Guidelines for Sampling of Antimalarial Drug Samples

In the USP DQI Antimalarial Drug Quality Monitoring Project in

Mekong Sub-region Countries

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1. General Considerations

Currently the project aims to carry out a monitoring activity for the quality of antimalarial medicines circulating and used in the Malaria Program in the selected sentinel site areas. Drug quality data obtained from this project will be reported to responsible authorities in each country for use in developing appropriate policies or strategies to improve the situation. Data will be also analyzed, classified, and disseminated, as appropriate, among participating countries in the Mekong Sub-region.

Sampling encompasses the operations designed to collect samples of different dosage forms of antimalarial drugs, namely: Chloroquine phosphate; quinine sulfate or quinine hydrochloride; sulfadoxine + pyrimethamine fixed-dose combination (FDC); mefloquine hydrochloride; tetracycline; artesunate and other artemisinin derivatives, including dihydroartemisinin, artemether, and arteether as used in different countries in this region.

1.1. Purpose of sampling

The purpose of sampling in this USP DQI Antimalarial Drug Quality Monitoring Project in Mekong Sub-region Countries (in collaboration with WHO) is to determine the quality antimalarial medicines collected in selected malaria sentinel sites participating in the project by testing for appropriate labeling, identity of active pharmaceutical ingredient(s) (API(s)), disintegration, and content of API(s). In certain instances, uniformity of dosage units by weight variation and dissolution tests may be required.

1.2. Sample definition and types

In this project, one sample of an oral dosage form (tablets or capsules) is at minimum 30 dosage units for single drug preparation (e.g., artesunate tablet) and minimum 50 units for fixed-dosed combination preparation (e.g., sulphadoxine + pyrimethamine tablet) from the same lot number and collected at the same location/outlet; one sample for an injectable dosage form is 10 units from the same lot number and collected at the same location/outlet.

Samples that pass tests should be kept for at least six months by the sentinel site of those samples that are not sent to the verification lab national; similarly for those samples that pass tests at the verification lab should be kept at the lab for at least six months. Samples that fail tests should be kept for at least one year at the verification lab.

The types of samples to be collected are finished dosage forms of chloroquine phosphate; quinine sulfate or quinine hydrochloride; sulfadoxine + pyrimethamine fixed-dose combination (FDC); mefloquine hydrochloride; tetracycline; artesunate; and other artemisinin derivatives of different dosage strengths.

1.3. Sample collector

The composition of the “sampling team” should consist of, but not be limited to:

1. Drug Regulatory Authority (DRA)
2. Malarial Control Program
3. Drug Quality Control Lab

The country should decide on actual composition of the sampling team and the choice should be approved by the DRA.

2. Sampling Method and Procedures

2.1. Sampling plan and sample size

Soon after the training of sentinel site personnel, each country should formulate a Sampling Team consisted of team members as described in point 1.3 above. The Team should then develop (in close cooperation and collaboration with the DRA, Malaria Control Program Manager, the National or State/Provincial Drug Control Lab) a plan to carry out the collection of samples as describe below:

Sample collection frequency

The collection should be carried out three times a year in four-month intervals, i.e., collections should be made every four months over a one-year period.

The Sampling Team at each sentinel site should arrange an appropriate schedule that takes into account the logistics and availability of resources. The sampling team should communicate this schedule to the verification lab (national or provincial) so the lab will be prepared to receive samples for verification testing.

Sample techniques

The use of official protocol is requested. Samples collected formally may be supplemented with samples collected by "mystery" shoppers, if the country wished to do so. The sample collection form should be completed for all samples collected using either technique.

Sample collection special precautions

Each sample collected must have a *Sentinel Site Drug Sample Collection and Testing Report Form*, properly filled out, and safely attached to or inserted into the sample container.

Samples must be kept and stored according to storage conditions required on the labels.

The source of a sample should be traceable. The Sampling Team should make every effort to collect samples that have an "identifiable" name of the drug product and its active ingredients API(s) and the manufacturer's address on the label. Also, where possible, samples should be in their original container or package. If the sampling team knows that a particular medicine has been transferred from the original container to a smaller container (for sale or dispensing purposes) which does not have proper labeling, additional samples should be taken from the original container as well. The team must write down the name of the product, API(s), and other information required on the *Sentinel Site Drug Sample Collection and Testing Report Form,* if this information is not on the label of the sample.

