Original Research Article

Pre- and post-marketing surveillance of drug quality at the National Health Laboratory, Bamako - Mali-2020

Abstract

Introduction: In a world marked by the spread of counterfeiting and substandard drugs, often without active ingredients or falsified active ingredients, greater vigilance by pharmaceutical regulatory authorities is necessary. The National Health Laboratory (LNS), in accordance with its mission, takes samples throughout the country in order to ensure their quality control.

Methods: Samples were taken in certain regions and the district of Bamako and analyzed according to the standards of the USP, BP and Ph. Int pharmacopoeias by identification and assay methods.

Results: This allowed us to analyze a total of 617 samples with 11 cases of non-compliance for a rate of 2%. The causes of the non-conformities were due to the absence of an active ingredient, an under-dosage of the active ingredient and technical and regulatory defects.

Conclusion: After one year of activity, our results showed that out of a total of 617 drug samples collected and analyzed, 606 were compliant with a rate of 98% against 11 cases of non-compliance or 2%. The causes of the non-compliance were due to the absence of an active ingredient, an under-dosage of the active ingredient and technical and regulatory defects.

Keywords: non-compliance, quality control, post-marketing, pre-marketing.

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].

Medicines regulation is a complex process that includes various regulatory instruments, such as authorization / registration for marketing following assessment of product documentation, inspection to verify manufacturers' compliance with the principles of good manufacturing practices (GMP) and approval of product information. It may also include Post-Marketing Surveillance (PMS) activities, such as maintaining product authorization and / or registration through variations or renewals, regular inspections of manufacturers, wholesalers and retailers, quality control tests, the use and disposal of drugs, pharmacovigilance and the implementation of regulatory measures in case a quality problem is found. When a product is made available to the public, it is not possible to predict every conceivable side effect or adverse event that could occur in large and diverse populations, and it may not be realistic for them. manufacturers to anticipate any manufacturing problems that might arise during large-scale operation[1; 2].

The quality of drugs can easily deteriorate through improper handling during distribution or storage before they reach patients. Quality control / quality assurance (QC / QA) of drugs in the distribution system to appropriate specifications is therefore an important prerequisite to ensure optimal results. It is therefore essential to carry out regular monitoring of the quality of

medicinal products through sampling missions and pre-marketing controls to guarantee their quality[3].
Post-market surveillance of drugs therefore plays an important role in uncovering the actual state of products in terms of safety, quality and efficacy that could pose a risk to users. It allows regulatory authorities to take appropriate measures for the withdrawal of falsified and substandard medicines from the market[4].
The National Health Laboratory(LNS) in accordance with its mission and as part of the pre- and post-marketing quality control of drugs, periodic samples are taken throughout the territory by LNS agents with the aim of to ensure the monitoring of drugs by their quality control at the laboratory with a view to safeguarding the health of populations.

MATERIALS AND METHODS:

Our material consisted of all the drugs analyzed from January 2020 to December 2020 at the LNS. Our data was collected using analytical certificates of drugs subject to quality control. The following information was collected: origin, place of collection, galenic form, therapeutic class, analytical methods, analytical equipment, analytical results.
Various analytical methods and tests are important for the development and manufacture of pharmaceutical formulations but also for their quality control. The evaluation was carried out according to the standards of the American Pharmacopoeia (USP), the British Pharmacopoeia (BP) and the International Pharmacopoeia by test methods (Friability, Disaggregation, Dissolution, pH, Average Volume, Coefficient of Variation of Weight, Loss on Desiccation), identifications (Thin Layer Chromatography, Minilab®, FTIR, RAMAN and assays (High Performance Liquid Chromatography, UV-Visible Spectrophotometry, Titrimetry) [5–8].

RESULTS AND DISCUSSION:

Out of a total of 617 drug samples taken and analyzed, 606 were compliant, a rate of 98% against 11 cases of non-compliance or 2%.

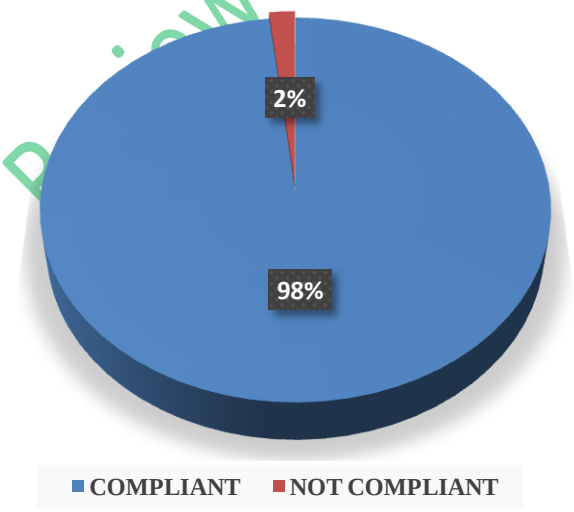

Figure 1: Global situation of samples according to their quality.

