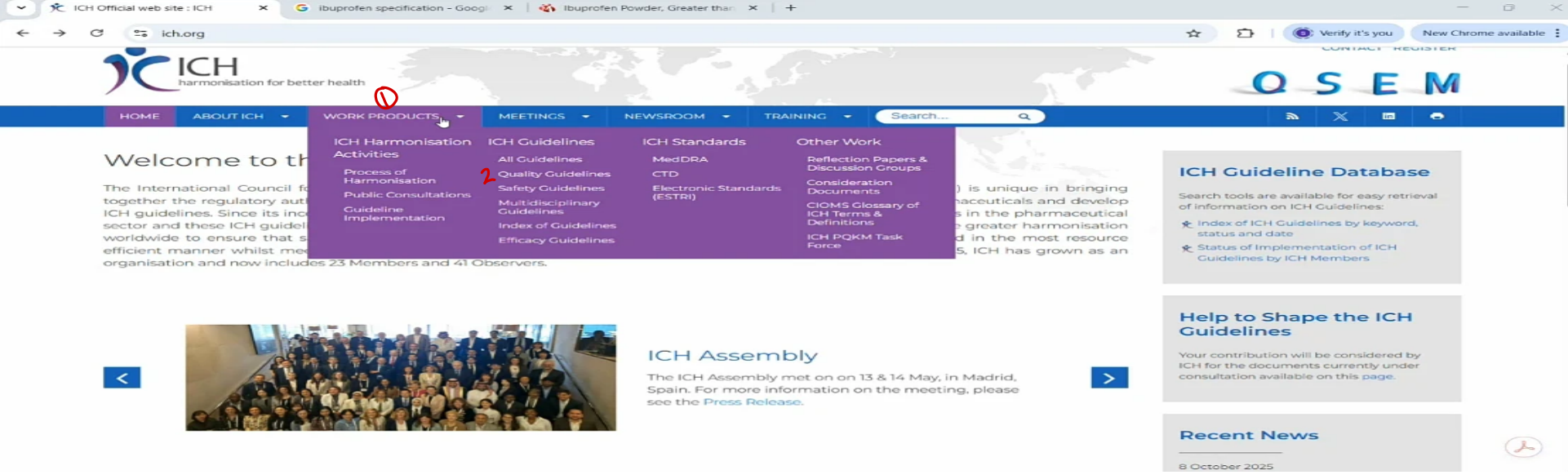
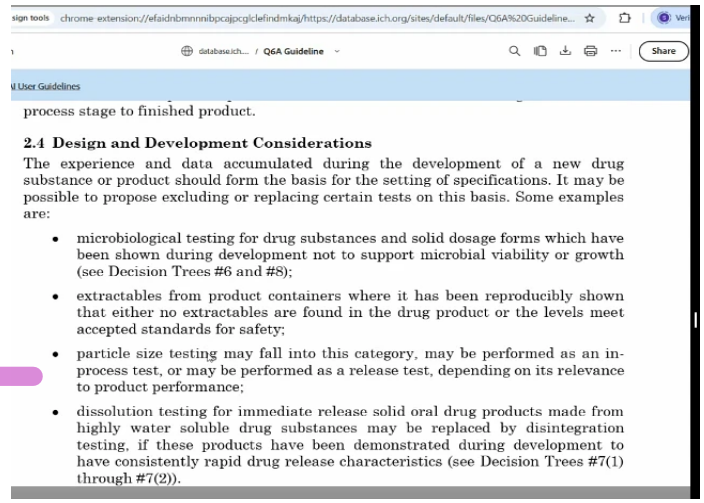
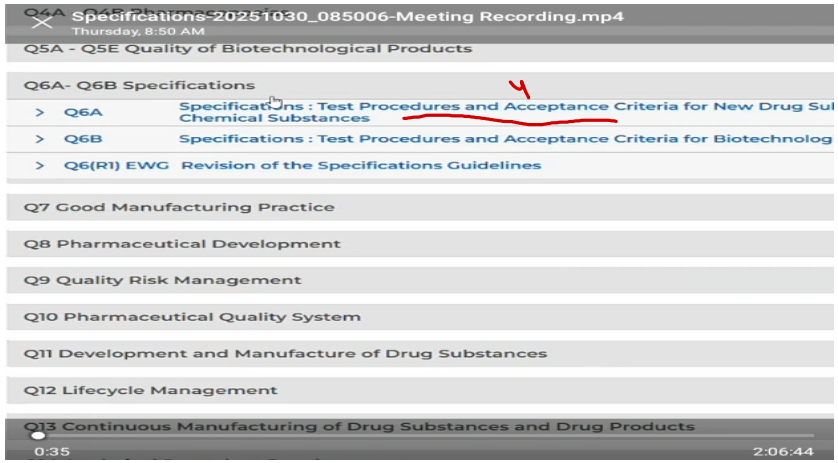


