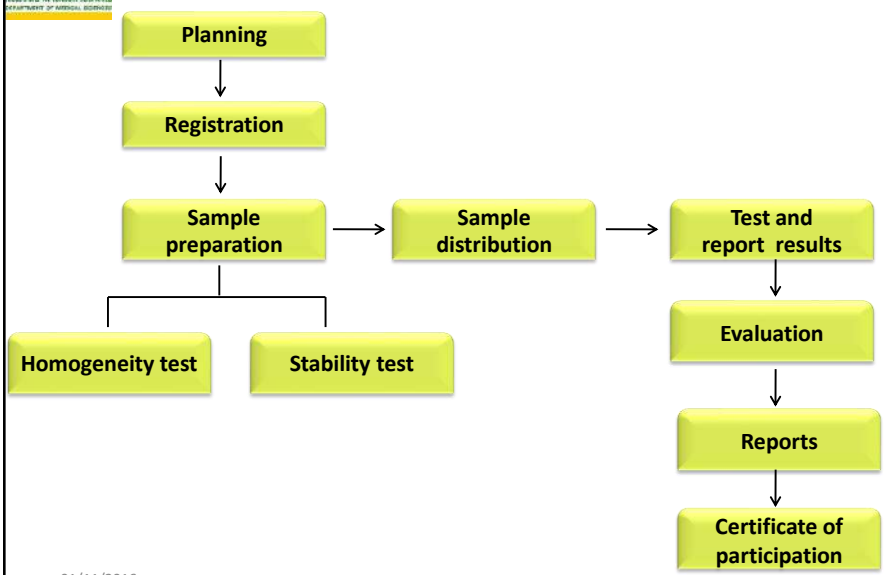
PT Provider : Procedure

Procedure



Planning

- Coordinator is responsible to prepare the plan which include the information a) – t) of 4.4.1.3

Example:

a) name and address of the PTP

Bureau of Drug and Narcotic (BDN)
Department of Medical Sciences
88/7 Tiwanon Road, A. Muang, Nonthaburi 11000 THAILAND
Tel. +66 2951 0000 ext. 99132, 99137
Fax +66 2580 5733
Email: pt_bdn@hotmail.com; pts.bdn@gmail.com

Planning

- Coordinator is responsible to prepare the plan which include the information a) – t) of 4.4.1.3

b) name, address and affiliation of the coordinator and other personnel involved in the design and operation of the PT scheme

1. Coordinator: Ms. Siriphorn Laomanacharoen
2. Responsible person:
   1. Ms. Masvalai Likitthanasrate
   2. Ms. Methinee Nimnoi
   3. Ms. Nanthanut Seesuwan
   4. Ms. Bumrung Pang-Ngarm
3. Quality control manager
4. Proficiency testing management team
5. Technical advisory team

Planning

- Coordinator is responsible to prepare the plan which include the information a) – t) of 4.4.1.3

c) the activities to be subcontracted and the names and addresses of subcontractors involved in the operation of the PT scheme

BDN has no policy of subcontract in any activities of proficiency testing provider.

d) criteria to be met for participation

-Participants who have competences to perform the analysis of gemfibrozil by High Performance Liquid Chromatography (HPLC) and use this technique in the routine work.

-Participants who are calibration laboratories.

Planning

e) the number and type of expected participants in the PT scheme

Number of participants:	20 - 60
Type of participant:	Quality control laboratories in pharmaceutical manufacturers Testing laboratories

f) selection of the measurand and or characteristic of interest, including information on what the participants are to identify, measure, or test for in the specific PT round

-Participants should determine the percentage content of $C_{15}H_{22}O_3$, calculated on as is basis.

-Participants should determine the pH value of the sample.

