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Research Article

Evaluation of the quality of the main antimicrobial drugs sold in pharmacies in Bamako (Mali) according to a risk-based sampling

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Abstract

Objectives: In a world marked by the increase in chemoresistance leading to the adoption of therapeutic combinations, the advent of generic multi-source drugs, the spread of counterfeiting and substandard drugs, often without active ingredients or falsified active ingredients, a greater vigilance by pharmaceutical regulatory authorities is needed. Drug quality control therefore plays an important role in detecting poor quality products on the market. Antimicrobial resistance (AMR) is a growing threat to public health. It occurs when vital antimicrobials can no longer effectively treat bacteria and other microbes. Worldwide, around 700,000 people die each year due to antimicrobial resistance and without global action it could lead to 10 million deaths a year by 2050. This study aimed to assess the quality of major antimicrobials sold in Bamako to determine the prevalence of falsified and substandard antimicrobials.

Methods: Samples were taken in some pharmacies in Bamako and analyzed according to the standards of the United State Pharmacopoeia (USP), British Pharmacopoeia (BP) and International Pharmacopoeia (IP) by identification and assay methods. Products that do not meet the required specifications described by these pharmacopoeias are declared non-compliant.

Results: A total of 151 samples were taken according to a protocol based on the risks, of which 145 were compliant and 6 non-compliant due to an under-dosage of active ingredient. We found 58% of unregistered drugs that came from India and China.

Conclusion: This study allowed us to detect 6 non-compliant products that were withdrawn from the market and regulatory measures were taken.

Keywords: Antimicrobial, quality control, non-compliance, AMR.

INTRODUCTION

In a world marked by several challenges including, among others, the increase in chemoresistance leading to the adoption of therapeutic combinations, the advent of multi-source generic drugs, the spread of counterfeiting and substandard drugs, often without active ingredients or falsified active ingredients, greater vigilance by pharmaceutical regulatory authorities is necessary[1].

Good quality drugs are essential for effective disease management. Substandard and falsified drugs can cause treatment failure and side effects, increase morbidity and mortality, and contribute to the development of drug resistance. Vulnerable populations and patients with co-morbidities are particularly at risk of being affected by receiving substandard or falsified drugs. Poor quality drugs also increase health care costs for patients and the health system as a whole, wasting resources that could otherwise be used for the benefit of public health[1].

Antimicrobial resistance (AMR) is a growing threat to public health. It occurs when antibiotics, antivirals, antifungals, and other life-saving antimicrobial drugs can no longer effectively treat bacteria and other microbes [2]. Some of these microorganisms can become resistant to multiple treatments and can evolve into what are commonly referred to as "superbugs" such as multidrug-resistant Staphylococcus aureus (MRSA) that do not respond to multiple antibiotics and lead to disease. prolonged, even death.

Worldwide, around 700,000 people die each year due to antimicrobial resistance and without global action it could lead to 10 million deaths a year by 2050 [3].

The causes of antimicrobial resistance include over-prescription and misuse of antibiotics, inadequate diagnostic tests to identify appropriate treatments, imperfect adherence to treatment regimens, widespread use of antibiotics in agricultural settings to promote the growth and proliferation of poor quality drugs [4]. The proliferation of substandard drugs as a significant factor in antimicrobial resistance is often overlooked, but very real. Poor quality drugs can contribute to antimicrobial resistance by being partially or totally ineffective in treating disease and infection, providing

sufficient exposure to surviving microbes to breed drug resistance [5].

With the aim of contributing to the fight against antimicrobial resistance, we undertook this study which consists of evaluating the quality of the main antimicrobial drugs sold in the district of Bamako to determine the prevalence of falsified and substandard antimicrobials on the basis of a risk analysis [6,7]

MATERIAL AND METHODS

Scope and Duration of the Survey: The survey covered some pharmacies in the district of Bamako identified by the MedRS tool over the period from September 2021 to February 2022.

