2.5.4.i Uniformity of Dosage Units

Published on: 08.11.2024 **Last date for comments:** 23.12.2024

This draft proposal contains monograph text for inclusion in the Indian Pharmacopoeia (IP). The content of this draft document is not final, and the text may be subject to revisions before publication in the IP. This draft does not necessarily represent the decisions or the stated policy of the IP or Indian Pharmacopoeia Commission (IPC).

Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

Description	Details
Document version	2.0
Amendments proposed for inclusion	IP 2026
Tentative effective date of Amendments	July, 2026
First draft published on IPC website for public comments	08.10.2024
Draft revision published on IPC website for public comments	-
Further follow-up action as required.	

2.5.4.i Uniformity of Dosage Units

Change **to: 2.5.4. Uniformity of Dosage Units**

This General Chapter has been harmonized with corresponding texts of the European Pharmacopoeia, the Japanese Pharmacopoeia and the United States Pharmacopeia.

Portions of the IP text that and are not part of the PDG harmonized text, are marked with symbols (♦♦).

[Note—In this chapter, uniformity of content and content uniformity are synonymous and unit and dosage unit are synonymous.

To ensure the consistency of dosage units, each unit in a batch should have a drug substance content within a narrow range around the label claim. Dosage units are defined as dosage forms containing a single dose or a part of a dose of drug substance in each dosage unit. ♦Unless otherwise stated,♦ the uniformity of dosage units specification is not intended to apply to solutions, suspensions, emulsions or gels in single-dose containers intended for local action following external, cutaneous administration.♦ The test for content uniformity is not required for multivitamin, single-vitamin and trace-element preparations.♦

The term 'uniformity of dosage unit' is defined as the degree of uniformity in the amount of the drug substance among dosage units. Therefore, the requirements of this chapter apply to each drug substance being comprised in dosage units containing one or more drug substances, unless otherwise specified elsewhere in this Pharmacopoeia.

The uniformity of dosage units can be demonstrated by either of two methods: content uniformity or ♦weight♦ variation (see Table 1).

The test for content uniformity of preparations presented in dosage units is based on the assay of the individual contents of drug substance(s) in a number of dosage units to determine whether the individual contents are within the limits set. The content uniformity method may be applied in all cases.

The test for ♦weight♦ variation is applicable for the following dosage forms:

(1) Solutions enclosed in single-dose containers and in soft capsules;

(2) Solids (including powders, granules and sterile solids) that are packaged in single-dose containers and contain no active or inactive added substances;

(3) Solids (including sterile solids) that are packaged in single-dose containers, with or without active or inactive added substances, that have been prepared from true solutions and freeze-dried in the final containers and are labelled to indicate this method of preparation;

(4) Hard capsules, uncoated tablets, or film-coated tablets, containing 25 mg or more of a drug substance comprising 25 per cent or more, by weight, of the dosage unit or, in the case of hard capsules, the capsule contents, except that uniformity of other drug substances present in lesser proportions is demonstrated by meeting content uniformity requirements.

The test for content uniformity is required for all dosage forms not meeting the above conditions for the ♦weight♦ variation test.♦Alternatively, products that do not meet the 25 mg/25 per cent threshold limit may be tested for uniformity of dosage units by weight variation instead of the content uniformity test on the following condition: the concentration Relative Standard Deviation (RSD) of the active substance in the final dosage units is not more than 2 per cent, based on process validation data and development data, and if there has been regulatory approval of such a change. The concentration RSD is the RSD of the concentration per dosage unit (*W/W* or *W/V*), where concentration per dosage unit equals the assay result per dosage unit divided by the individual dosage unit weight. See the RSD formula in Table 2♦.

Table 1 – Application of Content Uniformity (CU) and Weight Variation (WV) test for dosage forms

Dosage forms	**Type**	**Subtype**	**Dose and ratio of drug substance**	
			≥ 25mg and ≥ 25 per cent	< 25mg or < 25 per cent
Tablets	Uncoated		WV	CU
	Coated	Film coated	WV	CU
		Others	CU	CU

Capsules	Hard		WV	CU
	Soft	Suspensions, emulsions, gels	CU	CU
		Solutions	WV	WV
Solid in single unit containers	Single Component		WV	WV
	Multiple Components	Solution freeze-dried in final container	WV	WV
		Others	CU	CU
Solutions enclosed in single unit containers ♦ and into soft capsules♦			WV	WV
Others[a]			CU	CU

[a]Dosage forms not addressed by the other categories in this table including but not limited to suppositories, transdermal systems (patches), and semisolid preparations applied cutaneously and intended for systemic distribution of the drug substance.

Content Uniformity

Select not fewer than 30 units, and proceed as follows for the dosage form designated. Where different procedures are used for assay of the preparation and for the content uniformity test, it may be necessary to establish a correction factor to be applied to the results of the latter.

Solid dosage forms. Assay 10 units individually using an appropriate analytical method. Calculate the acceptance value (see Table 2).

Liquid or semi-solid dosage forms. Assay 10 units individually using an appropriate analytical method. Carry out the assay on the amount of well-mixed material that is removed from an individual container in conditions of normal use and express the results as delivered dose. Calculate the acceptance value (see Table 2).

Calculation of Acceptance Value

Calculate the Acceptance Value (*AV*) using the following formula for which the terms are as defined in Table 2.

$$|M - \bar{X}| + ks$$

Table 2

Variable	Definition	Conditions	Value
$\bar{X}$	Mean of individual contents ($x_1, x_2, \ldots, x_n$) expressed as a percentage of the label claim		
$(x_1, x_2, \ldots, x_n)$	Individual contents of the dosage units tested, expressed as a percentage of the label claim		
n	Sample size (number of dosage units in a sample)		
k	Acceptability constant	If n=10, then	2.4
		If n = 30, then	2.0
s	Sample standard deviation		?

