PHARMACEUTICAL QUALITY SYSTEM

11. Continual improvement is facilitated through the implementation of quality improvements appropriate to the current level of process and product knowledge.
12. Arrangements are in place for the prospective evaluation of planned changes and their approval prior to implementation taking into account regulatory notification and approval where required;

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PHARMACEUTICAL QUALITY SYSTEM

13. After implementation of any change, an evaluation is undertaken to confirm the quality objectives were achieved and that there was no unintended deleterious impact on product quality;
14. An appropriate level of root cause analysis (RCA) should be applied during the investigation of deviations, suspected product defects and other problems.

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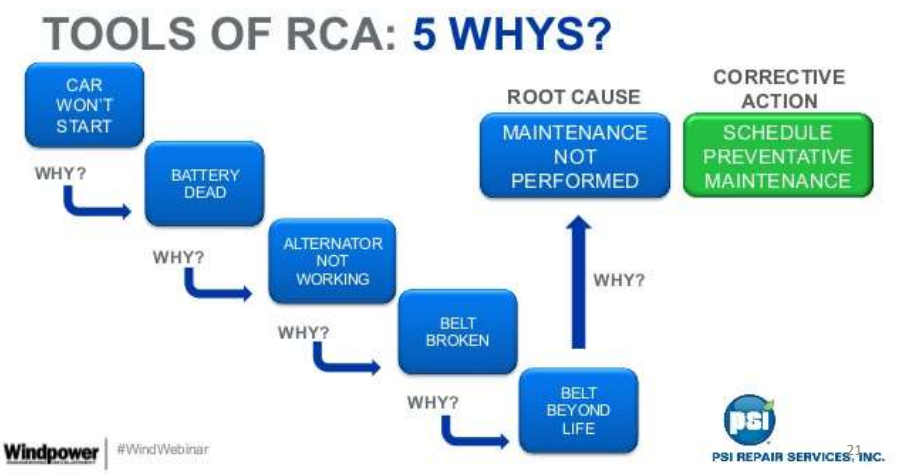
PHARMACEUTICAL QUALITY SYSTEM

What is RCA?



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PHARMACEUTICAL QUALITY SYSTEM

- In cases where the true root cause(s) of the issue cannot be determined, consideration should be given to identifying the most **likely** root cause(s) and to addressing those.
- Where human error is suspected or identified as the cause, this should be justified having taken care to ensure that process, procedural or system based errors or problems have not been overlooked, if present.
- Appropriate **corrective actions and/or preventative actions (CAPAs)** should be identified and taken in response to investigations.

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14. root Cause analysis

وهو سبب المشكلة، بدنا لحال لنوصل للسبب المشكلة، وهي سياسة ليعرفوا سبب المشكلة، زي المبرمجين وجماعة الـ It لما يكون عندهم مشكلة بال Code عشان يعرفوا سبب المشكلة وبس يعرفوا السبب يعملوا اشي اسمه previntion action عشان ماتصير المشكلة

أو Form "كابا" CAPA يكتبوا فيه ويعملوا reporting للمشكلة.

على سبيل المثال .. في عنا دواء، وال Distigration rate تاعها لازم يكون less than 50 min، بالبداية ما راح يصنعوا كميات كبيرة لأ راح يعملوا كميات قليلة ويحللوها بواسطة ال Qulity C، راح حلل هاد الدواء ووجد إنه ال Distigration طلع معاه 20 min

فهسا بده يعرف شو السبب .. بروح على ال Batch record الخاصة بالدواء، ويدور ويشوف شو سبب هاي المشكلة .. بروح على الوزنات .. بروح على أكثر من شغلة .. راح فحص ال Starch المضاف .. لقوا إنهم مغيرين نوعه .. ومعروف لما تغير النوع يلي إنت معتمده من ال Starch إنت هون راح تختلف عندك الخصائص الفيزيائية إذن حيصير عندك مشاكل ... شو للازم يصير هسّا؟ بروح أدور على ال prevention action يلي ممكن يكون مثلاً إني أضيف binder ثاني فوق الـ Starch ... هل هاد الشي على كيفي؟ لأ طبعًا ولازم آخذ عينة صغيرة من يلي صنعتهم وبطبق عليهم هاد ال action ...