Galenic forms

In our study, the most represented dosage form was the compressed form with 41.3% followed by the injectable form 36.1%. We found that the syrup form represented the greatest number of non-compliance, i.e. 54.54% of the total number of non-compliant products, followed by the syrup / suspension form with 36.36%.

Table I: Distribution of molecules according to the galenic form.

N°	Galenicforms	Effectifs	Percentage
1	Eye drops	1	0,2
2	Tablets	255	41,3
3	Capsules	24	3,9
4	Injection	223	36,1
5	Ointment / Cream / Lotion	7	1,1
6	Syrup / Suspension	52	8,4
7	Solution	55	8,9
Total		**617**	**100,0**

Pharmacological classes

We found that the predominant pharmacological class was antimalarials 24%, followed by antibiotics 19.4%. We also found that antimalarials contained the highest number of non-conformances, ie 45.45% of the total number of non-conforming products.

Table II: Distribution of molecules according to pharmacological class

N°	Pharmacological class	Effectifs	Percentage
1	Corticosteroids	5	0,8
2	Anesthesia	16	2,6
3	Analgesic / NSAID	51	8,3
4	Antihemorrhoid	1	0,2
5	Antihistamine	3	0,5
6	Antihypertensive	5	0,8
7	Antimicrobial	120	19,4
8	Antimalarial	148	24,0
9	Antiseptic	54	8,8
10	Anti-tuberculosis	7	1,1
11	Cough suppressant	7	1,1
12	Antiulcer	5	0,8
13	antiretrovirals(ARV)	77	12,5
14	Benzodiazepine	1	0,2
15	Others[1]	117	19,0
Total		617	**100,0**

Quality and manufacturer's country

Our results showed that the samples analyzed came mainly from India with 57.4% followed by China 16%. We also found that 13.1% of our samples were of unknown origin, these were mainly products of the Central Purchasing of Medicines (PPM).

Table III: Distribution of samples according to the country of origin.

N°	Country	Effectifs	Pourcentage
1	Germany	1	0,2

2	Austria	1	0,2
3	China	99	16
4	France	1	0,2
5	Ghana	24	3,9
6	India	354	57,4
7	Italy	1	0,2
8	Unknown	81	13,1
9	Nigeria	1	0,2
10	Mali	42	6,8
11	Swiss	9	1,5
12	UniUnited Kingdom	3	0,5
Total		617	**100,0**

Distribution / sampling circuit

In order to control the quality of our drugs by touching the entire distribution chain, samples were taken at all levels of the distribution circuit. This is how the samples were taken in large part from the Pharmacy Popular of Mali (PPM) 67.1% which is the local purchasing center, followed by samples taken during LNS post-marketing surveillance missions with 11.3%.

Tableau IV: Distribution of samples according to customer

N°	Customer	Effectifs	Percentage
1	CAMEG BURKINA	14	2,3
2	Direction de la Pharmacie et du Médicament (DPM)	3	0,5
3	Hôpital du Mali	4	0,6
4	Islamic Relief	21	3,4
5	LNS missions	70	11,3
6	Pharma Etoile Sarl	3	0,5
7	Pharmacie Populaire du Mali (PPM)	414	67,1
8	SE/HCNLS	67	10,9
9	SVPP	9	1,5
10	UFCP	2	0,3
11	UNIMED SARL	3	0,5
12	USAID/GHSC-PSM	7	1,1
Total		617	**100,0**

Assay methods

In our study among the assay methods, the HPLC technique was the most used, followed by UV-Visible spectroscopy and titrimetry with 38%, 36% and 26% respectively.