Sample size (number of units/sample)

- Minimum 30 for tablet or capsule dosage forms of single drug preparation;
- Minimum 50 tablets or capsules for fixed-dose combination preparations; and
- 10 for injectables.

This quantity/number of sample units should be sufficient for at least two complete screening tests using basic testing methods (physical/visual inspections, disintegration and thin-layer chromatography (TLC)) and assays described in section 1.1 (above) and one verification or confirmatory testing according to pharmacopeial specifications. (See further Annex 1 for level of testing).

Number of sample:
Every effort should be made to collect, whenever possible, at least five samples for each product per sentinel site per collection round.

In the subsequent round of sampling, if a specific drug product of the same lot/batch number is found at the same location, there is no need to collect this product again unless some unusual labeling, packaging, expiry date, manufacturing date or physical characteristics of the product are observed.

2.2. Sampling locations
A convenient sampling method is used in this project. In the effort to obtain geographically as well as drug-wise representative samples, sampling locations have been identified based on the following principles:

1. Sectoral coverage - sampling locations included in this project cover both the public and private sector supply and distribution systems, and both formal and informal channels;
2. Geographical coverage - both urban/suburban and rural areas of the sentinel sites selected;
3. Main route/flow of drug supply or distribution both from neighboring country (or countries) and province(s); and
4. Antimalarial drug-wise coverage – common antimalarial drugs and preparations from different brands/sources of manufacture and lots/batches are sampled (Table 1).

Sampling location selection follows to the schedule described below:

a. Provincial level: For the first year of the project, sampling locations will be concentrated in the selected provincial sites (see Table 2, below)

Table 2: Names of sentinel sites selected in each country.

PR China (Yunnan Province)	Laos	Vietnam	Cambodia	Thailand
1. Mang La	1. Sayaburi	1. Lai Chau	1. Pursat	1. Mae Hong Son
2. Rui Li	2. Savannaketh	2. Quang Tri	2. Pailin	2. Kanchanaburi
	3. Champasak	3. Daklak	3. Battambang	3. Chanthaburi/Trat
		4. Binh Phuoc	4. Preah Vihear	4. Ranong

b. Municipal, district and village level: Only municipalities and districts that belong to the selected provincial sites are selected. In the planning for sample collection in each provincial site, the Sampling Team should study the geographical map of the province and identify the districts located in each

province (in terms of number, surface area, port of entry/border with other province(s) or neighboring country based on the main circulation or distribution route of medicines, and physical access by car or walking).

Steps to locate municipalities and districts:

1. Draw a map and a plan to schedule for sample collection to cover municipalities or towns and districts in each provincial site;
2. Write down the names and numbers of municipalities or towns and districts and villages in each provincial site; and
3. Try to identify locations of the sampling sites (i.e. ports of entry, wholesalers or distributors; pharmacies; retail drug outlets; hospitals and clinics; and national malaria program warehouse) within each of the municipalities, districts and village based on principle 3 (above).

c. Selection of actual sampling location level:

1. Study as how many locations the Team is able to collect samples per round and plan accordingly; the selection should cover both formal and informal channels and give priority in the following order: ports of entry, wholesalers or distributors; pharmacies; retail drug outlets; hospitals and clinics; and national malaria program warehouse; and street venders.
2. Once a geographical area of sampling locations identified in a village of a district, the Team can select randomly and conveniently a site or sites taking into consideration of principle 3 (above) and order of priority when arrive in the village. In addition, every attempt has to be taken as to obtain samples from both public and private sectors (principle 1 – above).

Note:

In the subsequent round of sampling, the Team is encouraged to collect samples of antimalarial drugs or preparations of different lot/batch numbers from different manufacturers and distributors. Efforts should be made to collect any questionable antimalarial drug or sample from any suspicious outlet at any time.

2.3. Sampling record

A written record of the sampling operations carried out is shown in Annex 2. This form must be filled out and signed by all parties involved.

3. General Precautions to be Taken During Sampling Operations

All operations related to sampling should be performed with care. The “Sampling Team” should have all the tools needed to open the packages, containers, etc., at their disposal. That includes knives, pliers, sealable plastic bags, brushes to remove dust, amble or protect-from-light plastic storage containers, and material to re-close the packages (such as sealing tape). Likewise, they will need self-adhesive labels to indicate that a part of the contents has been removed from a package or container and documentation tools (notebook, permanent marker, air-block dark plastic bags).

