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Quality and Regulation Standards for Ventilator as Medical Devices in India

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ABSTRACT

The Drugs & Cosmetic act is meant to regularize safety & quality of medical devices, which is applied to all medical devices, implemented from 1st April 2020. Earlier 37 medical devices were regulated/ notified in India. The present study focuses on the devices which require regulations but still lack the quality check points for scrutiny from Central Drug standard control organization (CDSCO), Delhi. Furthermore, it aims to provide quality checklist for two upcoming devices (Ventilator) which is neither categorized nor regulated by Central Drug standard control organization, Delhi. Since the medical devices aid in diagnosing, treatment and palliative care, it is essential to check the quality such that it matches with the International standards. Post covid-19 outbreak ventilators have come under surveillance and notified as medical devices. The present study monitors all parameters for regulation of the ventilator. The survey based quality & regulation standards for ventilator as medical devices has been incorporated in this study.

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INTRODUCTION

The medical devices scenario is changing in India and is expected to reach USD 50 Billion by 2025. It is among the top 20 market for medical device around the world and fourth largest market in Asia. The Government of India has regulated /notified thirty-seven categories of devices as drugs, dated 11/02/2020. As per the notification, with effect from 01/04/2020, the medical devices with subsequent description would be synchronized as 'Drug' under the Drug & Cosmetics Act and Medical Device Regulation 2017. It was recommended by National Health Policy, 2017 to regularize medical devices [1]. Also establish an authoritarian body for medical devices in enjoin to monitor quality matching with international standards. In India, regulatory approval to 'low-risk' devices (Class A & B) are under the purview of State Licensing Authority and for 'high-risk' devices (Class C & D) are regulated by the DCGI, the Central Licensing Authority in India [1]. As per Drugs and Cosmetics Act 1940 and Rules thereunder, medical devices are defined as a devices such as apparatuses, instruments, appliances, implants, materials or other articles, used primarily or in combination, including software or accessories, designed by its manufacturer for humans and animals irrespective of primary intended action in, by any immunological, metabolic means and pharmacological action, but which may aid for one or more specific purposes of [2]:

(i) Diagnosing diseases, mode of avoidance, monitoring & treatment or alleviation of any diseases/ disorders

(ii) Diagnosis & treatment, palliative treatment or assistance for, any disability or injury.

(iii) Investigation, modification or replacement of the anatomic or of physiological process

(iv) Supporting & sustaining life.

(v) Disinfection of devices & Conception Control.

Further, it has been notified that from October 1, 2021, all currently unfettered medical devices should be registered by manufacturer or importers [3]. However, those medical devices, previously notified for regulation or regulated were exempted from the registration requirement. It is categorised under Class A (low-risk) & Class B (medium-risk) have to gain license prior to 11/08/2022, applied to all manufacturers, distributors, importers, retailers and whole seller. Further devices under Class C (medium high risk) & Class D (high-risk) have to gain license prior to 11/08/2023.

To obtain listing for medical devices, the manufacturers & importers must be authorized as acquiescent with ISO-13485 (Medical Devices, Quality Management Systems, Requirements for Regulatory Purposes). It is intended to cover all medical devices. Thus, medical devices sold in India are regulated by Medical Devices Regulations 2017 which have been further amended in April 2020. The medical devices that are not notified until 11/02/2000 (other than 37 categories), would be covered under new definition of medical devices and shall be referred to as "Newly Notified Medical Devices" [3].

The ("MDR Amendment") Medical Device (Amendment) Rules, 2020 is preamble for new section of registration of recently Notified Medical Devices. It is with the removal of 37 categories of previously notified devices from the necessity of registration.

As per first schedule of MDR following is list of 37 categories of devices which are notified or regulated before 11/02/2000 [4]. This list is generated in line with Global Harmonization Task Force (GHTF) countries (Australia, EU, USA, Canada etc.), because India largely follows GHTF principles of classification for medical devices. The 37 medical devices are enlisted in Figure 1.

In the present study, quality standards and regulatory requirements for the ventilators have been evaluated.