الملف





ننكبس على Q6A ونفتح الملف رح يكون فيه تعريف عنه وفي فهرس وكيف نطبقه ومتى

احنا كيف نعمل spacefication وبناءا على شو بحطها طبعا مصدر السلايدات هو gaidline ورح نشوف انه بالاخر السلايدات رح يصير عنا repetition للمواضيع

Company Details

IOL CHEMICALS AND PHARMACEUTICALS LTD

CERTIFICATE OF ANALYSIS

نميزها من خلال وجود result اخر اشي

Product Name	: IBUPROFEN IP	Batch No.	: 4000/1101/24/A-0043B
Date of Mfg.	: Jan. - 2024	Date of Analysis	: 05/02/2024
Date of Expiry	: Dec. -2028	A. R No.	: AR/FP/24/002375
Drug Lic No.	: 1689-OSP	Batch Qty	: 1000 Kg
Dispatch Qty	: 1000 Kg	Packing	: 20 X 50 Kg

Sr. No	TEST	SPECIFICATIONS	RESULTS
1.	Description	A White or almost white crystalline powder or colourless crystals; odour slight	White crystalline powder.
2.	Solubility	Freely soluble in acetone ,in chloroform,in ethanol(95%) and in ether,practically insoluble in water..It dissolves in dilute solutions of alkali hydroxides and carbonates.	Complies
3.	Identification A) Identification A, B) Identification B,C	A) By IR The infra-red absorbance spectrum obtained from the sample should be concordant with spectrum obtained with that Ibuprofen RS/WS or with reference spectrum of Ibuprofen. B) By UV Exhibits 2 absorption maxima, at about 264 nm and about 272 nm. The ratio of the absorbance measured at the maximum at about 264 nm to that	Complies Not applicable

Description

حكينا عنه قبل مثال لون البروده لازم يكون موضح

Seller Contac

Nandlal Bankat

Akhil Tody

1204, 12th F West, Mumb

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حكينا قبل عن البراميل الي توصل على المستودع وانه لازم يكون عليها label رغم ذلك لازم اتأكد منها(المادة الفعاله Api, drug substances تجي على المستودع بس ما تدخل عليه مباشره انما تنحط في منطقه اسمها curntins لحتى اعمل الها identification هسا دخلت طيب بكون عليها label لونه اصفر وهاي بعمل عليها sampling وبوديه علىQC بحلل العينه according the spacefication اذا أمورها تمام اطلعها واحط عليها label لونه أخضر انه وضعها ممتاز واذا لا بحط عليها label لونه احمر وهاي ممنوع تستخدم

هسا وصلنا لمرحله identification test: لازم يكون قادر انه يحكي انه هاي الماده هي ibuprofen مثلا.

① First ident A

اذا عملته كأني بحكي انه هاد اكيد هو ibuprofen زي البصمه يعني والغالب. يكون INR وفكرته عمله انه بحلل الماده ونتأكد من تحليلها اذا هاي الماده صح او لا من خلال refrance ويكون تفاصيلها بالضبط كل تيست. بال monograph

② second iden B,C,D

في tests لحالها ما بتكفى non spacefic فبدي test ثاني يأكد الي انه test الأول صح ويكونون هدول B يتضمن UV و C يتضمن TLC وكل هاد حتى اتأكد انه ibuprofen

طيب أيمتا اطبق test 1 or test 2 ؟؟ نفرض مثلا شركه ما عندها جهاز INR وعندها UV and TLC هون نعمل التست الثاني

بالنسبه لموضوع Appearance of solutions وفي عندي spacefic rotation ونوصل لموضوع related substances الي هو impurity وفي عندي نوعين منهم. وبحللهم عن طريق IBLC
1 هاد يكون unknown يعني ما بع ف شو هم
2 هاي بتكون known يعني بنعرف شو chemical structure الها
وفي عندي نوع impurity مفصول عنهم اسمه impurity F ومفصول عنهم لانه اله test لحاله. واسم التيست GC

Residual

ننحكي عن loss of water هاي تعطي indication عن water content
هاي لانه ضارة ما لازم تتجاوز حدود معينه بالفارماكوبيا واذا زدت عن هاي الكميه يعتبر المستحضر راسب

Sulfate ash

هاد بعكس inorganic solvents 🔥💥 بحرق الماده لتصير رماد وبحط عليها sulfuric acid وبرجع اسخنها على درجه حراره 800 ولازم ما تتجاوز نسبه ١٠/٣/٣٣