4. Packaging and Labeling of Samples

The container used to store a sample should not interact with the sampled material nor should it allow contamination. The samples should be in their original "unit" packaging and labeling, if applicable. It should also protect the sample from light, air, moisture, etc., as required by the storage directions for the material sampled. As a general rule, the container should be sealed and tamperproof. The container must be properly labeled and contain the information described in Annex 2. Drug samples should be kept in their original packaging, especially for blister pack preparations.

5. Transportation of Samples to the Testing Sites Where the Minilab Kit is Located, to National Laboratory, and to the Reference Lab(s)

Adequate care and measures have to be taken to ensure that samples are transported to where the tests are performed, including basic testing using the Minilab kit, national laboratories as well as reference labs, without any physical damage to the samples that might affect the physical/visual examinations.

Appropriate care should be taken to provide adequate packaging to protect samples during transportation, either by filling the container with cotton batting or foam, or by filling any residual space with a suitable material. All containers should be sealed and appropriately labeled.

6. Storage of Samples

Samples collected are packed, transported, and stored in such a way to prevent any deterioration, contamination, or adulteration. Samples collected should be stored in accordance with storage instructions for the respective drug. Closures and labels should be tamper-evident, that is, of such a type that unauthorized opening can be detected. When opening a sample container, the analyst or the person who opens it must date and initial it.

Annex 1: Testing Methods, Procedures and Testing Data Reporting

1. Testing methods and reference materials, substances and/or standards

- Basic testing at the sentinel site level: Testing methods and procedures described in the USP DQI Training Manual and the reference substances/product provided by USP DQI, including those provided with the GPHF-Minilab kits should be used. The tests cover:
  - Physical/visual inspection/examination
  - Simple disintegration
  - TLC (see Appendix 2 for General rules TLC result interpretation)

- Verification and confirmation tests: These tests should be performed by the national or provincial labs or at USP designated labs. Testing procedures and assay methods should be carried out according to the current official monographs in established pharmacopeias, including International Pharmacopoeia (IP), USP/NF, or if available national pharmacopeias.

2. Transportation of samples for verification and confirmation

- Sentinel site to National Drug Quality Control Lab (NDQC Lab) – Use of government channel or any other suitable means.
- NDQC Lab to reference lab (designated labs and USP-RDL lab) – Use WHO channel[1] USAID, or any other possible means that do not breach national or international regulations.
- Transportation costs – Malaria program and USP DQI is responsible for the charge incurred for the transport of drug samples from the NDQC Lab to the reference lab.

3. Testing costs

- USP DQI and WHO WPRO and WHO RBM Mekong will share the expenses of verification and confirmation tests.
- Invoices/bills of confirmatory testing charges are to be sent to WHO. Focal point for communication is the WHO RBM Mekong Coordinator, Dr. Krongthong Thimasarn.

4. Testing levels

Tests will be performed at three levels: sentinel sites; national lab (except for Yunnan China where the second level is district lab); and reference lab.

[1] Note to Thailand: Address to WHO/WR representative (no specific name) and CC: RBM Mekong.

Activity and requirements	Level of testing	Quantity/number of samples
Sample collection Basic testing: visual, disintegration and TLC	**Sentinel site**	Test: 100% of samples collected. Send: ▪ 100% doubtful samples to NDQC or designated Lab for verification ▪ 100% of failed samples ▪ 5-10% of passed samples
Verification: Validated methods or Pharmacopeial specifications	**NDQC or designated Lab**	Test: 100% samples received from sentinel sites. Send: ▪ 100% doubtful samples to reference lab for confirmation ▪ 100% of failed samples, where possible ▪ 5-10% of passed samples
Confirmation: Pharmacopeial specifications	**Reference Lab**	Test: all samples received from NDQC Lab/designated Lab

5. Testing data reporting

- In-country reporting:
  Regular reporting (every four months) – Each sentinel site sends a report covering the previous four (4) months' activity and performance to the focal point at national/provincial Malaria Control Program Center or the National/Provincial Drug Quality Control Lab (NDQC Lab), depending on the setup of each country.

  The Report from the National/Provincial Drug Quality Control Lab to DRA and key stakeholders should include a copy of the completed *Sentinel Site Drug Sample Collection and Testing Report Form* (Annex 2) and a copy of the *National Laboratory Testing Report Form* (Annex 3). All results (passed and failed) should be sent simultaneously to DRA and malaria program.

