



**SIAPS' Technical Assistance to Strengthen Medicines
Regulation in Namibia: 2011–2017**

December 2017



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Systems for Improved Access
to Pharmaceuticals and Services

**SIAPS' Technical Assistance to Strengthen Medicines Regulation in Namibia:
2011–2017**

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December 2017



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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

Pharmadex, NMRC, medicine, regulation, PMS (post-marketing surveillance)

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ACRONYMS AND ABBREVIATIONS

3TC	lamivudine
ABC	abacavir
ADR	adverse drug reaction
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
ARV	antiretroviral
AZT	zidovudine
d4T	stavudine
EFV	efavirenz
FDC	fixed-dose combination
FTC	emtricitabine
GDP	Good Distribution Practices
GMP	Good Manufacturing Practices
GRevP	Good Review Practices
HIV	human immunodeficiency virus
HR	human resource
I&L	Inspection and Licensing
MOHSS	Ministry of Health and Social Services
NMRC	Namibia Medicines Regulatory Council
PV	pharmacovigilance
OI	opportunistic infection
OPM	Office of the Prime Minister
PMS	post-marketing surveillance
QSL	Quality Surveillance Laboratory
SIAPS	Systems for Improved Access to Pharmaceuticals and Services
SOP	standard operating procedure
SPS	Strengthening Pharmaceutical Systems
TA	technical assistance
TB	tuberculosis
TDF	tenofovir disoproxil fumarate
TIPC	Therapeutics Information and Pharmacovigilance Centre
UNAM-SoP	University of Namibia School of Pharmacy
USAID	US Agency for International Development
WHO	World Health Organization

EXECUTIVE SUMMARY

The Namibia Medicines Regulatory Council (NMRC) is a statutory body established by the Medicines and Related Substances Control Act, Act 13 of 2003, to regulate the use of medicines in Namibia. Its mission is to serve the public by developing and maintaining internationally acceptable standards of medicines control. The four units of the NMRC work toward ensuring the availability of safe, efficacious, and quality-assured medicines in Namibia.

The Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program, funded by the US Agency for International Development (USAID) and implemented by Management Sciences for Health (MSH), is the follow-on project to the Strengthening Pharmaceutical Systems (SPS) Program (2007–2011), the Rational Pharmaceutical Management (RPM) Program, and RPM Plus (2000–2006). These predecessor programs provided technical assistance (TA) in pharmaceutical management and systems strengthening, beginning in the early 1990s. The SIAPS Project was initially planned for five years, from 2011–2016, but was later extended by a year. This report focuses on accomplishments of SIAPS in providing support to the NMRC, an agency of the Ministry of Health and Social Services (MOHSS).

The NMRC had protracted human resource (HR) and technical challenges that negatively impacted its mandate of ensuring availability of medicines even after the SPS Project in Namibia allocated most of its investment and efforts on HR development for pharmaceutical management. The NMRC's effectiveness was limited, largely due to these human and technical resource constraints. These challenges contributed to the rapid increase in the number of unassessed medicine registration applications/dossiers. The backlog extended beyond six months in 2011 and 2012 (annex A), measured by the time between the council's receipt of a dossier, reviewing it and giving feedback on outcome of the review to clients. Consequently, the procurement or importation of essential HIV medicines into the country was negatively affected. For example, new antiretrovirals (ARVs) not yet registered by the NMRC, could not be procured and stocked by the Central Medical Stores (CMS), unless the Health Ministry granted an exception to this requirement.

The overall goal of SIAPS is to improve access to quality pharmaceutical products and effective services for better health outcomes. For the period 2011–16, interventions by SIAPS focused on quality assurance and strengthening pharmaceutical governance. Overall, the program promoted and used a systems-strengthening approach that would result in positive and sustainable health impact. SIAPS pursued the following two general objectives regarding pharmaceutical regulation during the period:

- To expedite registration and introduction of newly recommended ARV formulations (including pediatric formulations) and to promote access to information on HIV/AIDS medicines registered in Namibia through a web-based platform
- To ensure safety and quality of medicines reaching patients by strengthening the post-marketing surveillance (PMS), monitoring and reporting of adverse drug

reactions (ADRs), and providing support to the Quality Surveillance Laboratory (QSL)

SIAPS helped improve pharmaceutical product quality by building the capacity of the NMRC to review medicine registration dossiers; inspect pharmaceutical manufacturing facilities and finished (imported) products at ports of entry and in the marketplace; to chemically test medicines compliance with established standards; and monitor overall compliance with applicable regulatory standards and norms. The quality assurance framework designed with assistance of SIAPS was used to identify, design, and implement interventions to strengthen medicines regulation in Namibia. SIAPS support mainly focused on the following areas:

- Capacity building/training in medicine dossier evaluation, good manufacturing and distribution practices, and quality control of medicines
- Conducting PMS of quality of medicines and supporting the QSL to chemically test the sampled medicines for quality according to specific standards
- Reconfiguration of the medicines registration tool, Pharmadex, to a web-based application to enhance transparency and efficiency of the registration process
- Implementation of a pharmacovigilance (PV) system for active surveillance of first-line ARV medicines to support the effectiveness of Namibia's antiretroviral therapy (ART) program in improving treatment and outcomes for persons living with HIV/AIDS.
- Support to the Therapeutics Information and Pharmacovigilance Centre (TIPC) of the NMRC on PV using spontaneous reporting of ADRs

In addition, SIAPS supported MOHSS in strengthening the management and regulation of medical devices and support equipment in Namibia, and in revising the National Medicines Policy, a crucial of pharmaceutical regulation and governance.

Although these interventions mainly targeted the NMRC staff at the national level, they also included regional pharmacists, veterinarians, and pharmacy professionals from the private sector including pharmaceutical industries which import medicines.

Forty-two health workers from the NMRC, public and private pharmacies, University of Namibia School of Pharmacy (UNAM-SoP), medicine importers and distributors, and regional health directorates were trained on the registration and quality assurance of pharmaceutical products for five days in 2014 (Anisfeld 2014b). The classroom training was followed by mentoring and continuous on-the-job training of new staff at NMRC and other personnel engaged in evaluation of dossiers for registration of ARV medicines, including new pediatric formulations, and other essential medicines. This was conducted in the format of organized dossier evaluation sessions, and was gradually transitioned to the NMRC for sustainability and continued improvement of the institution's efficiency in its operations. Support for the NMRC resulted in the reduction of the backlog that had accumulated for several years. This backlog declined from 222 dossiers to 13 between 2011–12 and 2017–18. The decline resulted in an increased percentage of dossiers processed within the same year, from 46.5% to 87.40%.

SIAPS supported the reconfiguration of the desk-top Pharmadex tool to a web-based application. NMRC staff were consulted and involved in determining how the new tool should be. The tool was customized and aligned to the processes and work flows of the NMRC. This user-requirements definition process resulted in the development, installation, and testing of the initial version of the new and improved tool to address NMRC's requirements. In addition, three hands-on training sessions were conducted to orient the staff on the system during the testing of the tool. On average, five NMRC staff members attended each training session. The new Pharmadex application, which is currently ready to use, is accessible to online users to register their products and access the registration database.

Analysis of PMS medicine samples showed that the overall medicine quality failure rate decreased between 2014 and 2016. However, the rate is still high, especially for medicines used for treating opportunistic infections (OIs). The improvements in post-marketing quality surveillance of medicines in Namibia are attributed to routine monitoring, health worker vigilance in reporting products of suspicious quality to NMRC, and NMRC's commitment to recalling substandard products from the market.

The active surveillance PV of the safety of ART in Namibia in 2012–2013 (Mengitsu 2014) demonstrated that an active PV system could be successfully implemented and conducted in sentinel sites. The results of the assessment, which was supported by SIAPS, were used to inform the design of PV strategies in Namibia, especially for the ART program.