Planning

g) a description of the range of values or characteristics, or both, to be expected for the PT items

-97.8-101.7.0% on as is basis
-pH value 7.0-8.0

h) the potential major sources of errors involved in the area of PT offered

HPLC
1. Change of concentration of sample and reference standard solution due to volatile solvent used
2. Suitability of chromatographic system
3. Calculation

pH
1. Variation of temperature
2. Incorrect calibration of pH meter
3. Solvent used should be carbon dioxide-free water

Planning

i) requirements for the production, quality control, storage and distribution of PT items

Packing condition:	PT samples will be packed in the control environment (temperature between 20 - 25◦C, humidity NMT 40%RH) by using glove box.
Container:	amber glass vial with screw cap
Distribution condition:	ambient
Storage condition:	at the temperature between 2-8◦ C and protect from light and humidity prior to analysis

Planning

j) reasonable precautions to prevent collusion between participants or falsification results, and procedures to be employed if collusion or falsification of results is suspected

Participants will be informed a priori of the penalty rule.

“Whenever any collusion between participants or falsification of results is proven by BDN, the results of those participants for the PT round concerned will be excluded from the performance evaluation.”

Planning

j) reasonable precautions to prevent collusion between participants or falsification results, and procedures to be employed if collusion or falsification of results is suspected

Participants will be informed a priori of the penalty rule.

“Whenever any collusion between participants or falsification of results is proven by BDN, the results of those participants for the PT round concerned will be excluded from the performance evaluation.”

Planning

k) a description of the information which is to be supplied to participants and the time schedule for the various phases of the PT scheme

Schedule for the PT scheme activities is as follows:

Activity	Schedule
Call for participation	December 2015
Deadline for registration	15 January 2016
Distribution of samples	February 2016
Deadline for submission of results	18 April 2016
Interim report for comments	June 2016
Final report	August 2016

Planning

l) for continuous PT schemes, the frequency or dates upon which PT items are to be distributed to participants, the deadlines for the return of results by participants and , where appropriate, the dates on which testing or measurement is to be carried out by participants

BDN does not organize continuous PT schemes.

Planning

m) any information on methods or procedures which participants need to use to prepare the test material and perform the tests or measurements

Method: Assay by HPLC according to the method in USP 38 on Gemfibrozil monograph

Reference: USP 38

Procedure: explain the details of the testing procedure

Planning

n) procedures for the test or measurement methods to be used for the homogeneity and stability testing of PT items and, where applicable, to determine their biological viability

Homogeneity:

Number of packing: 200 bottles, 200-220 mg of Gemfibrozil per bottle

Number of sampling: 10 bottles by random sampling using www.random.org

Procedure: according to ISO 13528:2015-Statistical methods for use in proficiency testing by interlaboratory comparisons, explain details of the procedure

Test method: assay by HPLC according to the method in USP 38 on Gemfibrozil monograph and General Chapters: <621> Chromatography, explain details of the test method

Evaluation: according to ISO 13528:2015-Statistical methods for use in proficiency testing by interlaboratory comparisons, explain details of the procedure and criteria of evaluation

Planning

Stability:

Period of sampling and stability test condition:

-PT samples at storage condition: every month from February to May 2016

-Control sample for transportation: perform the test upon receiving

Number of sampling: 3 bottles for each month by random sampling using www.random.org

Procedure: according to ISO 13528:2015-Statistical methods for use in proficiency testing by interlaboratory comparisons, explain details of the procedure

Test method: assay by HPLC according to the method in USP 38 on Gemfibrozil monograph and General Chapters: <621> Chromatography, explain details of the test method

Evaluation: according to ISO 13528:2015-Statistical methods for use in proficiency testing by interlaboratory comparisons, explain details of the procedure and criteria of evaluation

Planning

o) preparation of any standardized reporting formats to be used by participants

Bureau of Drug and Narcotic
Department of Medical Sciences

Result Report
Assay by High Performance Liquid Chromatography
Scheme code D6001R1

Determinandes	Gemfibrozil (% $C_{15}H_{22}O_3$ as is basis)
1	
2	
3	
Mean	
SD	
RSD (%)	

Resolution (between peaks of gemfibrozil and 2,5-dimethylphenol)	
Relative standard deviation of replication (standard solution)	

Planning

p) a detailed description of the statistical analysis to be used

Description of the statistical analysis including the criteria used in homogeneity test, stability test and evaluation of the results should be explained .

q) the origin, metrological traceability and measurement uncertainty of any assigned values

In case of determining the assigned value from CRM or one lab:

The assigned value is traceable to primary reference standard of USP reference standard.