- For-cause or emergency reporting (as necessary) – The site must report any "for cause" incidents to the NDQC Lab, which will verify the testing results and will take any necessary action. Measures may include convening a meeting with malaria program and the appropriate department/agency, for instance, DRA, FDD and MOH, for introducing an emergency alert, if necessary.

- Country and USP DQI and RBM Mekong:

USP DQI requires that the country data (including data of testing at sentinel site and national or provincial lab levels) sends quarterly report to USP DQI for analysis. The report should contain a copy of the completed *Sentinel Site Drug Sample Collection and Testing Report Form* (Annex 2) and a copy of the *National Laboratory Testing Report Form* (Annex 3). Should USP DQI require an electronic report format of aggregated results, it will request the country to provide accordingly. USP DQI responsible staff will work closely with WHO and the country focal point and will provide feedback and keep the National Labs informed regularly about the progress of the data analysis and compare to their own findings. The National Labs, in turn, should communicate the verification test results to the sentinel sites in a regular basis.

6. Supervision

A designated professional from the appointed lab (National Drug Quality Testing Lab or Provincial Lab) plus one supervisory staff member from the National Malaria Program or Provincial center will supervise the sentinel site through periodic visits. The supervisory visits will provide continued technical support and will ensure that standard procedures in sample collection, testing, and drug quality data documentation and reporting are being properly followed by the sentinel site staff.

- Supervisory visits should be scheduled as follows:
  - ⇨ First time, the first or second (1-2) month after operations begin;
  - ⇨ Thereafter, every four months.

Checklist for Sentinel Site "Drug Testing" Personnel

1. Collect samples (every 4 months) – Staff must follow the sampling procedure described in the course materials. Do not collect samples in 1 or 2 days only.

2. Complete a *Drug Sampling Receipt Form* for each sample collected and attach it to the sample container. Samples must be kept and stored according to storage conditions required on the labels (often in room temperature).

3. Testing – tests to be carried out by sentinel sites "drug testing" staff include:
   - physical/visual inspection,
   - simple disintegration, and
   - TLC.

4. Fill out the Drug Quality Report Form (see last page of training materials) with required information, data, and test results obtained –
   - Sign, date, and keep report in a safe place; keep with the leftover sample and retention sample (if applicable).
   - Store the "tested" TLC plates wrapped in foil; keep with the report and sample materials.

5. Sending sample for verification/confirmation – Enclose in the shipping case/parcel a copy of the completed *Sentinel Site Drug Sample Collection and Testing Report Form (Annex 2)* together with samples to the malaria program focal point or to the NLDQ Lab. The NLDQ Lab will conduct verification tests and provide feedback about the test results to the sentinel site; if further action is necessary, the NLDQ Lab will coordinate with the malaria program and others (DDF, FDA, MOH, and possibly WHO Country or Regional Office, and USP DQI) to make a decision as what to do next.

IMPORTANT NOTE:
Due to the sensitive nature of this activity and possible conflicts of interest, NO DATA or RESULT of any preliminary or initial test data obtained at the sentinel sites should be shared with or disclosed to third parties until it has been verified and discussed among the relevant authorities or agencies concerned (DRA, National Lab, and Malaria Program), and if applicable with USP DQI, and WHO RBM Mekong.

Annex 2: Sentinel Site Drug Sample Collection and Testing Report Form

Report No. ----------*/(province name)*

SAMPLE INFORMATION	
Sample Serial Number: _____/_____(Province name)	
Name of location/place where sample was taken	
Street address (with telephone and fax number, if applicable)	
Date of sampling	
Drug Name (trade or brand name)	
Generic or INN[1] name	
Dosage form and strength	
Manufacturer's Batch or Lot Number	
Manufacturing date	
Expiry date	
Registration or licensed number (if applicable)	
Manufacturer name and address	
Number of sample units taken (minimum 30 tablets or capsules; 50 for FDCs[2], and 10 for injectables)	
□ taken in original package	□ taken from bulk container
Brief physical/visual description of sample	
Name of collector(s)/date/sign	
Name of seller or representative identified of establishment where sample was taken	
PHYSICAL/VISUAL INSPECTION TEST	
Labeling (requirements)	
Brand Name of the drug sample (if applicable)	
Generic or INN name of active ingredient(s)	
Dosage form and strength	
Name of reference standard used (as claimed on label e.g. USP, BP, IP, EP)	
Manufacturer's Batch or Lot Number	
Name of manufacturer and address (with telephone and fax number if applicable)	
Manufacturing date	
Expiry date	
Storage conditions	

