Universal Tests / Criteria : New Drug Substances

d) Impurities:

Impurities in new drug subsances can be classified into the following categories (ICH Q3A):

1. **Organic impurities**
   - Starting materials
   - By-products
   - Intermediates
   - Degradation products
   - Reagents, ligands and catalysts

إذا اثبت انهم بس synthesis impurity ما بنتقلو معنا لل tablet

هاد بروح معنا على doseg form

2. **Inorganic impurities**
   - Reagents, ligands and catalysts
   - Heavy metals or other residual metals
   - Inorganic salts
   - Other materials (e.g., filter aids, charcoal)

Universal Tests / Criteria : New Drug Substances

*d) **Impurities:***

3. Residual solvents

Class 1 solvents: Solvents to be avoided

- Known human carcinogens, strongly suspected human carcinogens, and environmental hazards.
- E.g. Benzene, CCl4

Class 2 solvents: Solvents to be limited

- Non-genotoxic animal carcinogens or possible causative agents of other irreversible toxicity such as neurotoxicity or teratogenicity.
- Solvents suspected of other significant but reversible toxicities.
- E.g. Acetonitrile, Chloroform, Methanol, Dichloromethane, hexane

Class 3 solvents: Solvents with low toxic potential

- Solvents with low toxic potential to man; no health-based exposure limit is needed. Class 3 solvents have permitted daily exposure (PDE)s of 50 mg or more per day.
- E.g. Acetic acid, Ethanol, Ethyl acetate, Dimethyl sulfoxide, Acetone

Universal Tests / Criteria : New Drug products

d) impurities:

- Organic and inorganic impurities (degradation products) and residual solvents are included in this category.
- Organic impurities arising from degradation of the new drug substance and impurities that arise during the manufacturing process for the drug product should be monitored in the new drug product.
- Process impurities from the new drug substance synthesis are normally controlled during drug substance testing, and therefore are not included in the total impurities limit.
- However, when a synthesis impurity is also a degradation product, its level should be monitored and included in the total degradation product limit.

Universal Tests / Criteria : New Drug products

d) impurities:

- Acceptance limits should be stated for individual specified degradation products, which may include both identified and unidentified degradation products as appropriate, and total degradation products.
- When it has been conclusively demonstrated via appropriate analytical methodology, that the drug substance does not degrade in the specific formulation, and under the specific storage conditions proposed in the new drug application:

-→ degradation product testing may be reduced or eliminated upon approval by the regulatory authorities.

Specific Tests / Criteria : New Drug Substances

The following tests may be considered on a case by case basis for drug substances.

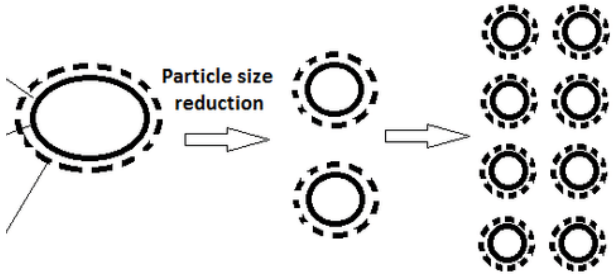
a) Physicochemical properties:

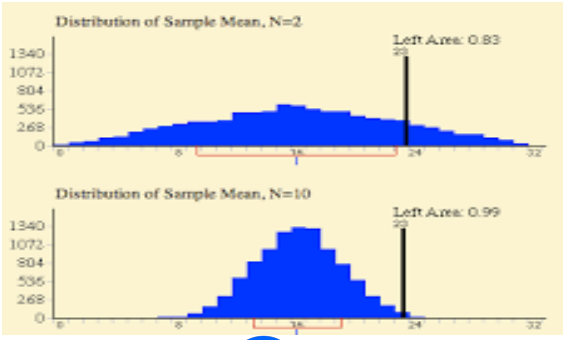
e.g. pH of an aqueous solution, melting point / range, and refractive index.

b) Particle size: هادspacific يا بحطها يا مابحطها

For some new drug substances intended for use in solid or suspension drug products, particle size can have a significant effect on dissolution rates, bioavailability, and / or stability.

In such instances, procedure for testing of size distribution and acceptance criteria should be provided.





