



กรมวิทยาศาสตร์การแพทย์
Department of Medical Sciences

PROFICIENCY TESTING PROGRAM 2020

Scheme Code D6305R1

Dissolution Test

Protocol No. D6305R1

Organized by

Bureau of Drug and Narcotic
Department of Medical Sciences
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Bureau of Drug and Narcotic
Department of Medical Sciences

D6305R1: Dissolution Test

1. ORGANIZER

Scheme Provider:

Bureau of Drug and Narcotic (BDN)
Department of Medical Sciences
88/7 Soi Bumrasnaradura Hospital, Tiwanon Road, Nonthaburi,
11000, THAILAND
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Scheme Coordinator:

Ms. Siriphorn Laomanacharoen
Pharmacist, Senior professional level
Email: pt_bdn@hotmail.com; pts.bdn@gmail.com
The scheme coordinator is responsible for all activities of the PT scheme.

2. OBJECTIVE

The objective of this Proficiency Testing (PT) scheme is to demonstrate that participants can accurately perform dissolution test. The scheme is based on the dissolution test of pharmaceutical product, fluconazole capsules, according to the method from the British Pharmacopoeia (BP) 2019 in Fluconazole Capsules monograph.

3. SUBCONTRACT

BDN has no policy to subcontract in any activity of this proficiency testing scheme.

4. CRITERIA FOR PARTICIPATION

Participants should have competences to perform dissolution test and use this technique in the routine work. Each participant is able to participate in the program for one set of PT sample.

5. NUMBER AND TYPE OF PARTICIPANTS

Number of participants: 20 – 70 laboratories
Type of participants: Quality control laboratories in pharmaceutical manufacturers and other testing laboratories



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6. SCHEDULE OF PT SCHEME

The frequency of this PT program is at least one round per 2 years. Schedule for the PT activities is as follows:

Activity	Schedule
Call for participation	December 2019
Deadline for registration	31 January 2020
Distribution of samples	April 2020
Deadline for submission of results	1 June 2020
Interim report for comments	August 2020
Final report	September 2020

For the most efficient PT program, all activities will be operated according to this time schedule. In order to keep time, participants are requested to feedback for registration and submission of result according to scheduled time. Participants should note that results submitted are not allowed to change or amend in any case.

7. REGISTRATION

Registration Fee:

Local participants	7,000.- Baht
Oversea participants	200.- USD (Including shipping handling)

Payment:

Local participants-

The payment should be made by Teller payment system at any branches of Krung Thai Bank Public Company Limited.

Oversea participants-

The payment should be made by bank transfer to

Account name:	DMSc Non-Fiscal Budget Account
Account number:	1301-034924
Bank name:	Krung Thai Bank Public Company Limited
Branch address:	Tivanon Road, Nonthaburi 11000, Thailand
Swift code:	KRTHTHBK

Method and Deadline for Registration:

Participants should register online via the website <https://www.bdn.go.th/pt> within **31 January 2020**. Registration by other means e.g. fax, Email will not be accepted.



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Terms and Conditions:

1. BDN reserves the right to occasionally delay the issue of PT program or use an appropriate substitute test material with prior warning to participants if the planned PT sample is not available according to the schedule of PT scheme.
2. The registration fees are nonrefundable.

More information can be viewed on the website <https://www.bdn.go.th/pt>.

8. PROFICIENCY TESTING SAMPLE

The sample of this scheme is pharmaceutical product, fluconazole 200 mg capsule.

9. HANDLING OF PT SAMPLE

Participants will receive (i) 10 capsules of fluconazole 200 mg capsule and (ii) a bottle of fluconazole reference standard for PT containing about 120 mg.

PT samples are packed in blisters and should be stored below 30°C. Reference standard are packed in 4-ml amber glass bottle and closed with plastic screw cap and should be stored between 2-8°C and protected from light and humidity until analysis. All of them are labeled which show the details of name, amount and storage condition and packed in vacuum plastic package. They are distributed in ambient condition.

PT samples are sent by express mail for local participants and by courier for oversea participants. It is the responsibility of the participants to contact BDN as soon as possible if they have not received the PT sample within the time schedule. In case of international transport for oversea participants, BDN cannot be responsible for any delays from the custom clearance. Upon receipt of PT sample, participants are requested to check physical conditions of PT sample as well as other substances provided and complete a PT sample acknowledgement form via the website <https://www.bdn.go.th/pt>.

10. TEST METHOD

Participants should determine the amount of fluconazole ($C_{13}H_{12}F_2N_6O$) dissolved and report the results as **percentage of the labelled content** of fluconazole ($C_{13}H_{12}F_2N_6O$) dissolved in 45 minutes with **one digit after the decimal separator**. In case number of digit reported is different from that specified in the protocol, the results will be rounded to one digit by BDN. If the right of the last decimal place is smaller than 5, it is eliminated and the preceding digit is unchanged. If the right of the last decimal place is equal to or greater than 5, it is eliminated and the preceding digit is increased by 1. Results reported with no digit after decimal separator or less than that specified in the protocol, 0 will be substituted. Range of percent labelled content for this PT sample is not less than 75 (Q)%.



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Participants should perform the dissolution test according to the method in Fluconazole Capsules monograph of BP 2019 according to the following procedure.