The present study focusses on the preparation of checklist for quality evaluation of the ventilators. Ventilator have not been notified yet, but it is an important device during the Covid-19 outbreak. Thus, it is very important to understand the quality standards and regulations for the ventilators.

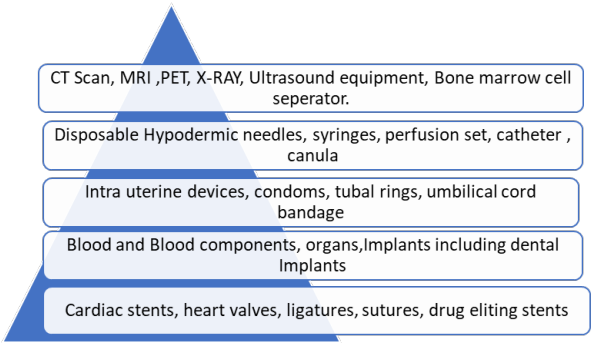

Figure 1: List of 37 Medical Devices Regulated in India

Authors aim to submit these data to CDSCO and propose to incorporate ventilator in the list of notified devices.

METHODOLOGY

Ventilators have become a necessary requirement during this catastrophic time of Pandemic of COVID-19. Novel coronavirus disease can root lung infections and foremost to complications such as lung collapse, acute respiratory distress syndrome, pneumonia, decreased lung capacity, Sepsis. Severe difficulties of COVID-19 are irreversible trauma to the lungs. The pneumonia that COVID 19 results into air sacs in the lungs crammed with fluids, restraining capability to inhale oxygen & causing briefness of breath, cough & death. Further of the lung alveolus are filled with fluid suppurated from the blood vessels in the lungs as COVID-19 pneumonia progresses, ultimately, shortness of breath leads to acute respiratory distress syndrome, a kind of lung failure. In the present study, literature search on quality standards of various ventilators was carried out followed by, survey based strategy designing, Questionnaires from the medical stake holders and followed by preparation of targeted check list was done. Data was collected from hospitals with respect to the list of ventilators, various modes on the basis of criticality of the patient, supplier and generation of oxygen, storage of oxygen, quality of water for dehumidification for ventilators.

Data Sources and Searches

We performed this research by following PRISMA checklist and flow diagram for systematic reviews including data collection for ventilators from official site Central drugs standard control organisation of Government of India, US Food and Drug Administration site for medical devices and EMA guidelines on Medical devices. We also surveyed hospitals in India for evaluation of Ventilator usage, Oxygen quality and water quality for dehumidification in India dur-

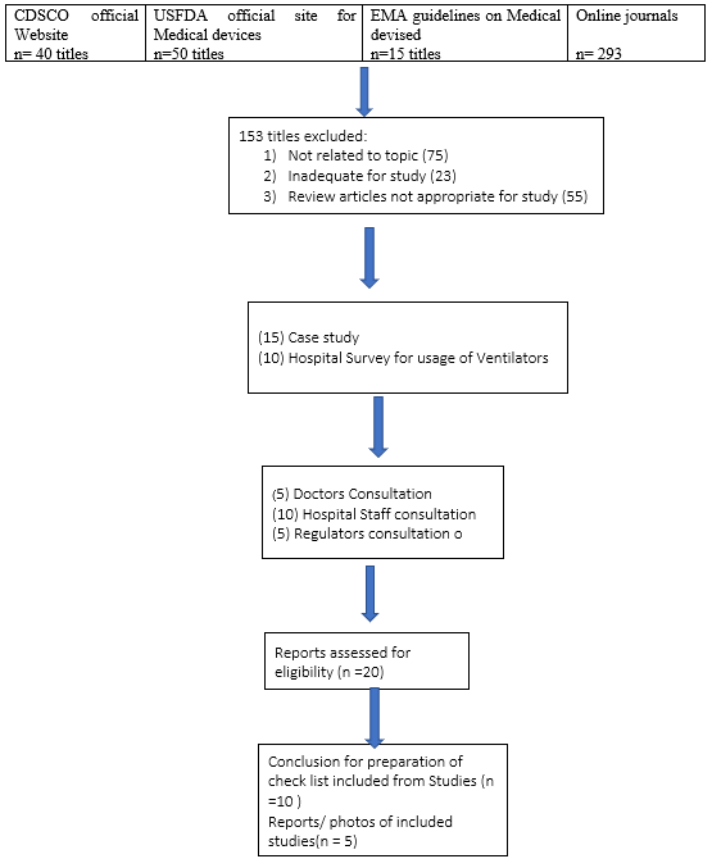

Figure 2: Shows Data Collected from Various Resources

ing this pandemic situation of COVID-19. The Figure 2 shows the data collected from various sources.