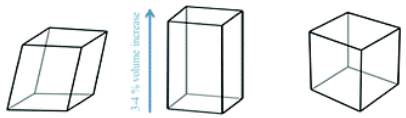
كيف يأثر particle size of active ingredients على stability
اذا كان بsusb يأثر على sedimentation وممكن يعمل kicking
ولو كان عندي powder كيف رح يتأثر فيه في عندي اشي اسمه hygroscopy محبه للماء اذا كانت particle size صغيره يعني بدها sarfuec area أعلى عشان absorption للماء أعلى فرح تمتص ماء أكثر مقا نه مع particle الأكبر واذا تمتص ماء أكثر رح تأثر على stability

هسا احنا عنا amorphous وفي عنا crysality ونادر نلاقي amorphous بالفارماكوبيا لانه مش stable
بالنسبه لل A, B, C crystaline يعني الها أكثر من form
طيب مثلا انا ما بدي crystaline B بدي A وهدول يختلفون عن بعض ب physochemical property ف احتمال يكون bioavailability مختلف فكيف اضمن انه النوع الي طلبته هو نفسه الي وصلني عن طريق تستات تعمل identification for polymorphic forms مثال الكلورو فينكول

Specific Tests / Criteria : New Drug Substances

c) Polymorphic forms:

In cases where different crystal forms exist which have been shown to affect drug product performance, bioavailability or stability, then the appropriate solid state should be specified.



Example: Part of Chloramphenicol monograph in USP

Melting range ⟨741⟩: between 149° and 153°.

Specific rotation ⟨781S⟩: between +17.0° and +20.0°.

Test solution: 50 mg, undried, per mL, in dehydrated alcohol.

Crystallinity ⟨695⟩: meets the requirements.

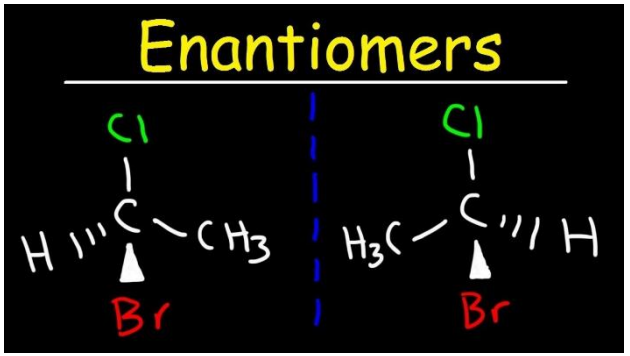
Bacterial endotoxins ⟨85⟩—Where Chloramphenicol is intended for use in preparing injectable dosage forms, it contains

Specific Tests / Criteria : New Drug Substances

d) Tests for chiral new drug substances:

For a drug substance developed as a single enantiomer:

1. The identity test(s) should be capable of distinguishing both enantiomers and the racemic mixture.
2. An enantioselective determination of the drug substance should be part of the specification.
3. Control of the other enantiomer should be considered in the same manner as for other impurities.



Specific Tests / Criteria : New Drug Substances

e) ***Water content:*** This test is important in cases where the new drug substance is known to be:

1. hygroscopic
2. degraded by moisture
3. is a hydrate.

The acceptance criteria may be justified with data on the effects of hydration or moisture absorption.

In some cases, a Loss on Drying procedure may be considered adequate; however, a detection procedure that is specific for water (e.g., Karl Fischer titration) is preferred.

Specific Tests / Criteria : New Drug Substances

f) Inorganic impurities:

The need for inclusion of tests and acceptance criteria for inorganic impurities (e.g., catalysts) should be studied during development and based on knowledge of the manufacturing process.

Procedures and acceptance criteria for:

A. sulfated ash / residue on ignition should follow pharmacopoeial precedents;

B. other inorganic impurities may be determined by other appropriate procedures, e.g., atomic absorption spectroscopy.

Specific Tests / Criteria : New Drug Substances

g) ***Microbial limits****:* There may be a need to specify:

1. the total count of aerobic microorganisms → 10^3
2. the total count of yeasts and molds → for oral solid 10^2 colony
3. the absence of specific objectionable bacteria (e.g., *Staphylococcus aureus, Escherichia coli, Salmonella, Pseudomonas aeruginosa*).

