Medicines & Healthcare products Regulatory Agency

MHRA

Rapidly Manufactured Ventilator System (RMVS)

Document RMVS001 - Specification

Issued by MHRA

Introduction

This is a specification of the minimally (and some preferred options) clinically acceptable ventilator to be used in UK hospitals during the current COVID-19 pandemic caused by SARS-CoV-2 virus. It sets out the clinical requirements based on the consensus of what is 'minimally acceptable' performance in the opinion of the anaesthesia and intensive care medicine professionals and medical device regulators. It is for devices, which are most likely to confer therapeutic benefit on a patient suffering with ARDS caused by SARS-CoV-2, used in the initial care of patients requiring urgent ventilation. A ventilator with lower specifications than this is likely to provide no clinical benefit and might lead to increased harm, which would be unacceptable for clinicians.

Intensive care medicine is a whole system of care and ventilators cannot be safely used on any patient without trained staff and other equipment and medicines. Where these impinge on the specification they are mentioned below.

It is proposed these ventilators would be for short-term stabilisation for a few hours, but this may be extended up to 1-day use for a patient in extremis as the bare minimum function. Ideally it would also be able to function as a broader function ventilator which could support a patient through a number of days, when more advanced ventilatory support becomes necessary.

Ventilation

1. At least 1, optionally 2 modes of ventilation
    a. Must have mandatory ventilation.
    b. Mandatory mode must be either (ideally) Pressure Regulated Volume Control, or a pressure controlled ventilation (PCV) or a volume controlled ventilation (VCV).
    c. PRVC/Pressure Controlled - a set pressure is delivered for the period of inspiration and the volume achieved is measured and displayed. Ideally PRVC, an adaptive mode where the tidal volume is set and the lowest possible pressure is delivered to achieve this volume. Pressure Control Ventilation where the user has to provide the adaptive control to achieve tidal volume is only acceptable if the tidal volume delivered is clearly displayed and the user can set patient specific upper and lower tidal volume alarms to alert to the need to adjust the pressure.
    d. Volume Control – the user sets a tidal volume and respiratory rate. The tidal volume is delivered during the inspiratory period. Acceptable only if additional pressure limiting controls are available, see Inspiratory Pressure section.
    e. Optional pressure support mode for those patients breathing to some extent themselves, e.g. BIPAP or SIMV-PC. The user sets an inspiratory pressure and an expiratory pressure. The ventilator can sense when a

patient starts to breathe in and apply the inspiratory pressure, then sense when the patient starts to breathe out and apply the expiratory pressure (this pressure is still positive but lower than the inspiratory pressure).

2. If the patient stops breathing in a spontaneous mode it must failsafe automatically onto mandatory ventilation.

3. Inspiratory airway pressure, the higher pressure setting that is applied to make the patient breathe in:

   a. Plateau pressure should be adjusted to achieve volume and be limited to 35 cmH_2O by default. It is acceptable if an option to increase this to 70 cmH_2O in exceptional circumstances is provided

   b. Peak pressure should be no more than 2 cmH_2O greater than plateau pressure.

   c. If volume control ventilation is used, the user must be able to set inspiratory airway pressure limit in the range at least 15 – 40 cmH_2O in at least increments of 5 cmH_2O.

   d. There must be a mechanical failsafe valve that opens at 80 cmH_2O.

4. Positive End Expiratory Pressure (PEEP). The pressure maintained in the breathing system during expiration.

   a. Range 5-20 cm H2O adjustable in 5 cmH_2O increments.

   b. Patient breathing system must remain pressurised to at least the PEEP level setting at all times.

5. Inspiratory:Expiratory ratio (I:E). The proportion of each breathing cycle that is spent breathing in compared to breathing out.

   a. 1:2.0 (i.e. expiration lasts twice as long as inspiration).

   b. Optionally adjustable in the range 1:1 – 1:3.