Selection of drugs and geographical areas

The selection of drugs for this quality survey was based on the purpose of the survey and the potential public health impact using a series of risk factors. The Drug Risk Assessment Tool (MedRS) was developed by USP/PQM Plus [8].

The following risk factors were considered:

- Drug stability
- GMP compliance (from manufacturers, if known)
- Complexity of the distribution chain
- Degree of exposure of the population
- Patient vulnerability
- Complexity of dosage form
- Therapeutic risk
- Degree of harm due to poor quality
- Availability of the drug during the survey period

This tool allowed us to identify the following drugs as drugs of interest based on the risk analysis of drugs according to the guideline for the implementation of risk-based post-marketing quality surveillance in low- and middle-income countries (LMIC) [7]. These are:

Artemether+Lumefantrine Tablet, Quinine Sulfate Tablet, Amoxicillin 250 Syrup, Amoxicillin + Clavulanic Acid 500 Tablet, Amoxicillin + Clavulanic Acid 125 Syrup, Benzathine Benzylpenicillin (1.2; 2.4 M) Injection, Ceftriaxone 1g Injection, Azithromycin 500 Tablet, Erythromycin 500 Tablet, Erythromycin 250 Syrup, Cotrimoxazole 960 Tablet, Doxycycline 100 Tablet, Ciprofloxacin 500 Tablet, Metronidazole 500 Tablet, Albendazole 400 syrup, Nystatin 500,000 IU Tablet.

Sample size

The total number of samples to be taken was calculated using the MedRS tool. This tool calculates the number of samples with a 95% confidence interval. Thus, on the basis of these analyses, a total of 151 samples including 111 antibiotics, 34 antiparasitics and 6 antifungals were collected.

Sample analysis in the laboratory

As the samples are essentially made up of antimicrobials and in order to contribute to the fight against antimicrobial resistance, the dosage of active ingredients was preferred. The analysis of the samples was carried out according to the monographs of the current pharmacopoeias [9–12].

Any sample that failed a test was examined according to LNS Out of Specification (OOS) procedures. Once the result is confirmed, it is not necessary to continue analyzing the sample until the next test.

RESULTS

Situation of the samples taken

A total of 151 were collected from pharmacies in the district of Bamako. When randomized facilities were not accessible or samples could not be obtained, other facilities were visited following the protocol substitution criteria.

Manufacturers and products collected

We found that a large majority of products came from India (44.4%) followed by France (23.2%) and China (15.2%). These results showed that the samples analyzed came mainly from India with 57.4% followed by China 16%. These results confirm those of Dembélé et al who found 45% and 17% respectively for India and China [13].

