

## What is Quality

- Quality: in simple words is the essential nature of a thing and the totality of its attributes which bear upon its fitness for its intended purpose



Sterility is always an essential quality?

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

7/10ct

المحاضرة الأولى  
الجودة.

## \* What is Quality

هي صفات نوعية، الصفات التي يبدّي ياها تكون موجودة بالمنتج عندي أو الخدمة، وكلمة جودة جاءت من "جيد" إظهارًا، فغالبًا يكون الشيء كويس.

يعني هي مجموع الصفات الملائمة للغرض المقصود  
(Fitness for its intended purpose.)

لو مثلاً حكمنا على التحميل إنه تدرب بسرعة، هل هي الصفة  
إياها دخل بالquality هل هي **related to quality**؟  
بالحقيقة لا، هاي أشياء و صفات موجودة فيها أملاً، بقدرش من  
خلافها اقيم جودتها!

نقرب الصورة أكثر، مثلاً هل مطلوب منا يكون كل منتج عندي  
يكون "Sterility"؟ برضه لا، مودائماً مطلوب مني يكون المنتج معقم  
إلا لأشياء معينة، هي **a good quality** لكن مودائماً مطلوبة!

الفكرة إنه بدي الصفات الملائمة للغرض المقصود.

## What is Quality

- The suitability of **either a drug substance or drug product** for its intended use. This term includes such attributes as the identity, strength, and purity. [ICH Q6A]
- The degree to which a set of inherent properties (of a product, system, or process) fulfills requirements [ISO 9000 / ICH Q9 and Q10].
- Every pharmaceutical product has established **identity, strength, purity, and other quality characteristics** designed to ensure the required levels of safety and effectiveness.
- Achieving quality means achieving these characteristics for a product

Slide credit: Dr. Isra Dmour and Prof. Nizar Al-Zoubi

## Quality, Quality Control and Quality Assurance

- **Quality control:**
  - The regulatory process through which industry measures actual quality performance, compares it with standards, and acts on the difference.
- **Quality assurance:**
  - Provision to all concerned the evidence needed to establish confidence that the activities relating to quality are being performed adequately.



Slide credit: Dr. Isra Dmour and Prof. Nizar Al-Zoubi

لو بدنا نحكي عن جودة من ناحية الصيدلة والأدوية :

ليش أنا بدي يكون عندي *good Quality*؟ لأنه أنا بكون غنت  
*Safety and effectiveness* للدواء، مادام *Quality* مخمونة ببقى  
 الفعالية والأمان للدواء مخمونة.

طيب شو الفرق بين *Drug substance* و *Drug product*؟



هو *active and*

*inactive ingredient*

يعني *product* كامل.



هو *active ingredient*

الموجودة بالدواء

وعشان في أمن الفعالية والأمان للدواء، لازم تجتمع فيه الصفات  
 التالية

① *Purity* → الدواء لازم يكون  
 نقى

③ *Strength*  
 ← مثلاً بدي عيار لدواء  
 يكون 250

② *Identity* → يعني مش احكي إنه  
 الدواء هاد *paracetamol*  
 وهو *Aspirin*، هويته  
 لازم تكون هتيرة.

بديش يكون 300 مثلاً!

← هاد الحكي كله موجود كتعريف عندي بالـ *ICH* راح نفضّل  
 فيه لقدام.

← عرفنا Quality هسا بدنا نعرف لفرده بين :-

## ① Quality control (ضبط الجودة)

م بدك تبجي تقارن product تبجك ، بالمعايير يلي إنت حطيتها وتشوف الفرده هل نجح ولا رسب وبناءً على النتيجة تتصرف.

مثال :-

أخذنا قبل Drug dissolution قبل بالصناعية وأخذنا إنه القيمة المقبولة على  $\frac{75}{30} = Q$  ، يعني يصير له release 75% على 30 دقيقة.

لما فحصت product تابعي كان 80% معناته المستحضر عندي راسب.