In general, the six-year support of the SIAPS project to the NMRC contributed to the strengthening of this regulatory agency, which in turn, contributed to improvements in service delivery to the clients. The registration process improved, to decrease the long-standing backlog of dossiers; PMS ensured safety and quality of pharmaceuticals; and implementation of web-based Pharmadex provided a means for clients/applicants to upload applications and follow up the progress of dossier review, which reduced workload for NMRC staff. SIAPS provided continuous TA for the restructuring of the NMRC.

BACKGROUND

Namibia has an estimated population of 2.1 million people (NSA 2013), which is distributed unevenly in urban centers and rural areas; and a sparse population density of 2.6 people/square kilometer. Namibia is one of the countries in Africa significantly affected by the epidemic of HIV/AIDS, a leading cause of morbidity and mortality in the country. The adult HIV prevalence rate is estimated at about 13.1%, and about 165,845 patients were on ART as at September 2017, according to the Namibian government's own database.

Limited capacity and efficiency of regulatory systems to monitor the quality, safety, and efficacy of medicines can compromise the overall effectiveness of patient-level health care services and endanger public health. A strong pharmaceutical regulatory system is considered an essential component of any health system. In Namibia, the NMRC regulates the country's pharmaceutical sector in a global environment where the circulation of substandard medicines has become a major public health threat. The NMRC is a statutory body, established in terms of the Medicines and Related Substances Control Act, Act 13 of 2003 (OPM 2003), to regulate the use of medicines in the country. Its mission is to serve the public by developing and maintaining internationally acceptable standards of medicines control. Namibia's Medicines and Related Substances Control Act 2003 mandates the NMRC to register and control medicines and related substances. The NMRC has four units: Pharmaceutical Inspection and Control, Medicines Registration, QSL, and TIPC (figure 1). The four units of the NMRC work toward ensuring the availability of safe, efficacious, and quality-assured medicines in Namibia. The Office of the Registrar of Medicines serves as the NMRC Secretariat and provides administrative and technical support to the council (Nwokike 2009).

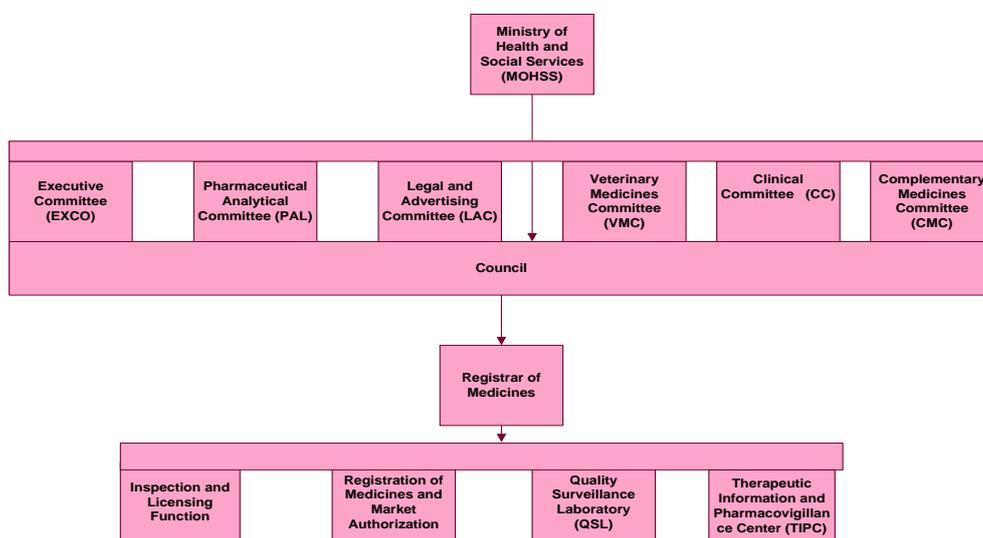


Figure 1. NMRC organizational structure and its location in the MOHSS

Strengthening the capacity of the NMRC requires prioritizing activities to ensure safety, quality, and efficacy of essential medicines and other health products in the country. The SPS Program that preceded SIAPS collaborated with the NMRC to develop a five-year strategic plan and helped streamline the registration process as well as NMRC's supportive systems and institutional capacity. SPS helped institutionalize systems that enable the NMRC to rely

on decisions by other stringent regulatory authorities and concentrate its limited resources on in-country monitoring for the quality, safety, and effectiveness of approved medicines.

The SIAPS Project continued supporting the regulatory systems using more robust approaches, to ensure the quality of medicines, which is essential for efficient disease management. In addition, NMRC applies various regulatory instruments to ensure the availability of good-quality medicines for patients in Namibia. These include (WHO 2015):

- Medicines authorization/registration for marketing through the technical assessment of products and supporting documentation, inspection of manufacturers' compliance with the principles of good manufacturing practices (GMPs), and approval of products' information
- PMS activities, including maintenance of products' authorization/registration through variations or renewals, regular inspections of manufacturers and wholesalers/distributors/retailers, quality control testing, and PV
- Implementation of regulatory actions should any medicine quality problem be found

The major functions of the NMRC include conducting technical assessments of medicine application prior to medicine registration and implementing an effective and robust PMS to monitor the quality of medicines registered in the country. These activities, including retraction and authorization, are driven and coordinated by the Office of the Registrar of Medicines. The other core functions include inspection and licensing, therapeutic information, and PV center activities and QSL services.

The NMRC continued to encounter critical HR and technical challenges that negatively impacted on its mandate of ensuring availability of medicines even after the SPS Project's pharmaceutical HR development interventions. The challenges largely contributed to the rapid growth of the number of unassessed medicine applications/dossiers (more than 63% of received dossiers in 2011 [annex B]) while long periods lapsed between receipts of a dossier and responding to clients on the outcome of the review.

Objectives of the Intervention

SIAPS in Namibia covered five intermediate results (IRs)/objectives, as shown in figure 2.

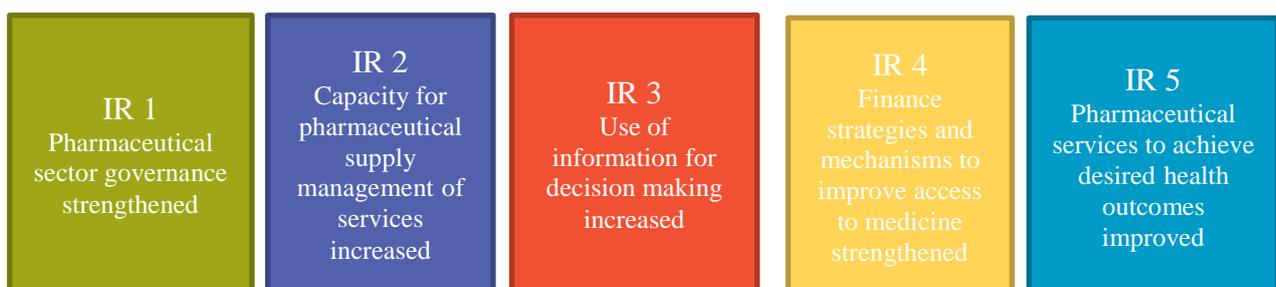


Figure 2. Intermediate results/objectives of SIAPS in Namibia

This report, however, focuses on SIAPS support on IR 1, the strengthening of pharmaceutical sector governance.