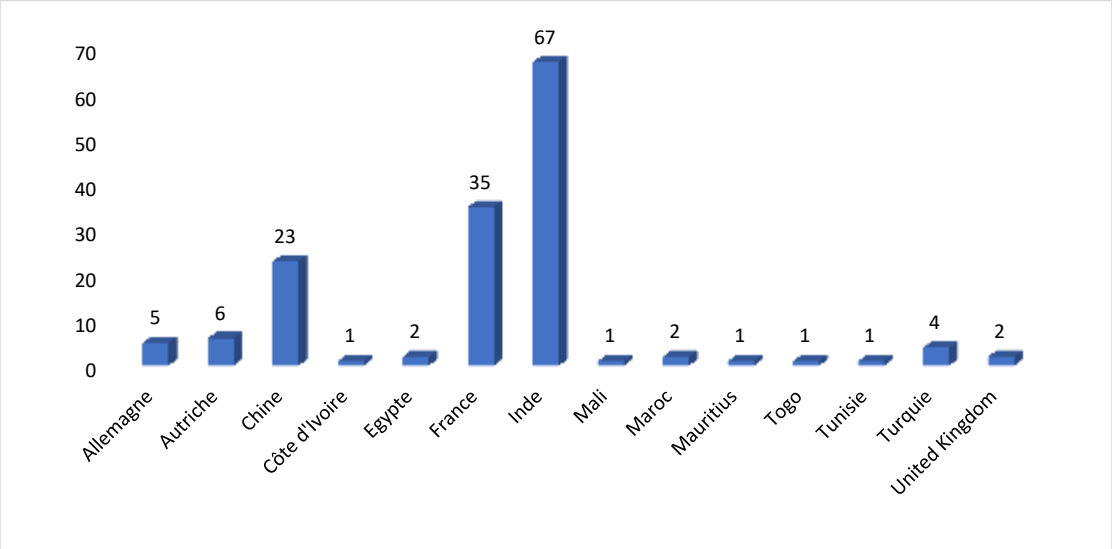

Figure 1: Situation products by origin.

Samples registration status

Only 42% of the drugs collected were registered, unlike PMS1 which were 31% [14].

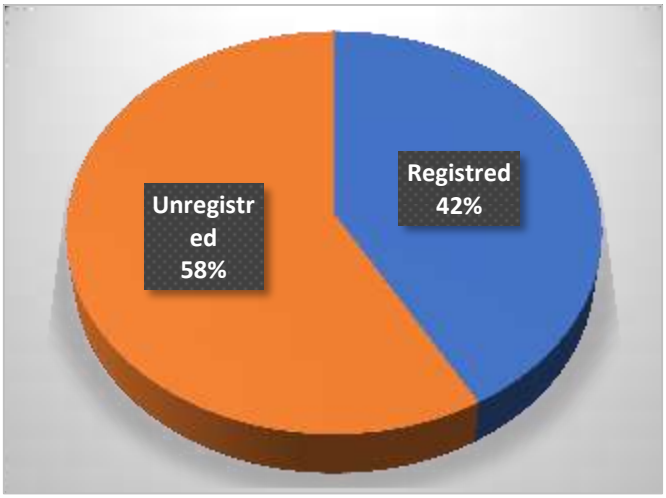

Figure 2: General registration status of the products.

We found that 73% of the samples from India and 70% from China were unregistered.

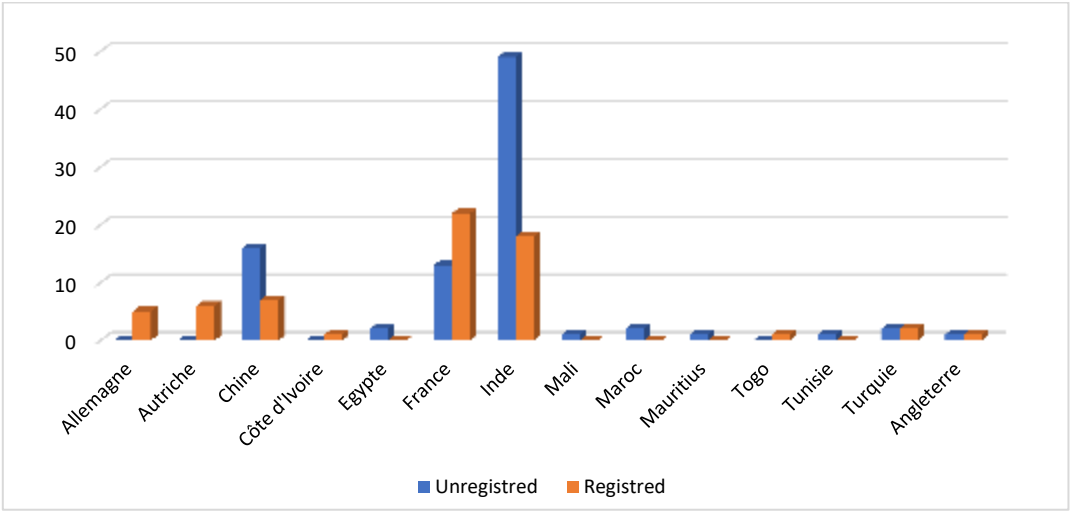

Figure 3: Situation of unregistered products by origin.