## ② Quality assurance (ضمان الجودة)

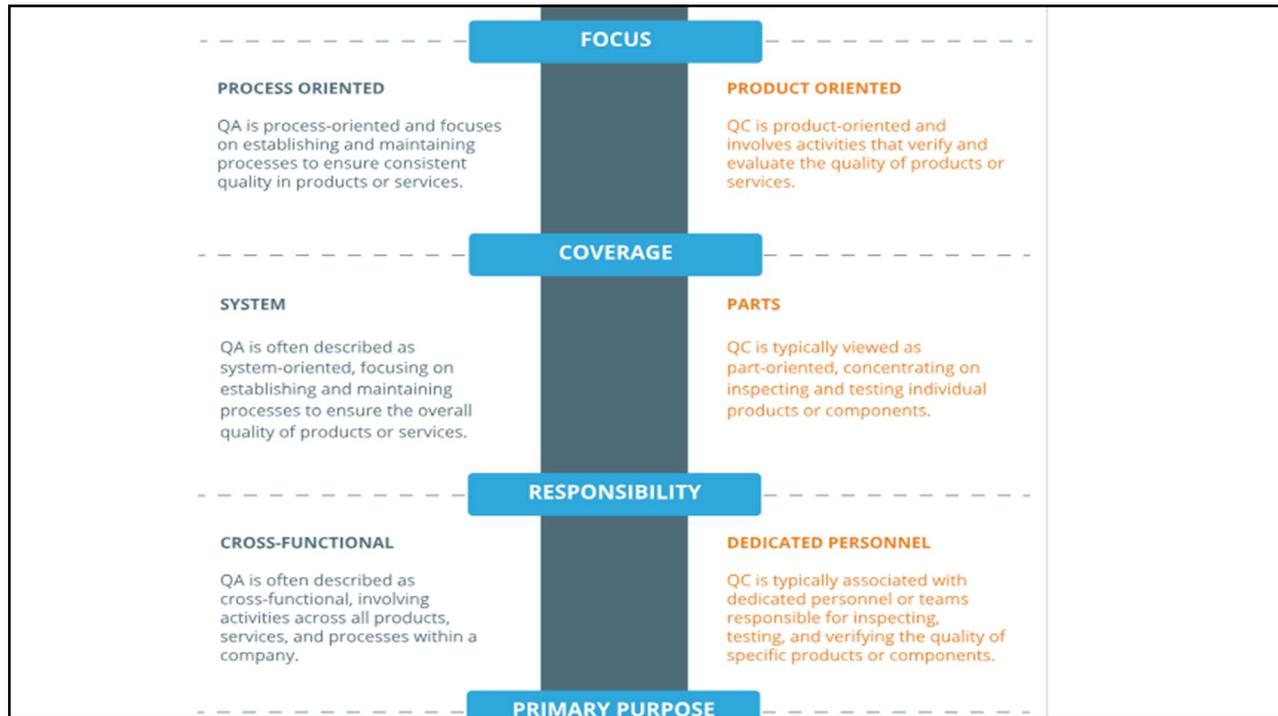
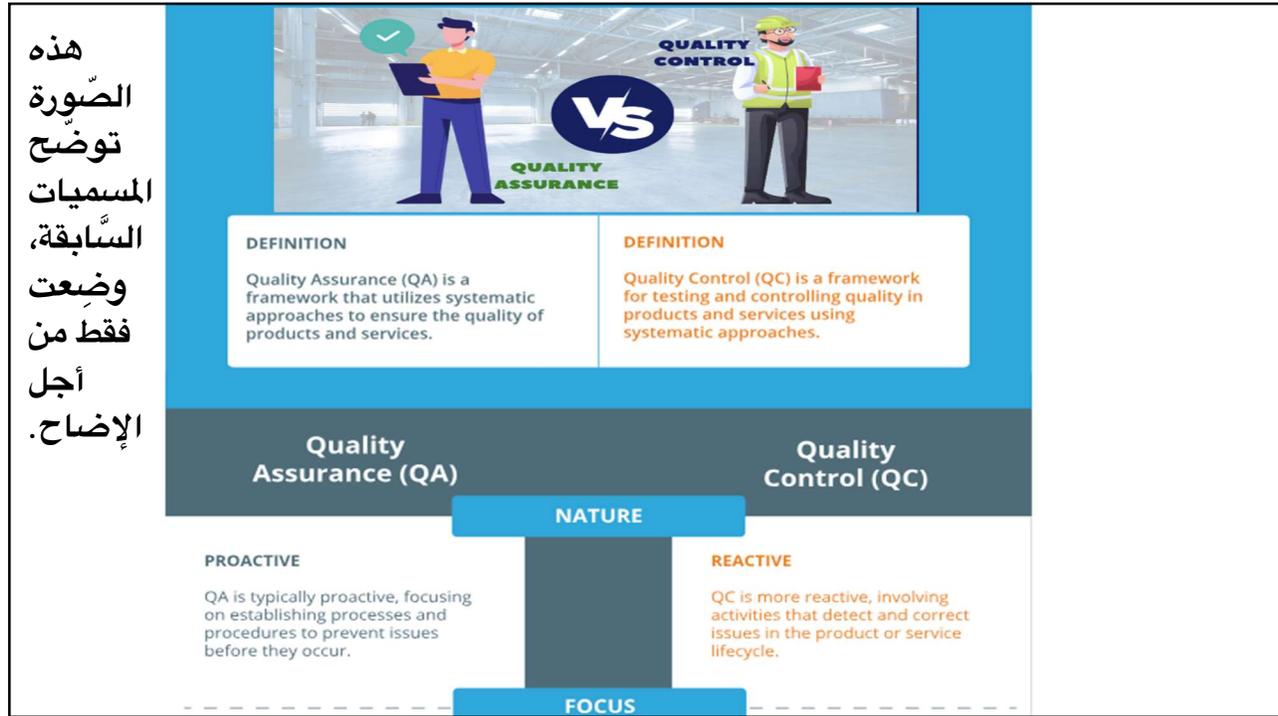
م بدنا نعرف هل طبقوا المعايير المطلوبة يلي وضعها Quality control لانهم نتوفر الأدلة الكافية لجميع الناس ، المعنيين بإثبات لثقة إنه المعايير تم تنفيذها على النحو الصحيح.