- These should be suitably determined using pharmacopoeial procedures.
- The type of microbial test(s) and acceptance criteria should be based on the Limit تتغير بالاعتماد عليهم

1. nature of the drug substance,
2. method of manufacture,
3. the intended use of the drug product:

ما بعملها لكل شي

- sterility testing may be appropriate for drug substances manufactured as sterile
- endotoxin testing may be appropriate for drug substances used to formulate an injectable drug product.

حكت مش فهم وعملت سكيب

Specific Tests / Criteria : New Drug products

- Additional tests and acceptance criteria generally should be included for **particular new drug products.**
- The ICH guidelines in Q6A presents a **representative** sample of both the drug products and the types of tests and acceptance criteria which may be appropriate.
- The specific dosage forms addressed include solid oral drug products, liquid oral drug products, and parenterals (small and large volume).
- Application of the concepts in this guideline to other dosage forms is encouraged.

Specific Tests / Criteria : New Drug products

Solid oral drug products:

a) Dissolution:

حتى كمان لـ الكريمات for systemic USP

- The specification for solid oral dosage forms normally includes a test to measure release of drug substance from the drug product.
- immediate-release dosage forms → normally Single-point measurements

يعني Limit من اقل من 85% وـ على مدة 30 دقيقة

- extended-release dosage forms → multiple time point sampling should be performed

في الفولتورين

- delayed-release dosage forms → two-stage testing (using different media in succession or in parallel, as appropriate). E.g pH: 1.2, 6.8

Specific Tests / Criteria : New Drug products

Solid oral drug products:

a) Dissolution:

- For immediate-release drug products where changes in dissolution rate have been demonstrated to significantly affect bioavailability, it is desirable to develop test conditions which can distinguish batches with unacceptable bioavailability.
- If changes in formulation or process variables significantly affect dissolution and such changes are not controlled by another aspect of the specification, it may also be appropriate to adopt **dissolution test conditions** which can distinguish these changes.
- Where dissolution significantly affects bioavailability, the acceptance criteria should be set to **reject** batches with unacceptable bioavailability. Otherwise, test conditions and acceptance criteria should be established which pass clinically acceptable batches

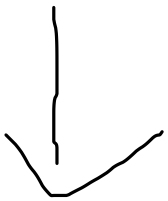
Specific Tests / Criteria : New Drug products

Solid oral drug products:

a) Dissolution:

- For extended-release drug products, in vitro / in vivo correlation (IVIVC) may be used to establish acceptance criteria when human bioavailability data are available for formulations exhibiting different release rates.
- Where such data are not available, and drug release cannot be shown to be independent of in vitro test conditions, then acceptance criteria should be established on the basis of available batch data.
- Normally, the permitted variability in mean release rate at any given time point should not exceed a total numerical difference of +/-10% of the labeled content of drug substance (i.e., a total variability of 20%: a requirement of 50 +/- 10% thus means an acceptable range from 40% to 60%), unless a wider range is supported by a bioequivalency study.

بقدر استغني عن dissolution بحاله وحده ويعتبر disintegration كافي لما يكون rapid dissolve وبعتبره هيك اذا)80٪ من الدواء ذاب او صار له release تماما خلال 15 دقيقه ضمن pH 1.2,6.8. هل هاد الشرط كافي اعتبره rapid. لا..... ولازم يكون الدواء الي داخل tablet high Soluble على physiological pH وهاي تكون لو أخذت maximum dose وذوبتها ب 250 مل من الماء يذوب تماما اذا تحقق هدول الشرطين ما بكون بحاجه dissolution



Specific Tests / Criteria : New Drug products

spacefic for solid doseg form يعتبر disintegration عنا
tablets and capsules وخص نص لازم تنحل البودره تبعهم قبل ما
dissolution يصير

Solid oral drug products:

b) Disintegration:

- For rapidly dissolving (dissolution >80% in 15 minutes at pH 1.2, 4.0 and 6.8) products containing drugs which are highly soluble throughout the physiological range (dose/solubility volume < 250 mL from pH 1.2 to 6.8), disintegration may be substituted for dissolution.
- Disintegration testing is most appropriate when a relationship to dissolution has been established or when disintegration is shown to be more discriminating than dissolution.
- In such cases dissolution testing may not be necessary.
- It is expected that development information will be provided to support the robustness of the formulation and manufacturing process with respect to the selection of dissolution vs. disintegration testing.

