Quality and Safety of HIV/AIDS Medicines in Namibia October 2015-September 2016

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Quality and Safety of HIV/AIDS Medicines in Namibia October 2015-September 2016

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About SIAPS

The goal of the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program is to assure the availability of quality pharmaceutical products and effective pharmaceutical services to achieve desired health outcomes. Toward this end, the SIAPS result areas include improving governance, building capacity for pharmaceutical management and services, addressing information needed for decision-making in the pharmaceutical sector, strengthening financing strategies and mechanisms to improve access to medicines, and increasing quality pharmaceutical services.

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Key Words

medicine regulation, quality assurance, post-market surveillance

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ACRONYMS AND ABBREVIATIONS

3TC	lamivudine
ABC	abacavir
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
ARV	antiretroviral
AZT	zidovudine
FTC	emtricitabine
EFV	efavirenz
HIV	human immunodeficiency virus
MOHSS	Ministry of Health and Social Services
NIMART	nurse initiated and managed ART
NMRC	Namibia Medicines Regulatory Council
NVP	nevirapine
OI	opportunistic infection
PMS	post-market surveillance
QSL	Quality Surveillance Laboratory
SIAPS	System for Improved Access to Pharmaceuticals and Services
TB	tuberculosis
TDF	tenofovir disoproxil fumarate
USAID	United States Agency for International Development
WHO	World Health Organization

BACKGROUND

Namibia is one of the southern Africa countries significantly affected by the HIV and AIDS epidemic, which is one of the leading causes of morbidity and mortality in the country. The country has however had a largely successful scale-up of antiretroviral treatment (ART) services, with public sector patient numbers increasing rapidly from about 400 in July 2003 to about 140,000 as at June 2015. Namibia's estimated population of 2.3 million people is distributed unevenly in urban centers and rural communities and has a sparse population density of 2.6 people/square kilometers.

The Namibia Medicines Regulatory Council (NMRC), which falls under the Ministry of Health and Social Services (MOHSS) directorate of Tertiary Health Care and Clinical Support Services is mandated by the Medicines and Related Substances Control Act 13 of 2003 to ensure quality, safety and efficacy of medicines in the country, and contribute to improving treatment outcomes. The quality and safety of antiretrovirals (ARVs) and related commodities are integral to the success of HIV and AIDS prevention and treatment. Among the key functions of NMRC are evaluating the quality and safety of medicines prior to their registration and conducting routine post-market surveillance (PMS) of the quality of registered medicines in the country.

The NMRC has not been able to effectively perform this function partly because of the lack of skilled pharmaceutical human and technical resources. Furthermore, the public sector pharmaceutical supply chain still experiences challenges in ensuring the uninterrupted availability of HIV and AIDS commodities and other essential medicines, which negatively affects the delivery of ART and TB treatment services.

The USAID-funded projects, i.e., Rational Pharmaceutical Management Plus, Strengthening Pharmaceutical Systems, and currently the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Project have provided technical assistance to the NMRC secretariat to help it fulfill its statutory mandate of protecting public health in Namibia. Our various interventions have focused on strengthening NMRC's regulatory capacity for ensuring that only quality-assured, safe, and efficacious ARV and other essential medicines reach patients. This abates the possibility of patients accessing poor-quality medicines and protects public health against the potential harmful effects of unsafe medicines, thus contributing to the success of HIV and AIDS programs. Over its five-year tenure, the SIAPS Project has assisted the NMRC in strengthening medicines registration, inspection and licensing, quality surveillance, and therapeutics information and pharmacovigilance.

Due to inefficient and labor-intensive procedures, the NMRC has previously experienced delays in the evaluation and timely registration of medicines, particularly new medicines or formulations for HIV, AIDS, TB, and maternal, neonatal, and child health. Such delays would deprive patients of the benefits of novel medicines and important innovations, like single pill, fixed-dose combinations.

The hurdles largely contributed to the rapid accumulation of unassessed medicine applications (dossiers), up to 711 by September 2014. Through various interventions introduced and supported by SIAPS, the backlog dropped to 254 applications by September 2015 (figure 1).