[1] INN is the International Non-proprietary name of a drug product
[2] FDCs stand for fixed-dose combination preparations

Packaging	
Material (blister pack/card, bottle, others specify)	
Unit dose per blister card or container stated	
Any print on the backing foil (if packed in blister pack or card)	
Description of dosage form	
Shape (circular, oval, flat sides, other)	
Uniformity of shape	
Uniformity of color	
No physical damage (cracks, breaks, erosion, abrasion, sticky)	
Other observations (no foreign contaminant, dirty marks, proper seal - for capsule)	

DISINTEGRATION TEST

Time of complete disintegration expected (30 minutes for uncoated tablet)	Time of complete Disintegration observed	Did the drug pass disintegration test?
----------	----- ----------	----------

RESULT OF TLC TEST (see Appendix 2 for TLC result interpretation)

Rf Standard: --------	Did the drug and the standard Spots have the same intensity? ----------	Did The sample pass quality by using the TLC Test?
Rf Sample:- --------	Was there any contaminant spot on TLC? ------- ----------	□ Yes □ No

FINAL COMMENTS

□ The sample passes basic testing

□ The sample failed basic quality testing (Reason:……..…….)

□ The sample is doubtful for its basic quality testing (Reason:……..……..…….……)

REPORT PREPARED BY:	REPORT REVIEWED BY:
Date: …….....	Date : …….
Name:…….	Name: ……
Signature: ……	Signature :……..……

ACTION TO BE TAKEN BY THE PROVINCIAL SENTINEL SITE[3]

Report the result to malaria program Date of report …….. Signature…….…….	Send the remaining sample units together with this Form to malaria program or to the National Lab for further testing Date……Signature…….

Reasons given for the chosen action:

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3 Action to be taken and communication between key agencies in the country should be dependent on individual country setting.

Annex 3: National Laboratory Testing Report Form

Report no. _____/[name of the lab]

SAMPLE INFORMATION *(This section should be filled out when receiving the incoming sample or if the repot is attached to the Sentinel Site Sample Collection and Testing Report Form, only discrepancies should be marked)*	
Sample Serial Number or Code (use the same number as the Sentinel Site Sample Collection and Testing Report Form	
Drug Name (trade or brand name)	
Generic or INN[4] name	
Dosage form and strength	
Manufacturer's Batch or Lot Number	
Manufacturing date	
Expiry date	
Registration or licensed number (if applicable)	
Manufacturer name and address	
Name and address (with telephone and fax number, if applicable)of location/place where sample was collected	
Date when the Lab receives sample	
Name of test requester or sender of the sample/date/sign	
PHYSICAL/VISUAL INSPECTION TEST	
Labeling (requirements)	
Brand Name of the drug sample (if applicable)	
Generic or INN name of active ingredient(s)	
Dosage form and strength	
Name of reference standard used (as claimed on label e.g. USP, BP, IP, EP)	
Manufacturer's Batch or Lot Number	
Name of manufacturer and address (with telephone and fax number if applicable)	
Manufacturing date	
Expiry date	
Storage conditions	
Expiry date or manufacturing date	
Storage conditions	
Packaging	
Material (blister pack/card, bottle, others specify)	
Unit dose per blister card or container stated	
Any print on the backing foil (if packed in blister pack or card)	
Description of dosage form	
Shape (circular, oval, flat sides, other)	
Uniformity of shape	
Uniformity of color	
No physical damage (cracks, breaks, erosion, abrasion, sticky)	
Other observations (no foreign contaminant, dirty marks, proper seal - for capsule)	

[4] INN is the International Non-proprietary name of a drug product

DISINTEGRATION TEST (IF TESTED)

Time of complete Disintegration expected	Time of complete Disintegration observed	Did the drug pass Disintegration test?
30 min	----------	----------

RESULT OF TLC TEST (IF TESTED) (see Appendix 2 for TLC result interpretation)

Rf Standard: -------- Rf Sample: --------	Did the drug and the standard Spots have the same intensity? ---------- Was there any contaminant spot on TLC plate? ----------	Did The sample pass quality by using the TLC Test? □ Yes □ No

DISSOLUTION TEST (IF TESTED, SPECIFY METHOD OR PROCEDURE AND ACCPETANCE CRITERIA……)

Result: ----------□ Passed □ Failed

OTHER TEST USED FOR VERIFICATION OF IDENTIFICATION AND CONTENT OF ACTIVE INGREDIENT (API)

Specify the test method(s) and reference to a pharmacopeial monograph e.g. IP 3rd ed., USP26
……

Identification	Name of API(s)	Results
	1.	□ Present □ Not present
	2.	□ Present □ Not present

Assay for content	Name of API(s)	Acceptance criteria	Results
	1.		
	2.		