Planning

r) criteria for the evaluation of performance of participants

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

s) a description of the data, interim reports or information to be returned to participants

The report includes the following information.

- Introduction: general description of PT scheme
- Participation: information of participating laboratories
- PT sample: sample preparation, results of homogeneity and stability testing
- Explanation of statistics used
- Results: result tables including assigned value, statistic summary data, z scores and bar chart of z scores
- Discussion of results: assigned value and traceability, measurement uncertainty, conclusion of overall performance and list of comments from participants
- Potential major sources of errors

Planning

t) a description of the extent to which participant and results, and the conclusions that will be based on the outcome of the PT Scheme are to be made public

The description that explain how to manage, if PTP should provide the participant's result to the public

u) actions to be taken in the case of lost or damaged PT items

In case of lost or damaged PT sample, participants should immediately inform BDN. The damaged PT sample should be returned to BDN. Replacement will be arranged 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.

Planning

-The plan should specify the responsible person on each activity and time frame.

-The plan is proposed to the meeting of the Proficiency Testing Management Team and Technical Advisory Team for the agreement.

-The plan is proposed to the director for the approval and the issued date.

Registration

-PT protocol and registration form are sent to participants.

PT protocol is the document that explains the information of the PT scheme operated in the year prepared by coordinator.

This information should be included:

1. name, address and contact details of PT provider and coordinator
2. details of how to apply and participation fees (if any)
3. criteria for participation
4. number (minimum and maximum) and type of participant
5. list of PT round to be organized and time schedule of PT sample distribution and deadline of submitting the result
6. details of each PT round : name and type of PT sample, measurand or characteristic of interest, information of test and test method, criteria for the evaluation of performance, potential sources of errors, storage condition of PT sample
7. policy of lost or damaged PT sample management
8. policy of confidentiality, collusion and falsification of results

Registration

-Code of participant in each PT round is randomly generated.

The code may be figures, for example 001, 002, 003….to the last number of registered participants.

Code of participant should be securely and confidentially kept by coordinator.

Sample preparation

PT sample can be

- Active pharmaceutical ingredients (raw materials)
- Pharmaceutical products (tablets, solution, etc.)
- Chemicals

Sample preparation

-PT samples are procured or prepared in appropriate amount to ensure that they are sufficient for using in the operation of the PT scheme.

Considering from:
-number of registered participant
-amount per container for a single use to perform the test
-amount of PT sample used for homogeneity and stability test
-compensation of damage and/or loss of PT sample

Sample preparation

-PT sample should be divided into the adequate amount per container for a single use to perform the test.

-The environment of packing procedure and the containers should be appropriate to protect damage or deterioration of PT sample. Temperature and humidity of packing area should be controlled and recorded.

Sample preparation

-Packing of PT sample

The sample number is labeled on each bottle according to the sequence of packing.
The number of packing (n) is number of PT samples packed in the final container which is set in the plan.

The sequences of packing are defined as follows,
Sample number 001 is the first packed bottle.
Sample number 002 is the second packed bottle.
Sample number 003 is the third packed bottle.
Sample number n is the last packed bottle.
(n = number of packing)

Sample preparation

-In case of pharmaceutical product, tablets or capsules, PT sample should not be removed from the original containers e.g. blisters or aluminum foil. The number of unit is exactly counted and distributed in the original container as the final container.

-The details of packed PT sample and packing condition should be recorded.

Sample preparation

-The labels should be securely attached to the container of individual PT samples throughout the operation of the PT scheme.

-The labels should inform the information of the PT sample as follows,

*Name of PT provider
*Code of PT
*Name of substance
*Approximate amount
*Storage condition
*Sample number

Sample preparation

- After packing, PT samples are kept in a tightly container and stored in a well identified area at the storage condition. The storage condition should be considered according to the type and physico-chemical property of PT sample. The information of storage condition can be obtained from Certificate of Analysis (COA), documents from manufacturer or pharmacopoeia.

Sample preparation : Homogeneity

-The homogeneity of PT sample should be tested and evaluated before distributing to participants ensure that all units of PT sample are identical.

