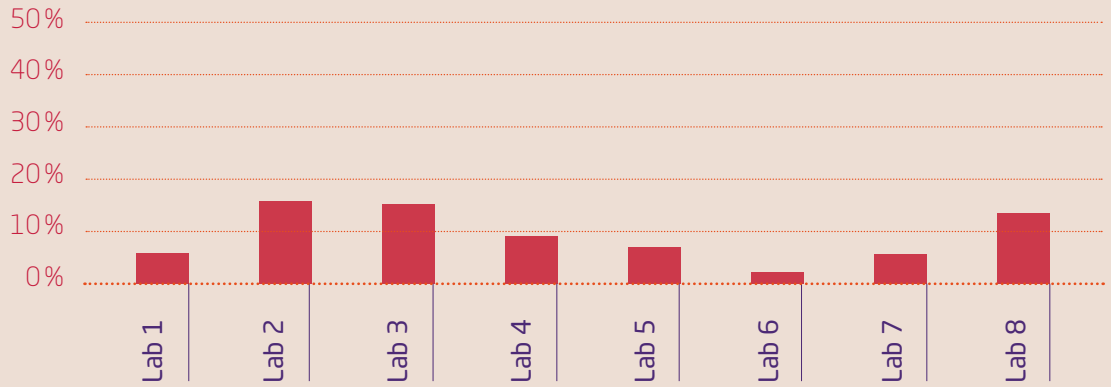
With a kit of 440 tests, it is possible to test 328 patient samples with half plates and 369 patient samples with full plates.

	Number of patient VL tests	Number of controls / standards
half-plate 1	41	14
half-plate 2	41	14
half-plate 3	41	14
half-plate 4	41	14
half-plate 5	41	14
half-plate 6	41	14
half-plate 7	41	14
half-plate 8	41	14
Total	328	112

	Number of patient VL tests	Number of controls / standards
plate 1	82	14
plate 2	82	14
plate 3	82	14
plate 4	82	14
plate 5	41	14
Total	369	70

Figure No 19: **Retesting rates observed in 8 laboratories at the end of the OPP-ERA project**

Review period: May to July 2019



Lesson learnt No 30

The short shelf life of the reagents and the difficulties in predicting the rate of HIV viral load testing activity (fluctuations in demand and consumption of viral load tests) suggests that the frequency of quantification exercises and orders should be adjusted.

Any inventory shortage has a profound impact on the entire viral load testing activity (inconsistency in activity within laboratories, fluctuation in demand from prescribers and unavailability of service for the patient). (Fig. No 20 and 21)

Tip

→ Ensure that the expiration dates proposed in the quotations when placing orders correspond to the period to be covered (take into account the estimated date of receipt).

Programmatic consideration

→ Plan biannual quantification exercises to adjust orders according to actual needs.
→ Plan a safety stock, depending on the period covered.
→ Plan quarterly or semi-annual deliveries to limit the risk of expiration.

Figure No 20 : **Causes of the 12 stockouts experienced over 3 years, within the framework of the OPP-ERA project**

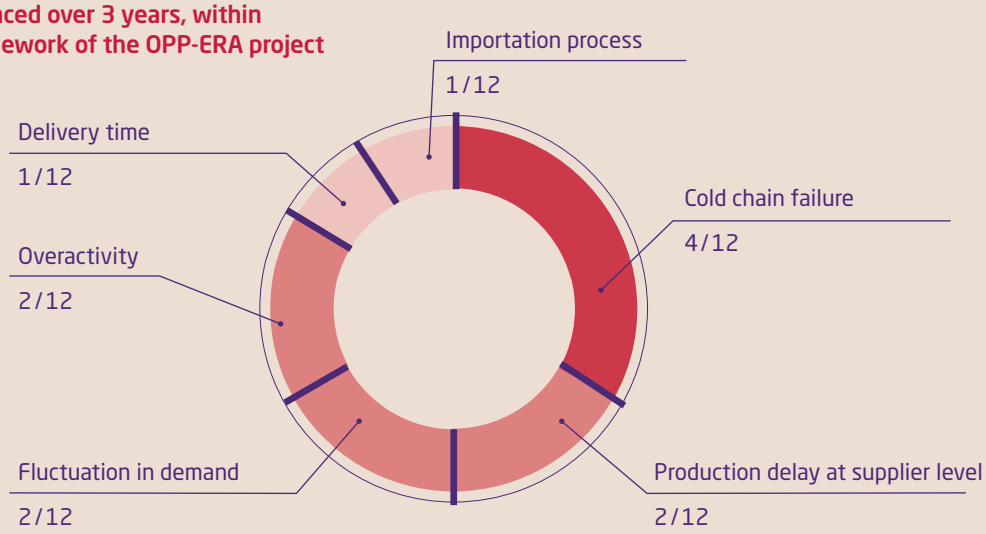
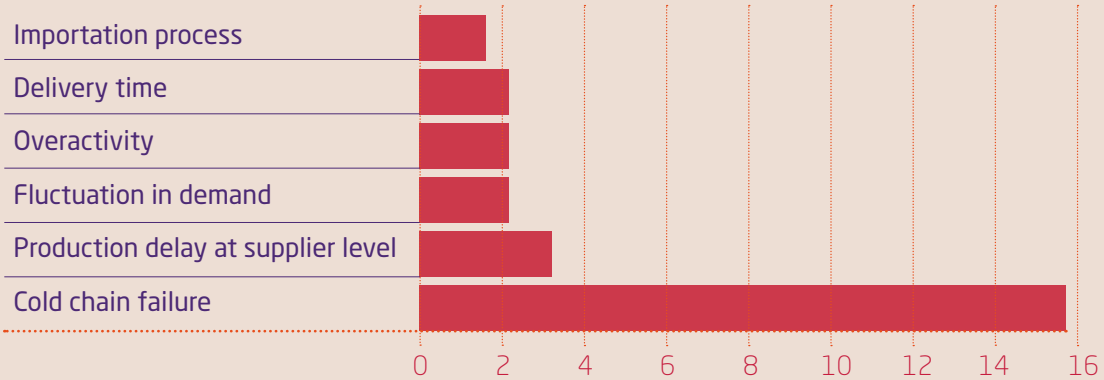


Figure No 21 : **Average duration of the stockouts in weeks depending on their cause, as experienced in the OPP-ERA project**



Lesson learnt No 31

The time between needs estimation and actual on-site delivery is variable and can be long. On OPP-ERA, despite a direct purchasing process with the supplier, this time was 5 months on average.

Programmatic consideration

→ Plan a period of 9 to 12 months between needs quantification and actual on-site delivery in the case of group purchasing on Global Fund grants, as the purchasing and procurement processes involve several stakeholders and must go through various validation steps.
→ Establish an annual procurement plan integrating the different sources of financing, order frequency and delivery frequencies; plan a biannual update in parallel with quantification exercises.
→ Set up regular monitoring of orders to quickly remove the obstacles that cause additional delays.

Lesson learnt No 32

The delays associated with importation and exemption procedures, before customs clearance, can be significant.

For example, the customs clearance of temperature dependent products sometimes took up to 14 days in the Republic of Côte d'Ivoire.

Programmatic consideration

→ Anticipate the arrival of laboratory products from an administrative and logistical point of view (filing in of files with the national authorities concerned, especially for equipment and temperature dependent products, etc.) and from a financial point of view (importation and exemption costs).

"The tools developed by OPP-ERA to handle the procurement are very user-friendly and easy to use"

Dr Yacouba Foupouapouognigni,
Laboratory Expert,
National Committee to Fight AIDS (CNLS),
Republic of Cameroon

Lesson learnt No 33

Cross-analysis of monthly inventory records and laboratory activity (number of viral load tests performed) contributes to the management of the activity and leads to the adjustment of needs projection, in line with demand (anticipation of possible shortages and minimization of losses).

Programmatic consideration

→ Make monthly inventories of reagents and quarterly inventories of consumables, with tools adapted to the field of the laboratory, and use them to manage the needs estimation.