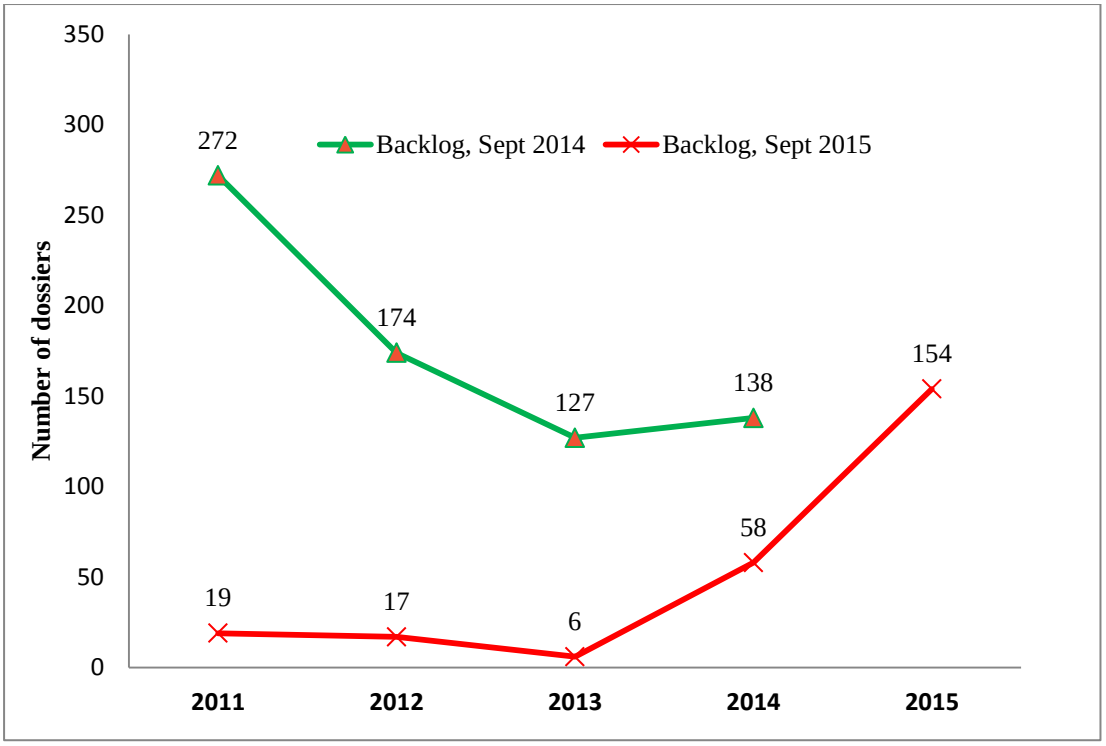

Figure 1. Number of applications pending review per year

In the last five years, SIAPS has provided technical assistance to the NMRC to strengthen its capacity for registration and quality testing by training technical staff in medicines dossier evaluation, developing guidelines for conducting the routine PMS of quality of medicines, and collecting medicine samples at selected ART and TB treatment sites for laboratory testing.

INTERVENTIONS

Medicines Registration

SIAPS mentored and provided guidance and technical support to NMRC staff and other personnel in conducting efficient dossier reviews for the registration of ARVs, anti-TB, and other essential medicines. Consequently, intensive dossier review sessions were organized and fully funded by NMRC after effective and successful transition of the activity to NMRC for sustainability.

Medicine Post-Market Quality Surveillance

SIAPS provided technical assistance to the NMRC to develop guidelines and collect medicine samples from seven priority regions (Kavango East and West, Khomas, Ohangwena, Omusati, Oshana, Oshikoto, and Zambezi) and one urban hotspot (Grootfontein [Otjozondjupa]). This was for the intensified PEPFAR-funded prevention and treatment scale-up interventions, such as decentralization of ART services through NIMART, to rapidly bring the epidemic under control.

The categories of samples collected included ARVs and medicines for opportunistic infections (OIs) in HIV/AIDS. Table 1 lists the samples and dosage forms collected during the exercise.

Table 1. Categories of medicines sampled

#	Category	Generic name	Strength	Dosage form
1	ARV	ABC/3TC	60 mg/30 mg	Tablet
2	OI	Co-trimoxazole	240 mg/5 ml	Suspension
3	OI	Co-trimoxazole	480 mg	Tablet
4	ARV	3TC/AZT	150 mg/300 mg	Tablet
5	ARV	EFV	600 mg	Tablet
6	ARV	TDF/FTC/EFV	300/200/600 mg	Tablet

The samples were tested by the national pharmaceutical quality surveillance laboratory (QSL) using recognized pharmacopoeia methods and specifications.

RESULTS/OUTCOMES

NMRC Performance in Medicines Registration

SIAPS continued to support NMRC to expedite medicines registration through intensive dossier evaluation sessions. In FY16, through this strategy that was fully funded by the Government of the Republic of Namibia, 229 medicine registration applications were reviewed and registered, of which 6.1% were ARV medicines (table 2).