-Choose a measurement method to use in the homogeneity test and measurand, which will be sensitive to inhomogeneity between the samples,

For example:

measurement method	measurand
Assay	%purity, %LA, amount/unit
pH measurement	pH value
Dissolution	%dissolve, %LA
Water determination	%water
Loss on drying	%Loss on drying

Sample preparation : Homogeneity

-Select a number (g) of the PT samples in the final container at random, where g ≥ 10.

The method of random sampling can be
*www.random.org
*Function RAND of Microsoft Excel

-Prepare two test portions, m = 2, from each sample using the appropriate techniques to minimized between-test-portion differences.

-Determine all test portions in a random order, obtain a measurement result on each, and complete the whole series of measurements under repeatability conditions

Sample preparation : Homogeneity

Evaluate the homogeneity test:

1) Checking for within sample variation (precision of the analyst) by using Cochran's test.

m = 2, the Cochran's test statistic should be calculated from

$$C = \frac{D_{max}^2}{\sum_{i=1}^{p} D_i^2}$$

Where
C = Cochran's test statistic
D_{max} = highest difference
D_i = difference of each pair of duplicates, for i = 1,2,…,p
p = number of data set = g

Sample preparation : Homogeneity

-Calculate Cochran's test statistic, *C*, and compare with the critical value from the table which gives values of 5% and 1% critical value (95% and 99% confidence, respectively) for *p* between 2 and 40 data set.

-If Cochran's test statistic is less than 5% critical value, there is no evidence of analytical outliers. The analysts who performed the test have good performance.

-If any outlier is detected, results must be inspected closely to see any errors and appropriate action must be taken. An outlier set should not be rejected unless it is significant at 99% confidence or any permanent analytical errors are found.

Sample preparation : Homogeneity

p	n = 2		n = 3		n = 4		n = 5		n = 6	
	1 %	5 %	1 %	5 %	1 %	5 %	1 %	5 %	1 %	5 %
2	—	—	0,995	0,975	0,979	0,939	0,959	0,906	0,937	0,877
3	0,993	0,967	0,942	0,871	0,883	0,798	0,834	0,746	0,793	0,707
4	0,968	0,906	0,864	0,768	0,781	0,684	0,721	0,629	0,676	0,590
5	0,928	0,841	0,788	0,684	0,696	0,598	0,633	0,544	0,588	0,506
6	0,883	0,781	0,722	0,616	0,626	0,532	0,564	0,480	0,520	0,445
7	0,838	0,727	0,664	0,561	0,568	0,480	0,508	0,431	0,466	0,397
8	0,794	0,680	0,615	0,516	0,521	0,438	0,463	0,391	0,423	0,360
9	0,754	0,638	0,573	0,478	0,481	0,403	0,425	0,359	0,387	0,329
10	0,718	0,602	0,536	0,445	0,447	0,373	0,393	0,331	0,357	0,303
11	0,684	0,570	0,504	0,417	0,418	0,348	0,366	0,308	0,332	0,281
12	0,653	0,541	0,475	0,392	0,392	0,326	0,343	0,288	0,310	0,262
13	0,624	0,515	0,450	0,371	0,369	0,307	0,322	0,271	0,291	0,243
14	0,599	0,492	0,427	0,352	0,349	0,291	0,304	0,255	0,274	0,232
15	0,575	0,471	0,407	0,335	0,332	0,276	0,288	0,242	0,259	0,220
16	0,553	0,452	0,388	0,319	0,316	0,262	0,274	0,230	0,246	0,208
17	0,532	0,434	0,372	0,305	0,301	0,250	0,261	0,219	0,234	0,198
18	0,514	0,418	0,356	0,293	0,288	0,240	0,249	0,209	0,223	0,189
19	0,496	0,403	0,343	0,281	0,276	0,230	0,238	0,200	0,214	0,181
20	0,480	0,389	0,330	0,270	0,265	0,220	0,229	0,192	0,205	0,174
21	0,465	0,377	0,318	0,261	0,255	0,212	0,220	0,185	0,197	0,167
22	0,450	0,365	0,307	0,252	0,246	0,204	0,212	0,178	0,189	0,160
23	0,437	0,354	0,297	0,243	0,238	0,197	0,204	0,172	0,182	0,155
24	0,425	0,343	0,287	0,235	0,230	0,191	0,197	0,166	0,176	0,149
25	0,413	0,334	0,278	0,228	0,222	0,185	0,190	0,160	0,170	0,144
26	0,402	0,325	0,270	0,221	0,215	0,179	0,184	0,155	0,164	0,140
27	0,391	0,316	0,262	0,215	0,209	0,173	0,179	0,150	0,159	0,135
28	0,382	0,308	0,255	0,209	0,202	0,168	0,173	0,146	0,154	0,131
29	0,372	0,300	0,248	0,203	0,196	0,164	0,168	0,142	0,150	0,127
30	0,363	0,293	0,241	0,198	0,191	0,159	0,164	0,138	0,145	0,124
31	0,356	0,286	0,235	0,193	0,186	0,155	0,159	0,134	0,141	0,120
32	0,347	0,280	0,229	0,188	0,181	0,151	0,155	0,131	0,138	0,117
33	0,338	0,273	0,224	0,184	0,177	0,147	0,151	0,127	0,134	0,114
34	0,332	0,267	0,218	0,179	0,172	0,144	0,147	0,124	0,131	0,111
35	0,325	0,262	0,213	0,175	0,168	0,140	0,144	0,121	0,127	0,109
36	0,318	0,256	0,208	0,172	0,165	0,137	0,140	0,118	0,124	0,106
37	0,312	0,251	0,204	0,168	0,161	0,134	0,137	0,116	0,121	0,103
38	0,306	0,246	0,200	0,164	0,157	0,131	0,134	0,113	0,119	0,101
39	0,300	0,242	0,196	0,161	0,154	0,129	0,131	0,111	0,116	0,099
40	0,294	0,237	0,192	0,158	0,151	0,126	0,128	0,108	0,114	0,097