بعد هيك بجيب الـ CAPA Form .. وبحط عليها المشكلة تاعتي

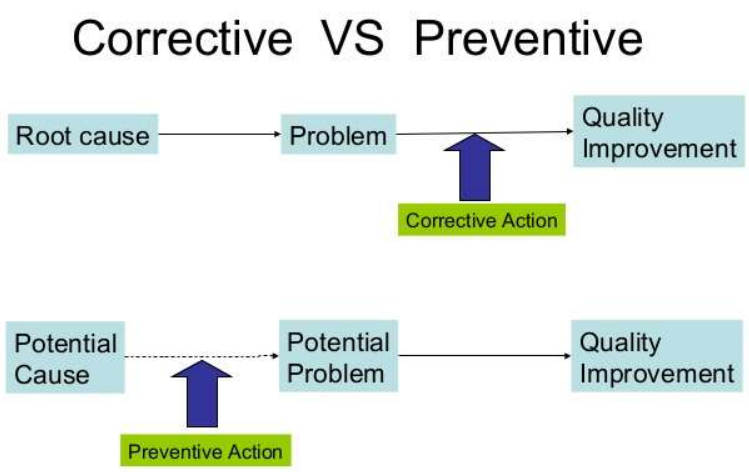
وكيف حليتها وشو؟ خلصت ... وهاد الـ Form يوقّع عليه الـ QA ويوافق عليه .. وينكبس وينضاف للـ Batch record.

وهاد هو الـ Corrective action .. أنقذت المنتج يلي بيدي ..

طيب! يش هو الـ preventive action هون؟ إنك تجيب Starch يلي إنت استخدمته جديد وتعمله Test وتفحص الـ Disintegration تاعه ... هيك قدرنا نعمل (RCA) .. ونتفادى هيك مشكلة ممكن تصير عندي مستقبلاً ..

في سلايدات حنا يفيتهم مثال تحت .. مش منزليتهم ..

PHARMACEUTICAL QUALITY SYSTEM



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PHARMACEUTICAL QUALITY SYSTEM

15. Medicinal products are not sold or supplied before a Qualified Person (QP) has certified that each production batch has been produced and controlled in accordance with the requirements of the Marketing Authorisation and any other regulations relevant to the production, control and release of medicinal products;
16. Satisfactory arrangements exist to ensure, as far as possible, that the medicinal products are stored, distributed and subsequently handled so that quality is maintained throughout their shelf life;
17. There is a process for self-inspection and/or quality audit, which regularly appraises the effectiveness and applicability of the Pharmaceutical Quality System.

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15. مصطلح QP مش موجود عنا بالأردن، موجود بأوروبا وهاي لازم
وهو شخص يكون عنده خبرة بال QA على الأقل سنتين ويكون
حافظ كل شي ويكون شخص مسؤول عن كل شي.. هاد الشي
مش مهم موجود بس هيك بالسلايد..

16. والخطة برضه بدها شرح وما حكت شي
زيادة

17. Self inspection → التفتيش الذاتي للشركة
يعني مزيد جوا الشركة بفتش إنه جميع العمليات
تتبع الإجراءات والجودة المطلوبة.

← باقي الكلام مكرر وهو واضح جدًا وشرحناه كله بالسلايدات
السابقة.

PHARMACEUTICAL QUALITY SYSTEM

- The Pharmaceutical Quality System should be defined and documented.
- A Quality Manual or equivalent documentation should be established and should contain a description of the quality management system including management responsibilities.

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PHARMACEUTICAL QUALITY SYSTEM

Quality Control

- Quality Control is that part of Good Manufacturing Practice which is concerned with sampling, specifications and testing, and with the organisation, documentation and release procedures which ensure that:
  - the necessary and relevant tests are actually carried out and,
  - that materials are not released for use, nor products released for sale or supply, until their quality has been judged to be satisfactory.

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PHARMACEUTICAL QUALITY SYSTEM

Quality Control

The basic requirements of Quality Control are that:

1. adequate facilities, trained personnel and approved procedures are available for sampling and testing starting materials, packaging materials, intermediate, bulk, and finished products, and where appropriate for monitoring environmental conditions for GMP purposes;
2. samples are taken by approved personnel and methods;
3. test methods are validated

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PHARMACEUTICAL QUALITY SYSTEM

Quality Control

4. records are made, manually and/or by recording instruments, which demonstrate that:
   - all the required sampling, inspecting and testing procedures were actually carried out.
   - any deviations are fully recorded and investigated;
5. the finished products contain active ingredients complying with the qualitative and quantitative composition of the Marketing Authorisation or Clinical Trial Authorisation, are of the purity required, and are enclosed within their proper containers and correctly labelled;

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PHARMACEUTICAL QUALITY SYSTEM

Quality Control

6. records are made of the results of inspection
7. testing of materials, intermediate, bulk, and finished products is formally assessed against specification. Product assessment includes a review and evaluation of relevant production documentation and an assessment of deviations from specified procedures;
8. no batch of product is released for sale or supply prior to certification by a Qualified Person.
9. sufficient reference samples of starting materials and products are retained to permit future examination of the product if necessary and that the sample is retained in the final pack.