Specifications: test procedures and acceptance criteria for new drug substances and new drug products: chemical substances

ICH Guidelines Q6A (www.ich.org)

Dr. Isra Dmour

Credit: Prof. Dr. Nizar Al-Zoubi

specification

ههي عباره عن lists تحتوي على tests لازم نكون رابطينها بrefrance analysis procedure. طيب لو انطلب منا نفحص assy كيف رح اعملها لازم يكون عنا مرجع بالا ضافه إلى acceptance criteria ما بنفع احكيله يكون assy وحيكون HPLC according USP35

يعني لو طلع معه 50 لا مش مسموح فلازم نكون حاطين اله acceptance criteria 98-102 اقل من98 ممنوع واعلى من102 ممنوع

المنتج تبعي لازم يطابق جميع spacefication الي يضعها ال manufacture ويوافق عليها المشرع الي هو regulatory authority

Definitions and general concepts

Specifications and acceptance criteria

Specification: A list of tests, references to analytical procedures, and appropriate acceptance criteria.

It establishes the set of criteria to which a drug substance or drug product should conform to be considered acceptable for its intended use.

Acceptance criteria: Numerical limits, ranges, or other suitable measures for acceptance of the results of analytical procedures.

- Example:
- Assay acceptance criteria 90-110%
- 110.5%--→ pass or fail??

Specifications and acceptance criteria

Example: Drug product specifications

Attribute	Acceptance Criteria (typical values)	Analytical Procedure (for example)
Identity	Matches Standard	IR or HPLC/UV
Appearance	Color, Imprint	Visual
Assay	90-110%	HPLC
Dose Uniformity	Statistical Criterion (USP)	HPLC or Weight
Release from Dosage Form	80% in 15 or 30 minutes	Stirred Aqueous Vessel
Impurities (Related Substances)	<1% to few %	HPLC
Microbial Limits Or Sterility	# of total aerobes and fungi per gram Pathogen (-)	Growth in special media
Water Content	Few %	Chemical or wgt. loss
Preservative Content	NLT 75% of Initial	HPLC

Specifications and acceptance criteria

Example: Drug product specifications

Table 2: Example of solid oral drug product specifications for early development.

Test Name	Test Method	Acceptance Criteria
Description Shape Colour	Visual	Product specific shape and colour
Identity by HPLC	HPLC	Consistent with reference*
Identity by UV	HPLC–PDA	Consistent with reference*
Assay by HPLC (% label claim)	HPLC	90.0–110.0%*
Degradation products by HPLC Individual unspecified Total	HPLC	 ≤1.0%* ≤5.0%*
Dissolution	HPLC or UV	Report*
Disintegration	USP<701>	≤15 min
Uniformity of dosage units	HPLC or weight variation	Corresponds to USP<905>*

Specifications and acceptance criteria

- "**Conformance to specifications**" means that the drug substance and / or drug product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria.
- Specifications are critical quality standards that are proposed and justified by the manufacturer and approved by regulatory authorities.

Specifications and acceptance criteria

- Specifications should focus on those characteristics found to be useful in ensuring the safety and efficacy of the drug substance and drug product.

- The quality of drug substances and drug products is determined by :

1. their design,
2. development,
3. in-process controls,
4. GMP controls,
5. process validation, and
6. by specifications applied to them throughout development and manufacture.

Definitions

specification → مقسوم إلى قسمين

* **Specific test:** A test which is considered to be applicable to particular new drug substances or particular new drug products depending on their specific properties and/or intended use.

هاد يكون يا موجود او لأ حسب

* **Universal test:** A test which is considered to be potentially applicable to all new drug substances, or all new drug products; e.g., appearance, identification, assay, and impurity tests.

يلا نحكي قصه هسا spacefic بعملها ل products جديد ولكن مش لكل المنتجات الجديده
مثلا بدي اشوف pH for tablets ما بزبط لانه موضوع pH يخص solution .
طيب هل موضوع isotonicity يعتبر universe لا لانه بخص بس solution
بالمختصر الي رح اكتبهم يعتبرون universal وغيرههم يعتبر specific الي هم
strength, impurity, description, identity نفسها لبعدين

Definitions

New drug substance: The designated therapeutic moiety, which has not previously been registered in a region or Member State (also referred to as a new molecular entity or new chemical entity).

- It may be a complex, simple ester, or salt of a previously approved drug substance.

New drug product: A pharmaceutical product type, for example, tablet, capsule, solution, cream, etc., which has not previously been registered in a region or Member State, and which contains a drug ingredient generally, but not necessarily, in association with excipients.