The interventions were designed to specifically address the challenges highlighted by the NMRC. First, the inefficiency in the registration of new medicines for HIV and AIDS treatment had needlessly prolonged the implementation of updated ART guidelines, which required the use of new medicines or formulations. Second, the NMRC lacked mechanisms for informing program managers and medical practitioners about new formulations that have been registered in Namibia. Third, lack of ADR data from health facilities hindered monitoring of the safety and quality of pharmaceutical products on the market. Based on these major challenges, SIAPS provided TA for the NMRC to do the following:

- Expedite registration and introduction of newly recommended ARV formulations (including pediatric formulations) and promote access to information on medicines for HIV/AIDS that are registered in Namibia, through a web-based platform
- Support the NMRC in ensuring the safety and quality of medicines reaching the patients in the community by strengthening PMS, monitoring of ADRs and reporting, and support to QSL services.

INTERVENTIONS

In 2011, SIAPS started providing comprehensive support to the four units of the NMRC: Medicines Registration, QSL, Pharmaceutical Inspection and Control, and the TIPC. SIAPS built on the work started by the SPS Program, which conducted a comprehensive assessment of the pharmaceutical regulatory system in Namibia. This assessment identified critical gaps in the medicine regulatory processes.

The SIAPS technical approach was modeled on the World Health Organization (WHO) health systems building blocks (figure 3). Following this framework, SIAPS placed emphasis on five specific building blocks—pharmaceutical governance, HR, information, financing, and service delivery—with a medical product overlay, to demonstrate the interrelation of systems for effectiveness and impact. Figure 3 demonstrates this approach.

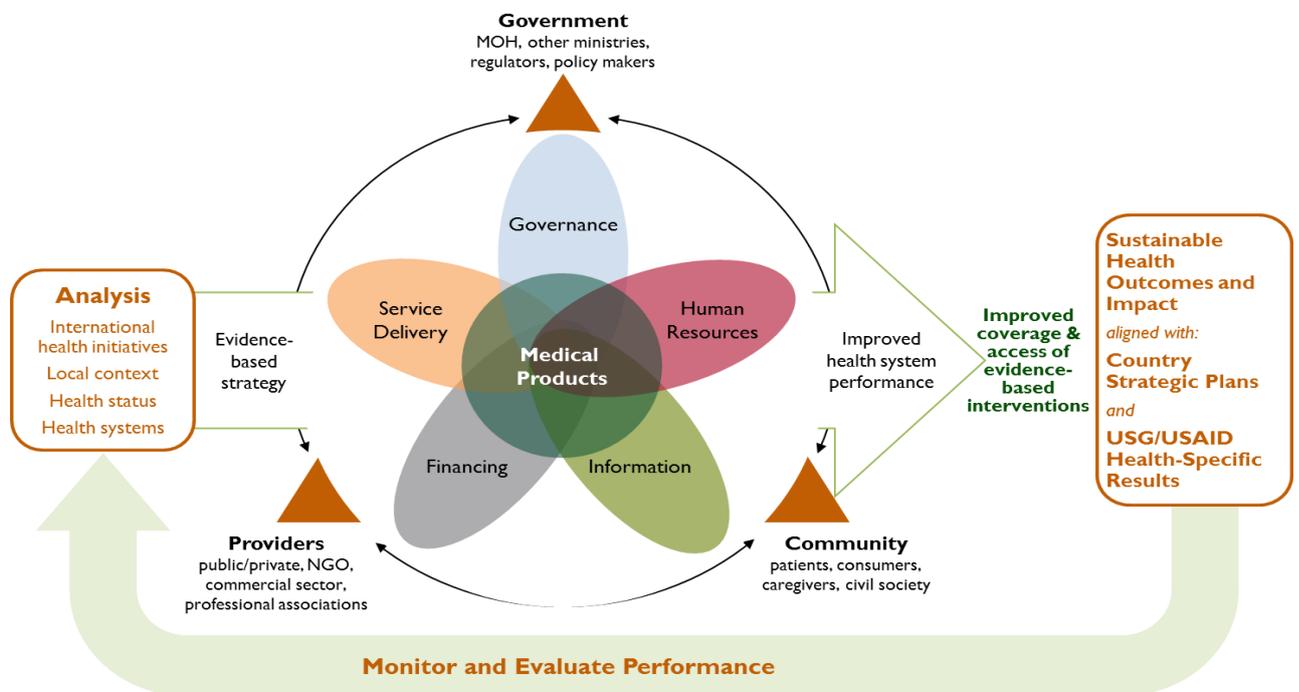


Figure 3. SIAPS pharmaceutical system strengthening approach (Factsheet 2013)

This framework has been a conceptual guide supporting the SIAPS team in Namibia in planning systematic capacity building approaches to strengthen the pharmaceutical system. In addition, this framework provides a more comprehensive view on how to design an integrated pharmaceutical capacity-building strategy. SIAPS interventions were aligned with Namibia’s strategic plan and US Government/USAID health-specific results to achieve sustainable development outcomes and impact on the life of the patient.

Use of poor-quality medicines can lead to lack of therapeutic response or prolong the treatment for a patient, exacerbate illness, contribute to resistance to medicines, and undermine patient confidence in the health care system. However, it was recognized that the NMRC had limited capacity to ensure the required standard of pharmaceutical products and

related services. Consequently, SIAPS focused on building the capacity at the NMRC to efficiently perform their pharmaceutical regulation and quality assurance role.

SIAPS helped systems for monitoring and ensuring pharmaceutical product quality by building capacity in the NMRC to review product documents, inspect manufacturing sites and products at ports of entry and in the marketplace, perform compliance testing with standards, and monitor overall compliance to applicable pharmaceutical standards and norms. SIAPS used a quality assurance system strengthening approach (figure 4), designed by MSH.

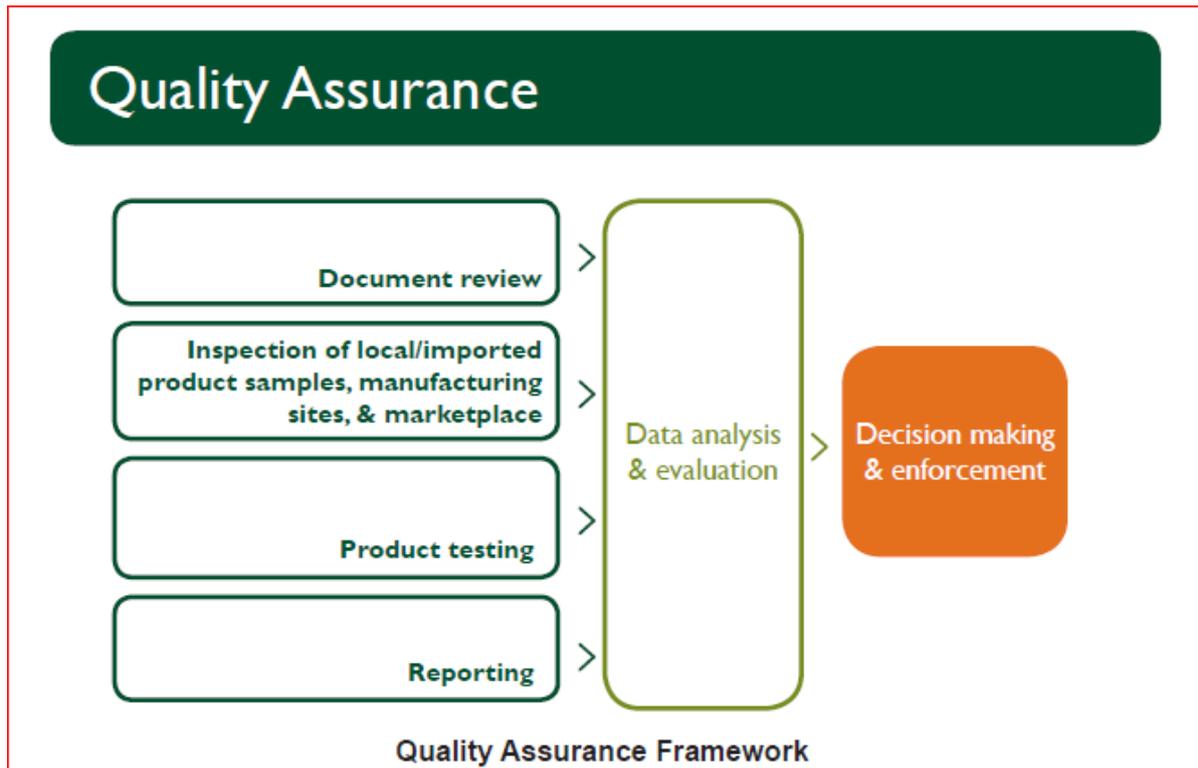


Figure 4. SIAPS pharmaceutical system strengthening approach: quality assurance (CPM 2011)