Products registration by pharmacological class

All antifungals were unregistered followed by antiparasitic and antibiotics with 76% and 49% respectively.

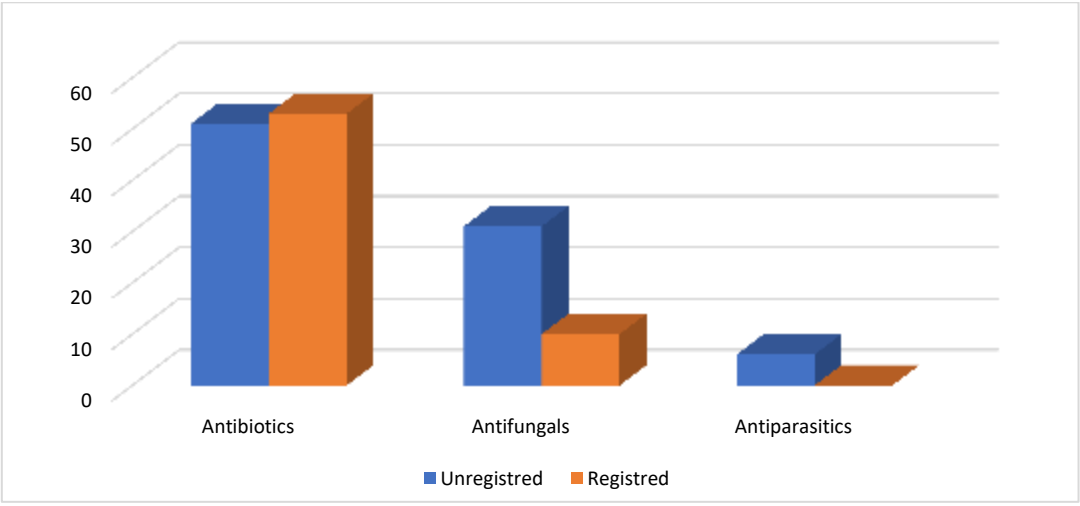

Figure 4: Products registration by pharmacological class

Products registration status by active ingredient

Among the antibiotics, all of the Cotrimoxazole samples were unregistered against 88% of the Benzathine Benzylpenicillin samples. On the other hand, all of the doxycycline samples were unregistred. Among the antiparasitics, all Quinine sulfate samples were unrecorded followed by Metronidazole 92% and Albendazole 78% samples. The antifungals consisted only of Nystatin which were all unregistered.

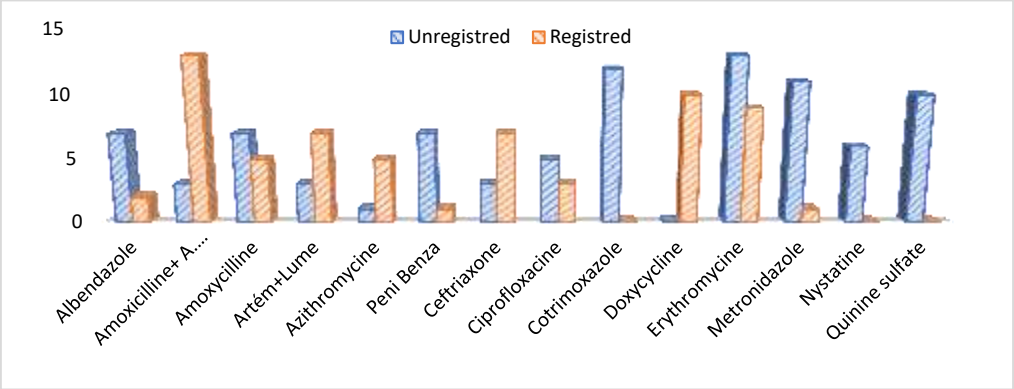

Figure 5: Product registration status by active ingredient.