2010 Recognition of Monograph and Reference Material Donors

USP acknowledges and appreciates the support of the following companies that participated in the USP standards-setting process by providing information for the development of new monographs or by donating reference standard candidate materials. The companies listed are those that either provided monographs that were published as proposals in 2010 or donated reference material candidates that were released as USP Reference Standards in 2010.

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عندي فحص ل microbiological لما يكون
عندي في substances بدي افحص micro وأثبت انه خلال التصنيع يضل ثابت على طول shelf life فراح المصنع على regulatory authority وحكاله بدي افحص micro لكل patch لانه عندي data..... هسا بقدر احكي ل regulatory خلال مرحله التسجل / التصنيع انه انا عندي إثبات انه ما تتغير النسبه طول فتره shelf life ف ما بدي افحص لكل patch انما لكل 5 patch وهو يوافق(بدنا ننتبه لشغله انه هاد الحكي بجوز ولكن لا يعني انه واقع فالشركان تفحص كل اشي عشان مش مستهله يصير مشكله من اشي مش مستاهل)

الامثله الي يطبق عليها تعمل إلهم spacefication على. release ما بمشي عليها patch to patch انما كل أسبوع أو كل فتره نفحص مجموعه من patch. مختلفة

- residual solvents and microbiological testing

إذا فشل التسيت وما طابقت acceptance criteria هون لازم ابلغ regulatory authority وانه هاد الحكي ما زبط وبطل عنا control على micro ولازم نرجع نعمل patch to patch release testing

GENERAL CONCEPTS

Periodic or Skip Testing

- Periodic or skip testing is the performance of specified tests at release on pre-selected batches and / or at predetermined intervals, rather than on a batch-to-batch basis with the understanding that those batches not being tested still must meet all acceptance criteria established for that product.
- This represents a less than full schedule of testing and should therefore be justified and presented to and approved by the regulatory authority prior to implementation.
- This concept may be applicable to, for example, residual solvents and microbiological testing for solid oral dosage forms.

GENERAL CONCEPTS

Periodic or Skip Testing

- This concept should generally be implemented post-approval.
- When tested, any failure to meet acceptance criteria established for the periodic test should be handled by proper notification of the appropriate regulatory authority(ies).
- If these data demonstrate a need to restore routine testing, then batch by batch release testing should be reinstated.

Release

ههاي معناها at time of manufacturing time zero والشركه تعمل release
لل patch بناءا على تحليلها ولكن release الفعلي للسوق يعمله JFDA تودي عينات من كل patch وتحليلها وبعدين تعمل release

Shelf-life

اما هاي دراسه من خلال stability وخلال تتبع المستحضر حتى خارج فتره دراسه stability

مثال عنا impurity وحكينا اكم لازم يكون limit تبعها وهاد المسموح
نروح نحكي قصه 🙄 هسا انا عندي generic name ولو قلنا انه shelf life اله 3 سنوات هل منطقي يطلع معي ١١/٣/٣٠٠٠٠٠ من اول ما بصنعه يعني على time zero طيب شو رح يصير بعد 3 سنوات فالمصنعين عملو spacefication narrower ل time zero فيقول بدي اياها على time zero تطلع معي ٢٠٢٥/٥/٩٠٠٠٠٠ وهيكك مسموح بملف التسجيل اسلم spacefication 2 هسا تمام ضيقت على حالي بالنسبه ولكن افضل لقدام
اما باليابان وامريكا! انت حر تعمل in house وتضيق على حالك وتلزم فيه بس انت بملف التسجيل بدك تسلم ملف واحد وهو shelf life وتلزم فيه

GENERAL CONCEPTS

Release Acceptance Criteria vs. Shelf-life Acceptance Criteria

- The concept of different acceptance criteria for release vs. shelf-life specifications applies to drug products only.
- It pertains to the establishment of **more restrictive** criteria for the release of a drug product than are applied to the shelf-life.
- Examples where this may be applicable include assay and impurity (degradation product) levels.
-

GENERAL CONCEPTS

Release Acceptance Criteria vs. Shelf-life Acceptance Criteria

- In Japan and the United States, this concept may only be applicable to in-house criteria, and **not** to the regulatory release criteria.
- However, an applicant may choose to have tighter in-house limits at the time of release to provide increased assurance to the applicant that the product will remain within the regulatory acceptance criterion throughout its shelf-life.

GENERAL CONCEPTS

In-process Tests

- **In-process tests**, are tests which may be performed during the manufacture of either the drug substance or drug product, rather than as part of the formal series of tests which are conducted prior to release.