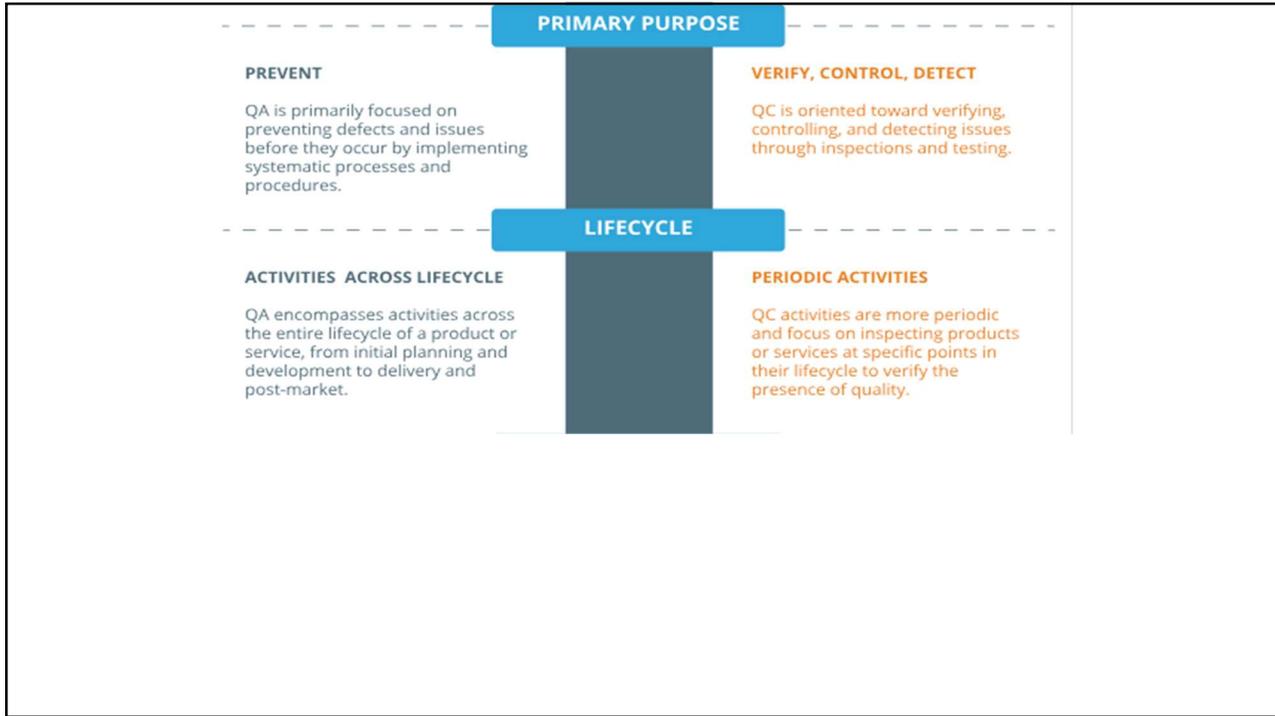
م ال assurance يعنى بعمليات و system و Quality control  
يعنى ب Testing و product

مع تحمي شوي عن ICH، في عنا بالعالم زي Guideline نتبها  
 لتتبع الدواء وتضمن كل شيء، يضمن الدواء ومنها Quality.  
 المعايير يلي يتم إتباعها في الأردن نفسها المتبعة في أوروبا مثلاً  
 والأردن إن هنت حديثاً لهايب ال ICH.  
 يعني هوننا جرد من الناس يلي تستشار لما تنطبق هاي المعايير  
 وال regulation.