Online toolkit in French

→ **Outil pour faciliter la gestion et le suivi des stocks des intrants :**
Fiche de stock, Fiche de comptage, Rapport d'inventaire, Fiche de suivi des températures, Fiche de transfert

→ **Manuel de procédures de gestion des approvisionnements et des stocks de réactifs et consommables de laboratoire**

→ **Aide-mémoire à l'attention des gestionnaires de stock des intrants et équipements de laboratoire**

→ **Définition des incoterms**

→ **Outil de sélection des intrants et équipements de laboratoire de charge virale**

→ **Outil de calcul des besoins en intrants pour la mesure de la charge virale du VIH sur plateformes ouvertes**

→ **Outil répertoriant les spécifications techniques requises et additionnelles pour l'acquisition d'extracteur et thermocycleur**

ENSURE COLD CHAIN MAINTENANCE

Lesson learnt No 34

Ensuring a continuous cold chain is a real issue. Transportation, receipt and storage of temperature dependent reagents must be carried out at negative temperatures (from -18°C to -30°C for Generic HIV Charge Virale Biocentric amplification reagents).

Any cold chain failure can influence the quality of the reagents and therefore the results given to patients.

The implementation of rigorous logistical procedures and their long-term follow-up is essential, including a warning system in the event of a cold chain failure and daily monitoring of temperatures by trained and available staff (including weekends and public holidays, which requires specific organization).

Temperature tracers are required for any national or international transport of temperature dependent reagents.

With regard to equipment, several systems can be considered within the laboratory to ensure 24-hour continuous electrical availability : generators or solar panels.

Each freezer must be equipped with an inverter. Freezers at -20° C or -40° C are preferred to those at -80° C, which consume a lot of energy and are not necessary except for the establishment of a plasma bank.

During the OPP - ERA project, 1 / 3 of all disruptions in laboratory activity were due to cold chain failures making the temperature dependent reagents unusable (all due to a failure of the electrical system).

Tip

→ Favour the shortest route for transportation of temperature dependent reagents : avoid air transport with stopovers; favour the nearest airport for receipt; identify a freight forwarder equipped to transport these products.
→ If necessary, identify local dry ice suppliers or use eutectic gels to ensure that the cold chain is maintained when receiving products, especially while waiting for customs clearance, or organize immediate transportation of temperature dependent reagents to the secured storage site (laboratory freezers or negative cold rooms in central purchasing offices).

Programmatic consideration

→ Ensure that a procedure is established at laboratory level to validate the quality of reagents upon receipt or in the event of suspected cold chain failure.
→ Consider central storage at the national level only if it can ensure the continuous maintenance of the cold chain (negative cold room or freezers to standards, electrical systems in place, staff trained and available, possible refrigerated transport to laboratories).
→ Adapt customs clearance procedures for temperature dependent reagents.

Online toolkit in French

→ **Emballage et Transport de Produits contenant des matières infectieuses**
→ **Check - list pour la gestion de la chaîne du froid**
→ **Guide pratique d'entretien et de maintenance préventive des réfrigérateurs et congélateurs de laboratoire**
→ **Outil pour faciliter la gestion et le suivi des stocks des intrants : Fiche de suivi des températures**

MONITOR AND MAINTAIN EQUIPMENT

Lesson learnt No 35

The evaluation of the site and especially of electrical requirements is a prerequisite for any equipment installation.
Indeed, even minor power outages jeopardize the laboratory's activity.
All critical equipment (extractors, thermocyclers and freezers) must be connected to a suitable uninterrupted power supply (UPS). (Fig. No 22)

Tip

→ Explore the possibility of group purchasing with suppliers (equipment and adapted UPS) to secure the equipment.

Programmatic consideration

→ Take into account the budget necessary for the essential electrical back up: purchase and installation of a generator (including an annual fuel budget) or solar panels (including regular maintenance and battery replacement).

Figure No 22 : **Examples of electrical capacities of critical equipment in an HIV viral load testing laboratory and adapted UPS, based on the experience of the OPP-ERA project**
The UPS must have integrated or additional stabilizers

Type of Equipment	Power consumption	Autonomy to be guaranteed	Required security
Extractor	180 VA	3h	UPS 3000 VA (for 1 extractor) or 5000 VA (for 2 extractors)
Thermocycler	950 VA	4h	UPS 3000 VA
Freezers - 20°C or - 40°C	60 à 100 VA	24h/24h	UPS 1500 VA or 3000 VA depending on the required autonomy
Fixed computer for Thermocycler	150 VA	4h	UPS 1500 VA
Fixed desktop computer	150 VA	4h	UPS 1500 VA

Lesson learnt No 36

OPP

During installation, and then during any relocation or replacement of any of the equipment (extractors or thermocyclers), the OPP platform requires a qualification that ensures that it is properly installed and produces the expected results.

Annual preventive maintenance is required for extractors and thermocyclers, including their calibration. These preventive maintenance operations are planned to ensure the availability of technicians and of the specific reagents (necessary for the calibration of thermocyclers).

Calibration of the micropipettes is also annual.

All other laboratory equipment also requires regular maintenance (hood, air conditioners, freezers, etc.).

Tip

OPP

→ Ensure the availability of reagents and consumables necessary for calibration as well as curative and preventive maintenance.
→ Take into account that OPPs require working with several suppliers and therefore having to use various maintenance modalities.

Online toolkit in French

→ **Dossier de vie des équipements de laboratoire : fiche de vie, fiche de rapport de panne, fiche d'inventaire des équipements, fiche d'identification, étiquettes "hors service" et "en panne"**
→ **Liste des contacts fournisseurs et prestataires de maintenance des équipements fournis par le projet OPP - ERA**
→ **Fiche de notification d'incident**
→ **Algorithme de gestion d'une panne ou d'un dysfonctionnement d'un équipement dans un laboratoire de biologie moléculaire**

Lesson learnt No 37

Equipment failures can block laboratory activity for several weeks and are at the root of the need for curative maintenance that must be considered in budgets.
A clear communication circuit for failure management (or alerts system) from the laboratories to the structures in charge of managing contracts with suppliers, allows the required maintenance service to be triggered without delay. Sharing the warranty and maintenance terms and conditions provided for in the contracts with laboratories greatly facilitates these communications.

Having several extractors in a laboratory allows for maintaining reduced activity in case of an extractor failure.

Programmatic consideration

→ Ensure that each equipment outside the warranty period is under a maintenance contract, with appropriate budget allocations and defined intervention times. Since it is difficult to quantify curative maintenance, which depends on the nature of the incident, it is rarely included in maintenance contracts with suppliers and must therefore be the subject of additional budgets that can be activated as often as necessary.
→ Define and regularly update a plan for monitoring equipment maintenance, ensuring a rapid response to curative maintenance needs.
→ Use and make available the tools for monitoring the life of equipment in laboratories.
→ Define a warning system, in case of equipment breakdown.
→ Identify a maintenance service provider, preferably locally. For equipment outside the warranty, consider using companies specializing in maintenance services, which may be separate from the supplier.
→ Consider integrating the price of preventive and corrective maintenance of equipment into the price of reagents.

4

PATIENT CARE

Collective efforts in recent years have resulted in a significant increase in the availability of HIV viral load testing in resource-limited countries.
However, the prescription of viral load test and the use of the results remain insufficient, as evidenced by the results of the OPP-ERA project.
It seems essential to continue building the capacity of the various stakeholders involved in the follow-up of people living with HIV and to improve the organization of patient care systems, so that viral load testing can really be used to improve patient care.

Online toolkit in French

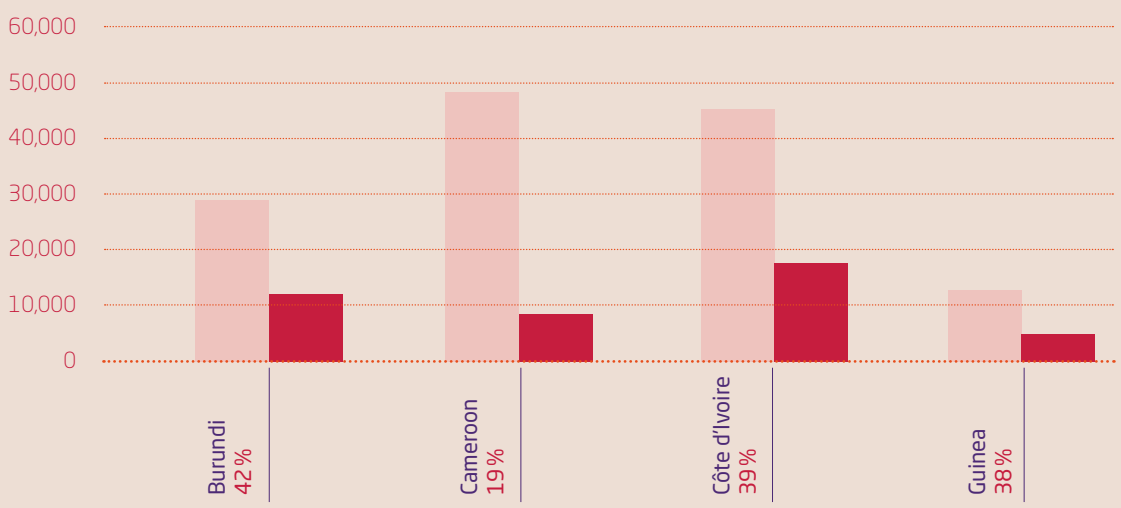
toolkit-chargevirale-oppera.solthis.org/prise-en-charge