➢ In-process tests which are only used for the purpose of adjusting process parameters within an operating range, e.g., hardness and friability of tablet cores which will be coated and individual tablet weights, are not included in the specification.

حكينا قبل عن الغرفه الي موجوده عندي داخل المصنع واسمها IPC فيها محلل وضابط ارتباط منQA وفي محلل من QC.
وحكينا قصه الماكينه وانا بدها متابعه حتى اتأكد انه المواد الي طلعت صحيحه او لا وانه كل فتره اعمل time interval بحسب من اوقات معينه ومن أماكن معينه من sample لاشيك عيلها

GENERAL CONCEPTS

In-process Tests

- Certain tests conducted during the manufacturing process, where the acceptance criterion is identical to or tighter than the release requirement, (e.g., pH of a solution) may be sufficient to satisfy specification requirements when the test is included in the specification.
- However, this approach should be validated to show that test results or product performance characteristics do not change from the in-process stage to finished product.

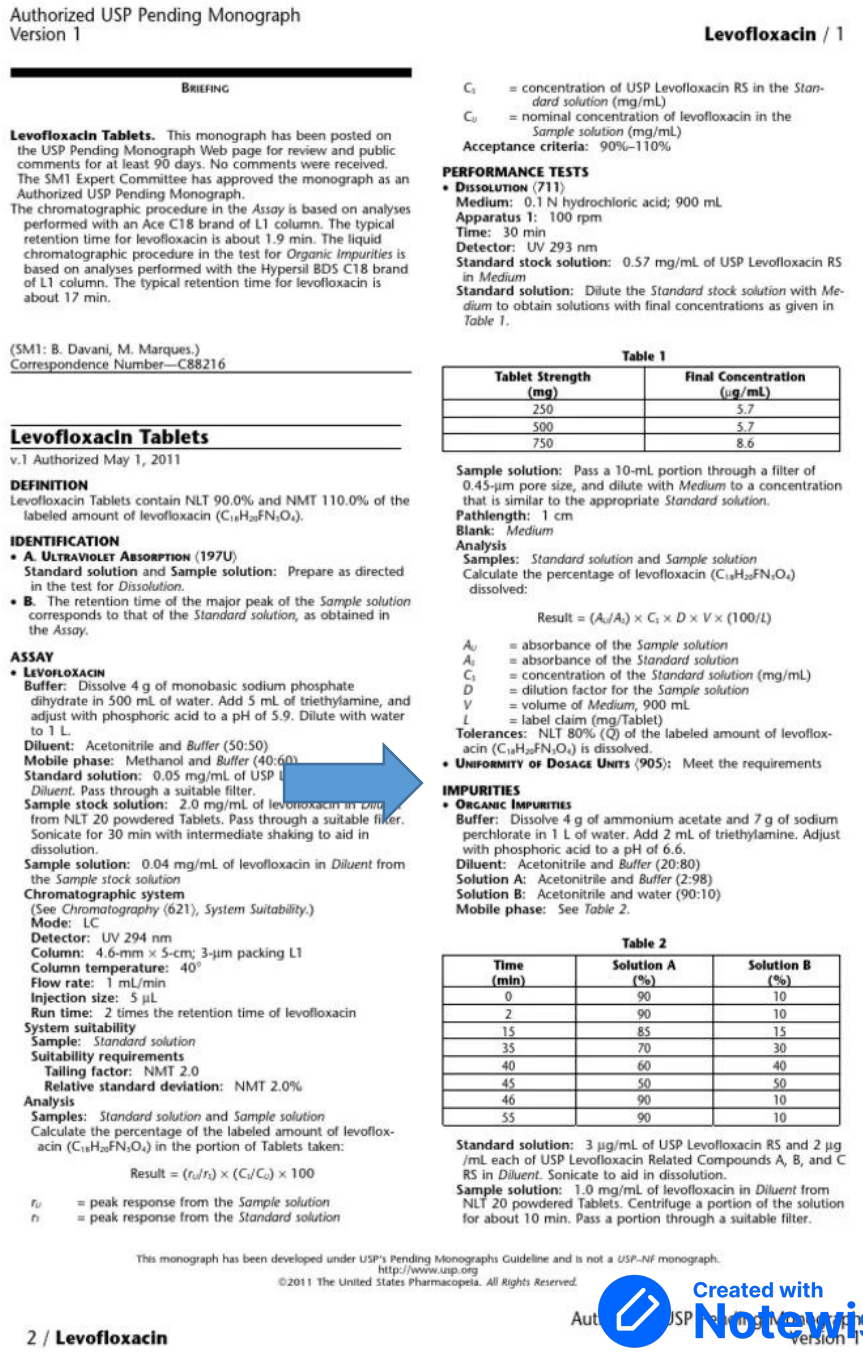
باختصار احنا عملنا دواء لأول مره حتى الماده الفعاله احنا اخترع
نحكي قصه أخرى لنفهم😶‍🌫️
هسا لما نقدم الملف لتسجيل الدواء ب FDA وما كان عندي data الي تسمح نحط acceptance criteria نهائيه (عنا impurity معينه limited غير هيك لسا ما كملت دراسه stability تبعها احنا حطيناه 1.5 وكان unknown وصار عنا shelf life وال limited كان 8٪ ما تغير فمسموح النا نعمل مراجعه لل acceptance criteria ونروح عليهم ونغير acceptance بدل ما كان 1.5 وهو عمره ما طلع عن 8٪ بحطوه 1٪ وبحكيلهم بدي اضيق على حالي واحطه 1٪