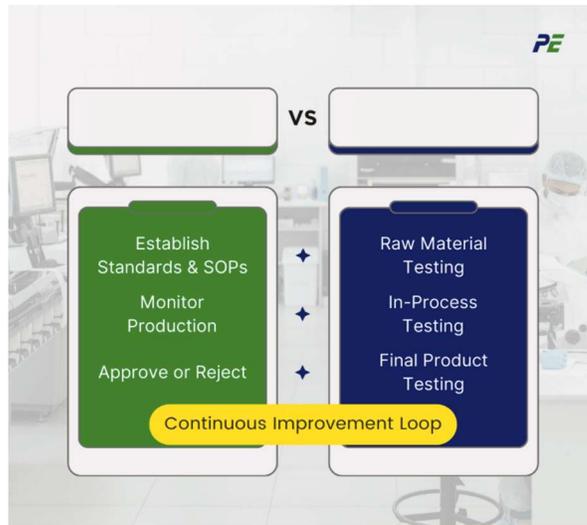
مع بالتالي هيك إنا إتخضع مفهوم أوضح لا Quality ويلي هو  
 "قد يتش المنتج عندي حقق المعايير الموضوعية وقد إيتش اتبع  
 هاي ال guideline (وقد يتش كان  
 Fulfills requirements)"

مع آخر سطرين مكتوبين بالاسلايد، افوض عندي تاخيص لكل الكلام  
 السابع.





Now, Place QA and QC in the proper place:





## Regulatory authorities Examples

1. **Jordan:** JFDA established in 2003
2. **USA:** The Food and Drug Administration (FDA).
3. **Europe:** The European Medicines Agency (EMA)
4. **UK:** The Medicines and Healthcare products Regulatory Agency (MHRA).

## Quality can impact safety and efficacy!

- Quality measures during development and manufacturing mitigate risks and ensure that only safe and effective drugs reach the market. Comprehensive documentation throughout the development process is required to support this.

من ودين أجا. كل هالأشياء مليه اهتموا بعلم، Quality، بدنا ندرس  
 ال History يا شباب ونعني عن الدواء يلي كنا نخرفه عن  
 إنه سبب كارثة للأمهات، لقامل وهو دواء "Thalidomide"  
 يلي على أساس يخفف من الغثيان يلي يجي للحامل وبتدهيك  
 ولدوا ذكفك بدون أطراف الله يعافينا وإيّاكم.

### \* Regulatory authorities Examples

عنا بكل دولة مشرف على تطبيعه هاي المعايير، معروف إنه  
 عنا بالأردن ماير دواء للسوية بدون ما يكون موافق عليه من قبل  
 (JFDA) وللك دولة مشرف من فيها، اقرأوهم.

قبل ما توجد JFDA كان مسؤوك عن هاي القمصين وزارة الصحة

## The roles of Jordan Medicines Regulator Drug Directorate in the JFDA



➤ The responsibilities include but not limited to:

1. Responsible for the registration of medicinal products (chemical and biological) whether locally manufactured or imported, and their follow-up after registration and re-registration.
2. Evaluates post approval changes for all medicinal products to facilitate medicines registration for medical security.
3. Pricing and re-Pricing of drugs
4. Approval of the importation of drugs
5. Receiving and evaluating all clinical studies protocols carried in Jordan and supervising and following up the clinical studies decisions.
6. Inspection
7. Product testing
8. Pharmacovigilance

## Example of the roles of international Medicines Regulator FDA

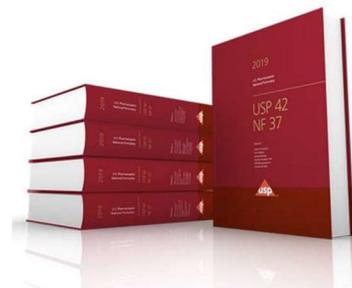
- The FDA, in addition to dosage forms, is also concerned about the drug development process, the protection of the human subjects during the drug testing phase, and post marketing drug safety.