6. Respiratory Rate. The number of breathing cycles every minute.

   a. Range 10 – 30 breaths per minute in increments of 2 (only in mandatory mode) can be set by the user.

7. Tidal Volume (V_t) setting, if provided. The volume of gas flowing into the lungs during one inspiratory cycle

   a. Must have at least one setting of 400ml +/- 10 ml.

   b. Ideally 350ml and 450 ml options.

   c. Optionally Range 250 – 600 ml in steps of 50ml.

   d. Even more optionally up to 800 ml.

   e. Optionally the ability to input body weight and have volume calculated as e.g. 6ml/kg of ideal body weight.

Gas and electricity

1. Incoming Gas Supply.
    a. All gas connectors and hoses must comply with BS EN ISO 5359:2014+A1:2017, ISO 5359:2014/AMD 1:2017 and BS 2050: 1978 Electrical Conductivity.
    b. Must connect to wall pipeline oxygen supply via BS 5682:2015 compatible probes (Schrader). If hose not permanently fixed to machine, then must connect with NIST (Non-Interchangeable Screw Thread to ISO 18082:2014/AMD 1:2017). Oxygen pipeline pressure is approximately 3.7 – 4.5 bar.
    c. Oxygen supply from wall outlets outside of ICU and theatres is limited to approximately 6-10 lpm (HTM_02-01_Part_A) and so provision for a gas reservoir will be required to manage peak inspiratory flow rates of up to 100 lpm
    d. Average oxygen consumption must be no more than 3 lpm. This may be allowed to increase as greater certainty is gained over oxygen supply.
    e. Optionally can connect to wall pipeline Medical Air (MA4, NOT SA7) via BS 5682:2015 compatible probes.
    f. Optionally can connect to ISO 7396-2:2007 compatible Anaesthetic Gas Scavenging System or an external activated charcoal absorber (If inhaled anaesthetic agents are being used).
    g. Optionally can operate using an oxygen concentrator device for input oxygen, these will typically be limited to 10 lpm.
2. Electricity Supply.
    a. Should connect to 240V mains.
    b. Should be PAT tested to the adapted IEC 60601, IEC 62353 standards
    c. Battery backup – see Unknown issues section. Must have 20 minutes back up battery in case of mains electricity failure.
    d. Optionally hot swappable batteries so that it can be run on battery supply for an extended period, e.g. 2 hours for within hospital transfer.
    e. Must avoid harmful RF or EM emissions that could interfere with other critical machinery.
3. Gas supply to patient.
    a. User must be able to control inspired oxygen proportion (FiO_2). The percentage of oxygen in the gas being breathed in by the patient. Room air is 21% oxygen.
    b. At least (50% or 60%) and 100% options
    c. Ideally variable between 30 – 100 % in 10% steps.

d. Patient breathing system connections: the ventilator must present 22mm outside diameter (OD) 'male' standard connectors to ISO 5356-1:2015 on both outlet and inlet ports for connection to user supplied 22mm 'female' connectors on the breathing system. These must be rigid and robust (not plastic) and separated by a minimum of 10 cm between centres to accommodate filter HMEs.

4. All elements in the gas pathway must meet biological safety and low-pressure oxygen safety standards, especially to minimise risk of fire or contamination of the patient's airway.

Infection control

1. All parts coming into contact with the patient's breath must be either disposable or able to be decontaminated between patients.
2. All external surfaces must be cleanable in the likely event that they get respiratory secretions or blood splatter on them. Cleaning would be by healthcare workers manually wiping using an approved surface wipe with disinfectant or cloths and approved surface cleaning liquid.
3. There will be a separately sourced HMEF-bacterial-viral filter between the machine and patient which may impact on resistance within the system, which may need to be accounted for with some designs. The pressure being delivered to the patient is the specified pressure. If the filter has a resistance of, say 2 cmH_2O at 30 lpm, the ventilator needs to output 37 cmH_2O to achieve a set 35 cmH_2O at the patient. This will need further detailed consideration. Viral filtering filters may have much higher resistance that may be clinically relevant.
4. Optionally include facility for hot water humidifier to be included in breathing system.