في حاله ثانيه إذا كان 1.5 وطلع عندي على بزيد 1.8 shelf life الحل هون انك توسعlimit على نفسك فتروح عليهم تحكيلهم بدي ارفعه ل2% هم بحكولك لا ياحبيبي هون ووقف😁 stability data لحالها ما رح تكفي فلازم تعمل كمان safety data انه هاي impurity بس وصلت ل 2 بالميه ما بتضر وزي ما قلت قبل انه هاد limit يحدد من manufacturers ويوافق عليه من regulatory authority ب justification

GENERAL CONCEPTS

Limited Data Available at Filing

- It is recognized that only a limited amount of data may be available at the time of filing, which can influence the process of setting acceptance criteria.
- As a result it may be necessary to propose revised acceptance criteria as additional experience is gained with the manufacture of a particular drug substance or drug product (example: acceptance limits for a specific impurity).



Authorized USP Pending Monograph
Version 1

Levofloxacin / 1

BRIEFING

Levofloxacin Tablets. This monograph has been posted on the USP Pending Monograph Web page for review and public comments for at least 90 days. No comments were received. The SM1 Expert Committee has approved the monograph as an Authorized USP Pending Monograph.
The chromatographic procedure in the *Assay* is based on analyses performed with an Ace C18 brand of L1 column. The typical retention time for levofloxacin is about 1.9 min. The liquid chromatographic procedure in the test for *Organic Impurities* is based on analyses performed with the Hypersil BDS C18 brand of L1 column. The typical retention time for levofloxacin is about 17 min.

(SM1: B. Davani, M. Marques.)
Correspondence Number—C88216

Levofloxacin Tablets

v.1 Authorized May 1, 2011

DEFINITION
Levofloxacin Tablets contain NLT 90.0% and NMT 110.0% of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$).

IDENTIFICATION
- **A. ULTRAVIOLET ABSORPTION** ⟨197U⟩
  Standard solution and **Sample solution:** Prepare as directed in the test for *Dissolution*.
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
- **LEVOFLOXACIN**
  Buffer: Dissolve 4 g of monobasic sodium phosphate dihydrate in 500 mL of water. Add 5 mL of triethylamine, and adjust with phosphoric acid to a pH of 5.9. Dilute with water to 1 L.
  Diluent: Acetonitrile and *Buffer* (50:50)
  Mobile phase: Methanol and *Buffer* (40:60)
  Standard solution: 0.05 mg/mL of USP L
  Diluent. Pass through a suitable filter.
  Sample stock solution: 2.0 mg/mL of levofloxacin in *Dil*
  from NLT 20 powdered Tablets. Pass through a suitable filter. Sonicate for 30 min with intermediate shaking to aid in dissolution.
  Sample solution: 0.04 mg/mL of levofloxacin in *Diluent* from the *Sample stock solution*
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 294 nm
  Column: 4.6-mm × 5-cm; 3-µm packing L1
  Column temperature: 40°
  Flow rate: 1 mL/min
  Injection size: 5 µL
  Run time: 2 times the retention time of levofloxacin
  System suitability
  Sample: *Standard solution*
  Suitability requirements
  Tailing factor: NMT 2.0
  Relative standard deviation: NMT 2.0%
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the percentage of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) in the portion of Tablets taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Levofloxacin RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of levofloxacin in the *Sample solution* (mg/mL)
Acceptance criteria: 90%–110%

PERFORMANCE TESTS
- **DISSOLUTION** ⟨711⟩
  Medium: 0.1 N hydrochloric acid; 900 mL
  Apparatus 1: 100 rpm
  Time: 30 min
  Detector: UV 293 nm
  Standard stock solution: 0.57 mg/mL of USP Levofloxacin RS in *Medium*
  Standard solution: Dilute the *Standard stock solution* with *Medium* to obtain solutions with final concentrations as given in *Table 1*.