SUPPORT THE PRESCRIPTION OF HIV VIRAL LOAD TESTING

Lesson learnt No 38

The prescription of HIV viral load test, which has been made possible in different countries through the OPP-ERA project, has improved little during this project. By the end of the project, less than half of the patients on antiretroviral therapy had had a viral load test within the year.
(Fig. No 23)

Figure No 23 : **Proportion of patients who received HIV viral load test on OPP compared to HIV cohorts in the care units in partnership with the OPP-ERA project in 2018**



Lesson learnt No 39

The prescription of HIV viral load test varies according to the HIV care units. There are disparities between care units; determinants can be multiple: number, training and availability of health staff; size of the HIV cohort; presence of psychosocial support workers; organization of the sample collection circuit; transportation cost for the patient to go for consultation; cost of the HIV viral load test (specific situation of the Republic of Cameroon until end of 2019), etc. (Fig. No 24)

Programmatic consideration

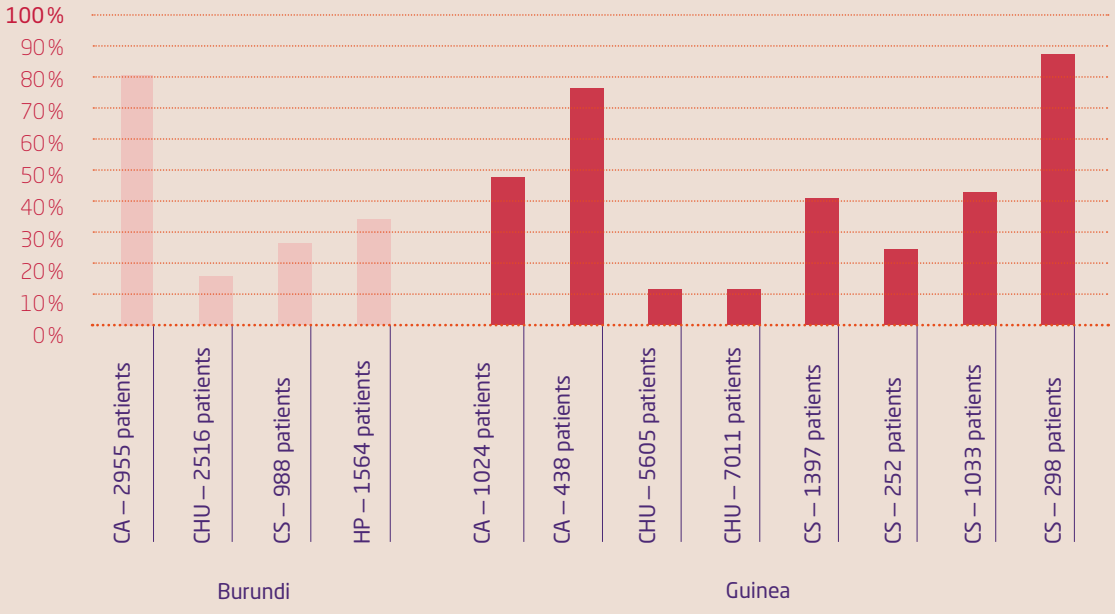
- → Inform prescribers of exam availability and of the practical arrangements (sample collection circuit and results reporting system).
- → Carry out practical training with prescribers on the benefits of viral load testing and repeat it frequently to take into account health staff turnover.
- → Anticipate the switch to Dolutegravir (DTG) for patients on ARV therapy: the viral load test prescription must be strengthened so that DTG is only used in patients with virological success in order to avoid the risk of developing resistance to Integrase inhibitors used as functional monotherapy.

Online toolkit in French

- → **Manuel de formation pour l'utilisation de la charge virale par les cliniciens**
- → **Module de formation théorique sur l'utilisation des résultats de charge virale VIH**
- → **Module de formation pratique sur l'utilisation des résultats de charge virale VIH (Cas cliniques)**

Figure No 24: **Proportion of the HIV cohort having had access to at least one HIV viral load measure in 2018**

Example of OPP-ERA project partner HIV care units in the Republic of Burundi and the Republic of Guinea - CC: community center, UH: university hospital, HC: health center, MH: main hospital



INCREASE THE USE OF VIRAL LOAD TEST RESULTS IN CASE OF VIROLOGICAL SUCCESS

Lesson learnt No 40

The overall virological success rate is satisfactory in the context of the OPP-ERA project (1st quantification of viral load in patients treated with Efavirenz and Nevirapine regimens with a low genetic barrier) and has remained relatively constant during the project.
(Fig. No 25 and 26)

Figure No 25: **Proportion of patients with an HIV viral load <1000cp/mL among patients who received viral load test on OPP in the partner laboratories of the OPP-ERA project in 2019, from January to July**

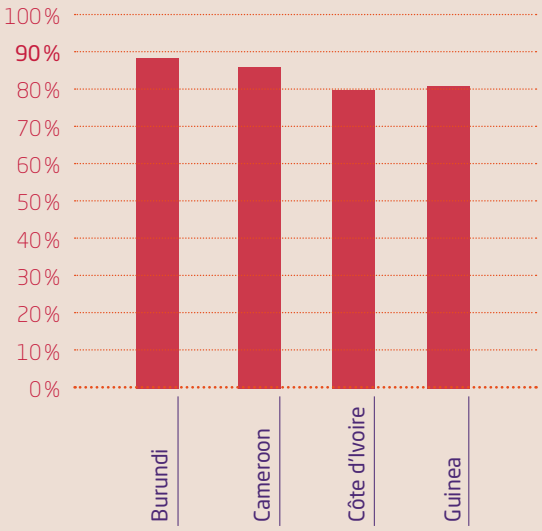


Figure No 26: **Proportion of patients with an HIV viral load <1000cp/mL in the Republic of Burundi and the Republic of Guinea, over 3 years as part of the OPP-ERA project**

Lesson learnt No 41

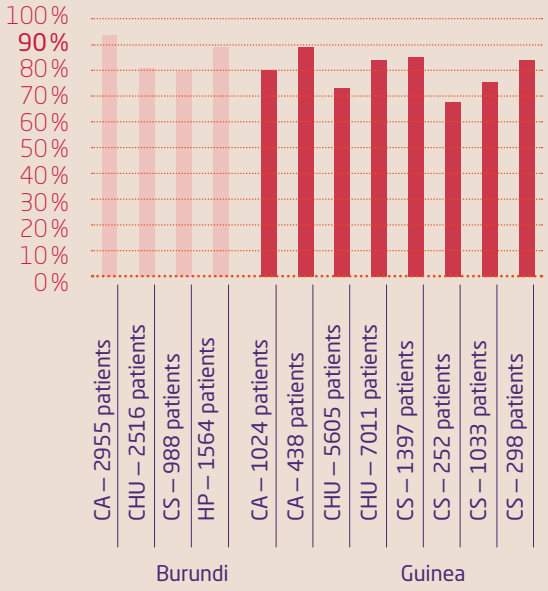
There are disparities between care units, reflecting differences in the quality of care, the determinants of which can be multiple: number, training and availability of health staff; size of the HIV cohort; presence of psychosocial support workers; organization of the search for the lost to follow-up; type of HIV care unit (community, private or public); procurement difficulties; type of patients cared for (children and adolescents, or adults). (Fig. No 27)

Programmatic consideration

→ Produce result analyses of virological success both at the national level to inform the 3rd 90th, and at the level of each site to identify the care units where the virological success rate is lower and to focus efforts on analyzing the determinants of their results and implementing appropriate corrective measures.

