Compressed Air in Pharmaceutical Industry

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Source of contaminations

- Intake air from surroundings (**oil, dirt/dust and moisture/ water vapour**, virus, bacteria, germ, micro-organisms)
- Compressor unit (*note : equipment uses oil for lubricants)* (including Air Receiver + Filters)
- Piping Distribution Systems and Fittings/ Accessories (rust/particles) → ?

Recommended Type

Oil Free Compressed Air :

Air compressed from initial pressure to final pressure using compressor in which the air is not in direct contact with any fluid or lubricant

Achieved by using Oil Free Rotary Screw and Centrifugal Compressors

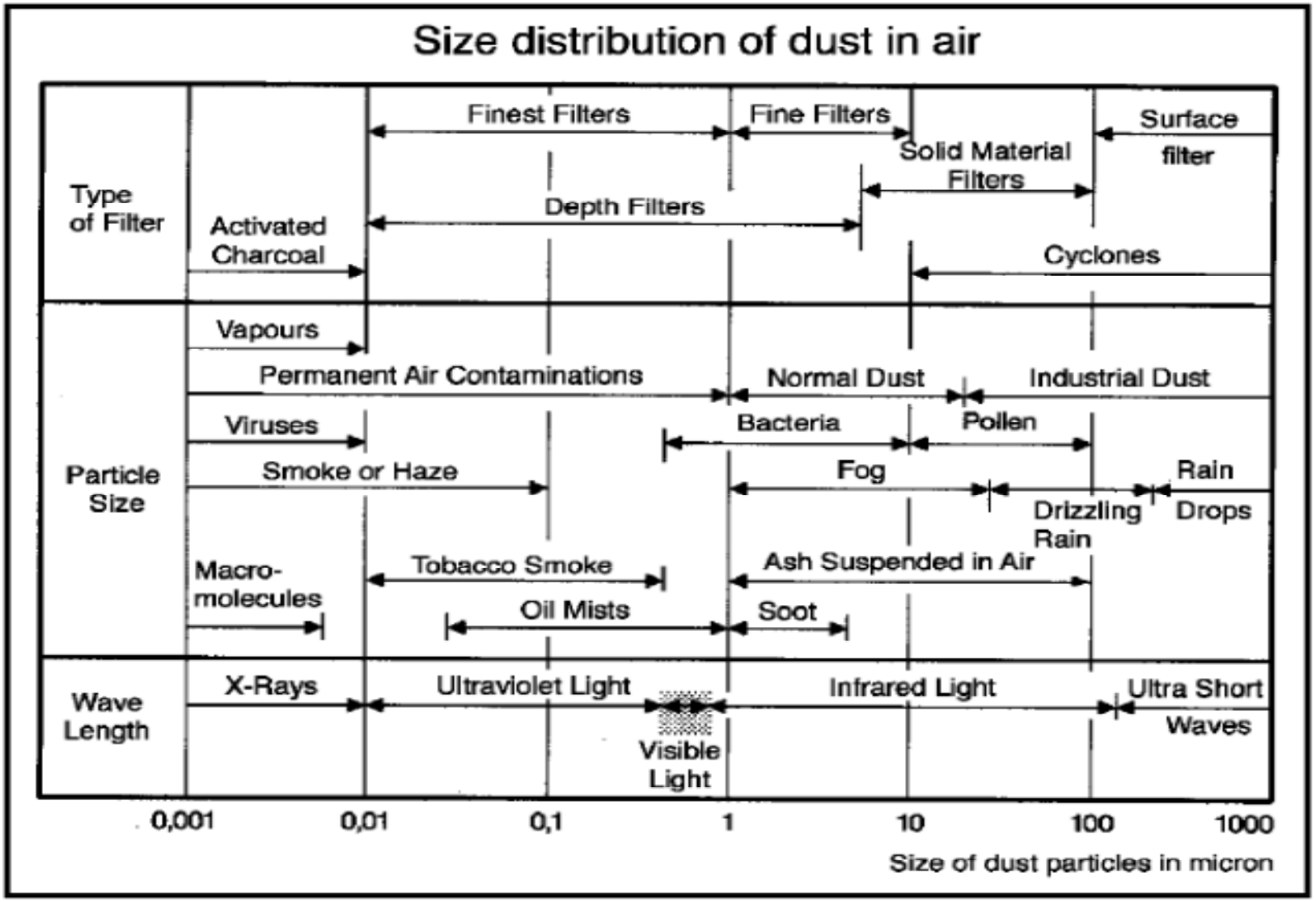
Up-date Air Quality Classes

- ISO 8573.1 Class 0
- Note : contamination cannot be eliminated but can be reduced → starting from the source and by *filtration – purification – separation* through various equipment, media filter