Sample preparation : Homogeneity

Evaluate the homogeneity test:

2) Estimate the within-sample standard deviation, , and between-sample standard deviation using analysis of variance.

The data from a homogeneity test are represented by $x_{t,k}$
where t represents the PT sample (t = 1, 2, 3, ….., g)
k represents the test portion (k = 1, 2)
If m = 2,

Sample averages:

$$\bar{x}_t = (x_{t,1} + x_{t,2})/2$$

Sample preparation : Homogeneity

Between-test portion ranges:

$$w_t = |x_{t,1} - x_{t,2}|$$

General average:

$$\bar{\bar{x}} = \frac{1}{g}\sum_{t=1}^{g} \bar{x}_t$$

Standard deviation of sample average:

$$s_x = \sqrt{\sum_{t=1}^{g} (\bar{x}_t - \bar{\bar{x}})^2/(g-1)}$$

Within-sample standard deviation:

$$s_w = \sqrt{\sum_{t=1}^{g} w_t^2/(2g)}$$

Sample preparation : Homogeneity

Between-sample standard deviation:

$$s_s = \sqrt{s_x^2 - (s_w^2/2)}$$

When PT samples are highly homogeneous, the between-sample variance, s_s^2 becomes negative when s_x is relatively smaller than s_w. In this case $s_s = 0$.

-Compare the between-sample standard deviation, s_s with the standard deviation for proficiency assessment

$$s_s \leq 0.3\,\sigma_{pt}$$

PT samples may be considered to be adequately homogeneous.

Sample preparation : Homogeneity

-Expand the criterion to allow for the actual sampling error and repeatability in the homogeneity test.
Calculate:

$$\sigma_{allow}^2 = (0.3\,\sigma_{pt})^2$$

and

$$c = F_1\sigma_{allow}^2 + F_2 s_w^2$$

where F_1 and F_2 are from standard statistical tables, for the number of PT samples selected and with each PT sample tested in duplicate.

If $s_s > \sqrt{c}$, there is evidence that the batch of PT sample is not sufficiently homogeneous.