Table 2. List of ARV medicines registered between October 2015 and September 2016

Applicant	Registered name	Approved active ingredient/s	Dosage form	Registration number
Aurobindo Pharma (Pty) Ltd	Truno 600/200/300 mg	EFV/FTC/TDF	Film-coated tablet	16/20.2.8/0024
Hetero Labs Limited	Abacavir sulfate and 3TC 600/300 mg	Abacavir sulfate and 3TC	Tablet	16/20.2.8/0029
Mylan Laboratories Ltd	3TC and AZT 30 mg/60 mg	3TC/AZT	Dispersible tablet	16/20.2.8/0035
Hetero Labs Ltd	Darunavir 400 mg	Darunavir	Tablet	16/20.2.8/0052
	Darunavir 600 mg	Darunavir	Tablet	16/20.2.8/0053
Strides Arcolab Limited	FTC and TDF 200/300 mg	FTC/TDF	Tablet	16/20.2.8/0055
Janssen-Cilag International NV	Prezista 100 mg/ml	Darunavir	Suspension	16/20.2.8/0074
Macleods Pharmaceuticals Ltd	Lopihope-R	Lopinavir-ritonavir	Tablet	16/20.2.8/0087
	Lamihope-SN	3TC, stavudine, NVP	Tablet	16/20.2.8/0088
Ranbaxy (SA) (Pty) Ltd	Aviranz Kid	EFV	Tablet	16/20.2.8/0093
Pharmacare Ltd, South Africa	Aspen Atazanavir 150	Atazanavir sulfate	Capsule	16/20.2.8/0162
	Aspen Atazanavir 200	Atazanavir sulfate	Capsule	16/20.2.8/0163
ViiV Healthcare UK Ltd	Triumeq	Dolutegravir sodium, abacavir sulfate, 3TC	Film-coated tablet	16/20.2.8/0216
Hetero Labs Ltd	Lopinavir and ritonavir 100 mg/25 mg	Lopinavir-ritonavir	Tablet	16/20.2.8/0220

During this period, there was delay in the ministerial appointment of the new members of the NMRC, which prolonged the number of days for approving medicines for registration, after dossiers had been evaluated by the technical experts at the NMRC secretariat.

From figure 2, the number of dossiers that constituted the backlog by September 2014 reduced from 711 in September 2014 to100 (sum of the green columns) in 2015 and finally dropped to 83 dossiers (sum of the blue columns) in 2016. Also, figure 3 shows that the number of dossiers that had stayed for more than four years without review dropped to less than 50 in 2015/2016. This is attributed to the intense efforts by NMRC and interventions supported by SIAPS to expedite medicine registration activities and ensure availability of quality HIV commodities for success of ART programs.

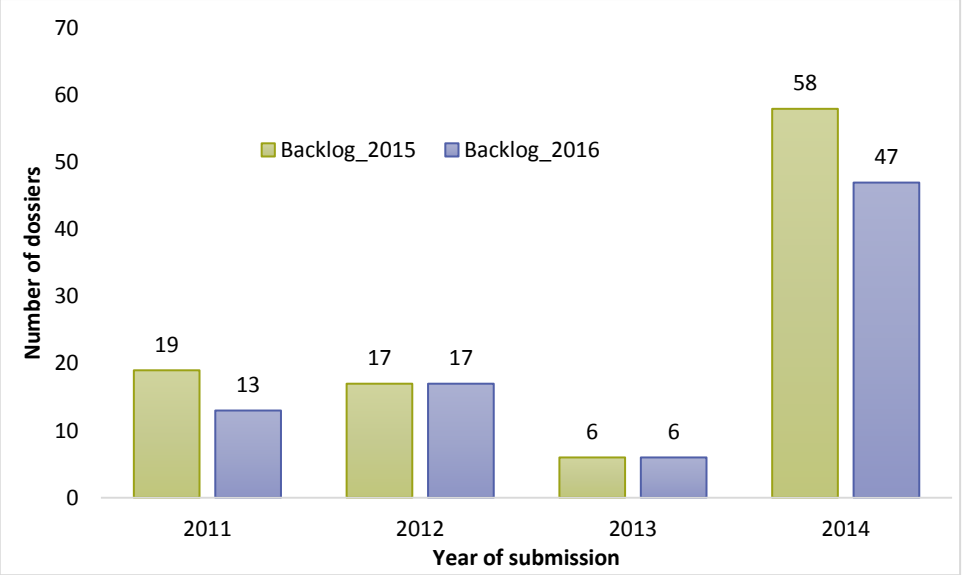

Figure 2. Breakdown of the NMRC dossier backlog (applications before 2015)