RESULTS AND DISCUSSION

Ventilator as a Medical Device

Medical ventilator is an instrument intended to supply mechanical ventilation by circulating oxygen into and out of the lungs, to bring breaths to a patient with shortage of breath or breathing difficulty. Patients with Acute respiratory distress syndrome (ARDS) are often not capable to breathe on their own and would need ventilator to hold up to help circulate oxygen in the body. Basic designs and modes of ventilators are on the basis of breaths such as,

1. Controlled/ /Mandatory breaths

- Volume Control Ventilation (VCV)
- Pressure Control Ventilation (PCV)

2. Supported breaths

- Pressure support ventilation (PSV)

3. Mixed breaths

- Synchronized Intermittent Mandatory Ventilation (SIMV)
- Assisted modes

Ventilator form is based on 3 parameters: trigger, cycle, and limit [5].

Trigger:

It is of two types they are- Patient-triggered & Time triggered.

1. Trigger: The kind of signal that initiates the inspiratory stage by the ventilator. It is of two types they are- Patient-triggered & Time triggered.
2. Cycle: The kind of signal that ends the inspiratory stage delivered by the ventilator. Volume-cycled ventilation: one time a preset volume exits the ventilator. Other types comprise time-cycled ventilation & pressure-cycled ventilation.
3. Limit: None of the value (like pressure, time) that should not be exceeded and which is precise by the operator.

Table 1: Classification of Ventilators

ACV (VCV)	PCV	SIMV-VC	SIMV-PC	PS	CPAP
Frequently used primary mode of ventilation. It catches breaths inhaled by the patient & decreases effort in breathing. Either assisted or controlled breath, of similar volume. ACV is ineffective for patients with short breath– it may induce both hyperinflation and respiratory alkalosis.	Less often used	Commonest mode used in combination. Appropriate mode for both supporting & weaning patients off the ventilator: allows the patient to practice independent breathing between assisted synchronized breaths. Patient-triggered if patient's breath is assessed: (i.e. intermittent) all of the sensed inspiration are assisted by the ventilator.	Less used than Synchronized intermittent mandatory ventilation	Mostly used in combination with SIMV to ensure volume-cycled backup.	It used to assess the potential for extubation in patients who require support from ventilation.
Time-Triggered: Time-triggered if patient's remain senseless: the ventilator delivers a programmed number of compulsory breaths in a minute. Patient-triggered if patient is breathing then all breaths are regulated by the ventilator.	It is required when control of peak airway pressures is important. for e.g Patients with barotrauma or undergone thoracic surgery.	Total Number of assisted breaths in a minute is determined by the operator. Time-triggered if patient's inspiratory effort is not sensed: Ventilator delivers a preset number of breaths in a minute. Volume-cycled:	Similar to PCV:	Operator sets the pressure that must be reached during each ventilator inspiratory phase.	It supplies constant circuit pressure specified by the operator throughout ventilation.

Continued on next page

Table 1 continued

ACV (VCV)	PCV	SIMV-VC	SIMV-PC	PS	CPAP
Volume-cycled: Inspiratory volume is a variable entity. Inspiratory phase ends when a calculated volume exits the ventilator	Where it permits the patient to maintain inflation volume and respiratory frequency. it is used to cut spontaneous breathing. It can be delivered through special face masks.	Inspiratory volume is an independent entity as it is set by the operator & does not change between breath.	Appropriate when control of peak airway pressures is important such as in patients with previous barotrauma or after thoracic surgery	It is always patient-triggered: All sensed inspiratory efforts are supported by the pressure set by the operator.	
	Inspiratory volume is a dependent variable as it is not set by the Operator.		It allows spontaneous breathing without assistance	Once flow in the airway reaches a level below a standard the pressure support is augmented.	
Inspiratory pressure is a dependent variable because it is pre-set & varies between the breaths Pressure-limited: previously set by the ventilator to stop the inspiratory phase in case of homeostasis.		Pressure-limited: Inspiratory pressure is a dependent variable as it is not monitored by the operator.Also predetermined by the ventilator to remove the inspiratory phase in case of lower level of airway pressure			