## You cannot test quality into a product

- Means that simply performing tests on a pharmaceutical product after it is manufactured does not guarantee its quality. Instead, **quality must be built into the product during its development and manufacturing process**. In other words, testing is essential to confirm that the product meets the necessary standards, but it cannot **create** quality if the product was not developed, formulated, or manufactured properly in the first place. The processes, materials, and controls used in manufacturing must be designed in such a way that the product consistently meets quality standards.
- This idea is central to **Quality by Design (QbD)**, which emphasizes designing processes that inherently ensure quality, rather than relying solely on testing the final product.

## Standards for pharmaceutical manufacturing

- Pharmacopoeias contribute to the overall control of the quality of medicinal products by providing authoritative statements of the standards that pharmaceutical substances and finished products are expected to meet, and provide definitive testing methods.



# BP Monograph

## Medicinal and Pharmaceutical Substances

- British Pharmacopoeia Volume I & II
- Monographs: Medicinal and Pharmaceutical Substances

### Magnesium Trisilicate



#### General Notices

(Ph. Eur. monograph 0403)

#### **Action and use**

Antacid.

#### **Preparations**

[Magnesium Trisilicate Mixture](#)

[Chewable Compound Magnesium Trisilicate Tablets](#)

[Compound Magnesium Trisilicate Oral Powder](#)

Ph Eur

#### **DEFINITION**

It has a variable composition corresponding approximately to  $Mg_2Si_3O_8 \cdot xH_2O$ .

#### **Content**

- — *magnesium oxide* ( $MgO$ ;  $M_r$  40.30): minimum 29.0 per cent (ignited substance),
- — *silicon dioxide* ( $SiO_2$ ;  $M_r$  60.1): minimum 65.0 per cent (ignited substance).

#### **CHARACTERS**

##### **Appearance**

White or almost white powder.

##### **Solubility**

Practically insoluble in water and in ethanol (96 per cent).

##### **IDENTIFICATION**

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← نيجي فخي عن roles لا FDA فأكيد هي لوحيدة يلي تهني  
 أكثر من تعاون لولة الأخرى اعزائي.  
 تشمل عندي المسؤوليات بشكل عام ما يأتي وذكرنا شوي ففهم مش  
 كلام لأجل لتوضيح :

### ① re-registration

مجنن تسجيل لوداد بناءً على المعايير المنقحة عليها وبعلا follow-up  
 بجد لتسجيل .

### ② Approval / ③ pricing and re-pricing

لنت بجد ما نترك المنتج على السوق، هل سعره تكفل عليه، لبتنا  
 عنن معايير محددة بده، مثلاً إعادة التسعير، زي على بسيل لثال  
 قنري لوداد قبل كان سعره 10 دنانير، والآن 5 دنانير  
 ويتم إعادة التسعير بده لشروط معينة

### ④ importation

الموافقة على السيراد الوداد.

### ⑤ Evaluating all Clinical studies protocols

يشرفوا على كل أي دراسات تقام بوجالنا .

### ⑥ inspection

~~التفتيش~~ (التفتيش) على الصيدليات بشكل عام

### ⑦ product testing

← وافحة بدهاش شرح .

### ⑧ pharmacovigilance

← اليقظة لودايت، رصد أي آثار  
 متعلقة بالأدوية لفحان استخدامها لفترة طويلة.

← سلاية Quality into a product داع تشرها بدين .

## \* Standards for pharmaceutical manufacturing

في داعي أشرح عن pharmacopoeias :

عني monograph تشرح لي صفات المواد يلي لازم تصنع  
أو يكون عني monograph يشرح لي الطرق العالية لعلية  
dissolution مثلاً ومكان توفر في طرق اختبارها  
للمنتج، وهو دستور محدد بشكل عام، مثلاً لو اتبعت طرق تصنيع  
دواء معين بناءً على معاييرهم وكتبته أنت كان مرجع صوم PP  
هل راج تعبها الـ USP طبعاً راج تعبها، بس لازم يكون PP  
محدد بالأردن مثل USP.