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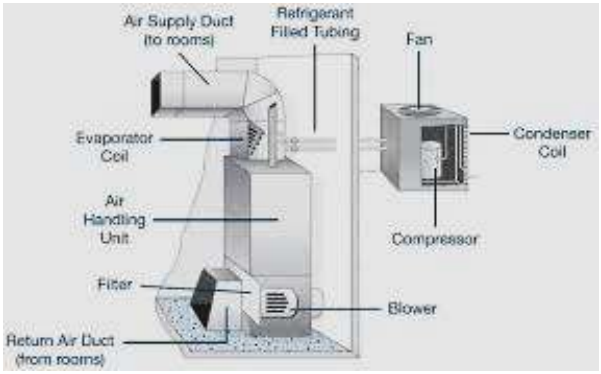
PHARMACEUTICAL QUALITY SYSTEM

Product Quality Review

- Regular periodic or rolling quality reviews of all authorised medicinal products should be conducted with the objective of verifying the consistency of the existing process:
  - A review of all batches that failed to meet specification(s)
  - A review of all quality-related returns, complaints and recalls and the investigations performed at the time
  - The qualification status of relevant equipment and utilities, e.g. HVAC (heating, ventilation, and air conditioning), water, compressed gases
  - A review of all significant deviations or non-conformances, their related investigations, and the effectiveness of resultant corrective and preventive actions taken

30

HVAC system



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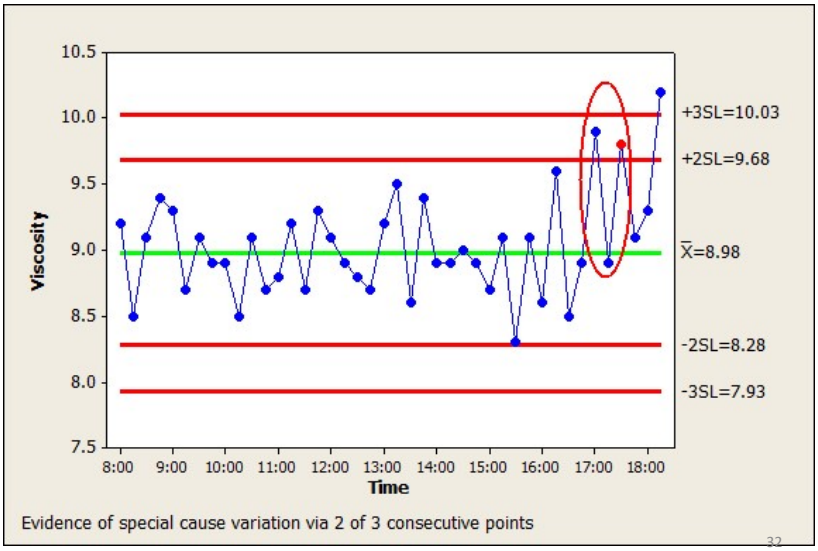
PHARMACEUTICAL QUALITY SYSTEM



Evidence of special cause variation via 2 of 3 consecutive points

32

(Quality Control)

بحكينا كثير عنه وواضح كل شي فيه .. وشارح بالسلايدات
شو وظيفتهم الاساسيّة وشو هي ال requrements المطلوبة
ويلي عندي عليها QC .. وإنه مهتم عندي بعملية ال Testing
.. إلخ
وحكينا إنه عملية ال recording لازم تكون be kept .. وكل شي
نعمله للمنتج مسجّل

...

ال QC تهتم عندي إنها تعمل مراجعات دوريّة منتظمة للمنتج
ولكل شي .. من هاي الأشياء يلي تعمل إلها مراجعة .