ISO 8573-1: 2001 Air Quality Classes

Quality Class	SOLIDS Max number of particles per m3			WATER Pressure Dewpoint		OIL & OIL VAPOR
	0.1-0.5 micron	0.5-1.0 micron	1.0-5.0 micron	°F	°C	mg/m3
0	As specified by user or equipment manufacturer and more stringent than class 1					
1	100	1	0	-100	-70	0.01
2	100000	1000	10	-40	-40	0.1
3	-	10000	500	-4	-20	1
4	-	-	1000	37.4	3	5
5	-	-	20000	44.6	7	-
6	-	-	-	50	10	-

Application	ISO 8573.1 Quality Class	SOLIDS Max number of particles per m^3			WATER Pressure Dewpoint		OIL & OIL VAPOR
		0.1-0.5 micron	0.5-1.0 micron	1.0-5.0 micron	°F	°C	mg/m3
Non-Contacting	2-4-1	100,000	1,000	10	37.4	3	≤ 0.01
Food and Food Surface Contact	2-2-1	100,000	1,000	10	-40	-40	< 0.01
Non-Contacting High Risk	2-2-1	100,000	1,000	10	-40	-40	≤ 0.01


Size distribution of dust in air
Type of Filter
Finest Filters
Fine Filters
Surface filter
Solid Material Filters
Depth Filters
Activated Charcoal
Cyclones
Particle Size
Vapours
Permanent Air Contaminations
Normal Dust
Industrial Dust
Viruses
Bacteria
Pollen
Smoke or Haze
Fog
Rain Drops
Drizzling Rain
Macro-molecules
Tobacco Smoke
Ash Suspended in Air
Oil Mists
Soot
Wave Length
X-Rays
Ultraviolet Light
Infrared Light
Ultra Short Waves
Visible Light
0,001
0,01
0,1
1
10
100
1000
Size of dust particles in micron

Parameters to be checked based on PIC Utility Inspection /

4.	Area of operation/Items **Pharmaceutical gases**	Notes	Crucial questions	Supporting documents
4.1.	Key design criteria (compressed air)	• air inlet-source, contamination risks • filters (pre –final) • suitability of materials • welding • prevention of contamination (receiver vessel) • valves	Source of Contamination : • **Oil** • **Moisture /water** • **Dust Particles** • **Microba**	Guide 3.1 0. Annex 15- 9-1 0
4.2.	Qualification	• (DQ, IQ, OQ? PQ) • solid contaminants, water, oil limits • capacity, filter pressure drops, alarm operation	• how do you assure that filters are replaced in time?	Guide 3.34, 3.38 ISO 8573 Compressed air 1-7 Annex 15- 2-1 8

Compressed Air in Pharmaceutical Facility

- Operation of Equipment (pneumatic system) →Packing Equipment : Blister Pack Machine, Powder Filling Machine etc.
- Vacuum cleaning system
- Spray system (coating, mixing and FBD)
- Others / Innovation : Tablet Press Machine, Capsule Filling Machine, Drying Container

Air Quality Testing

- During Performance Qualification (PQ)
- Check and Testing against major critical parameters (key design criteria)
  - **Solid** / Particle / Dust : Particle Counter Measuring Equipment → example Met One Particle Counter
  - **Liquid / Vapor / Moisture** : PDP (pressure dew point) → hygrometer
  - **Oil content** : Oil measuring kits →from Drager
  - **Microba / Viable Organism testing (Slit to Agar)** → Air Sampler (Biotest diagnostic air sampler)

FUNCTION Compressed Air in Pharmaceutical Production Use

- Compressed Air Generation (Air Compressor) and Distribution Piping System should be suitable for production of dry and oil-free compressed air, continuous distribution of Compressed Air in sufficient quantity and quality to the points of use (POU)/ user point.

COMPRESSED AIR QUALITY

- The compressed air quality must comply with the relevant ISO 8573-1 standard, quality class 1 for particles and oil residues (aerosol, liquid, and vapour), quality class 2 for humidity & liquid water *(class 1.2.1)*
- Quality requirements should be updated and revised if quality requirements are requested to higher standards.

- The Compressed Air Generation and Distribution/ Piping Systems should be constructed according to GMP requirements.
- Dead legs/zones after sterile filters should be avoided.

