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A Review on Cleanroom Gloves in Pharmaceutical Applications

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Abstract : This study intended to demonstrate the importance of having a standard quality of medical gloves and the requirement needed to meet the standard specifications set by regulatory authorities such as ASTM, EN, and ISO etc. The recent regulatory citations and warning letters revealed that major pharmaceutical companies in India had serious non-compliance issues in handling gloves into their receipt, testing, storage and issuance to production use. The gloves were tested to check the quality is within the limit as per ISO 2859-1.

The quality control test was carried out on sterile, non sterile and hypalon glove by following the ISO sampling procedure 2859-1 The tests includes visual examination test, water leak test for pinhole detection, physical dimension test, and pressure drop test for hypalon glove. The result of those test reveal that the gloves are meeting the standard requisites set by the different agency, hence the glove can be distributed and used in pharmaceutical clean room. Carrying out those tests will avail to avert the product from contamination, and transmission of disease between health care professional and the patient.

The reason behind the study on clean room glove is to demonstrate the importance of utilizing standard quality of clean room gloves. The recent regulatory citations and warning letters revealed that major pharmaceutical companies in India had serious non-compliance issues in handling gloves into their testing, storage and issuance to production use. It was found the use of non sterile glove in sterile area was in violation to cGMP. Clean room glove is one of the main sources of product contamination and using clean room glove as the contamination control kit can avail to reduce the product contaminations. In this study, the quality control tests for clean room glove were carried out as according to ISO, ASTM and EN.

Keywords : Clean room glove, Medical glove, Contamination.

Introduction

Key materials which are used in support of manufacturing or which arecoming in contact with the products during manufacturing that may not become partof final product.

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Direct quality impacting: Consumables which will have direct contact withproduct and directly affect the quality, purity, strength and safety of the final product.Examples are product filters, product contact tubing and process gases, polyethylene bags etc. Indirect quality impacting: Consumables which do not come into direct contact with the product and may affect the quality, purity, strength and safety of the product. Examples are gloves, garments, lubricants, wipes/mops, etc. Non-quality impacting: Consumables which will not affect the quality, purity, strength and safety of the product. Examples are engineering tools and housekeeping items etc.

Pharmaceutical gloves [1-2]

The recent past regulatory citations and warning letters revealed that major pharmaceutical companies in India had serious non-compliance in handling gloves into their receipt, testing, storage and issuance to production use.

Importance of gloves quality

- Gloves are used by medical professionals, such as doctors, surgeons, pharmacists and biochemists.
- All rely on medical gloves as an effective barrier against the transmission and spread of disease and blood and fluid-borne infectious agents.
- These are important to prevent the wide verity if diseases to both the patient and health professional.
- This also helps to prevent the cross contaminations.

Note: Wearing gloves is not a substitute for proper hand washing and hygiene, but using them gives greater protection.

Classification of Gloves[3-5]

Classification according to FDA based on surgeon's and patient examination gloves.

1. Surgeon glove
2. Patient glove

1. Surgeon glove:

These are future classified as follows:

→Powdered surgeon's glove
→Powdered free surgeon's glove

2. Patient glove:

These are future classified as follows:

→Powdered patient examination glove
→Powdered free patient examination glove

The selection of which glove to use is based on multiple factors, including type of procedure, need for chemical resistance, barrier effectiveness, fit, comfort and tactile sensitivity.

Table 1: Difference between examination gloves and surgical gloves

SlNo	Parameters	Examination gloves	Surgical gloves
1	Hand size	Ambidextrous in design	Surgical gloves are designed hand specific
2	Sterility	Non sterile	Sterile
3	Physical Dimensions	Thinner and shorter length	Thicker and longer
4	Process	Non critical	Critical

It is important to understand the application of consumables and criticality in usage of them in production and quality control aspects to define their pre-determined quality attributes. Though these consumables (Glove) are not a part of product composition, it is playing an important role in minimizing the contamination into the drug products. Hence, it is a right time to start the implementation of consumable management in pharmaceutical industry to meet product quality and safety requirements.

Table 2:Components of gloves

Name of Components	Functional property	Example
Antioxidant	To prevent the deterioration of rubber molecule	4-and 5 Methyl mercapto-benzimidazole sterically hindered polymeric phenol
Pigment	To differentiate by color	Titanium dioxide
Activator	To catalyze the reaction.	Active zinc oxide
Vulcanizing agent	A chemical process for converting natural rubber or related polymers into more durable materials via the addition of sulfur	Sulfur
Accelerators	Increasing the speed of cross linking between polymer and sulfur	Diisopropylxanthaogen poly (4) sulphide, Zinc diethyl Dithocarbamate, Sodium dibutyldithiocarbamate
Coagulant Agent	Uniform distribution of latex over the former	Calcium nitrate
Former Cleaning agent	To remove the organic metal	Nitric acid Sodium hypochlorite
Lubrication	To facilitate stripping (removing)the gloves from the molds at theend of the production line.	Silicon, Corn starch
Anti-webbing agent	A Deformer or an Anti-foaming agent/Anti-webbing agent is a chemical additive that reduces and hinders the formation of foam in industrial process liquids	Polymethylsiloxane
Thickener	A substance added to a liquid to make it firmer	Hydroxyethyl cellulose
Stabilizers	A thing used to keep something steady or stable)	Potassium caprylate, Potassium laurate, Potassium hydroxide, Ammonia.