Sample preparation : Homogeneity

g	20	19	18	17	16	15	14	13	12	11	10	9	8	7
F_1	1.59	1.60	1.62	1.64	1.67	1.69	1.72	1.75	1.79	1.83	1.88	1.94	2.01	2.10
F_2	0.57	059	0.62	0.64	0.68	0.71	0.75	0.80	0.86	0.93	1.01	1.11	1.25	1.43

Where m = 2

Sample preparation : Homogeneity

-When σ_{pt} is not known in advance, for example when σ_{pt} is the robust standard deviation of participant results, other criteria for determining sufficient homogeneity should be chosen for determining sufficient homogeneity.

a) General model for chemical application : Horwitz model
b) use information from previous rounds to estimate σ_{pt}
c) use data from a precision experiment
d) accept the risk of distributing PT sample that are not sufficiently homogeneous, and check the criterion after the consensus σ_{pt} has been calculated.

- In case of inhomogeneity, the PT sample should be discarded. The new PT sample should procured.

Sample preparation : Stability

-The stability of PT sample should be periodically tested to ensure that PT sample is stable

* in the storage condition : stable throughout the operation of PT round
* in transportation condition : stable during the sample distribution

-Select a number (g) of the PT samples in the final container at random, where g ≥ 2.

The method of random sampling can be

*www.random.org

*Function RAND of Microsoft Excel

Sample preparation : Stability

-Select a single lab using measurement method with good intermediate precision

-Measure g PT samples before the planned date of distribution. Replicated measurement should be made in a fully randomised order. Calculate the averages of the results for the before distribution as $\bar{y}_1$ (starting time).

-Reserve the remained g PT sample under conditions similar to the expected storage condition.

-After the closing date for return of results, measure the remaining g PT sample using the same lab, measure method and number of replicates, with all replicate in a randomised order. Calculate the averages of the results as $\bar{y}_2$.

Sample preparation : Stability

Evaluate the stability test:

-Compare the general average of measurements obtained before distribution data or from a prior homogeneity test with the general average of results obtained in the stability test.

The PT samples may be considered to be adequately stable if

$$|\bar{y}_1 - \bar{y}_2| \leq 0.3\ \sigma_{pt}$$

Sample preparation : Stability

If it is likely that the intermediate precision of the measurement method contributed to the inability to meet the criteria, one of the following options should be taken:

a) use an isochronous stability study
b) increase the uncertainty of the assigned value to account for possible instability
c) expand the criterion for acceptance by adding the uncertainty of the difference to

$$|\bar{y}_1 - \bar{y}_2| \leq 0.3\sigma_{pt} + 2\sqrt{u^2(\bar{y}_1) + u^2(\bar{y}_2)}$$

Sample preparation : Stability

If the criterion in equations

$$|\bar{y}_1 - \bar{y}_2| \leq 0.3\sigma_{pt}$$

and

$$|\bar{y}_1 - \bar{y}_2| \leq 0.3\sigma_{pt} + 2\sqrt{u^2(\bar{y}_1) + u^2(\bar{y}_2)}$$

is not met, the following option should be considered

- quantify the effect of instability and take it into account in the equation (for example with z' scores)
- examine the PT sample preparation and storage procedures to see if improvements are possible or
- do not evaluate participant performance

Sample preparation : Stability

-The criterion may be replaced by an appropriate statistical test for a difference between the two sets of data provided that the test takes due account of replication and provides assurance of identifying stability at least equal to that provided by equation: $|\bar{y}_1 - \bar{y}_2| \leq 0.3\sigma_{pt} + 2\sqrt{u^2(\bar{y}_1) + u^2(\bar{y}_2)}$

A t-test for significant difference at the 95% level of confidence, using the means for each PT samples (the number of units tested is 3 or more), may be used of identifying stability.

Sample distribution

-PT sample is wrapped with bubble plastic or cushion material if necessary and packed together with documents e.g. testing protocol, result report form and acknowledgement of PT sample form in the strong box to ensure that PT samples are in good condition when received by participants.

Sample distribution

-Testing protocol should explain the following,

* Introduction: details of PT sample and measurement, unit of measurement reporting basis and number of repeatability
* Test method and procedure
* References of the test method
* Measurand and/or other parameters to be reported by participant (if any)
* Number of digit after the decimal separator reported
* Deadline of submitting result
* Method for submitting result
* Name and address of coordinator

Sample distribution

-Acknowledgement of PT sample form should explain the following,
  * Name of participant
  * Date received
  * Sample number
  * Appearance of PT sample, container and parcel

-Additional PT sample is packed for the participants who are farthest in the north and south as the control sample for monitoring the stability from transportation.