Figure No 27: **Proportion of patients with virological success (HIV viral load <1000cp/mL)**

Example of OPP-ERA project partner HIV care units in the Republic of Burundi and the Republic of Guinea, In 2018 - CC: community center, UH: university hospital, HC: health center, MH: main hospital



Programmatic consideration

→ Adapt the care pathway (type of virological and clinical follow-up) to the profile of patients, particularly in the major care units, by distinguishing between new patients on ARVs, stable patients with therapeutic success and patients in virological failure.

Lesson learnt No 42

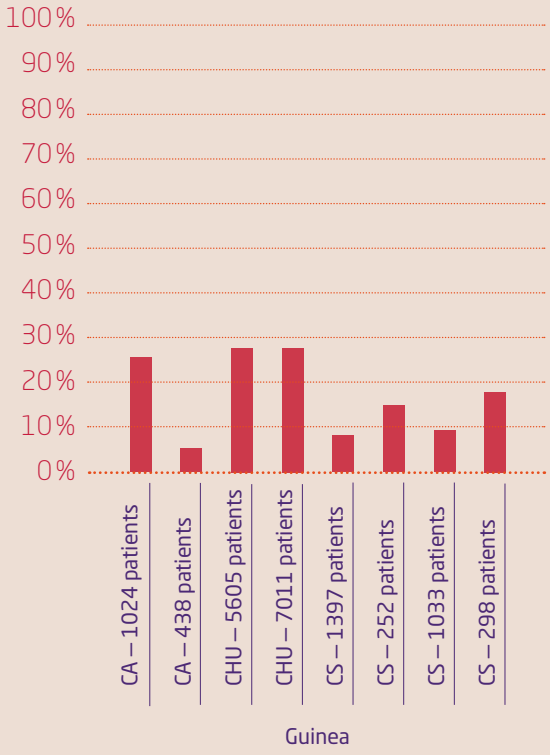
In the event of virological success, compliance with national recommendations is low: annual follow-up of HIV viral load in successful patients is not sufficiently respected.

The median number of viral load test per patient performed during the last 3 years of the project is only 1.3 (between 1.1 and 1.5 depending on the country).

Thus, the impact of the introduction of HIV viral load testing on improving patient care and care organization remains limited: the spacing of appointments for patients with viral load < 1000cp/mL (as recommended by WHO, to improve their quality of life and reduce caregiver workload) is slow to be implemented outside pilot care units. (Fig. No 28)

Figure No 28: **Proportion patients with virological success who received annual HIV viral load follow-up**

Example of OPP-ERA project partner HIV care units in the Republic of Guinea, in 2018 - CC: community center, UH: university hospital, HC: health center, MH: main hospital



STRENGTHEN THE USE OF VIRAL LOAD TEST RESULTS IN CASE OF VIROLOGICAL FAILURE

Lesson learnt No 43

The management of virological failure is problematic. The implementation of national algorithms (based on the WHO algorithm) for managing virological failure is insufficient: less than 15% of patients in virological failure received HIV viral load test within the recommended 3-6 months, although there are differences between care units. (Fig. No 29 to 32)

Figure No 29: **Proportion of patients in virological failure (HIV viral load ≥1000cp/mL) who received a control viral load within 3 to 6 months**

Example of OPP-ERA project partner HIV care units in the Republic of Burundi and the Republic of Guinea, in 2018 - CC: community center, UH: university hospital, HC: health center, MH: main hospital

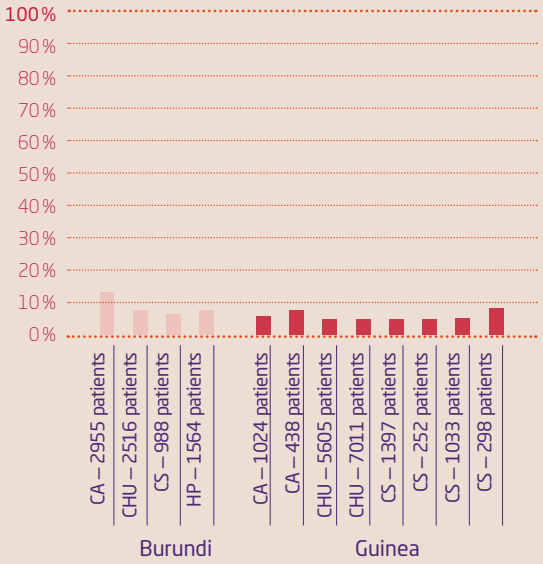
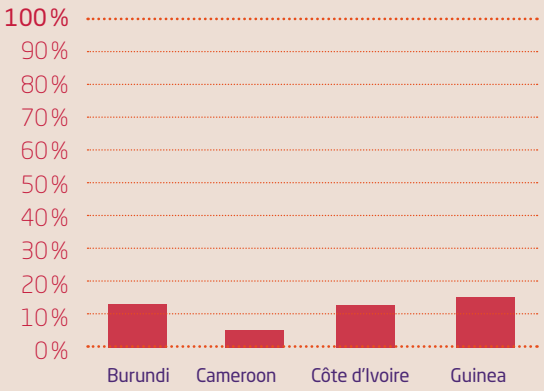


Figure No 30: **Proportion of patients in virological failure (HIV viral load ≥1000cp/mL) who received a control viral load within 3 to 6 months, in 2019, from January to July as part of the OPP-ERA project**



Lesson learnt No 44

Moreover, the change to 2nd line treatment is anecdotal. As a result of this low use, the epidemiological impact of the introduction of HIV viral load testing is also very limited: the rate of virological success has not improved during the OPP-ERA project due to the low number of viral load tests per patient and the low use of test results in case of virological failure.

Given the low use of HIV viral load results and a very low transition to 2nd line treatment, a minority of patients with virological failure benefit from appropriate care.

Figure No 31 : **Cascade of virological failure in the Republic of Burundi, Republic of Cameroon, Republic of Côte d'Ivoire and Republic of Guinea, cumulative data from 2016 to 2019**