① batches that failed to meet specification

لو سببت عندي batches بروح بعمل investigate على كل ال history
تاع ال product عشان أشوف كل المشاكل يلي صارت قبل ..
شو ال preventition يلي صارت قبل أو أنا حطيتها قبل

② Complaints and recalls → الشكاوي وهاي الأشياء

③ HVAC → ventilation → air conditioning → heating ←

وحكينا ال water ⇒
و ال Compressed gas

← يعني بدّي أتأكد .. هل الهواء والتكييف والحرارة وهاد كله تمام ولا لأ؟ مثلاً الحرارة للغرفة لازم تكون إلها range معيّن .. في قسم في ال QC مهتم بالتحكم بهاي الأمور .. مثلاً الهواء كل فترة يروحوا يجيبوا جهاز يشوف كمية ال dust بالغرفة عندي كم .. وكمان يفحصوا هل في MO ولا لأ ...

④ Corrective and preventive action

← برضه يهتموا بأنه يعملوا إلهم مراجعة .

PERSONNEL

- The manufacturer should have an adequate number of personnel with the necessary qualifications and practical experience.
- The responsibilities placed on any one individual should not be so extensive as to present any risk to quality.
- The manufacturer must have an organization chart in which the relationships between the heads of Production, Quality Control and where applicable Head of Quality Assurance or Quality Unit and the position of the Qualified Person(s) are clearly shown in the managerial hierarchy.

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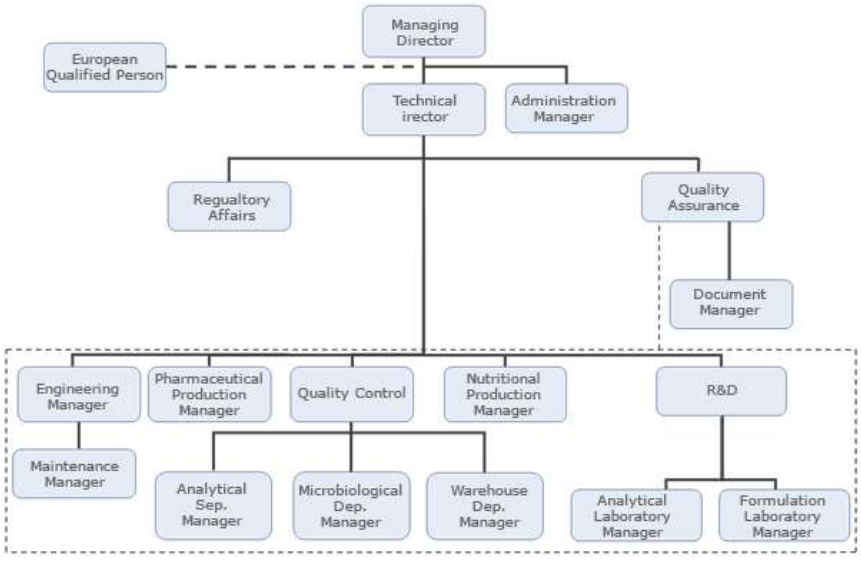

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PERSONNEL

- People in responsible positions should have
  - specific duties recorded in written job descriptions
  - adequate authority to carry out their responsibilities
- There should be no gaps or unexplained overlaps in the responsibilities of those personnel concerned with the application of Good Manufacturing Practice.
- Senior management has the ultimate responsibility to ensure:
  - an effective quality management system is in place to achieve the quality objectives,
  - roles, responsibilities, and authorities are defined, communicated and implemented throughout the organization.

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PERSONNEL

Key Personnel

- Senior Management should appoint Key Management Personnel including the head of Production, the head of Quality Control, and Qualified Person(s)
- Normally, key posts should be occupied by full-time personnel.
- The heads of Production and Quality Control must be independent from each other.
- For medicinal products manufactured within the European Union, a Qualified Person must ensure that each batch has been manufactured and checked in compliance with the laws in force in that Member State and in accordance with the requirements of the marketing authorization.

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PERSONNEL

Key Personnel

The **head of the Production Department** generally has the following responsibilities:

- To ensure that products are produced and stored according to the appropriate documentation in order to obtain the required quality;
- To approve the instructions relating to production operations and to ensure their strict implementation;
- To ensure that the production records are evaluated and signed by an authorised person;
- To ensure the qualification and maintenance of premises and equipment in his department,;
- To ensure that the appropriate validations are done;
- To ensure that the required initial and continuing training of his department personnel is carried out and adapted according to need.