Further, ventilators are classified based on the common modes of operation (Table 1) such as,

Controlled

It is utilized in crucially ill patients with abridged or absent respiratory drive. All impulsive patients are detected by the ventilator, afterwards assisted with a predetermined volume (or less normally pre-set pressure) specified by the operator. These modes are patient/time-triggered & volume/pressure-cycled.

1. Assist-control ventilation (ACV)/ volume-control (VC)/ ventilation (VCV).
2. Pressure-control (PC) / ventilation (PCV)

Spontaneous/Supported

It is used enhanced respiration, those who are capable to breathe impulsively. These modes are patient-triggered.

1. Pressure support (PS): approximately all impulsive patients are supported with a predetermined pressure specified by the operator.
2. Continuous positive airway pressure (CPAP): ventilator provides an unremitting circuit pressure.

Combined (controlled + spontaneous/supported)

Usually used in patients for continuation on ventilation. A predetermined number of patient breaths are assisted by the ventilator, as described for controlled, residual impulsive patient breaths are supported as described for the spontaneous/supported mode [6].

1. Synchronized intermittent mandatory ventilation (SIMV)-VC + PS
2. SIMV-PC + PS

Quality Parameters/Check List for Ventilators

Primary Checklist

1. Duly notarized valid copies of Quality record in respect manufacturing site (s)
2. Copy of Certificate following quality management system (ISO: 13485)
3. Qualification, Experience and responsibilities of key Technician
4. Detail list of Equipment and Instruments
5. Quality Management System as per medical devices Rules, 2017
6. Quality Manual including following points, Documents supporting the condition & need for a ventilator including oxygen concentrator, cough stimulator, suction pump or nebulizer (Table 2, Table 3) [2].

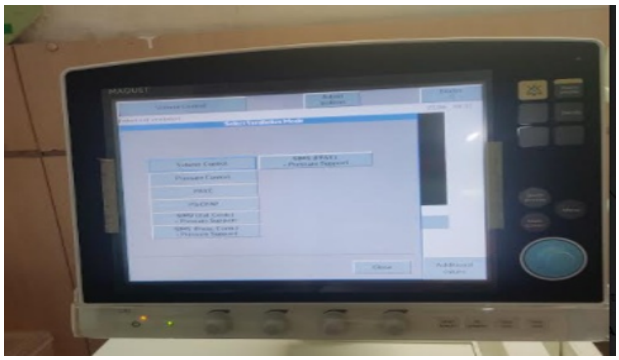

Figure 3: Ventilator Parameters

Water parameters for humidification in Ventilator

Infection Control

1. Sterile water is used for filing water reservoir of ventilators.
2. Sterile water is prepared by distillation of purified water.
3. In case of manually filing water reservoir, hygienic techniques should be used with personnel performing activity like washed hands, wearing gloves, preventing contamination from any other sources.
4. For active & passive humidification reusable Heated humidifiers &heat moisture should be disinfected with IPA or any other disinfectant while changeover from one patient to another.
5. When automatic feed system is used for single patient one dedicated water feed system should be provided & unused water in the reservoir remains sterile for use to the patient.
6. Water condensed from patient's circuit is infectious & should be disposed as per Environment Protection Act followed at hospital with strict precautions.
7. This water should never be circulated in either of humidifiers.