The quality assurance framework was used to identify, design, and implement the support provided to the NMRC for medicines regulation. SIAPS implemented activities to enhance capacity of the NMRC, based on approved annual work plans for USAID fiscal years (FYs) 12 to FY18 (October 2011–December 2017). These activities included the following:

- 1) Developed standard operating procedures (SOPs), checklists, forms, and guidelines for inspection and licensing (13), QSL (25), registration (13) and TIPC (5)
- 2) Developed and supported operationalization of guidelines for sampling and assessment of pharmaceuticals during PMS of quality of medicines
- 3) Conducted a gap analysis of the NMRC operations in January 2014, which informed training of HR

- 4) Trained pharmaceutical personnel for dossier review and medicines registration, good manufacturing and distribution practices, and quality control of medicines
- 5) Supported QSL in developing/updating guidelines, checklists, forms, and SOPs in 2011–12. Trained three QSL staff on GMPs for quality control laboratories, and provided on-the-job TA for QSL activities
- 6) Supported the NMRC in conducting PMS of medicines quality, using a strategy that NMRC developed with assistance from SIAPS
- 7) Supported the NMRC in reconfiguring the medicines registration tool, Pharmadex, as a web-based application, to enable more transparency and increase the efficiency of the registration process
- 8) Implemented an active surveillance PV system pilot program for first-line ARVs to support the effectiveness of Namibia's ART programs in improving the care and outcomes for persons with HIV and AIDS (Mengistu 2014)
- 9) Provided TA for the expedited registration of generic ARVs (including pediatric formulations) and strengthened systems for assuring the quality of ARVs and related medicines
- 10) Supported the TIPC in enhancing ADR reporting and analysis of reports
- 11) Assessed and projected cost-effectiveness of active surveillance PV of first-line ARVs compared to spontaneous reporting PV in Namibia
- 12) Continued to advocate for the transformation of the NMRC into an administratively and financially independent entity following agreement with technical experts in MOHSS on the transformation process, a critical step for the effectiveness, efficiency, and sustainability of pharmaceutical governance and regulation in the country

These interventions primarily focused on building the capacity of the NMRC. However, the training and mentoring also benefited regional pharmacists, pharmacy professionals from the private sector and pharmaceutical industry, veterinarians, and pharmaceutical import and export health care professionals. The intervention was augmented by periodic planning and review; continuous mentoring of NMRC staff on medicines regulation and control principles and implementation processes and support for the use of tools such as SOPs, checklists, guidelines, and computerized registration (Pharmadex); supporting the provision of PV and therapeutic information to the public; and compilation of progress report for reference in continued implementation of activities.

The results section of this report covers the achievements of the interventions.

RESULTS

This section narrates accomplishments of the collaborative NMRC- SIAPS interventions, over six years (2012–17). SIAPS TA to the NMRC contributed to streamlining the medicines registration processes, strengthening PV, and strengthening policies and procedures on and regulation of pharmaceuticals. The result was an increase in the number of registered ARVs and an increase of more than 70% in the number of multisource generic ARVs, including fixed-dose combinations (FDCs) and pediatric formulations. SIAPS also improved the electronic medicines registration tool (Pharmadex) and reconfigured it to be web-based, which supported over 1,580 product evaluations between 2012 and August 2017. There are 2,071 products currently on the NMRC register as of December 2017, since the year 1976. Comparing this result with the total registered 2,071 products, SIAPS assistance accounted for the registration of 76.29% of the products.

SIAPS developed or updated 56 SOPs/checklists/forms/guidelines for NMRC’s use as detailed in annex C, in the following categories:

- Inspection and licensing (13)
- TIPC (5)
- Registration (13)
- QSL (25)

A gap analysis of the NMRC operations was conducted in 2014. The findings guided NMRC, with SIAPS TA, in customizing training on medicines dossier evaluation and pharmaceutical GMPs; and in improving the efficiency of NMRC operations (Anisfeld 2014a). This contributed to expedited registration of quality, safe, and efficacious generic ARVs, including optimized pediatric formulations, as well as other essential medicines.

Capacity Building for Dossier Registration, Good Manufacturing and Distribution Practices, and Quality Control of Medicines

Forty-two health workers, including NMRC staff, public and private pharmacies, the UNAM-SoP, private medicines importers and distributors, regional pharmacists, and other health professionals were trained on the registration and quality assurance of pharmaceutical products in 2014 (Anisfeld 2014b; annex D). This training was followed by simulated dossier evaluation, with the support of SIAPS, which resulted in reduction of the backlog from the years 2012–15 (annex E). The trainees’ knowledge and skills were enhanced with on-the-job mentoring on dossier review.

SIAPS strengthened NMRC’s capacity for timely registration of second-line medicines for HIV/AIDS and TB, vaccines, and diagnostic devices. In the period 2012–17, the average number of days taken to review and approve an application for medicine registration decreased from over 53 days in 2013 to 48 days in 2014 and to 26 days in 2015. Of the 224 dossiers reviewed and registered for the duration of SIAPS, 6.1% were ARVs.

At least five intensified dossier evaluation sessions were conducted in October 2014, largely funded mostly by USAID through SIAPS; and in February, June, and September 2015, organized and funded by the NMRC with SIAPS TA. NMRC was able to organize and

funded three of the four review sessions because the activity was successfully transitioned to the council for sustained and continued improvement of the institution’s efficiency in its operations (Mbaziira 2015).

The reduction in dossier backlogs improved over the course of several years. The amount of backlog dossiers present in a given year as compared to new dossiers received in the same year declined from 222 in FY2012 to 13 in FY 2018. Thus the percentage of dossiers processed within the same period increased from 46.5% to 87.4% (table 1; figure 5).

Table 1. Dossiers received, processed and registered from 2011–12 through 2016–17*

Dossier status	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18	Total
Received	394	415	355	454	404	207	103	2,332
Processed	275	193	239	474	224	181	90	1,676
Registered	272	271	220	263	97	354	61	1,538
Backlog the same year	119	222	116	-20	180	26	13	656
% processed in the same year	70	46.5	67.3	104	55.4	87.4	87.4	71.86

*Year 2017–18 covers the period October–December 2017.