Situation of products by molecules

Erythomycin was the most represented active ingredient with 11.2% followed by Amoxycillin + Clavulanic acid (10.6%).

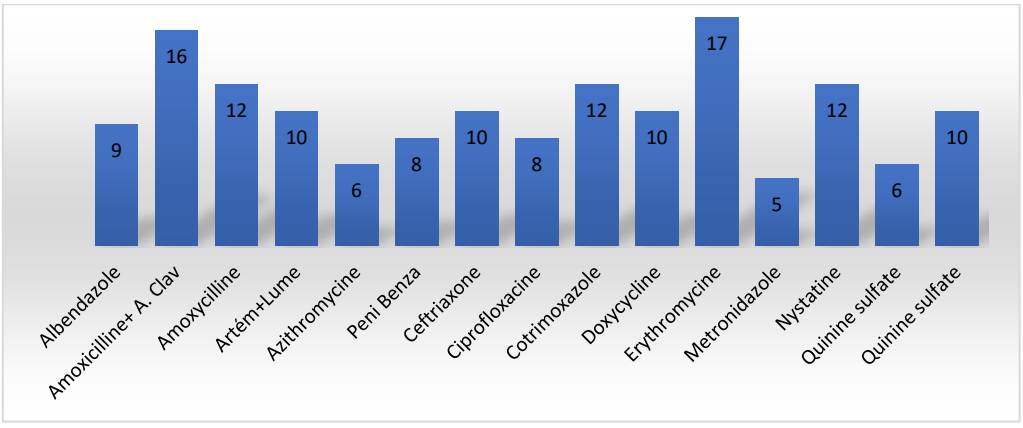

Figure 6: Situation of products by molecules.

Situation of products by pharmacological class

Antibiotics were the most represented pharmacological class with 69% followed by antiparasitics with 27%.

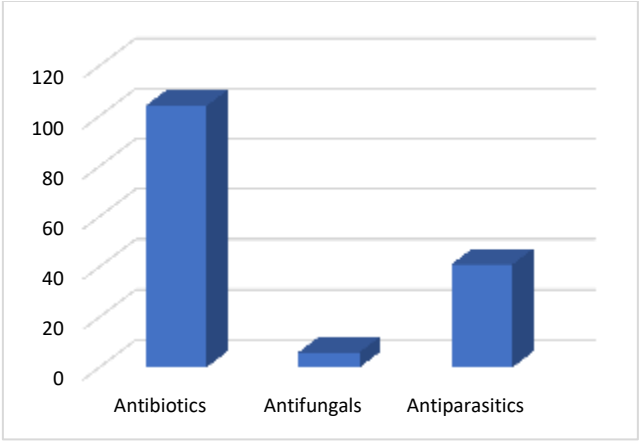

Figure 7: Situation of products by pharmacological class.

Situation of products by pharmaceutical form

Tablets were the most represented pharmaceutical form with 70% followed by suspensions with 17%.

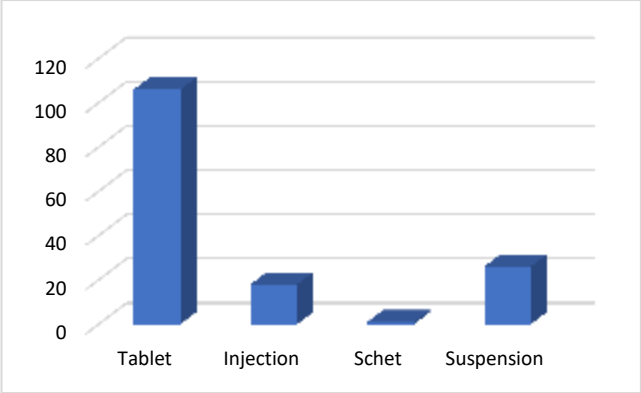

Figure 8: Situation of products by pharmaceutical form.