Monitoring and Alarms

1. Must alarm at:
   a. Gas or electricity supply failure.
   b. Machine switched off while in mandatory ventilation mode.
   c. Inspiratory airway pressure exceeded.
   d. Inspiratory and PEEP pressure not achieved (equivalent to disconnection alarm).
   e. Tidal volume not achieved or exceeded.
2. Monitoring – the following should be continuously displayed so the user can verify.

a. Current settings of tidal volume, frequency, PEEP, FiO_2, ventilation mode.

b. Actual achieved rates of tidal volume, breathing rate, PEEP, plateau pressure, FiO_2.

c. If it exists, in pressure support mode there must be real time confirmation of each patient breath and an alarm if below acceptable range.

d. Optionally CO_2 monitoring included.

Miscellaneous

1. ...st be reliable. It must have 100% duty cycle for up to 14 days.
2. Optionally it can be used beyond 14 days, the expected durability must be specified.
3. Can be floor standing.
4. Ideally small and light enough to mount on patient bed and orientation independent functioning.
5. Should be as robust as possible. For example, it may be dropped from bed height to floor.
6. It must be intuitive to use for qualified medical personnel, but these may not be specialists in ventilator use.
   a. Must not require more than 30 minutes training for a doctor with some experience of ventilator use.
   b. Must include Instructions for Use.
   c. Ideally instructions for use should be built into the labelling of the ventilator, e.g. with ‘connect this to wall’ etc.
   d. Must include clear labelling of all critical functions and controls using standard terms, pictograms and colours that will be readily recognised by UK healthcare staff.
7. Must have transparent design, supply chain, manufacture, quality assurance and testing processes that are of sufficient quality to enable MHRA officials to deem appropriate for usage in exceptional circumstances.
8. Must not be excessively cumbersome so that it would impede hospital operations or prevent easy movement within hospital premises.
9. Must be made from materials and parts readily available in the UK supply chain (anticipating increasing global restrictions on freight movement).
10. Standards – there are many standards that exist in this area. Below is a list of the most relevant ones. They are not formal regulatory requirements, but many are harmonised against regulatory requirements. Consider them as

helpful advisory standards for now. MHRA will lead an exercise to define which can be 'safely' relaxed for this emergency situation.

a. BS EN 794-3:1998 +A2:2009 Particular requirements for emergency and transport ventilators
b. ISO 10651-3:1997 Lung Ventilators for Medical Use - Emergency and Transport
c. BS ISO 80601-2-84:2018 Medical electrical equipment. Part 2-84. Particular requirements for basic safety and essential performance of emergency and transport ventilators – especially the parts on 'patient gas pathway' safety (very similar to IEC 60601)
d. ISO 80601-2-12:2020 Medical electrical equipment — Part 2-12: Particular requirements for basic safety and essential performance of critical care ventilators
e. BS ISO 19223:2019 Lung ventilators and related equipment. Vocabulary and semantics

Testing

1. It is accepted that full demonstration of compliance to ISO 80601-2-12:2020 is unrealistic in the time frame required for development. Nevertheless, compliance with the essential safety standards must be demonstrated for patient safety.

2. It is not anticipated that devices will be CE marked and approval by the MHRA will be through the "Exceptional use of non-CE marked medical devices" route.

3. When the current emergency has passed these devices will NOT be usable for routine care unless they have been CE marked through the Medical Device Regulations. The device must display a prominent indelible label to this effect.

4. Usability testing at both prototype and final production stages will be required. This should be done as a short Formative Usability Test to ISO62366 (this can be done in a day) in a realistic environment if possible. The user will be wearing complex protective clothing which includes: Eye goggles (in addition to spectacles if worn), Face shield, Plastic apron, Surgical gown, Two layers of gloves, usually nitrile non-handed small, medium, large variants, Gloves are donned in layers and sticky taped onto sleeves of gown in between layers

5. The user must be able to instantly see the settings selected and be able to easily operate all controls while dressed in protective gear. They may be required to remain so clothed and operating the ventilator for a number of hours without breaks.