Specific Tests / Criteria : New Drug products

Solid oral drug products:

c) Hardness/friability:

- It is normally appropriate to perform hardness and/or friability testing as an in-process control → normally not necessary to include these attributes in the specification.
- If the characteristics of hardness and friability have a critical impact on drug product quality (e.g., chewable tablets), acceptance criteria should be included in the specification.

Specific Tests / Criteria : New Drug products

Solid oral drug products:

d) Uniformity of dosage units:

- This term includes
  - the mass of the dosage form
  - the content of the active substance in the dosage form
- A pharmacopoeial procedure should be used.
- In general, the specification should include one or the other but not both.
- If appropriate, these tests may be performed in-process; however, the acceptance criteria should be included in the specification.

Specific Tests / Criteria : New Drug products

Solid oral drug products:

d) Uniformity of dosage units:

<905> UNIFORMITY OF DOSAGE UNITS (USP monograph) →

Table 1. Application of Content Uniformity (CU) and Weight Variation (WV) Tests for Dosage Forms

Dosage Form	Type	Subtype	Dose & Ratio of Drug Substance: ≥25 mg and ≥25%	Dose & Ratio of Drug Substance: <25 mg or <25%
Tablets	Uncoated		WV	CU
	Coated	Film	WV	CU
		Others	CU	CU
Capsules	Hard		WV	CU
	Soft	Suspension, emulsion, or gel	CU	CU
		Solutions	WV	WV
Solids in single-unit containers	Single component		WV	WV
	Multiple components	Solution freeze-dried in final container	WV	WV
		Others	CU	CU
Solutions in unit-dose containers and into soft capsules			WV	WV
Others				CU

Specific Tests / Criteria : New Drug products

Solid oral drug products:

e) Water content:

- A test for water content should be included when appropriate.
- The acceptance criteria may be justified with data on the effects of hydration or water absorption on the drug product.
- A detection procedure which is specific for water (e.g., Karl Fischer titration) is preferred.

Specific Tests / Criteria : New Drug products

Solid oral drug products:

f) Microbial limits:

- Acceptance criteria should be set for:
  - the total count of aerobic microorganisms,
  - the total count of yeasts and molds,
  - the absence of specific objectionable bacteria (e.g., *Staphylococcus aureus, Escherichia coli, Salmonella, Pseudomonas aeruginosa*).
- These should be determined using **pharmacopoeial procedures**, and at a sampling frequency or time point in manufacture which is justified by data and experience.

➢ The type of microbial test(s) and acceptance criteria should be based on the

1. nature of the drug substance,
2. method of manufacture,
3. the intended use of the drug product:

Specific Tests / Criteria : New Drug products

Solid oral drug products:

f) Microbial limits:

- In general, it is advisable to test the drug product unless:
  1. its components are tested before manufacture and
  2. the manufacturing process is known, through validation studies, not to carry a significant risk of microbial contamination or proliferation.

➢ With acceptable scientific justification, it should be possible to propose **no microbial limit testing for solid oral dosage forms. Why???**

Specific Tests / Criteria : New Drug products

USP 2012

ايام التعقيم اخخ

Table 1. Acceptance Criteria for Microbiological Quality of Nonsterile Dosage Forms