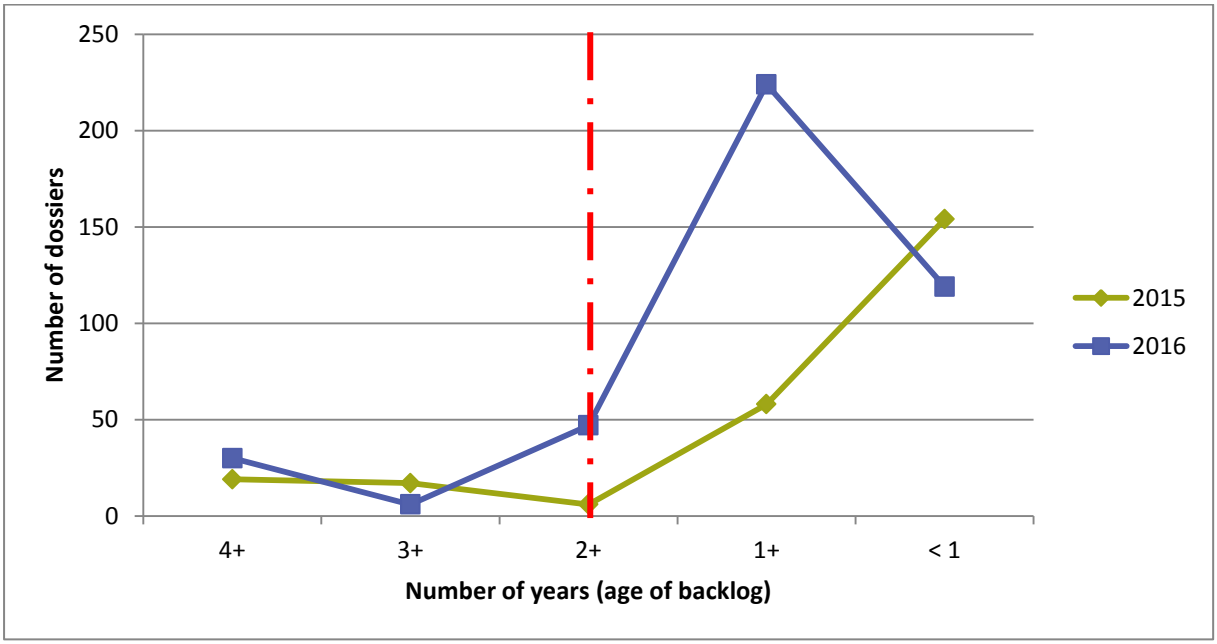

Figure 3. Age profile of the NMRC dossier backlog (years)

Post-Market Surveillance (Monitoring) of the Quality of Medicines

A total of 68 samples of ARVs and other essential medicines were collected from 15 public health facilities in 8 regions. The facilities included 6 primary health care clinics and 9 district hospitals. Table 3 shows the total number of samples collected by generic name.

All the samples were tested at QSL using the prescribed pharmacopoeia methods. Table 3 shows the results of the medicine sample tests, with an overall pass rate of 88.2% for all the samples collected and tested. The failures were recorded for co-trimoxazole suspension samples.

Table 3. Results of samples tested at NMRC QSL

Generic Name	Strength	Dosage form	# of samples	% results passed
ABC/3TC	60 mg/30 mg	Tablet	5	100%
Co-trimoxazole	240 mg/5 ml	Suspension	14	29%
Co-trimoxazole	480 mg	Tablet	14	100%
3TC/AZT	150 mg/300 mg	Tablet	10	100%
EFV	600 mg	Tablet	15	100%
TDF/FTC/EFV	300/200/600 mg	Tablet	10	100%
Total = 68		Overall = 88.2%		

RECOMMENDATIONS

The findings illustrate the importance of strengthening the PMS of medicine quality, and the results are of clinical and general public interest and should be disseminated in suitable media.

Routine monitoring of medicines quality at all levels of the country's pharmaceutical supply chain is critical for protecting public health.

CONCLUSIONS

The USAID-funded technical assistance to strengthening NMRC's pharmaceutical regulatory capacity has improved NMRC's efficiency in medicines regulation in Namibia. The backlog/number of dossiers pending regulatory review significantly reduced over the life of SIAPS. NMRC successfully assumed full responsibility and budgets for intensified medicines dossier reviews to accelerate the process and to shorten the time taken to evaluate applications and register medicines. This demonstrated commitment and sustainability of the interventions.

The quality and safety of medicines used in the ART program and other disease conditions are crucial for successful treatment outcomes. Through support from SIAPS, the NMRC began conducting routine surveillance of medicine quality in the country. The failure rate of the quality of sampled and tested medicines reduced between 2014 and 2016, although it was still high for medicines used for treating OIs. The improvements in the PMS of medicine quality in Namibia is attributed to routine monitoring, health worker vigilance in reporting products of suspicious quality to NMRC, and NMRC's commitment to recall sub-standard products from the market. The generally good quality and safety profile of the sampled ARVs and OI medicines indicates the positive effect of SIAPS support to NMRC in ensuring the quality of medicines used in the HIV, TB, and other public health programs in Namibia.