عرضت لذكورة النا على جهازها PP لأدوية معينة على شكل  
monograph، عرضت USP واد BP

TAKE IT EASY

More Examples (USP and BP)



## What is ICH?

- **I**nternational **C**onference on **H**armonization of Technical Requirements for registration of Pharmaceuticals for human use"



## Introduction + .

- ❑ The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use is an initiative that brings together regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of pharmaceutical product development and registration. Since its inception in 1990, ICH has gradually evolved, to respond to the increasingly global face of drug development.
- ❑ ICH's mission is to achieve greater harmonisation worldwide to ensure that safe, effective, and high-quality medicines are developed and registered in the most resource-efficient manner.

## ICH Mission

- To make recommendations towards achieving greater harmonization in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration.



## The Need to Harmonize

- For most countries, the 1960s and 1970s witnessed a rapid development in laws, regulations and guidelines for reporting and evaluating the data on safety, quality and efficacy of new medicinal products.
- The industry, at the time, was becoming more international and seeking new global markets; however, the divergence in technical requirements from country to country was such that industry found it necessary to duplicate many time-consuming and expensive test procedures, in order to market new products, internationally.
- Realisation was driven by tragedies, such as that with thalidomide in Europe in the 1960s.



## Initiation of ICH

- Harmonization of regulatory requirements was pioneered by the EC, Europe, in the 1980s, as the EC, Europe moved towards the development of a single market for pharmaceuticals. The success achieved in Europe demonstrated that harmonization was feasible.
  - At the same time there were discussions between Europe, Japan and the US on possibilities for harmonization. It was, however, at the WHO Conference of Drug Regulatory Authorities (ICDRA), in Paris, in 1989, that specific plans for action began to materialize.
  - Soon afterwards, the authorities approached International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) to discuss a joint regulatory-industry initiative on international harmonization, and ICH was conceived.
- 

## Purpose of ICH

- Promotion of public health through international harmonisation that contributes to:
    - Prevention of unnecessary duplication of clinical trials and post market clinical evaluations.
    - Development and manufacturing of new medicines. while maintaining safeguards on quality, safety, efficacy, and regulatory obligations to protect public health.
    - Reduction of unnecessary animal testing without compromising safety and effectiveness.
-

## ICH Guidelines

- ICH has developed over 50 harmonised Guidelines aimed at eliminating duplication in the development and registration process, so that a single set of studies can be generated to demonstrate the quality, safety and efficacy of a new medicinal product. These Guidelines also include the Common Technical Document (CTD), which describes the common format for the preparation of a well-structured CTD for applications that will be submitted to regulatory authorities.
  - In addition, the ICH is working to facilitate international electronic communication through the provision of Electronic Standards for the Transfer of Regulatory Information (ESTRI) that will meet the requirements of the pharmaceutical companies and regulatory authorities. A product of this has been the Electronic Common Technical Document (eCTD), which allows for the electronic submission of the Common Technical Document (CTD) from applicant to regulator.
- 

## ICH Guidelines

### ➤ Quality Guidelines: Q1 – Q14



Harmonisation achievements in the Quality area include pivotal milestones such as the conduct of stability studies, defining relevant thresholds for impurities testing and a more flexible approach to pharmaceutical quality based on Good Manufacturing Practice (GMP) risk management.

## ICH Guidelines

### ➤ Safety Guidelines: S1 – S12

Q



Guidelines to uncover potential risks like carcinogenicity, genotoxicity and reprotoxicity. A recent breakthrough has been a non-clinical testing strategy for assessing the QT interval prolongation liability: the single most important cause of drug withdrawals in recent years.

## ICH Guidelines

### ➤ Efficacy Guidelines: E1 – E22

Concerned with the design, conduct, safety and reporting of clinical trials. It also covers novel types of medicines derived from biotechnological processes and the use of pharmacogenetics/genomics techniques to produce better targeted medicines.