Route of Administration	Total Aerobic Microbial Count (cfu/g or cfu/mL)	Total Combined Yeasts/Molds Count (cfu/g or cfu/mL)	Specified Microorganism(s)
Nonaqueous preparations for oral use	10^3	10^2	Absence of *Escherichia coli* (1 g or 1 mL)
Aqueous preparations for oral use	10^2	10^1	Absence of *Escherichia coli* (1 g or 1 mL)
Rectal use	10^3	10^2	—
Oromucosal use	10^2	10^1	Absence of *Staphylococcus aureus* (1 g or 1 mL) Absence of *Pseudomonas aeruginosa* (1 g or 1 mL)
Gingival use	10^2	10^1	Absence of *Staphylococcus aureus* (1 g or 1 mL) Absence of *Pseudomonas aeruginosa* (1 g or 1 mL)
Cutaneous use	10^2	10^1	Absence of *Staphylococcus aureus* (1 g or 1 mL) Absence of *Pseudomonas aeruginosa* (1 g or 1 mL)
Nasal use	10^2	10^1	Absence of *Staphylococcus aureus* (1 g or 1 mL) Absence of *Pseudomonas aeruginosa* (1 g or 1 mL)
Auricular use	10^2	10^1	Absence of *Staphylococcus aureus* (1 g or 1 mL) Absence of *Pseudomonas aeruginosa* (1 g or 1 mL)
Vaginal use	10^2	10^1	Absence of *Pseudomonas aeruginosa* (1 g or 1 mL) Absence of *Staphylococcus aureus* (1 g or 1 mL) Absence of *Candida albicans* (1 g or 1 mL)
Transdermal patches (limits for one patch including adhesive layer and backing)	10^2	10^1	Absence of *Staphylococcus aureus* (1 patch) Absence of *Pseudomonas aeruginosa* (1 patch)
Inhalation use (special requirements apply to liquid preparations for nebulization)	10^2	10^1	Absence of *Staphylococcus aureus* (1 g or 1 mL) Absence of *Pseudomonas aeruginosa* (1 g or 1 mL) Absence of bile-tolerant Gram-negative bacteria (1 g or 1 mL)

Specific Tests / Criteria : New Drug products

Oral liquids:

One or more of the following specific tests will normally be applicable to oral liquids and to powders intended for reconstitution as oral liquids.

a) pH: Acceptance criteria for pH should be provided where applicable and the proposed range justified.

Specific Tests / Criteria : New Drug products

Oral liquids:

b) Uniformity of dosage units

In general, the specification should include weight variation or content uniformity test but not both.

If dispensing equipment (such as medicine droppers or dropper tips for bottles) is an integral part of the packaging, this equipment should be used to measure the dose. Otherwise, a standard volume measure should be used.

If appropriate, tests may be performed in-process; however, the acceptance criteria should be included in the specification.

For powders for reconstitution, uniformity of mass testing is generally considered acceptable.

Specific Tests / Criteria : New Drug products

Oral liquids:

c) Microbial limits

- Skip testing may be an appropriate approach where permissible.
- With acceptable scientific justification, it may be possible to propose no microbial limit testing for powders intended for reconstitution as oral liquids.
- Acceptance criteria should be set for:
  1. the total count of aerobic microorganisms,
  2. the total count of yeasts and molds,
  3. the absence of specific objectionable bacteria (e.g., Staphylococcus aureus, Escherichia coli, Salmonella, Pseudomonas aeruginosa).

Specific Tests / Criteria : New Drug products

Oral liquids:

d) Antimicrobial preservative content:

Acceptance criteria for preservative content should be established for oral liquids needing an antimicrobial preservative.

The lowest specified concentration of antimicrobial preservative should be demonstrated to be effective in controlling microorganisms by using a pharmacopoeial antimicrobial preservative effectiveness test.

هاي كثير مهمه هسا كيف نحدد shelf life من خلال نضل نتبع كل سنه من خلال stability لحتى نوصل لنقطه ممكن يزيد impurity او ينزل assay وهاد يكون shelf life طيب سؤال هل فش حدا بقيس assay of preservative هسا assay تبعه مسموح ينزل كثير بس هاد يتم تحديده اذا زاد نسبه micro يعني فشل preservative فليش نغامر لذلك خلال مرحله development يعملو اشي ليحددو rang الي يكون عليه preservative is وبعمل active antimicrobial preservative effective

Specific Tests / Criteria : New Drug products

Oral liquids:

d) Antimicrobial preservative content:

- normally performed at release → Under certain circumstances, in-process instead of release testing → however, the acceptance criteria should remain part of the specification.
- Antimicrobial preservative effectiveness should be demonstrated:
  - during development,
  - during scale up, and
  - throughout the shelf-life.