Performance requirements

- Gloves shall be sampled and inspected in accordance with ISO 2859-1. Gloveshall meet the following referee performance requirements
- Comply with requirement for sterility when tested in accordance sterility testmethod
- Be free from holes
- Have consistent physical dimensions
- Have acceptable physical property characteristics
- Have a powder residue limit of 2.0 mg
- Have a recommended aqueous soluble protein content limit of 200 $\mu g/dm^2$
- Have a recommended maximum powder limit of $15mg/dm^2$

Table 3: Routine release criteria of gloves

SL No	Test	Specification limits
1	Description	Off-white to pale yellow color cuff beaded,powder free rubber gloves**.**
2	Visual examination (Pouch)	Should be free from extraneous matter,sealing defects, damage and labeled as"Sterile"
3	Visual examination (Gloves)	Should meet AQL 1.5, G2 ISO 2859
4	Length	Not less than 480 mm.
5	Width	Between 102 mm to 114 mm
6	Thickness (Cuff)	Not less than 0.14 mm
7	Water leaktest (for pin holes)	Should meet AQL 1.5, G2 ISO 2859
8	Tensile strength-before ageing	>= 24 MPa Not less than 24 MPa
9	Tensile strength-after Ageing	>= 18 MPa Not less than 18 MPa
10	Ultimate Elongation-before Ageing	>= 750 % less than Not less than 750 %ageing
11	Ultimate Elongation-after	>= 560 % Not less than 560 %
12	Force at break- before Ageing	>= 9 N Not less than 9 N
13	Force at break- after ageing	>= 9 N Not less than 9 N
14	Protein content	<= 50 µg Not more than 50 µ g/dm2
15	Powder residue	<= 2 mg Not more than 2 mg/glove
16	Sterility	Must comply

How to don/doff the gloves

When the hand hygiene indication occurs before a contact requiring glove use, perform hand hygiene by rubbing with an alcohol-based handrub or by washing with soap and water.

I. HOW TO DON GLOVES:

1. Take out a glove from its original box

2. Touch only a restricted surface of the glove corresponding to the wrist (at the top edge of the cuff)

3. Don the first glove

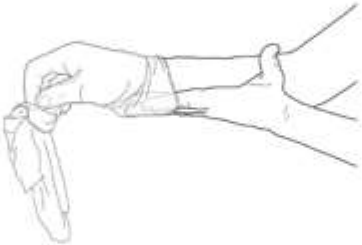
4. Take the second glove with the bare hand and touch only a restricted surface of glove corresponding to the wrist

5. To avoid touching the skin of the forearm with the gloved hand, turn the external surface of the glove to be donned on the folded fingers of the gloved hand, thus permitting to glove the second hand

6. Once gloved, hands should not touch anything else that is not defined by indications and conditions for glove use

II. HOW TO REMOVE GLOVES:

1. Pinch one glove at the wrist level to remove it, without touching the skin of the forearm, and peel away from the hand, thus allowing the glove to turn inside out



2. Hold the removed glove in the gloved hand and slide the fingers of the ungloved hand inside between the glove and the wrist. Remove the second glove by rolling it down the hand and fold into the first glove

3. Discard the removed gloves

4. Then, perform hand hygiene by rubbing with an alcohol-based handrub or by washing with soap and water

Sampling[6-8]

This sampling procedure has been followed while performing the quality control test for cleanroom gloves and the following sampling procedure (ISO 2859-1) are particularly for gloves only.

Sampling instruction

- Selected 2000 non sterile and 1000 sterile glove packs and conducted sampling in accordance with the sampling as given in sampling and inspection plan for gloves
- **Note-** Pack can be shipper or bags or container. Refer GRN for verifying number of packs received
- Randomly selected the packs and collected a quantity such that the total quantity was equal to the sample to be collected from the pack
- Check the sample collected, visually for gross obvious defects by referring table and annexure and record the details in observation sheet
- Record the observation in sampling observation sheet
- Additionally record the observed non-conforming items (AQL) level in sampling observation sheet

Test Procedure

A. Description

Sample glove was taken to the visual inspection table and checked each gloves for its appearance as described in specification and observation was recorded.

