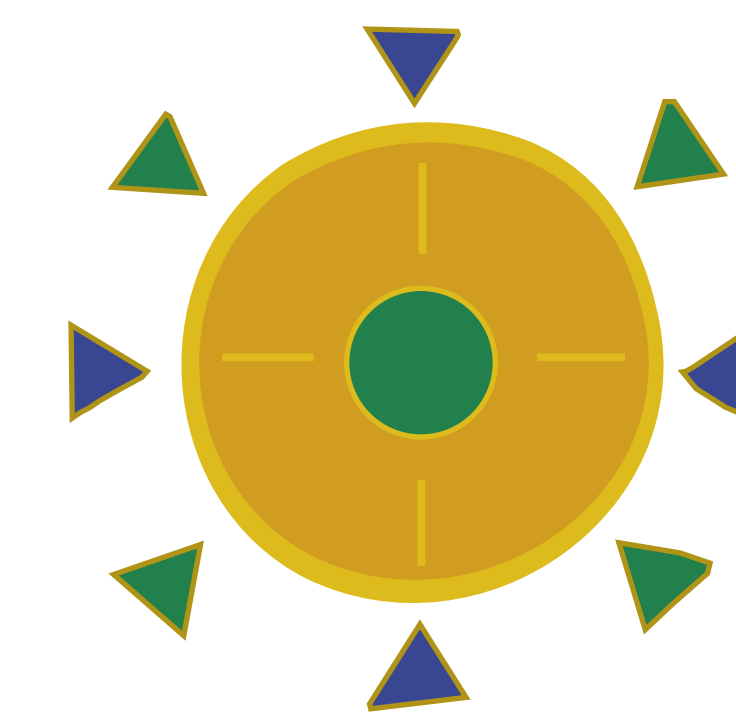


SEAM Tanzania



Quality Assurance: Proficiency Testing as a Tool to Assess the Performance of Visual TLC Quantitation Estimates

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Background

Thin-layer chromatography (TLC) has been used extensively for many years as a separation tool for an array of analytical applications. For example, TLC visual-detection test procedures to assess pharmaceutical product quality have been included in a convenient kit concept developed by the German Pharma Health Fund (GPHF) called the Minilab.

The Tanzania Food and Drugs Authority (TFDA) has established a drug product screening program using the Minilab testing technology. All inspectors participating in this program are pharmaceutical technicians or pharmacists who have had some prior laboratory training in volumetric laboratory procedures. Before they conduct the screening procedures in the field, the inspectors complete a one-week training program in properly performing the techniques incorporated in the Minilab. After completing the training program, inspectors were assigned the tasks of performing product screening tests for imported products at various ports-of-entry (POE) and performing postmarketing surveillance for selected products in their geographic areas. As a part of the TFDA Quality Assurance Program, a proficiency test procedure was established to provide assurance that the Minilab screening tests were being competently performed.

Proficiency Test Round 1

The proficiency test was conducted by providing each of the inspectors with powdered samples containing 100%, 40%, and 0% of the amount contained in a Minilab reference tablet. The samples were randomized so that the inspectors could identify the drug but not the amount of drug contained in the labeled sample packets. The inspectors assessed the quality of the samples using the Minilab screening procedures for that particular drug and were required to record whether the sample passed (if the spot size and/or intensity were similar to or higher than that of the 80% standard solution) or failed (if the size and intensity were lower). Table 1 summarizes the observations reported by the various inspectors.

The unexpected failure of most inspectors to identify significantly substandard products put in question whether the training programs and/or test protocols were adequate to develop sufficient capacity for the inspectors to discern the differences among products. To help improve this capacity, a performance qualification (PQ) test procedure was instituted.

Metronidazole, a drug in the Minilab inventory, was selected for the PQ test procedure. From Minilab standard tablets, each inspector prepared working standard solutions of metronidazole having concentrations of 4, 3, 2, 1.10, 1, and 0.80 mg/ml. The different working standard solutions were separately spotted on TLC plates, developed, and visualized at 256 nm. The inspectors were asked to write a brief report to indicate whether they could discern differences in spot size and intensity between the amounts of darkening for the solution concentrations of 5, 4, and 3 mg/ml, the solution concentrations of 3, 2, and 1.1, and the concentrations of 1.1, 1, and 0.8 mg/ml. All inspectors reported that they were able to discern in all cases the differences in spot sizes, which corresponded to 125%, 100%, 75% (5, 4, 3 mg/ml); 150%, 100%, 60% (3, 2, 1.1 mg/ml); and 110%, 100%, 80% (1.1, 1, 0.8 mg/ml).