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PERSONNEL

Key Personnel

The **head of the Quality Control Department** generally has the following responsibilities:

- To approve or reject, as he sees fit, starting materials, packaging materials, and intermediate, bulk and finished products;
- To approve specifications, sampling instructions, test methods and other Quality Control procedures;
- To approve and monitor any contract analysts;
- To ensure :
  - that all necessary testing is carried out and the associated records evaluated;
  - the qualification and maintenance of his department, premises and equipment;
  - that the appropriate validations are done;
  - that the required initial and continuing training of his department personnel is carried out and adapted according to need.

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PERSONNEL

Key Personnel

- The heads of Production and Quality Control and where relevant, Head of Quality Assurance or Head of Quality Unit, generally have some shared, or jointly exercised, responsibilities relating to quality. These may include:
  - The monitoring and control of the manufacturing environment
  - Plant hygiene
  - Training
  - Process validation
  - The retention of records

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PERSONNEL

Training

- The manufacturer should provide training for all the personnel whose duties take them into production and storage areas or into control laboratories (including the technical, maintenance and cleaning personnel), and for other personnel whose activities could affect the quality of the product.
- Training include:
  - the theory and practice of Good Manufacturing Practice,
  - Training appropriate to the duties assigned to personnels
- Training programs should be available, approved by either the head of Production or the head of Quality Control, as appropriate.
- Training records should be kept.

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PERSONNEL

Training

- Personnel working in areas where contamination is a hazard, e.g. clean areas or areas where highly active, toxic, infectious or sensitising materials are handled, should be given specific training.
- Visitors or untrained personnel should, preferably, not be taken into the production and quality control areas. If this is unavoidable, they should be given information in advance, particularly about personal hygiene and the prescribed protective clothing.

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PERSONNEL

Personnel Hygiene

- Detailed hygiene programmes should be established and adapted to the different needs within the factory.
- They should include procedures relating to the health, hygiene practices and clothing of personnel.
- All personnel should receive medical examination upon recruitment.
- Steps should be taken to ensure as far as is practicable that no person affected by an infectious disease or having open lesions on the exposed surface of the body is engaged in the manufacture of medicinal products.

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PERSONNEL

Personnel Hygiene

- Every person entering the manufacturing areas should wear protective garments appropriate to the operations to be carried out
- Eating, drinking, chewing or smoking, or the storage of food, drink, smoking materials or personal medication in the production and storage areas should be prohibited.
- Direct contact should be avoided between the operator's hands and the exposed product as well as with any part of the equipment that comes into contact with the products.
- Personnel should be instructed to use the hand-washing facilities.

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PREMISES AND EQUIPMENT

- Premises should be situated in an environment which, presents minimal risk of causing contamination of materials or products
- Premises should be carefully maintained, ensuring that repair and maintenance operations do not present any hazard to the quality of products.
- Premises should be cleaned and, where applicable, disinfected according to detailed written procedures.

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PREMISES AND EQUIPMENT

- Lighting, temperature, humidity and ventilation should be appropriate for the manufacture and storage of medicinal products and the accurate functioning of equipment.
- Premises should be designed and equipped so as to afford maximum protection against the entry of insects or other animals.
- Steps should be taken in order to prevent the entry of unauthorised people.

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PREMISES AND EQUIPMENT

Production Area

In order to minimize the risk of a serious medical hazard due to crosscontamination, dedicated and self contained facilities must be available for the production of particular medicinal products, such as:

- highly sensitizing materials (e.g. penicillins)
- biological preparations (e.g. from live microorganisms).
- Certain antibiotics,
- certain hormones,
- certain cytotoxics,
- certain highly active drugs and non-medicinal products

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PREMISES AND EQUIPMENT

Production Area

- For those products, in exceptional cases, the principle of campaign working in the same facilities can be accepted provided that specific precautions are taken and the necessary validations are made.
- The manufacture of technical poisons, such as pesticides and herbicides, should not be allowed in premises used for the manufacture of medicinal products

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PREMISES AND EQUIPMENT

Production Area

- Premises should preferably be laid out in such a way as to allow the production to take place in areas connected in a logical order corresponding to the sequence of the operations and to the requisite cleanliness levels.
- The adequacy of the working and in-process storage space should permit the orderly and logical positioning of equipment and materials so as to:
  - minimise the risk of confusion between different medicinal products or their components,
  - to avoid cross-contamination
  - to minimise the risk of omission or wrong application of any of the manufacturing or control steps.