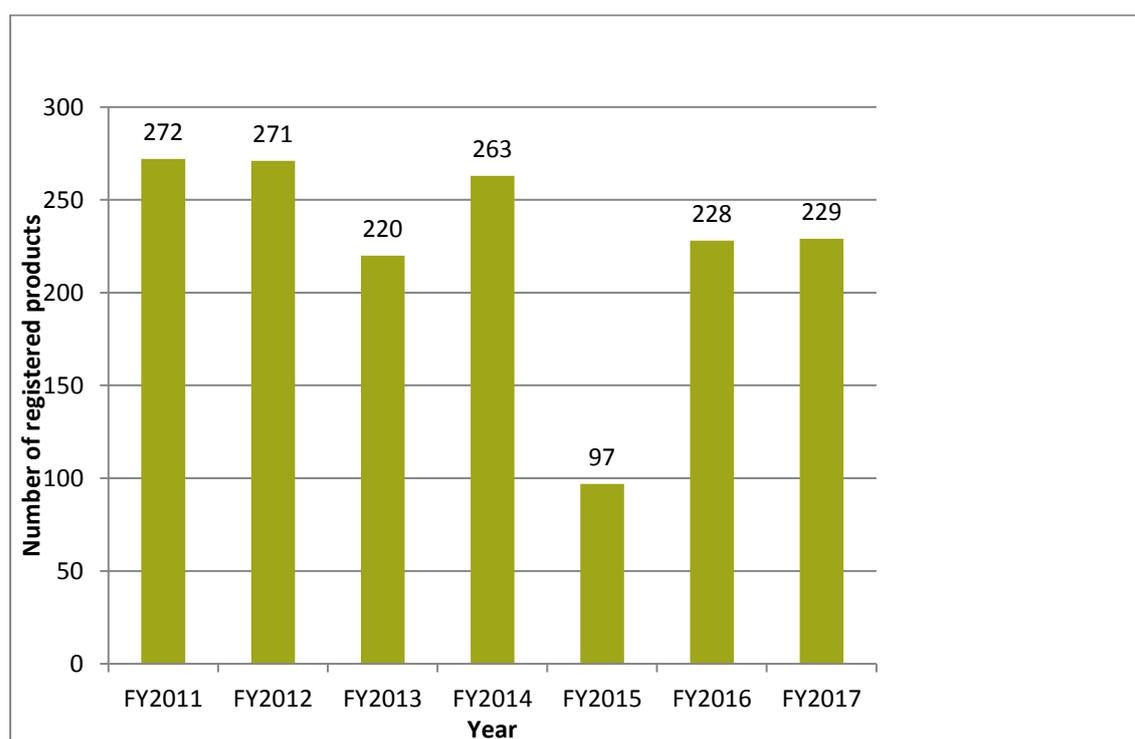


Figure 5. Number of registered products per year, 2011–17

Namibia adapted the 2013 revised WHO Treatment Guidelines for Antiretroviral Therapy, revising and launching new national guidelines in 2014. SIAPS provided TA to the MOHSS to manage the transition from d4T-containing ART regimens and FDCs to safer and more convenient ARV regimens and formulations for children to improve patient safety and adherence outcomes. The MOHSS revised the ART guidelines twice since 2011 and according to these guidelines, the preferred first-line treatment regimen for children included dispersible-tablet ARV formulations, including FDCs of ABC + 3TC and AZT + 3TC, which

meet the unique administration needs for children. For adults, the once-daily FDC (TDF + FTC + EFV) pills, which reduces the pill burden and has a potential for improving patient adherence, were expeditiously registered through the fast-track registration process, which SIAPS helped to create (Mbaziira 2014).

With SIAPS support to the MOHSS, the National Healthcare Technology Policy was updated and a comprehensive list of essential medical equipment for lower-level health facilities was completed. The updated documents and tools are intended to strengthen the management and regulation of medical devices and other essential health equipment in Namibia.

Reconfiguration of Pharmadex as a Web-Based System

SIAPS supported the reconfiguration of the desk-top Pharmadex into a web-based application. The tool was customized and aligned to the NMRC medicines registration processes and work flows (annex B). This improvement was to address the need for better coordination and efficiency within the NMRC. In addition, a report-generating module for managers was added. Three hands-on trainings were conducted during the testing of the tool, where the NMRC medicines registration staff were oriented on all modules of the tool. On average, five staff members attended each training session. The program is ready to use and offers options for online users to register their products and view the list of registered medicines.

Screenshot of NMRC’s Pharmadex interface with unique performance monitoring indicators (2017)

Post-Marketing Surveillance and Support to the QSL

Guidelines for PMS were developed and used for sampling and assessment of medicines in Namibia. SIAPS supported at least four field activities for sampling and collecting medicines in 2014 and 2015. The sampling covered 8 of Namibia’s 14 regions and 151 medicines in 2014–15. All samples were tested by the QSL and an independent WHO prequalified

laboratory in South Africa. Of the 151 samples collected, 13.9% (21) did not conform to pharmacopoeia specifications, and 36.8% were unregistered, of which 1.9% were substandard. After sharing this feedback with stakeholders including pharmaceutical manufacturers and importers in Namibia, the medicines quality failure rate reduced between 2014 and 2016. However, the failure rate of medicines for treating OIs is still high. The improvements in post-marketing quality surveillance of medicines in Namibia is attributed to routine monitoring, health worker vigilance in reporting products of suspicious quality to the NMRC, and the council’s commitment to recall substandard products from the market (Mbaziira 2016).

SIAPS TA enhanced the management capacity of the QSL in accordance with WHO prequalification requirements and its capacity to test PMS samples to monitor the quality of medicines in Namibia. The laboratory was able to test and release results of 88% (151) of the samples collected. SIAPS continued to provide TA to Pharmaceutical Control and Inspection and the QSL in FY11–16. Table 2 shows number and results of medicine samples received and tested by the QSL during the SIAPS support period.

Table 2. Number and results of medicine samples received/tested by the QSL in 2011–16

Samples	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16	Total
Received	247	351	232	162	278	350	1,620
Analyzed	213	262	253	181	201	365	1,475
Passed	211	253	237	178	185	342	1,406
Failed	8	9	16	12	16	23	84 (5%)
Backlog	68	89	68	46	77	34	Avg. 64
% backlog	28%	25%	29%	28%	28%	10%	25%

With SIAPS support, the NMRC revised its organizational structure; reviewed more than 50 SOPs, guidelines, checklists, and forms; and analyzed and developed job descriptions with full staffing details and submitted them to the Office of the Prime Minister (OPM) for approval (proposed structure in annex F.)

Pharmacovigilance System Enhanced

With SIAPS TA, active surveillance of the safety of first-line ARVs was carried out at the Windhoek Central Hospital and Katutura Intermediate Hospital ART clinics. The surveillance involved 457 patients (Mengistu 2014). The active surveillance for first-line ARVs done in 2012–13 demonstrated that an active PV system can be successfully implemented in sentinel sites. The results of the assessment were used to inform active surveillance PV in Namibia for ART as well as PV of other priority medicines, conditions, and populations (e.g., pregnant women).

With SIAPS TA, a cost-utility analysis of active surveillance PV of first-line ARVs versus spontaneous reporting PV in Namibia was completed. On the basis of Based on analysis findings, active surveillance PV was projected to be a highly cost-effective way to improve treatment for HIV in Namibia (Mann 2016)

SIAPS provided TA to the TIPC to train and create awareness among health care workers on PV and ADR reporting to TIPC for management. SIAPS supported the MOHSS to train 28 pharmacists, pharmacist assistants, and medical doctors, including lecturers from the University of Namibia’s School of Pharmacy and the National Health Training Center (NHTC) as TOT for PV/medicine safety surveillance for HIV and TB. The trainings were held in October 2014 and March 2015. In addition, SIAPS supported the TIPC in enhancing PV through annual national pharmaceutical support supervisory visits (2012–17) as well as annual pharmacists, doctors’ and dentists’ forums. The interventions raised awareness of health workers on issues of medicine safety and promoted a reporting culture among Namibian health professionals.

SIAPS also supported the TIPC in training 60 TB field promoters on community PV and ADR reporting to TIPC.