-Participants who receive control sample are requested to send back to BDN upon receipt.

-After the receipt of control sample, stability test should be tested immediately.

Report result

-The Result report received from participants are collected and kept in the securely and confidentially.

-The result should be arranged in the sequence of laboratory code.

-The participants' result should be identified which are outliers and missing values.

Evaluation

The performance can be determined by the following methods.

-Estimates of deviation (measurement error)

Performance of the participants can be calculated as the difference between the result reported by a participant and the assigned value.

$$D_i = x_i - x_{pt}$$

Where

D_i = measurement error

x_i = the result reported by a participant *i* for the measurement of a property of PT sample in one round

Evaluation

The difference, D_i may be expressed in the same units as the assigned value or as a percentage difference.

$$D_i\% = 100\,(x_i - x_{pt})/x_{pt}\ \%$$

Evaluation

- **z score**

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

Where

x_{pt} is the assigned value

σ_{pt} is the standard deviation for proficiency assessment

The interpretation of z scores is as follows

$\lvert z \rvert \leq 2.0$	is considered to be acceptable.
$2.0 < \lvert z \rvert < 3.0$	is considered to give a warning signal.
$\lvert z \rvert \geq 3.0$	is considered to be unacceptable.

Evaluation

- **z' score**

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 score

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

Where

$u(x_{pt})$ is standard uncertainty of the assigned value

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.

Evaluation

Assigned value: the methods for determining are as follows

-Formulation

PT sample can be prepared by mixing materials with different known levels of a property in specified proportions, or by adding a specified proportion of a substance to a base material. The assigned value is derived by calculation from the masses of properties used.

-Certified reference value

When the PT sample used in the proficiency test is a certified reference material (CRM), the certified reference value is used as the assigned value. The standard uncertainty of the assigned value is derived from the information on uncertainty provided on the certificate.

Limitation: expensive
CRM may be known to participants

Evaluation

Assigned value: the methods for determining are as follows

-Results from one laboratory

An assigned value can be determined by a single laboratory using a reference method such as primary method.

-Concensus values from expert laboratories

The assigned value is calculated as the robust average of the results reported by the expert laboratories, using Algorithm A in Annex C of ISO 13528:2005(E).

-Consensus values from participants results

The assigned value is calculated as the robust average of the results reported by the participants, using Algorithm A in Annex C of ISO 13528:2005(E).

Evaluation

Robust analysis: Algorithm A yields robust estimates of the mean and standard deviation of the data as follows

p = the items of data
x* = robust average
s* = robust standard deviation

1) Sort the p items of data into increasing order by:
$x_{(1)}, x_{(2)}, \ldots, x_{(p)}$

2) Calculate initial values for x* and s* as:
x* = median of x_i (i= 1, 2,…,p)

s* = 1.483 median of $|x_i - x^*|$ with (i= 1, 2,…,p)

Evaluation

3) Update the values of x* and s* as follows:

Calculate : $\delta = 1.5\, s^*$

For each x_i (i= 1, 2,…,p) calculate :

$$x_i^* = \begin{cases} x^* - \delta & \text{when } x_i < x^* - \delta \\ x^* + \delta & \text{when } x_i > x^* + \delta \\ x_i & \text{otherwise} \end{cases}$$

Evaluation

4) Calculate the new values for x* and s* as:

$$x^* = \sum_{i=1}^{p} x_i^* / p$$

$$s^* = 1.134 \sqrt{\sum_{i=1}^{p} (x_i^* - x^*)^2 / (p-1)}$$

5) Update the values of x* and s* several times using modified data in 3) and 4), until there is no change from one iteration to the next in third significant figures of the robust mean and robust standard deviation (x* and s*)

Evaluation

-When the assigned value is derived as a robust average, the standard uncertainty of the assigned value may be estimated as

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

The uncertainty of the assigned value can be assumed to include the effects of uncertainty due to inhomogeneity, transport, and instability.

Evaluation

Limiting the uncertainty of the assigned value

The uncertainty of the assigned value may be considered to be negligible and need not to be included in the interpretation of the results according to the following criterion.

