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The value of screening technologies in limiting falsified and substandard medicines: Lessons from Nigeria

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Background

All products that enter the legal market should be approved by the World Health Organization prequalification program, or be approved by a stringent regulatory authority and be manufactured at a Good Manufacturing Practices (GMP) certified site; however, in reality this is not always the case. Falsified and substandard medicines are becoming increasingly common, especially in emerging markets. A recent comprehensive study revealed that over a third of antimalarial medicines across Africa and Southeast Asia were unfit for use.[1] They had either been intentionally falsified or were substandard due to poor manufacturing.

Historically, Nigeria has had a significant problem with such products. In one study in 2001, 48% of the medicines sampled failed basic quality control testing.[2] From the formation of Nigeria's National Agency for Food and Drug Administration and Control (NAFDAC) in 1993, regulation of the medicine supply chain has been enhanced, coordination with other agencies such as customs and the department of health have increased, and medicine quality has slowly improved. NAFDAC carries out unscheduled inspections of local manufacturers every three months, and routinely inspects shipments from abroad. NAFDAC recently seized over N200 million ($1.2 million) of fake medicines, mainly antibiotics and oral contraceptives, as well as food and cosmetics, from China.[3]

NAFDAC has succeeded in reducing the amount of fake drugs on the market and frequently shuts down retail operations when sellers are unable to provide an invoice for their drugs or proof of a legal transaction.[4] The agency is also reviewing its laws with respect to convicted dealers of fake medicines to impose harsher penalties.

NAFDAC reports that 16% of products sampled in 2006 failed quality control, and a recent study by one of the authors of this paper found that about 12% of antimalarial

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products sampled from Lagos, Nigeria's most populous city, failed basic quality control.[5]

Assessing Field Technologies Project

Many of the policies implemented by NAFDAC and described above have been tried elsewhere, often with similarly successful results. NAFDAC has gone further though by implementing technologies to test for fake medicines in the field. In 2010, NAFDAC deployed the TruScan, a handheld Raman spectrometer made by US company ThermoFisher, to assist in screening medicines for quality. Today customs agents and NAFDAC personnel can test products on site enabling them to intercept fake products before they infiltrate the market. Counterfeiters have been arrested in Nigeria and as far afield as China. In September of this year, a US State Senator passed a resolution commending NAFDAC for its use of "cutting-edge technologies to fight drug counterfeiting".[6]

This paper assesses the value of TruScan technology by comparing a unique sample set of collected medicines screened with the TruScan against more established laboratory testing for content assay and dissolution. Since the TruScan has yet to be used to screen thousands of medicines in an emerging market, this type of comparison is essential to the widespread deployment of these types of technologies. Laboratory testing is not infallible, and no screening technique is perfect, but if the TruScan erroneously identifies too many fake products as genuine, this would essentially defeat the purpose of drug regulatory agencies using these technologies, likewise erroneously identifying too many genuine products as fake would waste valuable resources on expensive laboratory testing to confirm the results.

NAFDAC recently collected 6,419 samples of essential medicines, including antimalarials, antibiotics and analgesics from pharmacies across the country in order to assess their current quality. These products have all been screened with the TruScan and are currently being tested in the laboratory.

Thus far 2205 samples have been assessed in the laboratory and 14.5% (321 out of 2205) failed comprehensive quality control tests. These results indicate that while the number of poor quality products is far lower than it was a decade ago, substandard and fake medicines still persist, representing a danger to patients. A more comprehensive picture will be available in the future once testing is complete.

Comparative Results

Table 1 shows the comparison between the TruScan and laboratory results thus far. In roughly 90% of cases the TruScan and the laboratory results concur, indicating that the TruScan could be an effective screening device.

Table 1. TruScan and Laboratory Testing Results

	Passed Both		Failed Both		Passed TruScan® but failed Laboratory testing		Failed TruScan® but passed Laboratory testing		Total
Medicines	**Number**	**%**	**Number**	**%**	**Number**	**%**	**Number**	**%**	**Number**
Antibiotics	539	77.4	101	14.5	12	1.7	44	6.3	696
Antidiabetics	60	74.1	4	4.9	0	0.0	17	21	81
Antimalarials	712	69.9	174	17.1	22	2.2	111	10.9	1019
Analgesics and other products	372	91.0	5	1.2	3	0.7	29	7.1	409
Total	**1,683**	**76.3**	**284**	**12.9**	**37**	**1.7**	**201**	**9.1**	**2,205**

There are very few products (37 or 1.7% of the 2205 samples tested) that pass the TruScan but fail laboratory testing (resulting in a false positive rate of 11.5%). There are more samples (201 or 9.1% of the total sample) that fail the TruScan but are, in fact, good quality products according to laboratory testing (resulting in a similar false negative rate of 10.6%). From a public health perspective, this is a healthy result as few undesirable products are assumed to be of high quality.

Discussion

The TruScan is not the only method to identify dangerous products; analysis of packaging and pills can also identify poor quality products. The number of false negatives in this study was higher than ideal, which would increase the number of products analyzed in the laboratory and hence, costs.

However, the false positives and false negatives were not randomly distributed among the sample set. One product exhibited the most false positives - the antimalarial sulfadoxine pyrimethamine, which is known to have significant fluorescence making it more likely to pass TruScan testing when it is in fact poor quality. The products with the most false negatives were the artemisinin-based antimalarials because these exhibit the weakest Raman signal. Armed with this prior knowledge, either other screening techniques can be used on these products or TruScan testing of such products should be assessed by a qualified individual, preferably a spectroscopist.

Conclusion

Efforts to improve the drug supply in Nigeria by NAFDAC over the past decade have shown considerable success. The deployment of various screening devices, most notably the TruScan, have assisted in

this effort. While there is still a long way to go to ensure that every Nigerian always receives a quality medicine, Nigeria's experiences may assist other nations in combating the menace of falsified and substandard medicines.

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