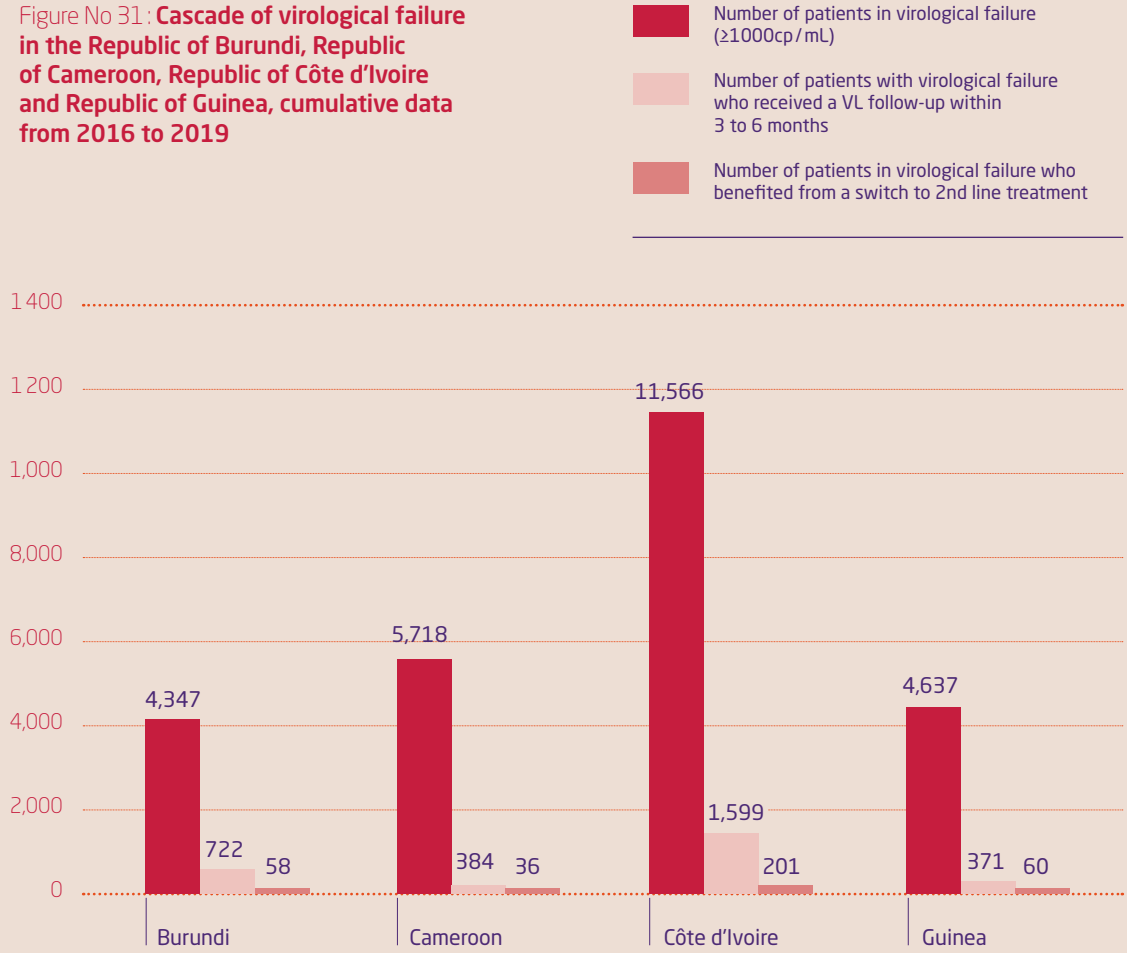
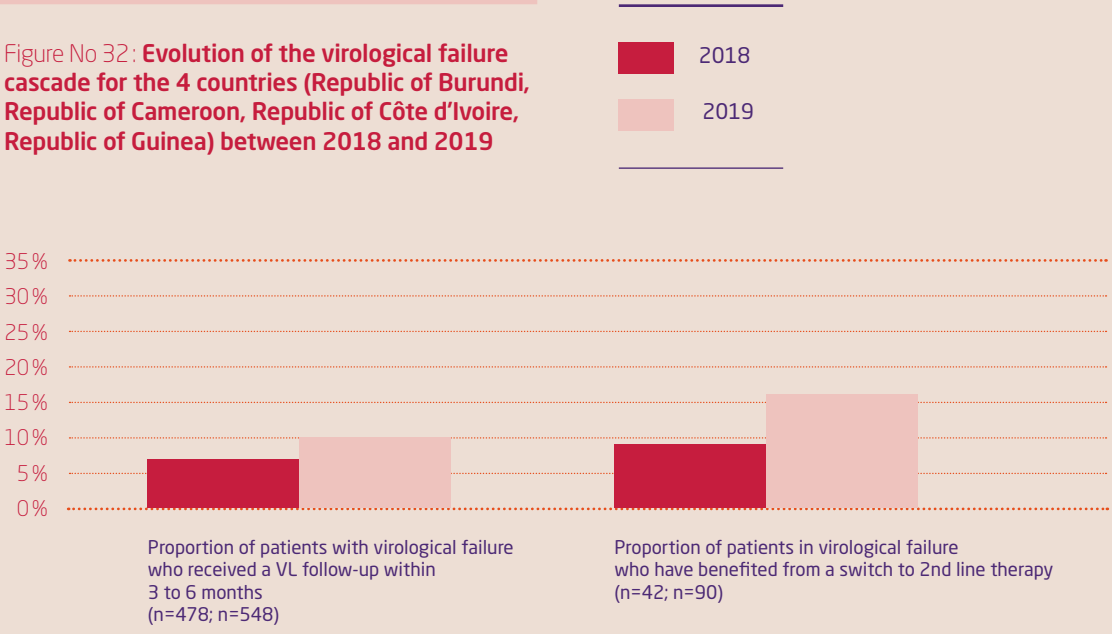


Figure No 32 : **Evolution of the virological failure cascade for the 4 countries (Republic of Burundi, Republic of Cameroon, Republic of Côte d'Ivoire, Republic of Guinea) between 2018 and 2019**



UNDERSTAND AND IMPROVE THE DIFFICULT MANAGEMENT OF VIROLOGICAL FAILURE

Lesson learnt No 45

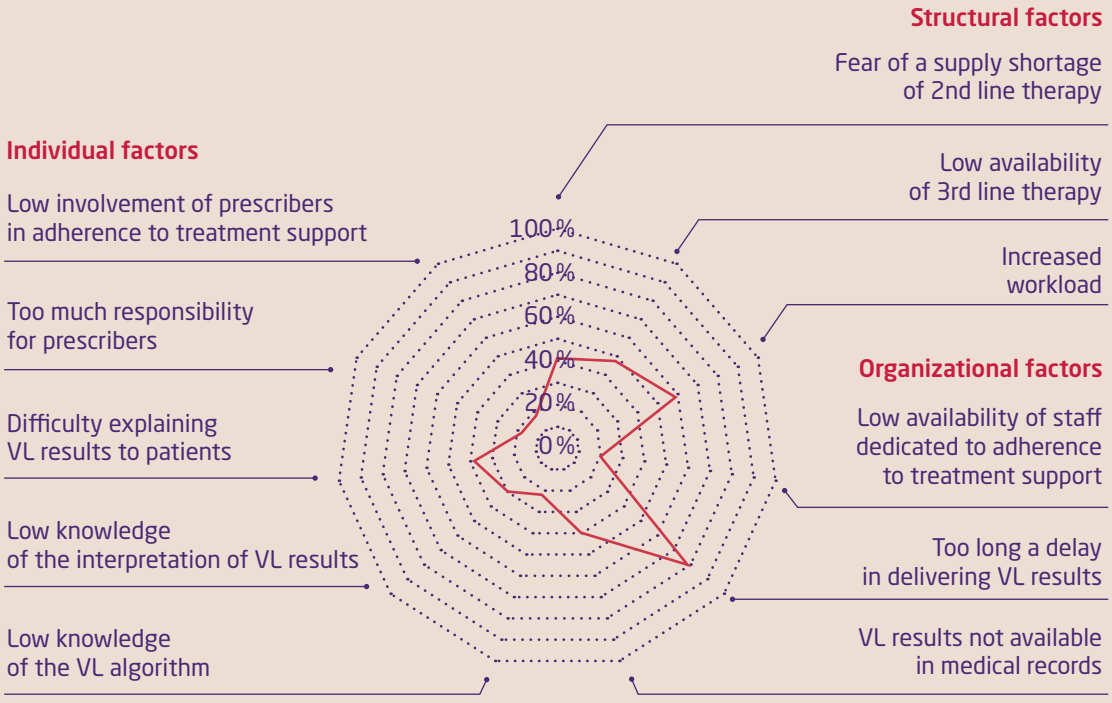
From the point of view of those responsible for National HIV / AIDS Program, in the context of implementing "treatment for all" recommendations and of reduced international funding, the cost of 2nd line treatments, which is higher than that of 1st line treatment, poses difficulties in prioritizing financially. It also leads those in charge of National HIV / AIDS Programs to limit the use of 2nd line therapy.

Lesson learnt No 46

From the point of view of prescribers, the main difficulties identified are structural (low availability and risk of stock shortage of 2nd line treatments, higher workload represented by the decision to switch treatment) and organizational (delay in receiving the result of the HIV viral load exam, unavailability of viral load results in medical records). The individual factors related to prescribers were not mentioned much in the survey addressed to them. (Fig. No 33)

Figure No 33: **Factors associated with low utilization of HIV viral load results by prescribers**

Survey on 56 prescribers (medical diploma 89%, median length of experience in HIV care: 6 years) from the Republic of Burundi, the Republic of Cameroon, the Republic of Côte d'Ivoire and the Republic of Guinea in 2019 as part of the OPP-ERA project



Programmatic consideration

→ Strengthen the use of clinical records and adapt patient follow-up tools by integrating HIV viral load monitoring.
→ Create registers identifying patients with a VL >1000 cp/mL.
→ Set up computerized medical records, to create warnings when the test is to be prescribed or to automate the prescription.
→ Reduce the time required to deliver results. Example of tools: SMS results reporting system and patient involvement (Venables E et al. PLOS One 2019), use of Point-Of-Care (Meloni ST et al. BMC Infect Dis. 2019).