Unknown Issues

1. How plentiful is 4 bar oxygen supply?
    a. Absolute minimum oxygen requirement is the human consumption of about 250 ml/min in a healthy person but upto 500 ml/min in severe sepsis. However, achieving this is only possible if certain breathing system designs are used and 'driving' gas is done by air.
        i. Specifically, would have to use circle breathing system with active CO_2 absorption. Is sufficient soda lime available?
    b. If consumption in the range 1-2 l/min is acceptable then a wider range of designs is possible, but some very basic designs are not.
    c. If consumption in the range 10l/min is acceptable then any possible design can be considered.
2. What is the resistance of HMEF-bacterial-viral filters that are to be used with the ventilator? Is it clinically relevant?
3. Is there any need to consider running from only low-pressure oxygen e.g. from a concentrator? This makes design more complex.
4. How plentiful is the supply of syringe drivers and drugs for sedation?
    a. If limited, then a vaporiser could be used to vaporise Isoflurane for sedation.
    b. This would need certain breathing system designs, mandatory AGSS and a supply of vaporisers.
5. If monitoring can be done by another machine it could be left out of the ventilator, but essential parameters must be available to the clinician.
6. Battery backup – Every current ventilator used inside hospitals has a battery backup, so users will expect it to be there and will behave as if it is, e.g. unplug it from the wall in order to rearrange cables or while manoeuvring the patient. However, this needs very careful thought to balance the risks. Including this in the spec means instantly trying to source 30,000 large, heavy batteries. Specifying a DC voltage (ie 12VDC) may well be the most sensible for the machine working voltage. Need the advice of an electronic engineer with military/resource limited experience before specifying anything here. It needs to be got right first time.

Glossary

ARDS – Acute Respiratory Distress Syndrome: a life-threatening form of respiratory failure where the lungs become severely inflamed due to an infection or injury and can't provide the body's vital organs with enough oxygen.

SIMV-PC – Synchronized Intermittent Mandatory Ventilation – Pressure Controlled: a mode of ventilation where the patient is allowed to take spontaneous breaths, the machine will assist the patients breathing when a spontaneous breath is taken. If the patient does not make a pre-set number of breaths a minute (i.e. 10) the machine provides mechanical ventilation to provide the set number.

PRVC – Pressure Regulated Volume Controlled: A mode of ventilation where a set tidal volume is delivered to the patient while maintain the lowest pressure possible in the airway, to avoid trauma.

BIPAP – Bilevel Positive Airway Pressure: a non-invasive ventilation mode that provides different levels of pressure when the patient inhales and exhales.

PEEP – Positive End-Expiratory Pressure: The lower pressure applied to the patient's airway to allow them to breathe out, but not too much.

EPAP – Expiatory Positive Airway Pressure: Similar to PEEP, pressure applied to the airway on patient expiration to prevent collapse of the airway.

HMEF – Heat and Moisture Exchange Filter: device fitted to the patient end of the breathing system, contains hydrophobic medium that absorbs heat and moisture from the patients exhaled breath and uses absorbed moisture to humidify inhaled gases. Can also filter bacteria and viruses, this will be used on all patients. WARNING can affect delivered pressure.

RF – Radio Frequency: Many medical devices are sensitive to RF interference. Care should be taken to ensure that this is kept to a minimum.

EM – Electro Magnetic Emissions: Many medical devices are sensitive to EM interference. Care should be taken to ensure that this is kept to a minimum.

Fi02 – Fraction of inspired oxygen: concentration of oxygen in the gas mixture that the patient inhales

AGSS – Anaesthetic gas scavenging system: where anaesthetic agents have been included in the gas mixture, this system is used to collect and remove exhales gas to avoid exposure to health care professionals.