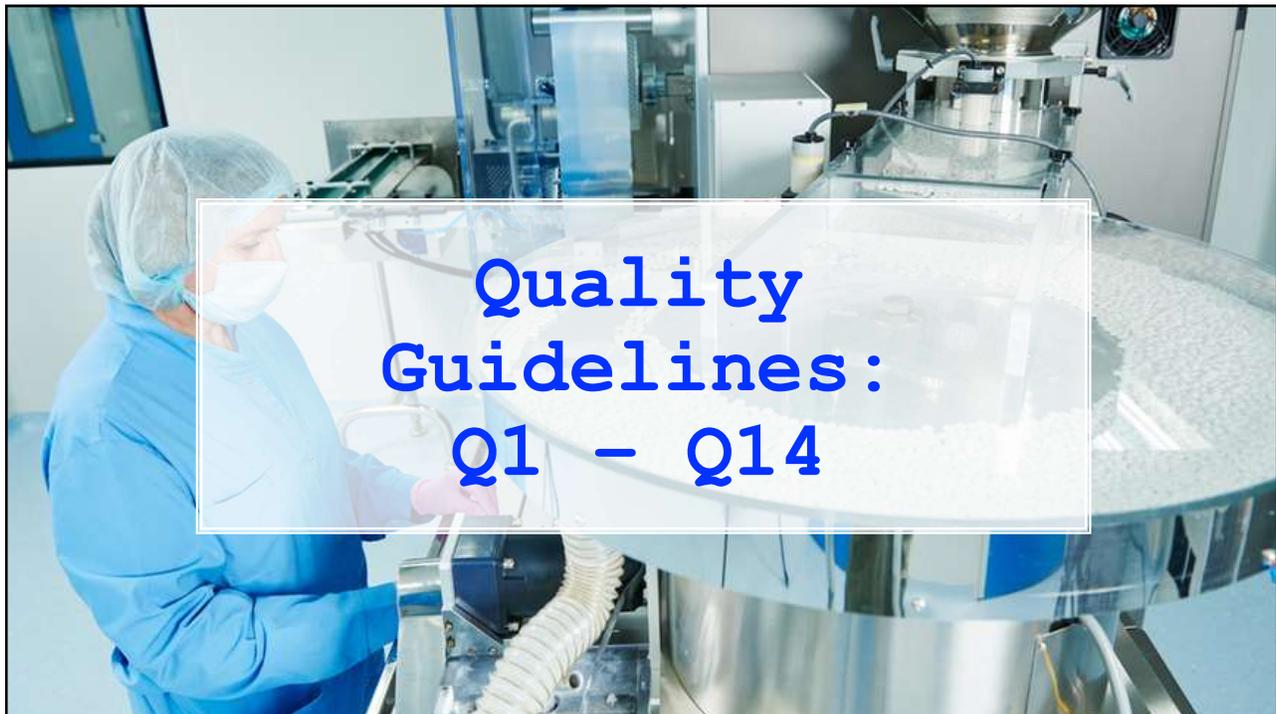


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# ICH Guidelines

## ➤ Multidisciplinary Guidelines: M1 – M15

Concerned topics which do not fit uniquely into one of the Quality, Safety and Efficacy categories. It includes the ICH medical terminology (MedDRA), the Common Technical Document (CTD) and the development of Electronic Standards for the Transfer of Regulatory Information (ESTRI).



- Stability
- Analytical validation
- Impurities
- Regulatory acceptance
- Quality of biotechnological products
- Specifications
- Good manufacturing practice
- Pharmaceutical development
- Lifecycle management

- Stability
- Analytical validation
  - ICH Q1A (R2) Stability testing of new drug substances and drug products
  - ICH Q1B Photostability testing of new active substances and medicinal products
  - ICH Q1C Stability testing: requirements for new dosage forms
  - ICH Q1D Bracketing and matrixing designs for stability testing of drug substances and drug products - Scientific guideline
  - ICH Q1E Evaluation of stability data
  - ICH Q1F Stability data package for registration in climatic zones III and IV
- Lifecycle management

- Stability
- Analytical validation
- Impurities
  - ICH Q2(R2) Validation of analytical procedures
  - ICH Q14 Analytical procedure development
- Specifications
- Good manufacturing practice
- Pharmaceutical development
- Lifecycle management

- Stability
- Analytical validation
- Impurities
  - ICH Q3A (R2) Impurities in new drug substances
  - ICH Q3B (R2) Impurities in new drug products
  - ICH Q3C (R9) Residual solvents
  - ICH Q3D Elemental impurities
- Pharmaceutical development
- Lifecycle management

- ICH Q4B Evaluation and recommendation of pharmacopoeial texts for use in the ICH regions
- ICH Q4B Annex 1 Residue on ignition/sulphated ash
- ICH Q4B Annex 2 Test for extractable volume in parenteral preparations
- ICH Q4B Annex 3 Test for particulate contamination: sub-visible particles
- ICH Q4B Annex 4A Microbiological examination of non-sterile products: microbial enumeration tests
- ICH Q4B Annex 4B Test for microbiological examination of non-sterile products: tests for specified microorganisms - Scientific guideline