Compliance with Specifications

Global Results

Out of 151 samples tested, 145 were compliant, i.e. a rate of 96% and 6 non-compliant, corresponding to a rate of 4%. Which is identical to that obtained by Dembélé et al [13].

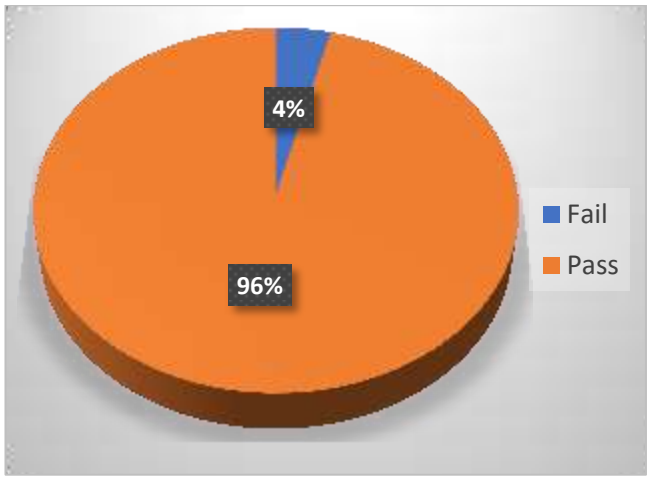

Figure 9: Global situation of products according to compliance

Results by Therapeutic indication

All the cases of non-compliance encountered consisted solely of antibiotics, including 3 samples of Erythromycin and 2 samples of Benzathine Benzylpenicillins. Among these non-compliant samples, none was registered in Mali.

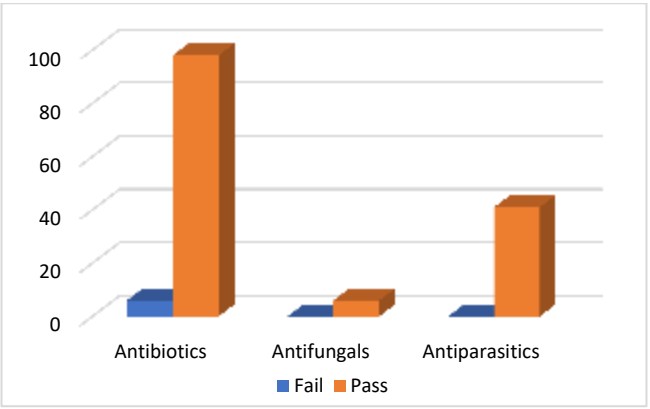

Figure 10: Results by Therapeutic indication.

DISCUSSION

Test methods and data quality

In accordance with the Guidance document for implementing risk-based post-marketing quality surveillance in low- and middle-income countries, we conducted sampling by using a risk-based approach. The total number of samples to be taken was calculated using the MedRS tool. This tool calculates the number of samples with a 95% confidence interval. Non-compliant samples were subject to OOS processing in accordance with our procedure which in its chapter 6.2.1 which describes out-of-specification results and. All data has been submitted for review and approval by the laboratory's quality control functions in accordance with our procedure for the control of technical records, which in its chapter 6.4 describes the provisions specific to the certificate analysis and controls required before final approval.

As the samples are essentially consisting of antimicrobials and in order to contribute to the fight against antimicrobial resistance, the dosage of active ingredients was preferred. The analysis of the samples was carried out according to the monographs of the current pharmacopoeias.

Results interprétation

In this study, a large majority of the products came from India (44.4%) followed by France (23.2%) and China (15.2%). These results confirm those of Sidibé et al who found 45% and 17% for India and China respectively [15], and those of Dembélé et al who found 45% and 17% respectively for India and China [13]. Also, all antifungals were unregistered followed by antiparasitic and antibiotics with 76% and 49% respectively. Among the antibiotics, all of the Cotrimoxazole samples were unregistered against 88% of the Benzathine Benzylpenicillin samples. On the other hand, all of the doxycycline samples were unregistred. Among the antiparasitics, all Quinine sulfate samples were unrecorded followed by Metronidazole 92% and Albendazole 78% samples. The antifungals consisted only of Nystatin which were all unregistered.