FINAL COMMENTS

□ The sample meets standards
□ The sample does not meet standards
(Reason:……..……..)
□ The sample is doubtful for its quality testing
(Reason:……..……..……..……...
…… and further testing is needed at a reference lab)

REPORT PREPARED BY:	REPORT REVIEWED BY:
Date: …….....	Date : …….
Name:…….	Name: ……
Signature: ……	Signature :……..……

ACTION TO BE TAKEN BY THE NLDQC*		
1. Report to responsible authorities	Report in writing to e.g. MOH Drug Regulatory Authority and the Malaria Program Date and sign…… ……	
2. Send samples to the Reference Lab for confirmatory testing. They should always be accompanied by a Request Form (Appendix 1)	Send to	☐ Bureau of Drug and Narcotics Lab in Thailand
		☐ National Institute for Drug Quality Control in Viet Nam
		☐ USP Lab
	Date:……. Signature:…….	

* Action to be taken and communication between key agencies in the country should be dependent on individual country setting.

Appendix 1: Test Request Form

Request submitter: …….....	For National Lab Use Only
Contact details: Telephone: ……... Fax: …….. Email: …….. Street address: …… …….. …….. ……..	Project or Receipt Number: ……. Receiving Officer: ……. Date:…….
Date of request:……	
Type of request: (check where applied)	
□ Verification testing □ Confirmation testing □ Others (specify)…….	
Tests request for: (check where applied) □ Identification of active ingredient(s) (API)(s) □ Dissolution □ Assay for content of active ingredient(s) (API)(s) □ Others (specify)……	
Suggested Method to be used (check where applied) □ International Pharmacopeoia (specify Edition number or Year) □ U.S. Pharmacopeia (specify Edition number or Year) □ Other (specify)……	
Desired Completion Date:…….. Provide reasons for the date:…….	
Attachments and/or materials provided with this Request Form: □ Samples (if more than one sample, attach a separate list of the samples with names and other details e.g. sample code) □ Sentinel Site Drug Sample Collection and Testing Report Form □ Others (specify)…….	
Please send invoice/bill of testing charge to:…… Telephone: …… ……Fax: ……. Email: …… Street address: …….. ……... ……...	

Note:

1. *For verification and confirmatory testing, if identification test failed ⇨ there is no need to perform test/assay for content.*
2. *Report of testing results should be sent to Dr. S. Phanouvong, unless otherwise specified, at 12601 Twinbrook Parkway, Rockville, Maryland 20852, U.S.A. UNITED STATES PHARMACOPEIA. Fax: +1 301 816 8374; Email: sxp@usp.org*

Appendix 2: General Rules for Interpreting TLC Results

This simple guideline uses the percent **R_f error**, defined below, to determine the fate of a sample based on simple TLC.

R_f Sample Error = {|R_f (standard) – R_f (sample)| / R_f (standard)} x 100%

Example

From multiple TLC experiments, the following R_f values were obtained:

R_f (standard) = 0.55
R_f (sample) = 0.53

Then, R_f Sample Error = {(0.55 – 0.53)/0.55} x 100% = 3.6 %

Interpretation of TLC Results

Based on the typical R_f values, broadness of TLC spots and simple error analysis[1], some broad rules can be applied to interpret TLC results. It is important to note that these rules should only be considered semi-quantitative and not absolute.

1. When R_f Sample Error is **5% or less**, the sample can be considered **"Pass"**

2. When R_f Sample Error is **10% or more**, the sample can be considered **"Fail"**

3. When R_f Sample Error is **between 5% and 10%**, the sample can be considered **"Doubtful"**

Note:

1. If the TLC chamber and plates were not well saturated, or if the saturation has been disturbed the spots may not be horizontal and this could give high R_f sample error.
2. Always make TLC in duplicate and compare the R_f of both runs.
3. When R_f sample error is more than 5%, always make another duplicate run under optimal conditions to double check the doubt.

[1] *Quantitative Chemical Analysis*, 6th Edition. Daniel C. Harris, W. H. Freeman, New York, 2003.