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

If the criterion is not met, the followings should be considered.

a) select method for determining the assigned value such that its uncertainty meets the criterion

b) use the uncertainty of the assigned value in the interpretation of the results by using z' score

Evaluation

Limiting the uncertainty of the assigned value

c) If the assigned value is derived from participant results, and the large uncertainty arises from differences between identifiable sub-populations of participants, report separate values and uncertainties for each sub-population (for example, participants using different measurement methods).

d) inform the participants that the uncertainty of the assigned value is not negligible, and evaluations could be affected

If none of a) - d) apply, then the participants shall be informed that no reliable assigned value can be determined and that no performance scores can be provided.

Evaluation

Standard deviation for proficiency assessment: the methods for determining are as follows

-By perception of experts

The standard deviation for proficiency assessment may be set at a value that corresponds to the level of performance which the technical experts of PT provider believe that it is reasonable for participants.

-By experience from previous rounds of a proficiency testing scheme

The standard deviation for proficiency assessment can be determined by experience with previous rounds for the same measurand with comparable property values and where participants use compatible measurement procedures.

Evaluation

Standard deviation for proficiency assessment: the methods for determining are as follows

-By use of a general model

The standard deviation for proficiency assessment can be derived from a general model for the reproducibility of the measurement method.
General model for chemical application : Horwitz model

$$\sigma_R = \begin{cases} 0.22\ c & \text{when } c < 1.2 \times 10^{-7} \\ 0.02\ c^{0.8495} & \text{when } 1.2 \times 10^{-7} \le c \le 0.138 \\ 0.01\ c^{0.5} & \text{when } c > 0.138 \end{cases}$$

c is the mass fraction of the chemical species to be determined
where $0 \le c \le 1$

Evaluation

Standard deviation for proficiency assessment: the methods for determining are as follows

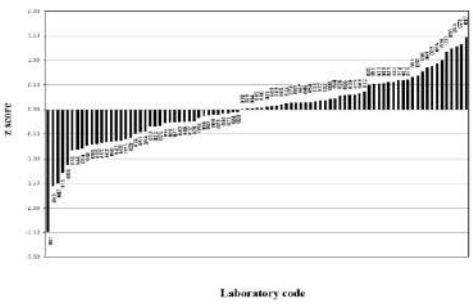
-From data obtained in the same round of a proficiency testing scheme

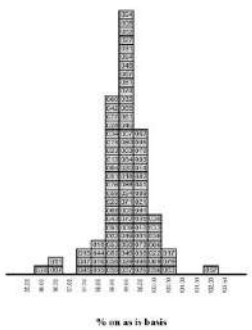
The standard deviation for proficiency assessment is calculated from the results of participants in the same round. A robust estimate of the standard deviation of the results reported by all the participants,calculated using robust analysis: Algorithm A, should be used to calculate.

Evaluation

-Graph should be made in order to simplify the presentation and interpretation and showed in the report.

-The mean of each participant and the z-score should be presented by histogram or bar-plots.





Evaluation

-The graph should enable each participant to see where participant's results fall in relation to those obtained by the other participants.

-Laboratory code should be used to represent the participants so that each participant is able to identify their own results but not able to determine which participant obtained any other result.

Reports

-The report should explain the general details of the PT round and the results of all participants, together with the performance evaluation and discussion of the result.

-Interim report is previously issued for reviewing the result recorded and giving comments by participants.

-The draft of interim report should be proposed for the consideration, and/or comments from Proficiency Testing management team and Technical advisory team

Reports

-Comments and/or corrections from participants on interim report should be collected and included in the final report. The draft of final report should be proposed for the consideration, and/or comments from Proficiency Testing management team and Technical advisory team. Then, the final report should be proposed to the BDN director for the approval.

-Interim/final report, letter informed code number of participant and Acknowledgement of interim/final report are packed in the secure and sealed envelope and sent to participants via EMS.

-The identity of interim/final report should be set by using report number

Certificate of participation

-Participants whose results are sent and evaluated by BDN will be certified for the participated round.

-The certificate should be proposed to the BDN director for the approval and issued date.