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PREMISES AND EQUIPMENT

Production Area

- Where starting and primary packaging materials, intermediate or bulk products are exposed to the environment, interior surfaces (walls, floors and ceilings) should:
  - be smooth
  - be free from cracks and open joints
  - not shed particulate matter
  - permit easy and effective cleaning and, if necessary, disinfection.
- Pipework, light fittings, ventilation points and other services should be designed and sited to avoid the creation of recesses which are difficult to clean.
- As far as possible, for maintenance purposes, they should be accessible from outside the manufacturing areas.

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PREMISES AND EQUIPMENT

Production Area

- Production areas should be effectively ventilated, with air control facilities (including temperature and, where necessary, humidity and filtration) appropriate both to the products handled, to the operations undertaken within them and to the external environment.
- Weighing of starting materials usually should be carried out in a separate weighing room designed for that use.
- In cases where dust is generated (e.g. during sampling, weighing, mixing and processing operations, packaging of dry products), specific provisions should be taken to avoid cross-contamination and facilitate cleaning.

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PREMISES AND EQUIPMENT

Production Area

- Production areas should be well lit, particularly where visual on-line controls are carried out.
- In-process controls may be carried out within the production area provided they do not carry any risk for the production.

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PREMISES AND EQUIPMENT

Storage Areas

- Storage areas should be of sufficient capacity to allow orderly storage of the various categories of materials and products:
  - starting and packaging materials,
  - intermediate, bulk and finished products,
  - products in quarantine,
  - released, rejected, returned or recalled.
- Segregated areas should be provided for the storage of rejected, recalled or returned materials or products.

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(personal)

- طبعًا لهمني يكون عندي العدد الكافي من الموظفين المؤهلين للعلبة ولهيك وظيفة .. وأهم شي يكون حس المسؤولية عندهم عالي .. ويكون هم المسؤولية مش أكبر من عاتقهم .. في مخطط بيسلايد 34 يوضح فيه الموظفين ودوجاتهم وعلاقتهم ببعض.

أهم الوظايف .. Key personnel برضه مايحتاج لشرح يحكيلي عن طبيعة الشغل لكل منصب في الإدارة .. إحترامهم

...

وعندي وظيفة رئيس لـ QC وأهمها مايلي

① The monitoring of Manfacurnng enviroment
↳ يراقبوا بيئة التصنيع

② Hygiene → زي العمال تاع دواء الضغط والعضاد يلي عكيته

③ Training → أكيد راح يأهلوك كشخص ويدربوك على الأجهزة وكيف تتعامل معهم

④ process validation

⑤ retention of records

"personnel Hygrene"

← تهمني يتبع معايير النظافة الشخصيّة .. يكون خالٍ من الأمراض .. وكيش فحص تحص النظافة .

Health , clothing of personnel, hygrene

← صير إ QC والمدير لل QA والمدير تاع الإنتاج ممنوع يكونوا نفسهم يعني نفس الشخص عشان مايصير عشي over-lab

← بالنظافة .. ممنوع المكياج .. ممنوع المسكاراة .. ممنوع اي شي .. حتى الملتحي يكون مخطي لحيته .. الحمامات مفصولة عن الإنتاج .

"premises and equipment"

← بيئة الشركة الموجودة فيها تهمني تكون بعيدة عن مسببات التلوّث

يجب صيانة الجنب بعناية .. التطهير والنظافة مهمين الحرارة .. الرطوبة وكل هاي الأمور

الأشخاص يلي يدخلوا الجنب .. في تهاريج مش اي حد يدخل

=) production area

نظرًا لسمّية بعض المواد والأدوية وخاطرها .. في إجراءات
لازم نتخذها وهن هاي الأدوية مايلي : ذاكرهم بالسلايد
.. الهرمونات مثلًا .. مثل البروجيسترون .. الموظفين يلي
مكلفين إنهم يصنعوه .. قبل ما نوظفهم بعملوا إلهم Test
عستوى الهرمون عندهم .. خلال عملية الإنتاج .. كل اسبوع
بشيكوا على مستوى هاد الهرمون عندهم ... وقت بيرتفع مباشرة
بخيروا الشامل .. عشان الموظف
الباقي كله واضح .. مايحتاج تفريغ
مثلًا مبيدات الحشرية ممنوع تتصنع في مصانع الأدوية ..

عمّت