Specific Tests / Criteria : New Drug products

Oral liquids:

e) Antioxidant preservative content:

- Release testing for antioxidant content should normally be performed.
- Under certain circumstances, where justified by developmental and stability data,
  - shelf-life testing may be unnecessary,
  - in-process testing instead of release testing → the acceptance criteria should remain part of the specification.

Specific Tests / Criteria : New Drug products

Oral liquids:

f) Extractables:

- Tests and acceptance criteria for extractables from the container/closure system components (e.g., rubber stopper, cap liner, plastic bottle, etc.) are considered appropriate for oral solutions packaged in:
  - non-glass systems
  - glass containers with non-glass closures.

Package material المواد الي تطلع من formula على (بس ما بوصلها) اذا كانت solution

"Extractables are compounds that can be extracted from the **container closure system** when in the presence of a solvent."

U.S. Food and Drug Administration (FDA)

هي الي تصير بال formula وتصير فيها

"Leachables are compounds that leach into the **drug product formulation** from the container closure system as a result of direct contact with the formulation."

U.S. Food and Drug Administration (FDA)

Specific Tests / Criteria : New Drug products

Oral liquids:

f) Extractables:

- Generally, where development and stability data show evidence that extractables are consistently below acceptable and safe levels, elimination of this test can normally be accepted.
- This should be reinvestigated if the container/closure system or formulation changes.

Specific Tests / Criteria : New Drug products

Oral liquids:

g) Alcohol content:

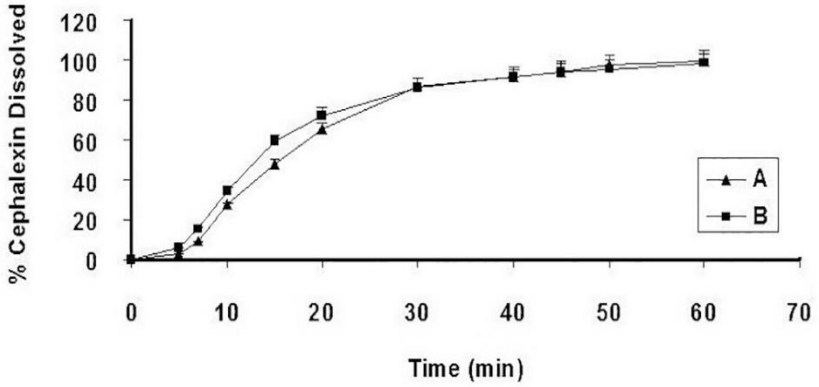
- Where it is declared quantitatively on the label in accordance with pertinent regulations, the alcohol content should be specified.
- It may be **assayed or calculated**.

Specific Tests / Criteria : New Drug products

Oral liquids:

h) Dissolution:

- In addition to the attributes recommended immediately above, it may be appropriate (e.g., insoluble drug substance) to include dissolution testing and acceptance criteria for:
  - oral suspensions
  - dry powder products for resuspension.
- The testing apparatus, media, and conditions should be pharmacopoeial, if possible, or otherwise justified.

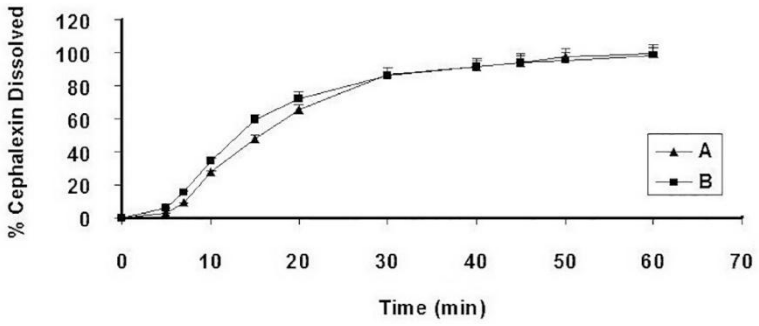


Specific Tests / Criteria : New Drug products

Oral liquids:

h) Dissolution:

- Single-point measurements are normally considered suitable for immediate-release dosage forms.
- Multiple-point sampling, at appropriate intervals, should be performed for modified-release dosage forms.
- Acceptance criteria should take into account the dissolution profiles of the batches that showed acceptable performance in vivo.