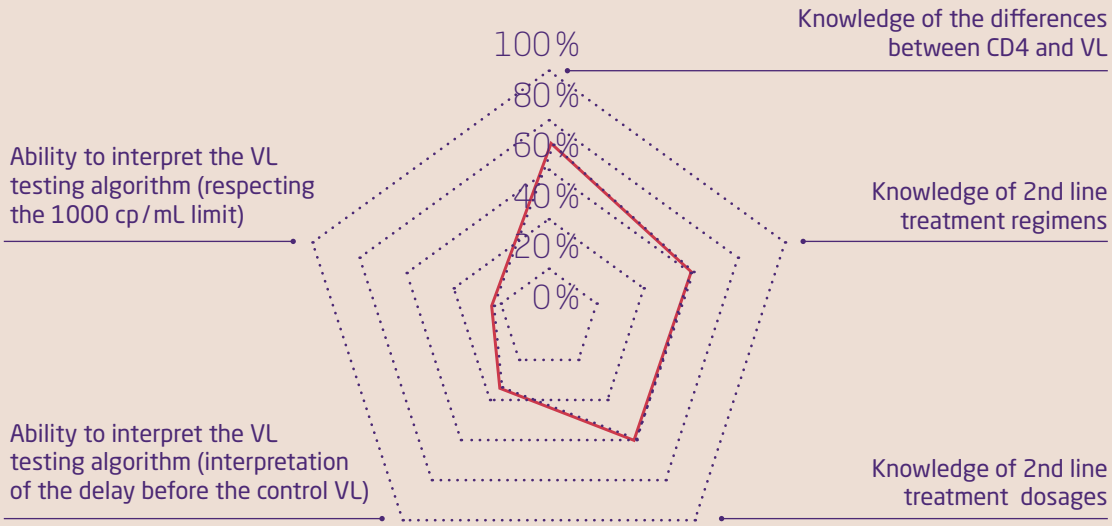
Lesson learnt No 47

The HIV viral load testing algorithm appears to be well known to most clinicians, but its interpretation is poorly understood. The 3 to 6 month period before controlling the viral load is sometimes applied too strictly: a test performed after this period (which is frequent) is wrongly considered uninterpretable.

The limit of 1000 copies/mL is only respected in a quarter of prescribers. Even a slight decrease in this value is misinterpreted as a marker of success of adherence to treatment support, and as an encouragement to continue efforts to hopefully fall below the 1000 copies/mL limit. The change to 2nd line is associated with high viral load. (Fig. No 34)

Figure No 34: **Assessment of knowledge of viral load testing and of the national HIV viral load testing algorithm**

Survey on 71 prescribers (medical diploma 87%, median length of experience in HIV care: 6 years) from the Republic of Burundi, the Republic of Cameroon, the Republic of Côte d'Ivoire and the Republic of Guinea in 2019 as part of the OPP-ERA project.



Programmatic consideration

→ Carry out practical training with the sharing of clinical cases (management of virological failure, choice of 2nd line treatment), in the presence of prescribers and all caregivers involved in the care of PLHIV (especially in the event of delegation of tasks to psychosocial support workers, mediators, community partners, etc.).
→ Set up specific training courses to report virological failure and support patients.
→ Ensure that national patient management algorithms are understood, especially for those with viral loads ≥1000 copies/mL and those with virological failure under 2nd line treatment; or adapt them.
→ Organize multidisciplinary clinical consultation meetings involving prescribers, community stakeholders, program managers and laboratory technicians/biologists.
→ Identify staff specialized in the care of patients with virological failure (example of practices: establishment of HIV viral load champions, Sunpath et al. Public Health Action 2018).
→ Ensure the continuous availability of 2nd line treatments in the care units and inform prescribers of their availability.

Lesson learnt No 48

Caregivers are not trained to inform the patients about their virological failure, their words are often guilt-ridden and dramatic, and present switch to 2nd line treatment as a sanction.
Nor are caregivers trained to support patients on 2nd line treatments, exposing the patients to the risk of a new virological failure, all the more dramatic as 3rd line treatments are only rarely available.

Programmatic consideration

→ Set up specific training courses on how to inform patients about virological failure.

Online toolkit in French

→ **Guide de l'annonce de l'échec virologique et de l'accompagnement des patients**


OPPERA
Outil d'évaluation des coûts de la gestion des déchets des tests de charge virale
Laboratoires de niveau 2 de sécurité biologique
EXPERTISE FRANCE
anrs
Solthis
OPPERA 33

5

ECONOMY

Beyond the effective implementation of OPP viral load testing in the 4 countries of the OPP-ERA project, one of the objectives was to participate in the revitalization of the viral load testing market. The analysis of market trends showed the expansion and diversification of the viral load test offer.

The search for efficiency is a key issue for health systems whose resources are unfortunately limited. Viral load tests must be offered at a reasonable cost and optimized, in order to extend the offering to as many patients as possible.

A study of the full costs associated with viral load testing and waste management illustrates the human and material resources required within any health system wishing to build a robust and sustainable viral load test offer.

Online toolkit in French

Rubrique **Laboratoire** sous thématique : **Evaluation des coûts.**

toolkit-chargevirale-oppera.solthis.org/laboratoire

EXPAND AND DIVERSIFY THE HIV VIRAL LOAD TEST OFFER

Lesson learnt No 49

Prior to the open polyvalent platforms (OPPs), the HIV viral load testing market was not very competitive. It was an oligopolistic market (with many buyers but few sellers, since only four large companies shared the viral load testing market).
The available equipment was also integrated, without the possibility of using several suppliers.

Programmatic consideration

→ Acting on the offering by proposing new viral load testing tools opens the market to new manufacturers and thus increases competition between suppliers, with a view to triggering a price reduction per HIV viral load test, for the benefit of patients and of the health system as a whole.

.

Figure No 35 : **Number of references and potential suppliers identified during the February 2017 market study, OPP-ERA**

	Extractors	Extraction reagents	Thermocyclers	Amplification reagents
Number of identified references potentially usable in open systems	44	76	45	71
Number of suppliers involved	38	63	26	58

OPP

Lesson learnt No 50

However, a significant offering has been developed with many suppliers producing equipment and reagents that could be combined to form OPP platforms (confirmed within the framework of the OPP-ERA project by a market study and a questionnaire). However, not all combinations are possible. At the time of the project, the instructions for use for Generic HIV Charge Virale Biocentric amplification reagents, only mentioned 5 thermocycler references. (Fig. No 35)

Lesson learnt No 51

The attractiveness of the Molecular Biology market and the dynamism of its players are illustrated by the numerous fusions and acquisitions of companies. Thus, the positions of the various market operators cannot be considered as stable.

OPP

The example of the acquisition of Biocentric by Hain and then Brucker illustrates the interests of large groups specializing in diagnostic equipment for innovative solutions and their openness to opportunities.

Lesson learnt No 52

The HIV viral load testing market has been undergoing rapid changes for several years with a diversification of the offering in which open platforms have participated.

OPP

Thus, OPPs have been a source of innovation, because these systems are:

- open: i.e. offering the possibility of using various reagents and equipment that is compatible with each other, thus allowing the buyer to choose between several references;
- flexible: adaptable to contexts where the demand for viral load testing and therefore the volume of activity are variable, and allowing the diagnosis and biological monitoring of different pathologies - Hepatitis B and C, TB.

Lesson learnt No 53

The obvious need for scientific technical validation to demonstrate compatibility between different pieces of equipment and with reagents is a major challenge for open systems during certification processes. Each amplification reagent is labelled for a specific combination of machines.

OPP

The technical validation of the reagents / equipment pairing requires time and significant technical skills.

Programmatic consideration

→ Select suppliers whose equipment is compatible with the reagents chosen and mentioned in the instructions for use of these reagents.

Lesson learnt No 54

To ensure the quality and safety of reagents for diagnosis and biological monitoring, they are subject to specific international regulatory requirements (WHO prequalification, use authorized by the regulatory authorities of the Global Harmonization Task Force - GHTF -, purchase authorized by the WHO Review Committee).
To access the market funded by international donors, suppliers must demonstrate that they meet these quality and safety requirements, regardless of the country of use.