Table 1: Results of proficiency test round 1

Inspector	Drug	0%	40% ¹	100%
1	Amoxicillin	+	=	+
	Artesunate	+	=	+
	Metronidazole	+	=	+
2	Sulfadoxine-pyrimethamine	+	=	+
	Amoxicillin	+	=	+
	Artesunate	+	=	+
3	Metronidazole	+	=	+
	Sulfadoxine-pyrimethamine	+	=	+
	Amoxicillin	+	=	+
4	Artesunate	+	=	+
	Metronidazole	+	=	+
	Quinine sulfate**	+	+	+
5	Amoxicillin	+	=	+
	Artesunate	+	=	+
	Metronidazole	+	=	+
6	Sulfadoxine-pyrimethamine	+	=	+
	Amoxicillin	+	=	= ²
	Artesunate	+	=	= ²
7	Metronidazole	+	+	+
	Sulfadoxine-pyrimethamine	+	=	+
	Amoxicillin	+	=	+
8	Artesunate	+	=	+
	Metronidazole	+	=	+
	Sulfadoxine-pyrimethamine	+	=	+

** Quinine sulfate was substituted for sulfadoxine-pyrimethamine, as the inspector is allergic to SP.
¹ The (=) notation indicates that the observer reported that the 40% sample spot was the same intensity as the 100% reference spot. This would allow a substandard product to pass the test.
² The observer reported that the 100% sample spot was substandard when compared to the 100% reference spot. This would result in an acceptable sample being submitted to the laboratory for testing by the legal standard methods.

Proficiency Test Round 2

Following the successful PQ exercise, a second proficiency test was submitted to the same nine inspectors who had completed the PQ and performed daily screening of samples. Three blinded samples containing 0%, 50%, and 100% of the reference drug level of each of three candidate drugs were given to each inspector. The results of round 2 proficiency testing are summarized in Table 2.

Discussion

The round 2 proficiency test procedure demonstrated, as did the round 1 tests, that all inspectors were able to discern the 0% content samples, corresponding to the wrong drug or non-drug in the sample. In round 2, all inspectors correctly identified the 100% content samples. Despite this extensive effort, two of the inspectors failed to correctly identify any of the three substandard samples and two other inspectors failed to identify the quinine substandard samples. The two inspectors who failed to correctly identify any of the three substandard samples in round 2 similarly failed to identify any correctly in round 1. Those inspectors may not have acquired sufficient technique and/or did not have sufficient visual acuity to correctly perform these assessments and should be excluded from the program until the necessary competencies have been achieved.

The above-cited performance deficiencies could call into question the desirability of widely deploying TLC technology as a deterrent to the distribution of substandard products in the marketplace; all inspectors correctly identified in all instances the 0% content samples, corresponding to non-drug or wrong drug in the sample. However, inappropriately identifying substandard products as being satisfactory could create an ill-founded confidence in the quality of products in the marketplace, which could pose a public health hazard. A balance will need to be struck between wide deployment of the TLC technology and assuring that competent assessments are made. Individuals who cannot successfully complete the proficiency testing protocol should be excluded from performing these assessments.

Conclusion

The Minilab technology and packaging provides an inexpensive, low-technology, nonlaboratory-based testing option to assess product identity, disintegration, and drug content, which is of value in resource-limited settings. When in the hands of competent persons, it provides an opportunity to identify substandard, fake, or wrong drugs inexpensively and quickly. Our work here has shown that to use the Minilab successfully, however, it is important to include proficiency testing in the implementation plan to provide an added measure of confidence in these screening tests and identify additional training needs or other interventions.

Table 2. Proficiency Test Round 2

Inspector	Drug	0%	50%*	100%
1	Co-trimoxazole	+	+	+
	Metronidazole	+	+	+
2	Quinine sulfate	+	+	+
	Co-trimoxazole	+	+	+
3	Metronidazole	+	+	+
	Quinine sulfate	+	+	+
4	Co-trimoxazole	+	+	+
	Metronidazole	+	+	+
5	Quinine sulfate	+	+	+
	Co-trimoxazole	+	+	+
6	Metronidazole	+	+	+
	Quinine sulfate	+	=	+
7	Co-trimoxazole	+	=	+
	Metronidazole	+	=	+
8	Quinine sulfate	+	=	+
	Co-trimoxazole	+	=	+
9	Metronidazole	+	+	+
	Quinine sulfate	+	+	+

* The (=) notation indicates that the observer reported the 50% sample spot as being the same as the reference spot (100%). This failure would allow a substandard product to pass the test.