In FY2014, SIAPS also provided support to the TIPC in analyzing ADR-reported data for the period 2011–13. The review revealed that the highest frequencies of ADRs reported during the period were associated with skin disorders. In particular, Stevens-Johnson syndrome, which is a serious reaction, accounted for the highest number (94 reports out of 218). With regard to ADRs associated with blood disorders, anemia 96/97 (99%) was associated with AZT (Chinedum 2014). Furthermore, most reactions reported were serious in nature.

With SIAPS TA, the TIPC compiled and disseminated four editions of *Medicines Watch*, a quarterly newsletter providing information on treatment to health care workers. Compilation and production of *Medicines Watch* was successfully transitioned to the MOHSS.

Figure 6 provides a detailed summary of SIAPS support as focused on PV from 2011 to 2016.

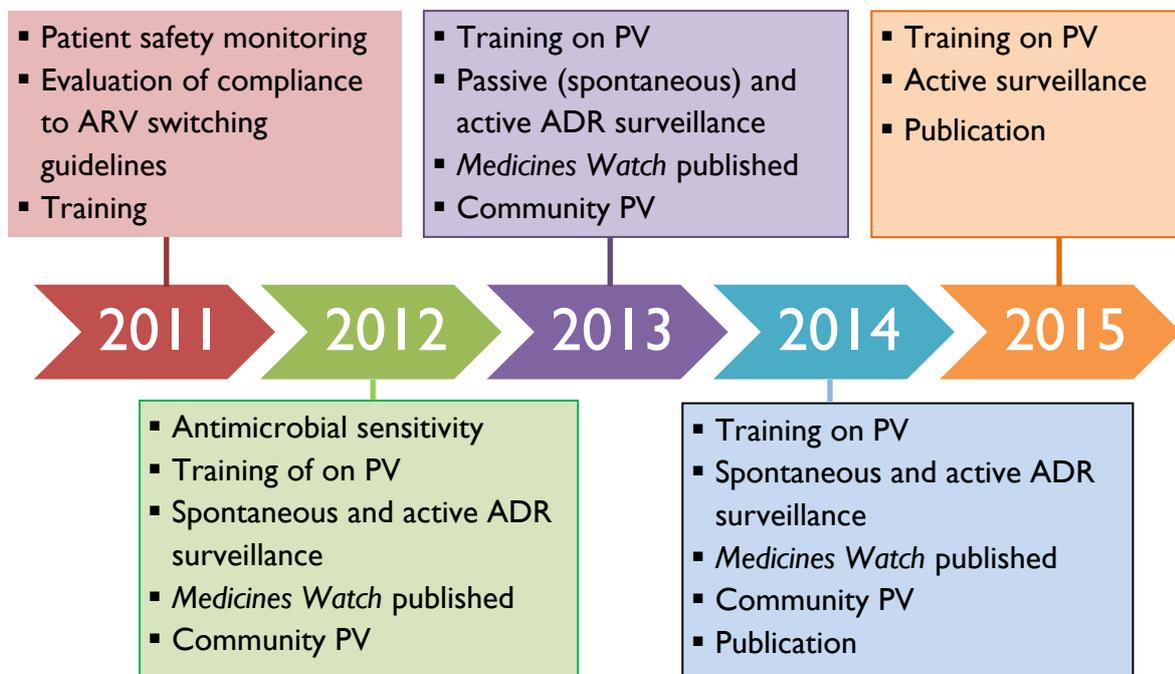


Figure 6. Key PV strengthening activities (Mazibuko 2016)

DISCUSSION

Despite the few staff at the NMRC during the period 2011–2017, SIAPS provided TA to all four units of the council, playing a significant role in the improvement of NMRC's regulatory functions. Trainings by SIAPS equipped NMRC technical staff, other pharmacy personnel from the MOHSS and the private sector with knowledge and skills in Good Distribution Practices (GDP), GMP, Good Review Practices (GRevP), and active and spontaneous PV for enhanced patient safety. By involving in the training non-NMRC staff such as MOHSS regional pharmacists; pharmacists from the UNAM-SoP and from the private sector, SIAPS increased the pool of technical experts locally available to perform key regulatory functions. This made it possible for NMRC to utilize the trained staff in dossier review and evaluation, which reduced the backlog of dossiers over the years, especially from 2014 onwards. As of December 2017, the NMRC did not have a backlog of dossiers beyond six months.

With SIAPS support, the efficiency of registration of ARV and other medicines increased by 49%. This is attributable to the intensified efforts by NMRC and to the interventions supported by SIAPS to expedite medicine registration (Mbazira 2016). However, the average processing efficiency of NMRC remains at 71.9%, indicating that further effort needs to be made in making medicines available in the country. Part of SIAPS' assistance included organizing intensive sessions for reviewing and processing medicine dossiers, which the NMRC has since then taken over. The NMRC intensified medicines dossier reviews to accelerate the process and shorten the time taken to evaluate application files and to register medicines. Three of the four (75%) dossier review sessions held in FY15 were organized and financed by the NMRC, which shows their commitment to sustain interventions supported by the USAID-funded SIAPS program. The takeover of the financing of this activity is commendable and ensures the sustainability of the regulatory strengthening interventions. Therefore, this is an example of how SIAPS worked with its client (NMRC) to sustain project (donor)-supported activities.

Continuous TA by SIAPS on the revision of the ART guidelines while simultaneously supporting the NMRC in expediting the registration of ARVs, using the fast-track registration, has contributed to the efficient and effective transition of patients to safer, more patient-friendly and convenient products, which encourage better patient adherence to treatment. Namibia introduced pre-exposure prophylaxis (PEP) to its ART services in 2014. SIAPS supported the registration process and the registration of a generic fixed dose medicine containing TDF/FTC (Ricovir EM[®]), which has enabled high-risk and vulnerable Namibians to access this highly effective method of preventing HIV transmission.

The limited skills capacity of the NMRC, in terms of both numbers and type of technical expertise of the staff has been a major constraint that prevented the NMRC from fully optimizing its operations. For sustainability, SIAPS advised the NMRC to transform itself into an autonomous organization. This effort has been accepted by MOHSS management and the new structure was endorsed by the government. In addition, the NMRC is in the process of implementing the web-based Pharmadex, which enables online submission of dossiers whereby applicants fill in the information online. This will lessen the burden of NMRC staff having to reenter applicants' information into the database, and contribute to efficiency of the review, communication, and approval of medicines for registration.

Routine post-marketing surveillance of the quality of medicines revealed the presence of counterfeit medicines on the Namibian market. WHO defines a counterfeit medicine as one that is deliberately and fraudulently mislabeled with respect to identity and/or source. Thus, counterfeit medicines include both branded and generic products and even products with correct/wrong/insufficient/no active ingredients, or fake packaging (WHO 2013). In the assessment of 151 samples tested in 2014, 13.9% (21) did not conform to pharmacopoeia specifications, 36.8% were unregistered, and 1.9% were substandard, based on the test results from the QSL and a WHO-prequalified laboratory in South Africa. These findings demonstrate that further work needs to be done by the NMRC to solve this problem. The presence of counterfeit medicines on the global market is a widespread public health concern with significant direct and indirect impact on human health and quality of life. It may result in the use of products lacking efficacy and thus impacting on treatment outcomes as well as the risk of developing microbial resistance to medicines. Thus, the Namibian Government and stakeholders should create awareness about this threat and develop strategies to promote inter-sectoral coordination between public and private stakeholders.

SIAPS provided TA to the TIPC to pilot an active surveillance PV system for first-line ARVs, which was conducted at two sentinel ART sites (Windhoek Central and Katutura Intermediate Hospitals). The incidence, severity and risk factors for adverse events in persons receiving first-line highly active ART at the two sentinel sites were determined. These data, together with the findings of the comparative cost-effectiveness analysis of active versus spontaneous PV, provided key inputs in informing the potential national expansion of an active surveillance PV program. The MOHSS/TIPC may review and implement recommendations.