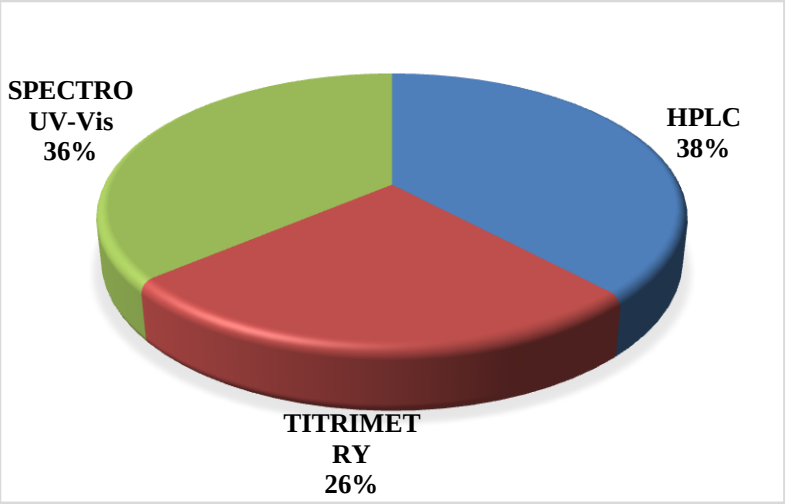

Figure 1: Distribution of assay methods.

Test and identification methods

In our study of the test methods, the uniformity of dosage units (UDU), pH and volume were the most used test methods.The colored test was the most widely used identification technique followed by TLC and FTIR.

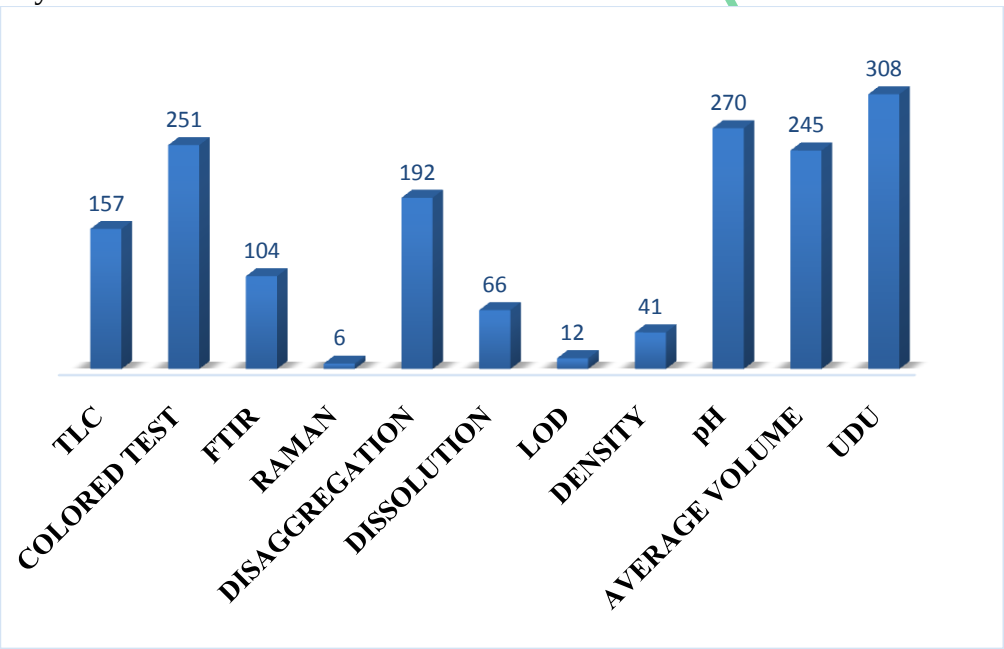

Figure 1: Distribution of testing and identification methods.

CONCLUSION:

The proliferation of sources of supply and illicit sale of drugs as well as the inadequate conditions of their storage and the non-observance of good manufacturing practices can cause, with acuteness, problems at the level of the quality of the drugs available on the market. The LNS National Health Laboratory, in accordance with its mission and as part of the pre- and post-marketing quality control of drugs, takes periodic samples throughout the country for their quality control at the Laboratory. After one year of activity, our results showed that out of a total of 617 drug samples collected and analyzed, 606 were compliant, a rate of 98% against 11 cases of non-compliance or 2%. The causes of the non-conformities were due to the absence of an active ingredient, an under-dosage of the active ingredient and technical-regulatory defects and mainly affected antimalarials 24%, followed by antibiotics 19.4%. The results of these analyzes were transmitted to the socio-health authorities who proceeded with the withdrawals of these poor quality drugs thus safeguarding the health of the populations

and advice was given in order to maintain the quality of the drugs at the points of sale and storage.

CONFLICT OF INTEREST:

No conflict of interest associated with this work.

ACKNOWLEDGMENTS:

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