CONSTRUCTION REQUIREMENTS

- Appropriate materials of manufacture must be selected and specified in accordance with GMP regulations depending on the specific application and process requirements.
- All materials, instruments and instrument enclosure materials shall be of durable type.
- Compressed air contact parts should be made from FDA accepted materials (food grade standard)

CONSTRUCTION REQUIREMENTS

- Surface finish on compressed air contact parts should be such that adherence of particle or liquids is minimized.
- Join materials, then it should be crevice free and flush with the adjacent material.
- The surface finish shall be the same standard as the adjacent material.

CONSTRUCTION REQUIREMENTS

- Non compressed air contact parts should be made of FDA accepted materials.
- The surface finish on non product contact parts should be such that cleaning of the surface made easy (easily cleaning)
- All pipes should be complete drainable and possible to sanitize

CONSTRUCTION REQUIREMENTS

- The piping must be passivated in factory with adequate passivation solutions and should be repassivation after completely installed
- Compressed Air Generation and Distribution shall operate in such a way that the compressed air produced flows smoothly through the pipe works to the point of use.
- Stable pressure compressed air at all point of use (looped system preferable)

CONSTRUCTION REQUIREMENTS

CLEANABILITY and IDENTIFICATION

- The outer surface of Compressed Air Generation and Distribution Piping System should be easy to clean.
- Identification and flow direction should be available (marked)

Parameters, Specification and Limits (URS)

The Items could be slightly different depend of Users

Parameter	Specification	Limits
Particles 0,5 µm < d ≤ 1,0 µm	ISO 8573-1, quality class 1: max. 1 particle per m^3	max. 1 particle per m^3
Particles 1,0 µm < d ≤ 5,0 µm	ISO 8573-1, quality class 1: No particle per m^3	No particle per m^3
Humidity & liquid water	ISO 8573-1, quality class 2: Humidity ≤ 0,117 g/m^3 Dew – point temperature:≤ -40 °C	Humidity ≤ 0,117 g/m^3 Dew – point temperature: ≤ -40 °C

Total oil (aerosol, liquid, and vapour)	ISO 8573-1, quality class 1: ≤ 0,01 mg/ m^3	≤ 0,01 mg/ m^3
Materials of construction: Parts with compressed air contact before sterile filtration:	AISI 304 Food grade FDA accepted material	Material certification 2.2 (EN 10204) Material certificate
Surface finishes	Grit 240	Declaration of supplier
Materials of construction: Parts with compressed air contact after sterile filtration:	AISI 316L Food grade FDA accepted material	Material certification 3.1 (EN 10204) Material certificate
Surface finishes	Ra ≤ 0,8 µm, electropolished Welds Ra ≤ 1,6 µm	Measurement of surface finish
Materials of construction: Parts without compressed air contact:	AISI 304 Food grade FDA accepted material	Material certification 2.2 (EN 10204) Material certificate
Surface finishes	Easy to clean (Grit 240)	Declaration of supplier
Materials of construction:	PTFE or EPDM	Material certificate

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Surface finishes	Easy to clean (Grit 240)	Declaration of supplier

Parameter	Specification	Limits
Non metallic materials (gaskets diaphrams, o-rings)		
Material of construction: signs and name plates Installation of tags	Durable type. They shall be GMP compliant and resistant against cleaning detergents. Withstand temperature influence and mechanical demands	Material certificate Material certificate
General Design of Equipment	Complete drainage of all utility lines is assured, the equipment is fully drainable. Drain valve at the lowest point of air tank. Sterile filter at points of use. Integrity test of sterile filters.	
Site acceptance tests	Pressure test for whole system. Leak tightness test.	
Passivation	The piping must be passivated in factory with adequate passivation solutions.	Passivation documentation

Other Parameters

EHS Critical Parameters (Engineering Parameters Not To Be Validated)

Parameter	Specification	Limits
Guarding	Independently operation, without presence of an operator	
Air tank	Safety valve	
Noise level	75 dB (A)	± 3 dB (A)
Emergency stop	Emergency stop at compressor to be installed.	Easy to reach.

Inspection on Compressed Air

- Drawings and installed (reality)
- Maintenance Program
- Change Control

"Check List In logical order "

- √ Contact with product or with process equipment
- √ Type of product – non sterile – terminally
- √ Name tag/ labelling and identification of the system
- √ Connections – risk of mix-up
- √ Identity all other used gases

"Check List In logical order "

- √ Changing systems for filters
- √ SIP systems / CIP
- √ Back-up systems
- √ Capacity vs. consumption
- √ Maintenance program
- √ Calibration program
- √ SOP's
- √ Records
- √ Breakdown / emergency including challenges o alarm systems

Reference :

- PIC/S PI 09-3 Aide Memoire September 2007
- Manufacturer Manual : Atlas Copco and Ingersoll Rand
- Pharmaceutical Facility Management, JPS Kohli