In summary, SIAPS comprehensive TA to the NMRC, including developing SOPs and guidelines, mentoring, on-the-job training, and advocating for the transformation of the NMRC structure led to the desired outcomes. The NMRC proposal submitted to the OPM will ensure the council's autonomy both administratively and financially. In the proposed structure, the number of staff and the professional mix will enable the council to function more efficiently to solve current ongoing challenges.

The NMRC registered 1,538 medicines in the last seven years. This accounts for 65.9% of the total medicine dossiers received. WHO indicates that developed countries' time for providing marketing authorization of medicinal products is an average of 15–25 days. In developing countries, the period is shorter in terms of average approval times, even for new products, than in developed countries, which have the largest pharmaceutical market share (WHO 2004). The main reasons for this short period may be that most of the product registrations are based on Stringent Regulatory Authority (SRA) countries approval documentation. The main challenge of the slow pace of product evaluation and registration has been shortage of staff for carrying out NMRC's activities and insufficient budget to hire as well as frequent attrition of staff.

CONCLUSION AND RECOMMENDATIONS

SIAPS's continued support to strengthen NMRC not only improved the efficiency and reduced the backlog of applications for medicine registration but also motivated the MOHSS to put more resources into drug registration. The NMRC has taken over financing of intensified medicines dossier reviews to accelerate the process and shorten the time required to evaluate applications and register medicines, which demonstrates commitment and sustainability of the interventions.

Training provided on GDP, GMP, and GRevP built the capacity and increased the pool of locally available technical personnel. These included NMRC technical staff, MOHSS pharmacists, lecturers at the UNAM-SoP, and pharmacists from the private sector. They were trained in current medicine dossier review practices, including the globally accepted Common Technical Documents (CTD) format and other regulatory aspects of GMP and GDP to ensure patient safety for medicines approved for sale in Namibia.

The TIPC is operational and serves as the official MOHSS center for PV and therapeutics information, with a clear mandate to provide both proactive and query-response therapeutic information to health care workers as well as serving as a reference unit on PV by collecting and monitoring ADR reports spontaneously generated by facilities.

SIAPS assistance in strengthening spontaneous PV created awareness among health care workers and provided training to TB field promoters on community PV and ADR reporting. This enabled health facilities to continuously report PV and ADRs and overcome the tendency for reporting fatigue among practitioners in health care facilities.

According to analysis of ADR data from 2011 to 2013, most reactions reported were serious in nature. Continuous monitoring and targeted trainings efforts are essential to reduce medicine harm to patients.

Post-marketing surveillance of quality of medicines, implemented by the NMRC with support from SIAPS, contributed to improvements in routine monitoring, health worker vigilance in reporting products of suspicious quality to the NMRC, and the NMRC's commitment to recalling substandard products from the market. The findings from PMS activities illustrate the importance of strengthening Namibia's post-marketing quality surveillance of medicines. The NMRC has to strengthen post-registration medicine quality monitoring. Regulatory decisions and actions based on the outcomes may include the recall of products that do not conform to specifications. The measures taken so far are commendable, although the actions need to be expedited. Routine monitoring of medicines quality at all levels of the country's pharmaceutical supply chain is critical for protecting the public.

Reconfiguration of Pharmadex from a desktop to a web-based system enabled the staff to become more transparent. When fully functional, applicants will be able to process and monitor their application/s online, thereby reducing the time required to process the dossiers and make the process transparent. The NMRC should start using the final version of the system and enable the applicants to access the tool.

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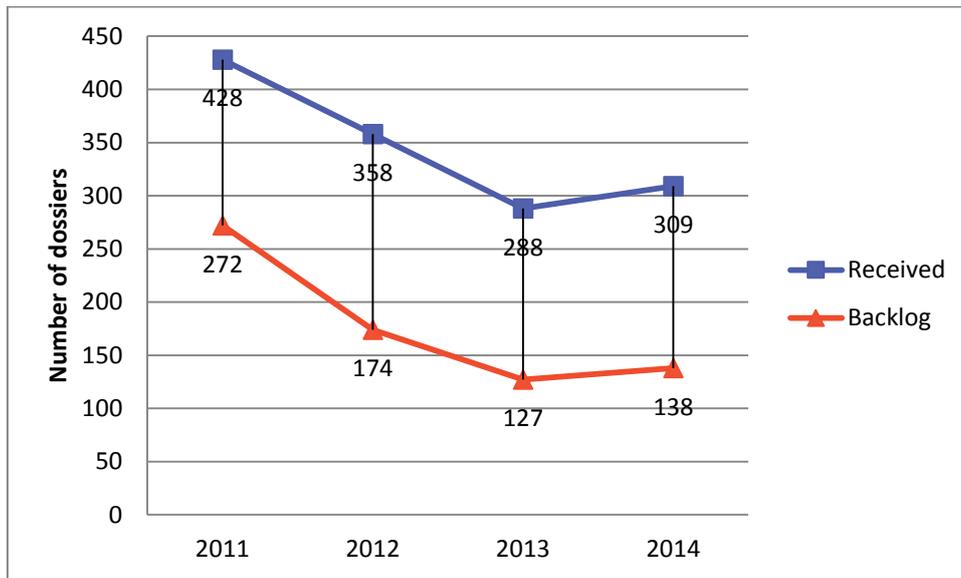
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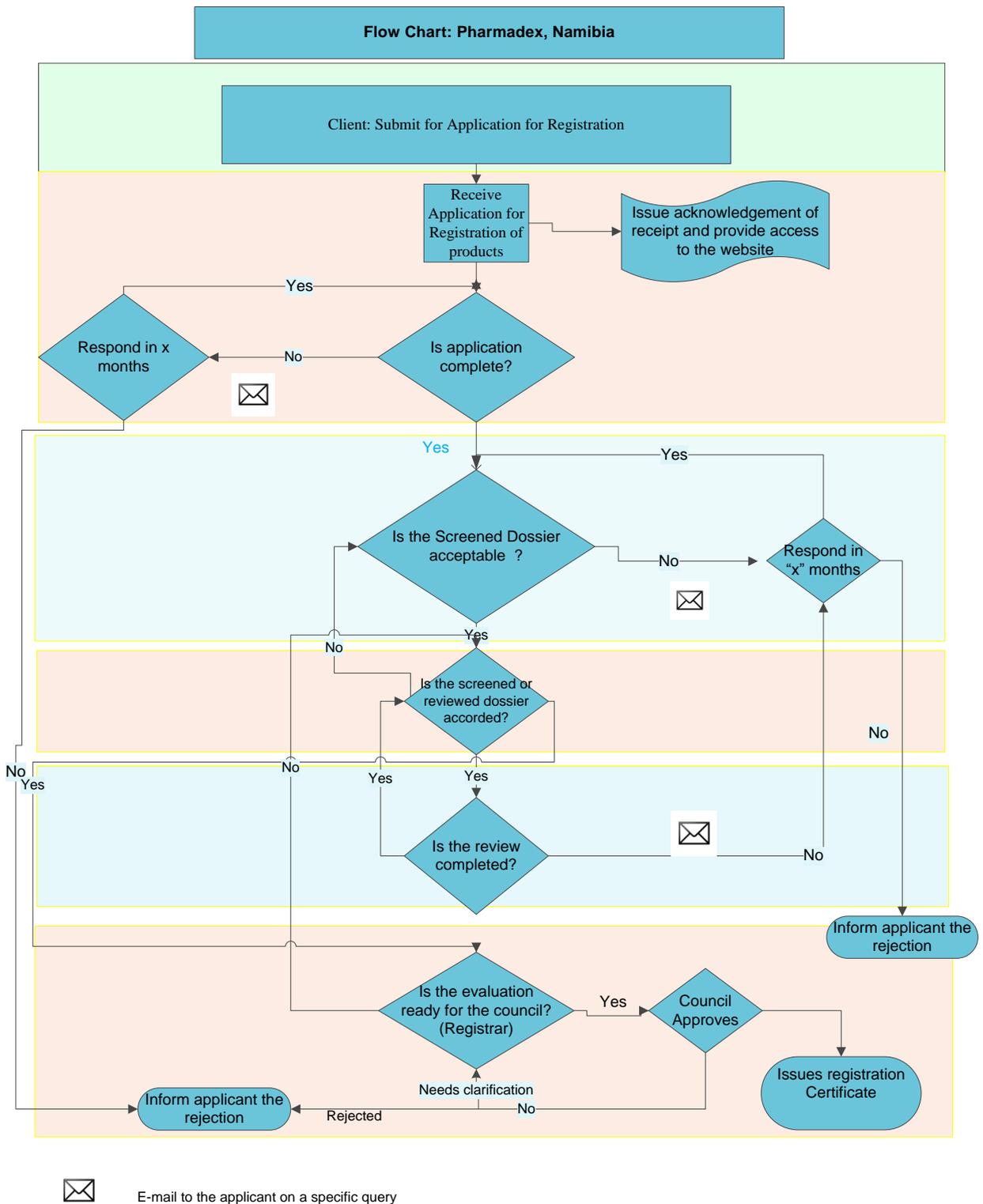
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ANNEX A. DOSSIERS RECEIVED AND BACKLOG, 2011–14