OPP

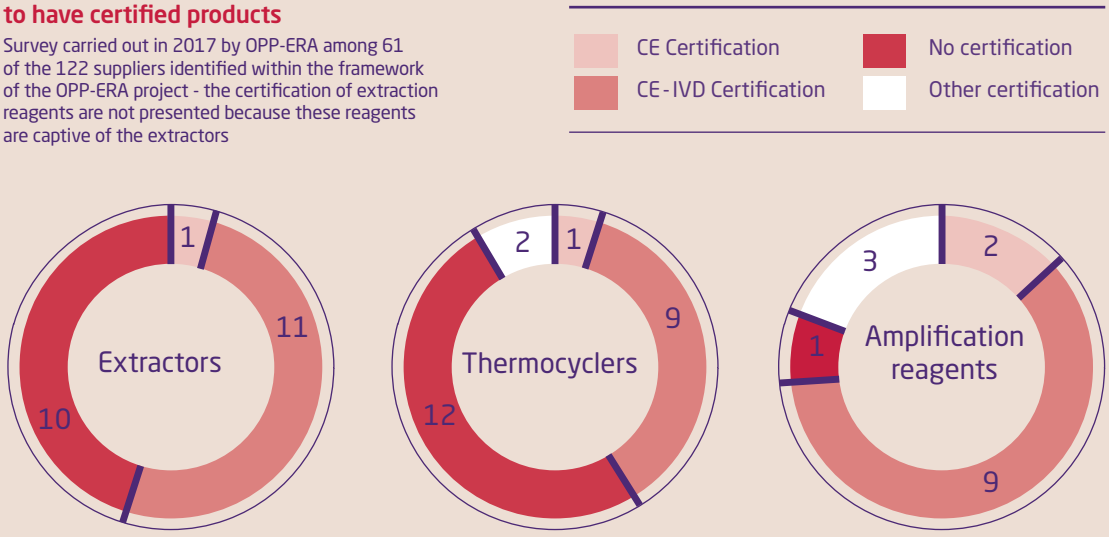
In addition, at the time of publication of this Guide, it appears that the concept of openness is being questioned in the context of obtaining WHO prequalification. The fact that the constituent elements of OPPs must correspond to each other may allow technological alliances between certified manufacturers. (Fig. No 36)

Programmatic consideration

→ Select suppliers whose reagents and corresponding equipment are already certified (or at least engaged in certification processes).

Figure No 36 : **Proportion of suppliers claiming to have certified products**

Survey carried out in 2017 by OPP-ERA among 61 of the 122 suppliers identified within the framework of the OPP-ERA project - the certification of extraction reagents are not presented because these reagents are captive of the extractors



OPP

Lesson learnt No 55

Although the need for HIV viral load testing coverage remains high, particularly in West and Central Africa, the limited interest of potential new suppliers is certainly multifactorial: constraints related to the validation of the creation and the deployment of a maintenance service in the sub-region, underestimation of demand, anticipation of an access barrier (especially if the costs cannot be covered by the health system and if they do not know the international aid financial instruments), etc.

ANALYZE THE COSTS OF PERFORMING HIV VIRAL LOAD TESTING

Lesson learnt No 56

The costs of performing HIV viral load testing provided by the suppliers of the different available platforms are not directly comparable and are underestimated since they do not include all the costs necessary to perform HIV viral load testing.
Hidden costs generally include: the cost of continuous training, laboratory staff time, sample collection, infrastructure and operating costs, or even waste management. These hidden costs can have a significant impact on prices.
Most costs vary from one laboratory to another (salaries, daily working time, transportation costs, infrastructure requirements and equipment purchases, etc.) as well as the actual consumption of consumables and reagents.
A full-cost comparison is therefore necessary. (Fig. No 37 and 38)

Tip

Take into account the following cost categories when calculating the full cost:

- → Human resources costs: salaries paid related to the average time spent directly or indirectly by the staff to perform HIV viral load tests
- → Training costs: all expenses incurred to train laboratory staff in HIV viral load testing
- → Costs of small equipment and supplies: consumables and small disposable equipment used for sample preparation, extraction and amplification
- → Reagent costs: extraction and amplification reagents required for an HIV viral load test (including retesting)
- → Small non-medical equipment: additional supplies required
- → Equipment costs: inventory of the laboratory's technical platform, associated maintenance and depreciation
- → Infrastructure costs: construction, plumbing and electrical system costs
- → Operating costs: expenses necessary for operation (energy, etc.)
- → Transportation costs: sample collection and transportation

Programmatic consideration

- → Estimate the full cost before choosing an HIV viral load technique.

Figure No 37: **Evaluation of the unit cost of an HIV viral load test by cost components, in euros**

2013-2016 period, OPP-ERA project
Converted into dollars at the rate of $1.20 / €

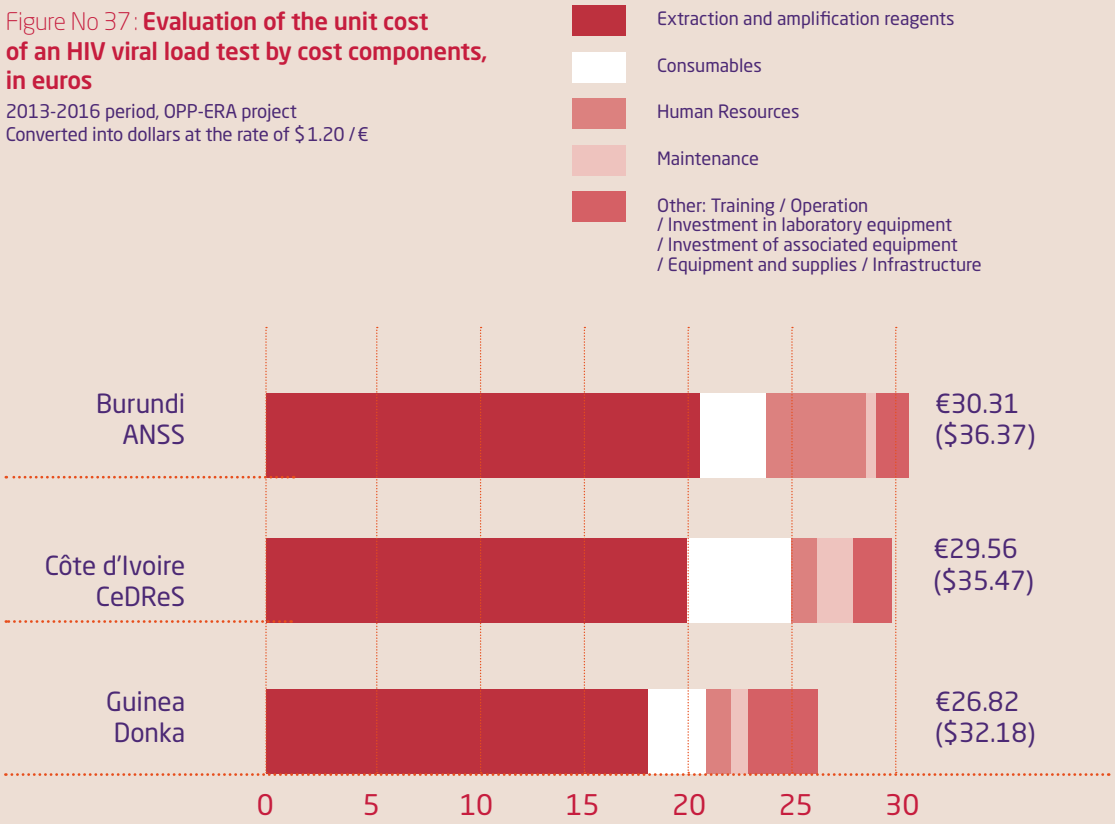
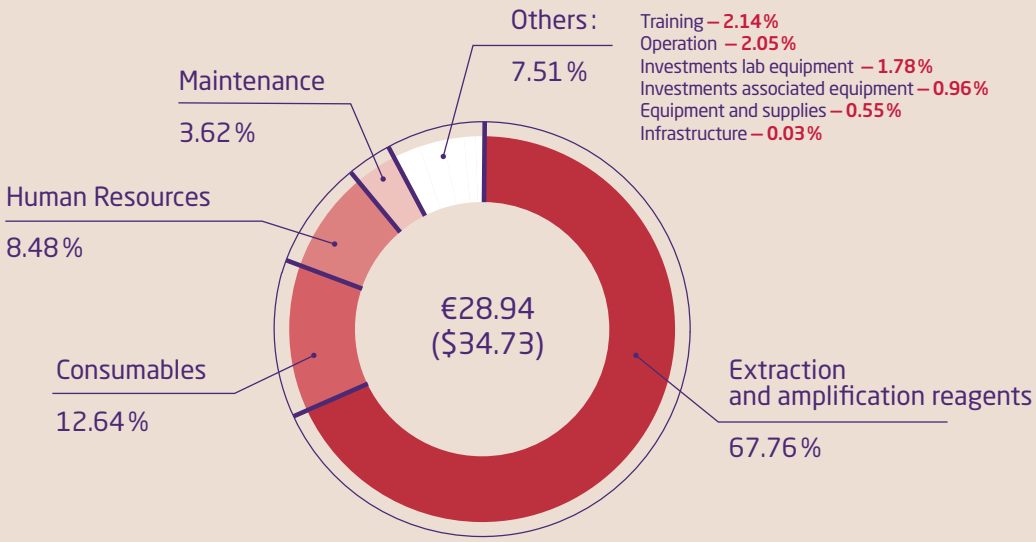