- Impurities

- Regulatory acceptance

- Quality of biotechnological products

- ICH Q4B Annex 4C Test for microbiological examination of non-sterile products: acceptance criteria for pharmaceutical preparations and substances for pharmaceutical use - Scientific guideline
- ICH Q4B Annex 5 Disintegration test
- ICH Q4B Annex 6 Uniformity of dosage units general chapter
- ICH Q4B Annex 7 Dissolution test
- ICH Q4B Annex 8 Sterility test
- ICH 4 QB Annex 9 Tablet friability
- ICH Q4B Annex 10 Polyacrylamide gel electrophoresis
- ICH Q4B Annex 11 Capillary electrophoresis
- ICH Q4B Annex 12 Analytical sieving
- ICH Q4B Annex 13 Bulk density and tapped density of powders
- ICH Q4B Annex 14 Bacterial endotoxins tests

- Stability
- Analytical validation
- Impurities
- Regulatory acceptance

- Quality of biotechnological products

- ICH Q5A(R2) Guideline on viral safety evaluation of biotechnology products derived from cell lines of human or animal origin - Scientific guideline
- ICH Q5B Analysis of the expression construct in cell lines used for production of rDNA-derived protein products - Scientific guideline
- ICH Q5C Stability testing of biotechnological/biological products
- ICH Q5D Derivation and characterisation of cell substrates used for production of biotechnological/biological products - Scientific guideline
- ICH Q5E Biotechnological/biological products subject to changes in their manufacturing process: comparability of biotechnological/biological products - Scientific guideline

- ICH Q6A specifications: test procedures and acceptance criteria for new drug substances and new drug products: chemical substances - Scientific guideline
- ICH Q6B Specifications: test procedures and acceptance criteria for biotechnological/biological products - Scientific guideline

- Quality of biotechnological products

- **Specifications**

- Good manufacturing practice
- Pharmaceutical development
- Lifecycle management

- Stability
- Analytical validation
- Impurities
- Regulatory acceptance
- Quality of biotechnological products
- Specifications

- **Good manufacturing practice**

- Pharmaceutical development

- ICH Q7 Good manufacturing practice for active pharmaceutical ingredients

## \* ICH \*

→ أموا مجموعة من المؤسسات العالمية المختصة بالأدوية وقررت توطد هاي regulator، لأنه تقريريًا كلهم زي بعض بس في اختلافات جدًا بسيطة، فقرروا ينشئوا ICH كمرجع واحد الكل يربطه كثير أسباب أهمها كثرة الأدوية يلي ممكننا عنها قبل ونحان بسبب توسع الشركات يلي صادت مبيعاتها عالميًا.

→ هاد شرع لتقريبًا 6 سلايدات من ICH، يعني أولي عن منه وتحت الخرفين من ICH وأهدافه، حاجتنا جوا شرع ابتداء، إقرارهم فقط. وسعت الدكتوراة مش مطلوب منهم فقط Guidelines لل ICH.

→ شو هو CTD ?

أو Common Technical Document هو ملف تسجيل الدواء وصويف لكل نظام وهدوها ICH

→ راج فحبا عن أو Section بال ICH هو

① Quality (Q1 - Q14)

بيشرفي عن GMP (Good manufacturing practice) المصنع ممنوع يصنع الدواء إذا ما معاه شهادة GMP، متعين كيف تفحص، لنقاوة المنتج، كيف تصنع الدواء موجود، كيف نقل Test لل dissolution موجود، كل حاجة.

## ② Safety ( $S_1 - S_{12}$ )

في الخطي أو risk تأتي carcinogenicity يلي مسببات لسرطان  
وإلى genotoxicity السمية الجينية ... و reprotoxicity ..

## ③ Efficacy ( $E_1 - E_{22}$ )

في كيف يدي أعرف إنني لواء هاد effect، يشمل كل شيء.

## ④ Multidisciplinary ( $M_1 - M_{15}$ )

في فيه زي قاموس يرتوي على المصطلحات الخاصة بالأدوية وطب  
التصنيع مثل CTD  
في quality راج ندخل فهم يشاير الحالة بالتفصيل تمامًا.

تمّ بحمد الله تفريغ المحاضرة الأولى، نفع الله بكم جميعاً، فلتجعلوا نيّة دراستكم خالصة لأجل الله، ولأجل نصره أهلنا في غزّة، كلاً منّا يجابه على جبهته الخاصة، فسلوا الله الثبات والقوّة.

دعواتكم.



Believe

**YOURSELF**

CO