RSD	Relative Standard Deviation (the sample standard deviation expressed as a percentage of the mean)		*100s / $\bar{X}$*
M (case 1) To be applied when T ≤ 101.5	Reference Value	If 98.5 per cent ≤ $\bar{X}$ ≤ 101.5 per cent, then	*M = $\bar{X}$ (AV=ks)*
		If $\bar{X}$ < 98.5 per cent, then	*M = 98.5 per cent (AV=98.5 - $\bar{X}$ + ks)*
		If $\bar{X}$ > 101.5 per cent, then	*M = 101.5 per cent (AV= $\bar{X}$ – 101.5 + ks)*
M (case 2) to be applied when T > 101.5	Reference Value	If 98.5 per cent ≤ $\bar{X}$ ≤ T, then	*M = $\bar{X}$ (AV=ks)*
		If $\bar{X}$ < 98.5 per cent, then	*M = 98.5 per cent (AV=98.5 - $\bar{X}$ + ks)*
		If $\bar{X}$ > T, then	M = T per cent *(AV= $\bar{X}$ - T + ks)*
Acceptance Value (AV)			General Formula $\lvert M - \bar{X} \rvert + ks$ Calculations are specified above for the different cases.
L1	Maximum allowed range for acceptance value		L1= 15.0 unless otherwise specified
L2	Maximum allowed range for deviation of each dosage unit tested from the calculated value of M	On the low side, no dosage unit result can be less than 0.75 M while on the high side, no dosage unit result can be more than 1.25 M (This is based on an L2 value of 25.0)	L2 = 25.0 unless otherwise specified
T	Target content per dosage unit at time of manufacture, expressed as a percentage of the label claim. Unless otherwise stated, T is equal to 100 percent or T is the manufacturer's approved target content per dosage unit.		

♦Weight♦ variation

Carry out an assay for the drug substance(s) on a representative sample of the batch using an appropriate analytical method. This value is result *A*, expressed as percentage of label claim (see Calculation of Acceptance Value). Assume that the concentration (weights of active substance per weight of dosage unit) is uniform. Select not less than 30 dosage units, and proceed as follows for the dosage form designated.

Uncoated or film-coated tablets. Accurately weigh 10 tablets individually. Calculate the content expressed as percentage of label claim, of each tablet from the ♦weight♦ of the individual tablet and the result of the assay. Calculate the acceptance value.

Hard capsules. Accurately weigh 10 capsules individually, taking care to preserve the identity of each capsule. Remove the contents of each capsule by a suitable means. Accurately weigh the emptied shells individually, and calculate for each capsule the net ♦weight♦ of its contents by subtracting the ♦weight♦ of the shell from the respective gross ♦weight♦. Calculate the drug substance content of each capsule from the ♦net weight♦ of the individual capsule ♦content♦ and the result of the a*ssay*. Calculate the acceptance value.

Soft capsules. Accurately weigh accurately 10 intact capsules individually to obtain their gross ♦weights♦, taking care to preserve the identity of each capsule. Then cut open the capsules by means of a suitable clean, dry cutting instrument such as scissors or a sharp open blade, and remove the contents by washing with a suitable solvent. Allow the occluded solvent to evaporate from the shells at room temperature over a period of about 30 minutes, taking precautions to avoid uptake or loss of moisture. Weigh the individual shells, and calculate the net contents. Calculate the drug substance content in each capsule from the ♦weight♦ of product removed from the individual capsules and the result of the assay. Calculate the acceptance value.

Solid dosage forms other than tablets and capsules. Proceed as directed for hard capsules, treating each unit as described therein. Calculate the acceptance value.

Liquid ♦or semi-solid♦ dosage forms. Accurately weigh the amount of liquid ♦or semi-solid♦ that is removed from each of 10 individual containers in conditions of normal use. If necessary, compute the equivalent volume after determining the density. Calculate the drug substance content in each container from the ♦weight♦ of product removed from the individual containers and the result of the assay. Calculate the acceptance value.

Calculation of Acceptance value

Calculate the acceptance value (*AV*) as shown in content uniformity, except that the individual contents of the units are replaced with the individual estimated contents defined below.

$x_1, x_2, ..., x_n$ = individual estimated contents of the dosage units tested, using the formula:

$$x_i = w_i \times \frac{A}{\bar{W}}$$

where,

$w_1, w_2, ..., w_n$= individual weights of the dosage units tested;

A = content of drug substance (percentage of label claim) obtained using an appropriate analytical method (assay);

$\bar{W}$ = mean of individual ♦weights♦ ($w_1, w_2, ..., w_n$).

Criteria. Unless otherwise specified, apply the following criteria.

Solid, semi-solid and liquid dosage forms. The requirements for dosage uniformity are met if the acceptance value of the first 10 dosage units is less than or equal to $L1$ per cent. If the acceptance value is more than $L1$ per cent, test the next 20 dosage units and calculate the acceptance value. The requirements are met if the final acceptance value of the 30 dosage units is less than or equal to $L1$ per cent and no individual content of ♦any♦ dosage unit is less than $(1 - (0.01)(L2))\ M$ nor more than $(1 + (0.01)(L2))\ M$ ♦as specified♦ in the calculation of acceptance value under content uniformity or under ♦weight♦ variation. Unless otherwise specified, $L1$ is 15.0 and $L2$ is 25.0.