Procedure:

Comply with the dissolution test for tablets and capsules, Appendix XII B1.

TEST CONDITIONS

- (a) Use Apparatus 1, and rotate the basket at 100 revolutions per minute.
- (b) Use 900 mL of 0.1M hydrochloric acid, at a temperature of 37°, as the medium.

PROCEDURE

- (1) After 45 minutes withdraw a sample of the medium and measure the absorbance of the filtered sample, diluted with the dissolution medium, if necessary, to produce a solution containing 0.0056% w/v of Fluconazole, at 261 nm, Appendix II B using dissolution medium in the reference cell.
- (2) Measure the absorbance of a 0.0056% w/v solution of fluconazole reference standard in dissolution medium at 261 nm using dissolution medium in the reference cell.

Details of the method are described in the testing protocol which can be downloaded via auto Email from website <https://www.bdn.go.th/pt>. PT sample as well as analytical procedure should be handled and operated in the same manner as performing routine work.

11. ASSIGNED VALUE

The assigned value used to calculate z score is based on the consensus value from participants using the robust mean calculated according to robust analysis: Algorithm A in Annex C of ISO 13528:2015 (E) -Statistical methods for use in proficiency testing by interlaboratory comparisons. The assigned value will not be disclosed to public until the report is issued.

The standard uncertainty of the assigned value x_{pt} is estimated as

$$u(x_{pt}) = 1.25 \times \frac{s^*}{\sqrt{p}}$$

Criteria:
If

$$u(x_{pt}) < 0.3 \sigma_{pt}$$

then, the uncertainty of the assigned value is negligible and need not to be included in the interpretation of the results.

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12. STANDARD DEVIATION FOR PROFICIENCY ASSESSMENT

Standard deviation for proficiency assessment used to calculate z scores is set as 3.0% that corresponds to the level of performance and the expected precision of the test method or techniques and according to fitness for purpose.

13. PERFORMANCE EVALUATION

Participants will be assessed on the differences between their results and the assigned value. The z score is used for the performance evaluation as

$$z_i = \frac{(x_i - x_{pt})}{\sigma_{pt}}$$

z_i = z score

x_i = measurement result from participant

x_{pt} = assigned value

σ_{pt} = standard deviation for proficiency assessment

The interpretation of z score is designated as follows.

$|z| \leq 2.0$: acceptable

$2.0 < |z| < 3.0$: warning signal

$|z| \geq 3.0$: unacceptable

When $u(x_{pt}) > 0.3\sigma_{pt}$, then the uncertainty can be taken into account by expanding the denominator of the performance score and calculated as z' score

$$z'_i = \frac{x_i - x_{pt}}{\sqrt{\sigma_{pt}^2 + u^2(x_{pt})}}$$

The interpretation of z' score is as same as z score and using the same critical values of 2.0 and 3.0, depending on the design for the PT scheme.

For warning signal or unacceptable results, it is recommended that participants should investigate root causes and take necessary corrective actions.



14. POTENTIAL MAJOR SOURCES OF ERRORS

1. Formation of bubbles.
2. Composition, volume or temperature of the dissolution medium.
3. Sampling position
4. Sampling time
5. Interference due to contamination from the filter.
6. Floating of sample in basket

15. REPORT

An interim report is issued to provide each participant with an early indication of performance. In general, the interim report is issued about two months after the deadline for submission of results via the website <https://www.bdn.go.th/pt>. Participants are requested to check and review for any correction and/or comment. The final report is issued via the website <https://www.bdn.go.th/pt> after the correction and/or comment of interim report has been completed.

The report includes the following information.

- Introduction: general description of PT scheme
- Name and contact details of proficiency testing provider and scheme coordinator
- Participation: information of participating laboratories
- PT sample: description, sample preparation
- Homogeneity and stability assessment
- Assigned value, including measurement uncertainty and standard deviation of proficiency assessment
- Results: result tables including statistic summary data, z scores and bar chart of z scores
- Discussion of results: conclusion of overall performance and comments on participants' performance
- Potential major sources of errors

16. CONFIDENTIALITY, COLLUSION AND FALSIFICATION OF RESULTS

The identities of participants are protected by means of laboratory codes which are randomly assigned in each PT round. These codes and performance evaluation are confidential and are not disclosed to other persons unless agreed by the participant for a regulatory or recognition purpose. Participants can access their personal information in the website <https://www.bdn.go.th/pt> by using username and password which can keep their information confidentially. For security purpose, participants are recommended to change username and password in case of changing the responsible person who can access the information in the website.

This PT scheme is conducted in the belief that participants will perform the analysis and report results with scientific professional. Where any collusion between participants or falsification of results is proven by BDN, the result of that participant for the PT round concerned will be cancelled for performance evaluation.



17. LOST OR DAMAGED OF PROFICIENCY TESTING SAMPLE

Auto Email will be sent to participants after sample distribution. In case of lost or damaged PT sample, participants should immediately inform BDN via <https://www.bdn.go.th/pt>. In some cases, the damaged PT sample should be returned to BDN. Replacement will be arranged within 1 week if the PT samples are proved to be lost or considered not suitable for analysis. The deadline of submitting result will be extended to appropriate date if necessary.