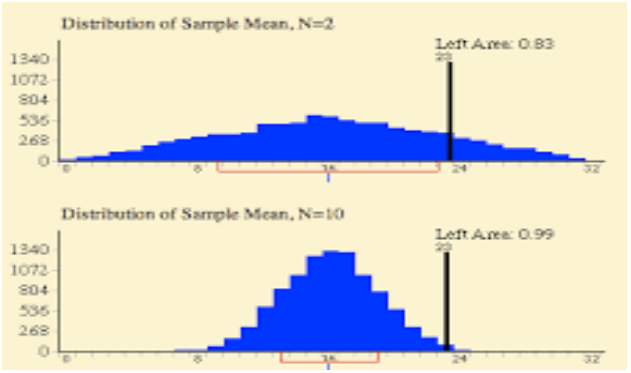


Specific Tests / Criteria : New Drug products

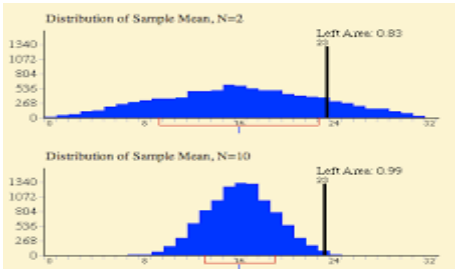
Oral liquids:

i) Particle size distribution:

- Quantitative acceptance criteria and a procedure for determination of particle size distribution may be appropriate for oral suspensions.
- performed at release→ in-process test when justified by product development data.



Specific Tests / Criteria : New Drug products

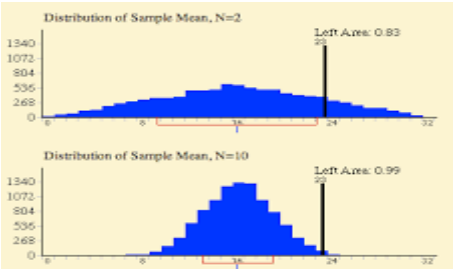


Oral liquids:

i) Particle size distribution:

- If these products have been demonstrated during development to have consistently rapid drug release characteristics, exclusion of a particle size distribution test from the specification may be proposed.
- Particle size distribution testing may also be proposed in place of dissolution testing; justification should be provided.
- Developmental data should be considered when determining the need for either a dissolution procedure or a particle size distribution procedure.

Specific Tests / Criteria : New Drug products



Oral liquids:

i) Particle size distribution:

- The acceptance criteria should include acceptable particle size distribution in terms of the percent of total particles in given size ranges. The mean, upper, and / or lower particle size limits should be well defined.
- The potential for particle growth should be investigated during product development; the acceptance criteria should take the results of these studies into account.

Specific Tests / Criteria : New Drug products

Oral liquids:

j) Redispersibility:

- For oral suspensions which settle on storage (produce sediment), acceptance criteria for redispersibility may be appropriate.
- The procedure (mechanical or manual) should be indicated. Shaking may be an appropriate procedure.

Specific Tests / Criteria : New Drug products

Oral liquids:

k) Rheological properties:

- For relatively viscous solutions or suspensions, it may be appropriate to include rheological properties (viscosity/specific gravity) in the specification.

l) Reconstitution time:

- Acceptance criteria for reconstitution time should be provided for dry powder products which require reconstitution.

m) Water content:

- For oral products requiring reconstitution, a test and acceptance criterion for water content should be proposed when appropriate.

Specific Tests / Criteria : New Drug products

Parenteral Drug Products :

a) Uniformity of dosage units

b) pH: Acceptance criteria for pH should be provided where applicable and the proposed range justified.

c) Sterility: All parenteral products should have a test procedure and acceptance criterion for evaluation of sterility. Where data generated during development and validation justify parametric release, this approach may be proposed for terminally sterilized drug products.

d) Endotoxins/Pyrogens: A test procedure and acceptance criterion for endotoxins, using a procedure such as the limulus amoebocyte lysate test, should be included in the specification.

Pyrogenicity testing may be proposed as an alternative to endotoxin testing where justified.

Specific Tests / Criteria : New Drug products

Parenteral Drug Products :

e) Particulate matter: Parenteral products should have appropriate acceptance criteria for particulate matter.