Out of 151 samples tested, 145 were compliant, i.e. a rate of 96% and 6 non-compliant, corresponding to a rate of 4%. Which is identical to that obtained by Dembélé et al [13]. All the cases of non-compliance encountered consisted solely of antibiotics, including 3 samples of Erythromycin and 2 samples of Benzathine Benzylpenicillins. Among these non-compliant samples, none was registered in Mali.

Results: A total of 151 samples were taken according to a protocol based on the risks, of which 145 were compliant and 6 non-compliant due to an under-dosage of active ingredient. We found 58% of unregistered drugs that came from India and China.

CONCLUSION:

This study allowed us to detect 6 non-compliant products that were withdrawn from the market and regulatory measures were taken to ensure health and guarantee access to quality medicines for health and the well-being of populations.

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Conflicts of Interest: None

References

1. WHO | WHO Global Surveillance and Monitoring System [Internet]. WHO. [cité 27 nov 2020]. Disponible sur:

http://www.who.int/medicines/regulation/ssffc/surveillance/en/

2. CDC. What Exactly is Antibiotic Resistance? [Internet]. Centers for Disease Control and Prevention. 2020 [cité 27 nov 2020]. Disponible sur: https://www.cdc.gov/drugresistance/about.html
3. 160518_Final paper_with cover.pdf [Internet]. [cité 27 nov 2020]. Disponible sur: https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf
4. Rousham EK, Unicomb L, Islam MA. Human, animal and environmental contributors to antibiotic resistance in low-resource settings: integrating behavioural, epidemiological and One Health approaches. Proc Biol Sci. 11 2018;285(1876). https://doi.org/10.1098/rspb.2018.0332
5. Antimicrobial resistance [Internet]. [cité 27 nov 2020]. Disponible sur: https://www.who.int/westernpacific/health-topics/antimicrobial-resistance
6. http://www.who.int/medicines/areas/quality_safety/quality_assurance/Local-manufacturing.pdf.
7. pqm-annual-report-2017-12-web.pdf.
8. MedRS | Log In [Internet]. [cité 29 déc 2021]. Disponible sur: https://medrsv2.com/
9. USP-NF USP [Internet]. [cité 7 juill 2021]. Disponible sur: https://online.uspnf.com/uspnf/section/monographs-usp
10. BP 2021 (Ph. Eur. 10.5 update) - British Pharmacopoeia [Internet]. [cité 7 juill 2021]. Disponible sur: https://www.pharmacopoeia.com/bp-2021?date=2021-07-01
11. The International Pharmacopoeia [Internet]. [cité 7 juill 2021]. Disponible sur: https://digicollections.net/phint/2020/index.html#d/b.6.2.2.3
12. GPHF | The GPHF-Minilab™ [Internet]. [cité 7 juill 2021]. Disponible sur: https://www.gphf.org/en/minilab/
13. Dembélé O, Coulibaly S, Dakouo J, Koumaré B. Pre- And Post-Marketing Control Of Drug Quality At The National Health Laboratory, Bamako-Mali. Universal Journal of Pharmaceutical Research. 15 janv 2022; https://doi.org/10.22270/ujpr.v6i6.696
14. Dembélé O, Coulibaly S, Cissé B, Cissé M, Dakouo J, Cissé N, et al. Risk-Based Post-Marketing Surveillance (RB-PMS) of antimalarial drugs and maternal, neonatal and reproductive health (MNCH) in Mali. Journal of Drug Delivery and Therapeutics. 7 mars 2022;12:6-10. https://doi.org/10.22270/jddt.v12i2.5223
15. A Sidibé O. Quality control of medicines antimalarials in seven (07) administratives regions of Mali and Bamako district: operationalization of minilab kits. Published online 2012. Accessed April 2, 2021.