Figure No 38: **Average distribution by cost components of an HIV viral load test**

2013-2016 period, OPP-ERA project
Converted into dollars at the rate of $1.20 / €



Online toolkit in French

→ **Outil d'évaluation des coûts de la charge virale**
→ **Guide utilisateur pour l'outil d'évaluation des coûts de la charge virale**

Lesson learnt No 57

Price negotiations are possible with suppliers, especially when large volumes of purchases are anticipated.
The OPP-ERA project has thus contributed to lowering the price of viral load test reagents. (Fig. No 39)

Figure No 39: **Price evolution by reagent during the OPP-ERA project**

* negotiated minimum degressive price, depending on the volume of purchases
** amount negotiated in euros (converted into dollars at the rate of $1.20 / €)

	Reagent prices in 2014	Reagent prices in 2019
Extraction kit	$6.5	$4.94*
Amplification kit	$12.41	$9.08**

Lesson learnt No 58

Depending on the context (including allocated resources and procurement circuits), the costs of HIV viral load tests on OPP correspond to the costs observed in the market, all platforms combined.

Programmatic consideration

→ Periodically repeat full cost comparisons in real life situation.

Lesson learnt No 59

Some of the costs associated with performing HIV viral load tests are sometimes underestimated or underfunded, resulting in payment difficulties that undermine all viral load testing activity. These issues mainly concern the costs related to sample transportation, infrastructure and waste management, or the salaries of all persons directly or indirectly involved in carrying out the tests.
If these costs cannot be absorbed at the level of care units, laboratories or National HIV / AIDS Programs, they tend to destabilize the service offering. Conversely, full cost recovery improves the robustness of the service offering.

Programmatic consideration

→ Anticipate the recovery of all these costs before the start of the viral load testing activity, to provide for smooth operation and a continuous activity, without forcing the laboratories to carry out the viral load testing activity when they do not have the necessary resources.
→ Consider offering free HIV viral load testing for patients whenever possible.

TAKE INTO ACCOUNT AND ESTIMATE THE COST OF WASTE MANAGEMENT AND WASTE TREATMENT

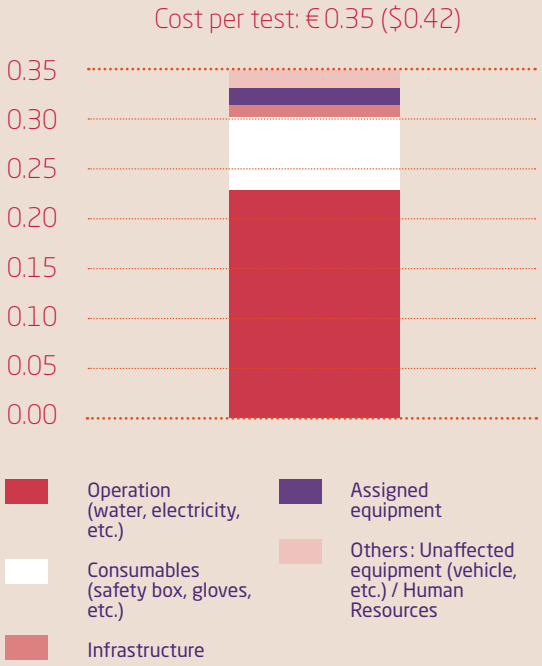
Lesson learnt No 60

The waste generated by the viral load testing activity, whatever the technique used, is potentially hazardous (including toxic waste of chemical or biological origin, carrying infectious and epidemic risks). Due to their environmental and health impact, the issue of waste management and treatment should be integrated from the initial assessment of the laboratory site, as well as into national standards and cost calculations. (Fig. No 40)

Tip

→ Take into account the following cost categories in calculating the cost of waste management and waste treatment: human resources, consumables (safety box, gloves, masks, etc.), equipment directly related to viral load testing waste management (incinerator, etc.), equipment indirectly related to viral load testing waste management (generator, etc.), maintenance, overhead costs (water, electricity, etc.) and infrastructure.

Figure No 40: **Cost evaluation of waste management by test, at ANSS in the Republic of Burundi, in euros**
2013-2016 period, OPP-ERA project
Converted into dollars at the rate of $1.20 / €



Programmatic consideration

→ Define standards and protocols for waste management.
→ Systematically take into account the means necessary to reduce the ecological and health impact in the management of care and in the granting of international funding for the activities to be implemented.
→ Estimate the full costs of waste management and waste treatment before choosing the HIV viral load testing technique, and then carry out follow-up studies.

Online toolkit in French

→ **Outil d'évaluation des coûts de la gestion des déchets des tests de charge virale**

ACKNOWLEDGEMENTS

Our acknowledgements go to all those who have actively participated in the implementation of the OPP-ERA project and who helped in producing this Guide:

For their collaboration and support during the 6 years of the project.

The Ministries of Health, the National HIV / AIDS Programs and CNLS of the 4 implementing countries.

For their continued involvement in our partnership.

The civil society as well as the teams and management of the community structures, HIV care units and laboratories, and especially, in the Republic of Burundi: the National Association for the Support of HIV-positive and AIDS patients, Muyinga Hospital, Kamenge University Hospital and Gitega Hospital; in the Republic of Cameroon: Laquintinie hospital of Douala, Central Hospital of Yaoundé, Regional Hospital of Bertoua and Centre Pasteur of Cameroon, including the Annex of Garoua; in the Republic of Côte d'Ivoire: the Diagnosis and Research Centre on AIDS and other opportunistic diseases, and the Treatment Research and Training Centre; in the Republic of Guinea: the National Institute of Public Health and Donka Hospital; as well as the virology laboratory of the Necker-Enfants Malades Hospital in Paris.

For their commitment to us
and the implementation of this project full of surprises.

All the Expertise France, Sidaction and Solthis teams.

For writing this Guide.

Guillaume Breton, Natasha Dubois Cauwelaert, Emilande Guichet, Olivia Marc, ainsi que Anthony Billaud, Benjamin Coriat, Franck Lamontagne, Christine Rouzioux, Nadia Yakhelef.

For their contribution to reflection and proofreading.

Jean-Claude Agaman, Guillaume Bado, Sophie Calmettes, Mathilde Casabonne, Angéline Inamahoro, Francine Karemera, Samuel Kabore, Emilio Lumia, Laurent Malato, Madeleine Mbangue, Léa Mérillon, Ildéphonse Nduwayo, Anicet Nyawakira, Louis Pizarro, Olivia Sylla, Tamba Kallas Tonguino, Roland Tubiana, Isabelle Zangre.

For enhancing the content of this Guide and for their creativity.

Rachel Domenach, Jasmine Irakoze, Anne Klepper.

For the technical coordination and the management of this Guide
and of the last year of the project, and their participation in the writing.

Sophie Ouvrard and Jeanne Roussel.

For ensuring the scientific coordination of the project
and for their financial contribution.

ANRS.

Unitaid, for funding the project and for the support provided
by its teams over the past 6 years,

and especially Smiljka de Lussigny and Lélio Marmora; as well as Loveena Dookhony, Philippe Duneton, Lorenzo Llewellyn Witherspoon, Sarah Mascheroni, Robert Matiru, Gélise Mccullough, Ombeni Mwerinde, Ademola Osigbesan, Sara Padidar, Julien Pouille, Anna Laura Ross and Matthieu Vittot.

And finally, for their support in preparing for the transition.

The Global Fund Secretariat teams for the Republics of Burundi, Cameroon, Côte d'Ivoire and Guinea.

Solthis,
for the members of the OPP-ERA consortium.

Photo credit:
Loic Delvaux / Agence MAPS
Africa Global Vision – Guinea
Anna Surinyach

All rights reserved. 2019
© OPP-ERA
https://chargevirale-oppera.solthis.org/

Graphic design:
Atelier c'est signé (Mora Prince)

Layout:
Mora prince, Paola Marti

Translation from French to English:
Murielle Jackson, Thérèse Benoit

This Guide has been developed within the OPP-ERA project:

OPP-ERA

Implemented by:

Solthis

anrs

EXPERTISE FRANCE

Sidaction

Supported and funded by:

Unitaid
Innovation in Global Health