This will normally include acceptance criteria for:

1. visible particulates and / or clarity of solution,
2. for sub-visible particulates as appropriate.

f) Water content:

For **non-aqueous** parenterals, and for parenteral products for reconstitution, a test procedure and acceptance criterion for water content should be proposed when appropriate.

Loss on drying (LOD) is generally considered sufficient for parenteral products, if the effect of absorbed moisture vs. water of hydration has been adequately characterized during development.

In certain cases a more specific procedure (e.g., Karl Fischer titration) may be preferred.

Specific Tests / Criteria : New Drug products

Parenteral Drug Products :

g) Antimicrobial preservative content:

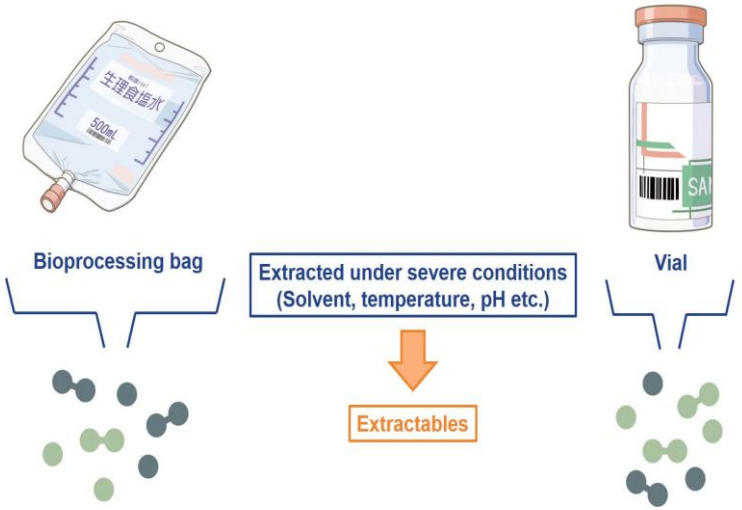
- For parenteral products needing an antimicrobial preservative (e.g. multidose vials).
- The **lowest** specified concentration of antimicrobial preservative should be demonstrated to be effective in controlling microorganisms by using a pharmacopoeial antimicrobial preservative effectiveness test.

Specific Tests / Criteria : New Drug products

Parenteral Drug Products :

i) Extractables:

- Control of extractables from container/closure systems is considered significantly more important for parenteral products than for oral liquids.
- However, where development and stability data show evidence that extractables are consistently below the levels that are demonstrated to be acceptable and safe, elimination of this test can normally be accepted.
- This should be **reinvestigated** if the container/closure system or formulation changes.



Specific Tests / Criteria : New Drug products

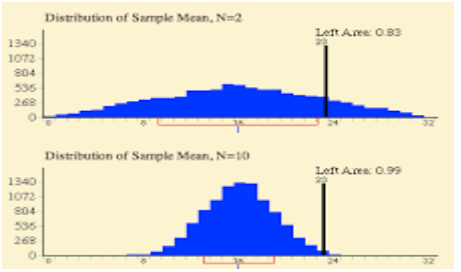
Parenteral Drug Products :

j) Functionality testing of delivery systems:

- Parenteral formulations packaged in pre-filled syringes, autoinjector cartridges, or the equivalent should have test procedures and acceptance criteria related to the functionality of the delivery system (e.g.inj. volume).
- Under certain circumstances these tests may be performed in-process.
- Data generated during product development may be sufficient to justify skip lot testing or elimination of **some or all a**ttributes from the specification.

لو عندي قلم انسولين لازم احدد الجرعه اول اذا فيه volume
معين انه كل حقنه فيها volume كذا

Specific Tests / Criteria :
New Drug products



Parenteral Drug Products :

k) Osmolarity: When the tonicity of a product is declared in its labeling, appropriate control of its osmolarity should be performed.

l) Particle size distribution:

Quantitative acceptance criteria and a procedure for determination of particle size distribution may be appropriate for injectable suspensions.

Particle size distribution testing may also be proposed in place of dissolution testing, when development studies demonstrate that particle size is the primary factor influencing dissolution; justification should be provided.

m) Redispersibility: similarly to oral liquids

n) Reconstitution time: similarly to oral liquids