B. Visual examination

Sample glove was taken to the visual inspection table and checked each gloves for visual examination of physical defects such as rupture/cut/lumps/crack/beadlesscuff etc; as per inspection G1 AQL 1.5 (for non-sterile glove) and observation was recorded.

C. Length of the glove

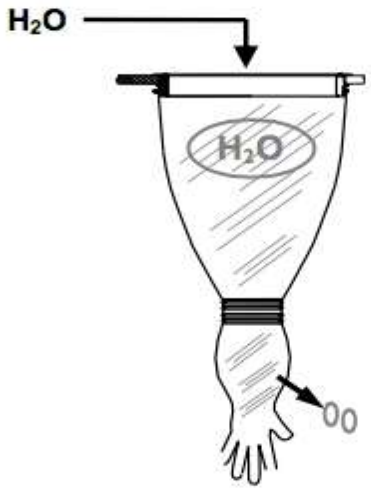
Gloves were placed flat on an even surface and measured the length by measuring the distance from the middle finger tip of the glove to the cuff edge using measuring graduated rule and observation was recorded.

D. Width of the glove[9]

Gloves were placed flat on an even surface, folded the thumb portion of the glove and measured the width by measuring the distance between end of the thumb to the end of the small finger and observation was recorded.

E. Water Breakthrough Test or Leak Test

The water breakthrough test utilized water pressure to inflate the glove. Visual inspection of the glove was carried out to find the presence of pinhole, which can be indicated by droplets of water on the surface of the glove[10]. The test was carried out byfilling the glove with 1 litre of water and then it was hanged in order to observe for the leakage after2 minutes.



Advantage

Pinholes in fingertips are more easily recognized.

F. Pressure drop test

The pressure drop test measures the pressure decay as an indicator of a leaky glove[11].

Procedure

Fixed the hypalon glove to the gauntlet and it was verified for any wrinkle on the glove port glove and closed the glove integrity testing cabinet door. The integrity tester was switched on and after the completion of inflation phase, stabilization phase was carried out for 420 sec. After the completion of stabilization phase, measurement phase was started. In this phase pressure decay per unit time of the glove was measured over the defined measurement time i.e. 360 sec. After the completion of test, result were displayed in the "**Port status screen**" and recorded.

Pressure Drop Test

Acceptance criteria : The pressure drop of gloves must NMT 150 pa at set pressure of 2000 pa and test time of 6 minutes.

Table 4: Set parameter for gloves integrity testing

Set parameters	Set value
Start/Test pressure	2000 pa
Inflate time out	180 sec
Stabilization time out	420 sec
Pulse count	25 Nos
Test time or holding time	360 sec
Pressure decay limit	150 pa

G. Thickness of glove

Thickness of the gloves was expressed in millimetres using dial micrometre in three different locations such as finger, palm and cuff.

Summary and Conclusion:

It is important to utilize standard quality of gloves and there should be congruous quality system regulation, sampling should be done as per ISO 2859-1 by inspectors of the quality control laboratory and performing those tests and meeting those tests acceptance limit will assure that clean room/medical gloves are safe to utilize.

This project work was carried out to understand the importance of clean room glove in pharmaceutical application and the mandatory tests which are needed to be performed as per regulatory agency. The results were found to be good and within acceptance limits. A summary of each test carried out for description, visual examination, length, width, water leak test or pinhole test and pressure drop test studies are as follows:

A. **Description:**

The description test has been performed to check whether description given by the manufacture is meeting with the recorded observation.It was found to be satisfactory for all the three gloves.

B. **Visual examination:**

The visual examination test has been performed to checkwhether it was free from extraneous matter and free fromrupture/cut/lumps/crack. It was found to be satisfactory for all the three gloves.

C. **Length:**

The test to measure the length of the clean room glove has beenperformed to check whether it was meeting with the manufacturer's certificate of analysis. The length plays important role in controlling the contamination ofthe product, where longer length glove allows the sleeve to be tucked into theglove, thus eliminating contamination problem. It was found to be satisfactoryfor all the three gloves.

D. **Width:**

The test to measure the width of the clean room glove has beenperformed to check whether it was meeting with the manufacturer's certificateof analysis. It was found to be satisfactory for all the three gloves.

E. **Water leak test:**

Water leak test has been performed to check the presence ofpinholes in the gloves through which the microbes can migrate which leads tocontamination of the product. It was found to be satisfactory for all the threegloves.

F. **Pressure drop test:**

Pressure drop test has been performed to hyplaon glove only, to detect the pinhole by using the pressure drop decay method. It wasfound to be satisfactory.Based on the test performed on cleanroom gloves, it was concluded that the cleanroom gloves met those specifications set by the agencies; therefore they weresafe to be utilized in pharmaceutical cleanroom, medical examiner, dental examiner,health care technicians and associated workers[12].

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