Table 2: Shows Parameters and Acceptance Criteria for Ventilator

Parameters	Acceptance Criteria
Respiratory Rate	Generally, 4-20 breaths per minute delivered by Ventilator
Pressure	Minimum-10 to 20 cm water above peak inspiratory pressure Maximum- 35 cm water
Tidal Volume	5-15 cc/kg volume of gas delivered during each ventilator breath
Fraction Inspired Oxygen (FIO2)	21 to 100% of oxygen delivered to patient from ventilator to keep Partial pressure of oxygen in blood (PaO2)> 60 mmHg & saturated Oxygen (SaO2)> 90%.
I:E ratio (Inspiratory: Expiratory ratio)	1:1.5 to 1:2 unless inverse ratio ventilation ratio [6]

Table 3: Shows Oxygen Test and Acceptance Criteria

Test	Acceptance Criteria
Description	Clear Colourless Gas
Carbon Monoxide	Upto 2 ppm
Moisture	Up to 150 ppm
Carbon Dioxide	24 ppm
Total hydrocarbon	0.1 ppm
Purity	NLT 99 %
Particular Matter	0.2 mg/m^3

8. For preventing water condensation & entrapment Luer lock port for aspirating condensation could be used or high-pressure air could be passed.
9. Passive humidifiers could be used for 48 hours or for a week with some patients
10. Active humidifiers must be changed daily
11. Either of the humidifier must be changed if not working aptly or visible particles or unless until mentioned by the manufacturer [6].

Other Parameters

1. To prevent dryness of discharge formidable humidification with humidity level of 33-44 litre with temperature flanked by 34°C & 41°C with a RH of 100% is maintained.
2. Minimum of 33 mg water per litre is suggested to arrest mucosal dryness which may cause due to insufficient or humidity less than 25 mg water per litre for 24 hours (Figure 3).
3. Maintain normal respiration condition is 36-44 water per litre
4. The humidifiers provide adequate heat & moisture to avoid damage to the alveoli's.

Medical Necessities when with Suction Pump Function

For adequate suction pump function, the recipient must have clearing secretions in given clinical conditions such as:

Cancer surgery, laryngitis, thyroid gland cancer, dysfunction of the swallowing muscles, tracheostomy & unconsciousness. Coverage is determined by diagnosis of the condition. It is required to administer albuterol (J7611, J7613), arformoterol (J7605), budesonide (J7626), cromolyn (J7631), formoterol (J7606), ipratropium (J7644), levalbuterol (J7612, J7614), or metaproterenol (J7669) for the management of obstructive pulmonary disease, cystic fibrosis, HIV [7, 8].

Filtered Nebulizer Requirements

Nebulization is a common method of medical aerosol drugs devices. To deliver a drug by nebulization, it is dispersed in a liquid. After application of a dispersing force (either a jet of gas or ultrasonic waves), the drug particles are contained within the aerosol droplets, which are then inhaled.

It is essential to manage Pentamidine to beneficiaries with pneumocystis, HIV, or complications of organ transplants. Controlled dose inhalation drug delivery system to deliver dosage of Treprostinil inhalation solution (J7686) & iloprost (Q4074) all of

the following criteria should be followed:

The pulmonary hypertension is disorder affecting right ventricle of heart. (Unlike valvular heart diseases, ventricular disease.). It is different from disorders of the respiratory system (like COPD, interstitial lung disease, obstructive sleep apnoea or other sleep disordered breathing, alveolar hypoventilation disorders, etc.). The recipient has any of the following condition including primary pulmonary hypertension, human immune deficiency virus (HIV) infection, connective tissue disease, cirrhosis.

CONCLUSION

The checklist for medical devices is standardized & regulated by epitome body (CDSCO, India). Indian markets for medical devices can only be pushed by the intervention of authority in this unexplored sector of Asian country. In comparison with countries of the west & north, Indian agencies have proposed the regulatory standards for various unnotified medical devices like Ventilators. Ventilators have become an essential requirement during this catastrophic time of havoc Pandemic of COVID-19. Sustaining the life of many needy people, hence provides the backbone to the health sector during this testing time of covid-19. Depending upon the criticality of the patients various modes of the ventilators are set to maintain the pressure and air volume. It is highly beneficial for patients with respiratory disorders and suffering from other ailments. Regulatory standards on these devices will help in maintaining quality and availability of these devices Pan-India.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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