Table 1

Tablet Strength (mg)	Final Concentration (µg/mL)
250	5.7
500	5.7
750	8.6

Sample solution: Pass a 10-mL portion through a filter of 0.45-µm pore size, and dilute with *Medium* to a concentration that is similar to the appropriate *Standard solution*.
Pathlength: 1 cm
Blank: *Medium*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of levofloxacin ($C_{18}H_{20}FN_3O_4$) dissolved:

$$\text{Result} = (A_U/A_S) \times C_S \times D \times V \times (100/L)$$

A_U = absorbance of the *Sample solution*
A_S = absorbance of the *Standard solution*
C_S = concentration of the *Standard solution* (mg/mL)
D = dilution factor for the *Sample solution*
V = volume of *Medium*, 900 mL
L = label claim (mg/Tablet)
Tolerances: NLT 80% (Q) of the labeled amount of levofloxacin ($C_{18}H_{20}FN_3O_4$) is dissolved.
- **UNIFORMITY OF DOSAGE UNITS** ⟨905⟩: Meet the requirements

IMPURITIES
- **ORGANIC IMPURITIES**
  Buffer: Dissolve 4 g of ammonium acetate and 7 g of sodium perchlorate in 1 L of water. Add 2 mL of triethylamine. Adjust with phosphoric acid to a pH of 6.6.
  Diluent: Acetonitrile and *Buffer* (20:80)
  Solution A: Acetonitrile and *Buffer* (2:98)
  Solution B: Acetonitrile and water (90:10)
  Mobile phase: See *Table 2*.

Table 2

Time (min)	Solution A (%)	Solution B (%)
0	90	10
2	90	10
15	85	15
35	70	30
40	60	40
45	50	50
46	90	10
55	90	10

Standard solution: 3 µg/mL of USP Levofloxacin RS and 2 µg /mL each of USP Levofloxacin Related Compounds A, B, and C RS in *Diluent*. Sonicate to aid in dissolution.
Sample solution: 1.0 mg/mL of levofloxacin in *Diluent* from NLT 20 powdered Tablets. Centrifuge a portion of the solution for about 10 min. Pass a portion through a suitable filter.

This monograph has been developed under USP's Pending Monographs Guideline and is not a *USP–NF* monograph.
http://www.usp.org

GENERAL CONCEPTS

Limited Data Available at Filing

- When only limited data are available, the initially approved tests and acceptance criteria should be reviewed as more information is collected, with a view towards possible modification.
- This could involve loosening, as well as tightening, acceptance criteria as appropriate.

Parametric Release

يلا مثال رقم الف! لنفرض عنا product termenal sterilize يعني معمول اله تعقيم وهو داخل Package
فلو عملت تعقيم على درجه حراره 200 مثلا ووقت نص ساعه وعملت الفحص طلع sterile مره ومرتين وثلاث هسا هاي parameters انو كل مره على نفس الوقت ونفس الوقت يطلع sterile ف بقدر اعمل الها pass بناءا على انه طلول هاي process الحراره ما نزلت عن 200 والوقت ما قل عن 30 دقيقه
ما بمسك عينه وبروح اعمل الها زراعه لاشوف اذا معقمه او لا عشان اعمل. release for product
انما نعمل parametric release

Alternative Procedures

اما هاد.. مثال احنا ممكن نستخدم طريقه بدل طريقه بالتحليل
عندي tablet وهاي tablet ما بصير الها degradation خلال عمليه التصنيع ف انا بقدر اعمل الassay test على Release عن طريق UV..... يعني هسا assay بحلله عن طريق HPLC الي يحلل drugs content ولكن UV قادر انه يحلل كمان drug content طيب ليش ما رحت علىUV من اول لانه انا عندي impurity بدها تحليل وهاد اصلا عن طريق HPLC عصفورين بحجر واحد)(impurity and assay
ولو حضرت tablet هاي خلال عمليه التصنيع زي مااخذنا بالصنايعه ما بصير الهاdegradation ف رح نحلل assay حتى نقدر نعرف هل. نروح coating or not بعدها هل ناجحassay اوديه علىblastering وبدل ما امشي كل هاي الخطوات بقدر اعمل release مبدأي يعني اوخذ indication عن طريق UV حللassay وطلع معي ناجح بكمل على coating بعدها حللassay روح علىpackeging ولكن بس خلصنا كل اشي وصار المدراء داخل الكرتون وبدي اعمل release for finish product هون لازم ارجع احلل. Method الموجوده داخل spacefication الي هي chromatography

لاحقي سريع

GENERAL CONCEPTS

Parametric Release

- Parametric release can be used as an operational alternative to routine release testing for the drug product in certain cases when approved by the regulatory authority.
- Sterility testing for terminally sterilized drug products is one example. In this case, the release of each batch is based on satisfactory results from monitoring specific parameters, e.g., temperature, pressure, and time during the terminal sterilization phase(s) of drug product manufacturing.
- These parameters can generally be more accurately controlled and measured, so that they are more reliable in predicting sterility assurance than is end-product sterility testing.