Source: Mbaziira 2015

ANNEX B. MEDICINE REGISTRATION PROCESS FLOWCHART FOR TRAINING OF STAFF



ANNEX C. LIST OF SOPS, CHECKLISTS, FORMS, AND GUIDELINES DEVELOPED OR UPDATED FOR THE NMRC

Inspection and licensing

- 1) Checklist for GMP audits
- 2) Checklist for Inspection of a Hospital Pharmacy
- 3) Checklist for Inspection of Community Pharmacy
- 4) Checklist for Inspection of Distribution and Wholesale Outlets
- 5) Checklist for Inspection of Private Clinics
- 6) Checklist Inspection of Dispensing Medical Practitioners' Premises
- 7) Guidelines on Training and Qualification of GMP Inspectors
- 8) Inspection of a Hospital Pharmacy SOP
- 9) Inspection of Community Pharmacy SOP
- 10) Inspection of Dispensing Medical Practitioners Premises SOP
- 11) Recall or Withdrawal of a Medical Product SOP
- 12) Scope of Inspections SOP
- 13) SOP Register I&L

TIPC

- 1) AMR Case Reporting
- 2) Editing TIPC Publications
- 3) EM_ 14 Jul _AMR Data Collection and Documentation
- 4) Responding to Queries
- 5) SOP Register TIPC

Registration

- 1) Dossier Screening Checklist
- 2) Guidelines for Importation of Unregistered Medicines
- 3) Guidelines for Section 27 Applications
- 4) Medicine Registration Application Form
- 5) Medicine registration Guidelines
- 6) Post Registration Amendment Guidelines
- 7) Registration Process Algorithm
- 8) SOP - Format of Registration - Application Numbers
- 9) SOP for Entering Dossiers into PharmDex Database
- 10) SOP for Numbering of Minutes of Council
- 11) SOP for Registration Dossier Receiving
- 12) SOP Register Registration
- 13) SOP-for-SOPs

QSL

- 1) Authorization and Processing of Deviation from SOPs
- 2) Calibration and Maintenance of Lab Equipment SOP
- 3) Complaints SOP
- 4) Confidentiality SOP

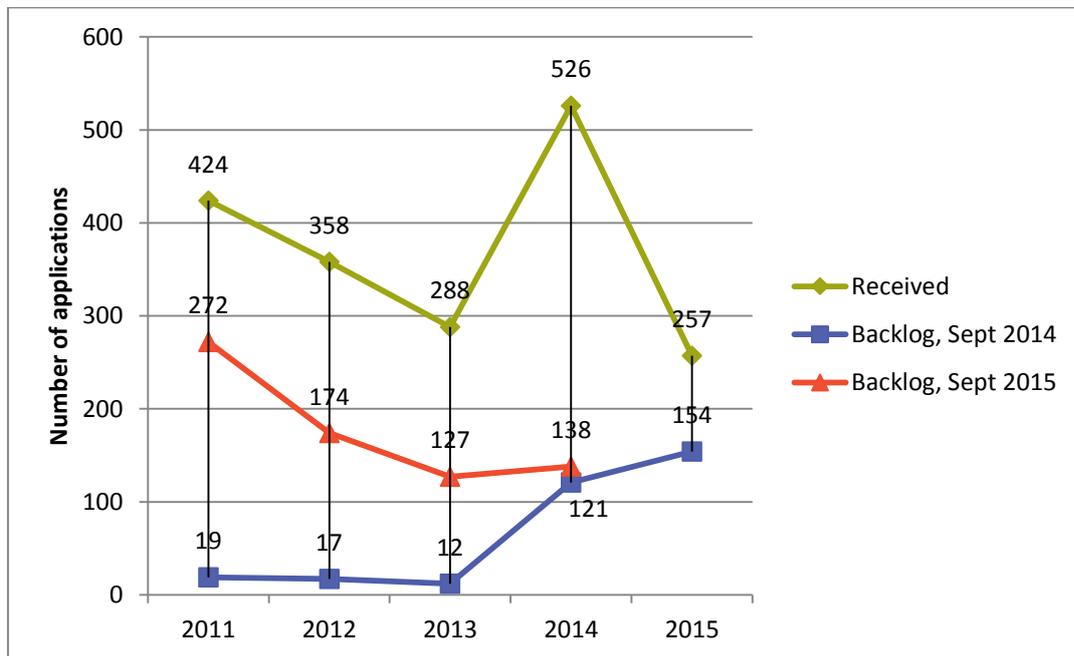
- 5) Control of Data SOP
- 6) Control of Non-conformances SOP
- 7) Control of Records SOP
- 8) Corrective and Preventive Actions SOP
- 9) Document Control SOP
- 10) Estimation of Uncertainty of Measurement SOP
- 11) Handling of Test Items
- 12) Health and Safety Guidelines
- 13) Health and Safety SOP
- 14) Internal Audits SOP
- 15) Maintenance of Integrity
- 16) Maintenance of Ref Standards and Materials SOP
- 17) Management Reviews SOP
- 18) Proficiency Testing SOP
- 19) Purchasing Services and Supplies
- 20) Reporting Results
- 21) Review of Requests Tenders and Contracts SOP
- 22) SOP for Sampling at CMS 2010 3
- 23) SOP Register QSL
- 24) Staff Development and Training
- 25) Validation of Nonstandard Analytical Methods SOP

ANNEX D. PARTICIPANTS WHO ATTENDED THE DOSSIER EVALUATION TRAINING WORKSHOP, MAY 12–16, 2014, AFRICA HOTEL, WINDHOEK



Last row left: Mr. Johannes Gaeseb (Registrar, NMRC) and participants; the lecturer, Mr. Michael Anisfeld, is in the second row center. Photo by MSH staff, Namibia.

ANNEX E. TRENDS IN MEDICINE REGISTRATION APPLICATION BACKLOG, 2011–15



Source: Mbaziira 2015

ANNEX F. PROPOSED AUTONOMOUS NMRC ORGANOGRAM