GENERAL CONCEPTS

Parametric Release

- Appropriate laboratory tests (e.g., chemical or physical indicator) may be included in the parametric release program.
- It is important to note that the sterilization process should be adequately validated before parametric release is proposed and maintenance of a validated state should be demonstrated by revalidation at established intervals.
- When parametric release is performed, the attribute which is indirectly controlled (e.g., sterility), together with a reference to the associated test procedure, still should be included in the specifications.

GENERAL CONCEPTS

Alternative Procedures

- Alternative procedures are those which may be used to measure an attribute when such procedures control the quality of the drug substance or drug product to an extent that is comparable or superior to the official procedure.

Example:

- For tablets that have been shown not to degrade during manufacture, it may be permissible to use a spectrophotometric procedure for release as opposed to the official procedure, which is chromatographic.
- However, the chromatographic procedure should still be used to demonstrate compliance with the acceptance criteria during the shelf-life of the product.

GENERAL CONCEPTS

Pharmacopoeial Tests and Acceptance Criteria

- References to certain procedures are found in pharmacopoeias in each region. Wherever they are appropriate, pharmacopoeial procedures **should be** utilized.

Evolving Technologies

- New analytical technologies, and modifications to existing technology, are continually being developed. Such technologies should be used when they are considered to offer additional assurance of quality, or are otherwise justified.

هاي صارت كثير لما ظهر UPLC صارت USP, BP, regulatory authority تحول عليه فصار تكنيك جديد. بدنا نتكيف معها

GENERAL CONCEPTS

Impact of Drug Substance on Drug Product Specifications

- In general, it should not be necessary to test the drug product for quality attributes uniquely associated with the drug substance.

Example:

- It is normally not considered necessary to test the drug product for synthesis impurities which are controlled in the drug substance and are not degradation products.

هاي ماده كيمياويه صنعناها خلال chemical synthesis وتفاعلات المواد مع بعضها. وهاي ينتج عنها impurity شوايب مش كل ال solvent تبخر ضل جزء منه فمثلا ibuprofen الي صنعته رح اوخذ منه 30٪ واحطه داخل tablet الي هي finish product وأخذت معها impurity and residual solvent فهاد هو impact تبع drugs substances على drugs products هسا هل في داعي افحص residual solvent داخل drugs products ؟ هسا الجواب لا لانه الماده لا تفنى ولا تستخدث من العدم ومصدر ال اسيتون مثلا من عمليه تصنيع الدواء فمش مهم اصلا

اما الاشي الثاني الي بأثر على drug substances هو impurity وفي عنا نوعين من impurity داخل API

① synthesis impurities

هاي بسبب التصنيع والها اسم ثاني هو process impurity يعني انا خلطت مادهA مع طلعت C فضل جزء. يكاد لا يذكر من الماده A ونوع ثاني على نفس الي فوق ولكن تم اضافه catalyst وهاد يتفاعل مع احد المواد وعمل impurity ولكن فش داعي افحص ها لأنها خاصه بعمليات الصناعه ما بتنتقل معها ك drugs products من حيث spacefication وحكينا زيها residual solvent

② degradation impurity

اما هاد ناتج عن active ingredients نفسه صار اله hydrolysis او تفاعل معه الضوء او اكسده هاي لازم نضل نتبع معها

في عنا نوع ثالث وهاد كتر مهم الي نو synthesis impurity ولكن تتفاعل مع الدواء وتزيد خلال storage نتجت عن طريقق synthesis ولكنها فيها chemical structure وممكن بطريقه ما يتفاعل مع iboprofen وتزيد هاي بتابعها مع ال drug products

الدكتوره رح يكون السؤال واضح لما تسأل بالامتحان عن أي نوع

GENERAL CONCEPTS

Reference Standard

- **A reference standard, or reference material**, is a substance prepared for use as the standard in an assay, identification, or purity test.
- It should have a quality appropriate to its use.
- It is often characterized and evaluated for its intended purpose by additional procedures other than those used in routine testing.
- For new drug substance reference standards intended for use in assays, the impurities should be adequately identified and / or controlled, and purity should be measured by a quantitative procedure.