Supplementary Material

Testing of pandemic ventilators under early and agile development

1 GirVent Description

1.1 Design

The GirVent ventilator (GirTec AG, Sulgen, Switzerland) is a compact mechanical emergency ventilator (<5kg) intended for use in patients with acute or chronic respiratory failure or respiratory insufficiency (Figure 1). The pressure generated during inspiration as well as during expiration (PIP and actively generated PEEP) is provided by a turbine blower. There is a total of one port for the intake of fresh air and the exhaust of used air. The inspiratory and expiratory phases are controlled by the opening and closing of a solenoid valve inside the ventilator.

Supplementary Figure 1 Illustration of the GirVent ventilator. The ventilator has five control knobs for setting the parameters; plateau pressure, PEEP, respiratory rate, I:E ratio and the trigger sensitivity. The measured values with the flow and pressure sensors at the distal end of the patient tubing are displayed on an LCD screen. An additional pressure gauge indicates the pressure at the proximal end of the patient tubing.
The tested patient tubing system consists of a double lumen tube with a mass flow sensor and an integrated pressure sensor at the distal end of the tube. The tubing system is connected to two standard ports; for the intake of fresh air during inspiration and the exhaust of exhaled air.

**Supplementary Figure 2** Schematic representation of the operating concept of the girvent. The system can be operated either with low pressure O\(_2\) or with high pressure O\(_2\). The low pressure O\(_2\) is injected into the patient circulatory system via a reservoir, while the high pressure O\(_2\) is added via a throttle valve. A PID controller regulates the applied pressure via the pressure sensor attached at the patient tubing system.

### 1.2 Controls and monitoring

**Basic Controls**

The parameters on the Grivent are set using analog rotary dials. Five parameters can be set on the ventilator; the plateau pressure can be set from 15-35 cmH\(_2\)O, the PEEP can be set from 2-15 cmH\(_2\)O, the respiratory rate can be set from 5-30 bpm, the I:E ratio can be set from 1:1-1:3, and the trigger sensitivity can be set from 0-2 mbar.

**Pressure-Control Mode and Trigger Signals**

At the time of the measurements for the study, the GirVent could be operated in one mode, the pressure-controlled continuous mandatory ventilation (PC-CMV). The pressure generated in the ventilation system (ventilator and patient tubing system) is controlled by an actively controlled solenoid valve. The expiration port of the valve is closed during inspiration and open during expiration. By controlling the opening and closing of the solenoid valve, the PEEP can be actively regulated. The pressure and flow sensor attached at the distal end of the patient tubing system is used for the internal feedback of the PID controller of the turbine blower. The pressure sensor is also used for triggering in assisted ventilation mode. The trigger signal is transmitted via an adjustable threshold through the measured negative pressure drop in the pressure sensor.
**OXYGEN SUPPLY**

O₂ supply can be provided both from a pressure source (high-pressure mode) and admixture of O₂ from a low-pressure source via an injector (low-pressure mode). In the low-pressure mode, the O₂ source is connected to a standard connection for low-pressure oxygen (0.25 bar). The O₂ supplied with the low-pressure port is first distributed into a two-liter balloon reservoir and then aspirated during inspiration. The pressure in the balloon reservoir, hence, the amount of O₂ supplied during inspiration, is controlled by the O₂ supply flow from the O₂ source. In high pressure mode, the pressure source is connected to a standard port for high pressure O₂ (max. 4.5 bar). The O₂ is injected into the patient tubing system during inspiration via a port on the inspiratory output of the ventilator.

**MONITORING**

The GirVent has a digital LCD display for monitoring all adjustable parameters. In addition, an analog manometer display continuously displays the instantaneous pump pressure. The digital display has four text lines; i.e. inspiratory pressure, PEEP, respiratory rate, I:E ratio, trigger pressure threshold, O₂ supply mode and for error messages or alarms. Further, the following alarms are implemented; inspiratory Paw exceeded or not achieved, end expiratory pressure exceeded or not achieved and failure of electricity or gas supply.
2 Differences to MHRA recommendation

**Supplementary Table 1** Overview of the elements tested presented our test protocol and the MHRA specification. The MHRA specification covers a broad range of scenarios in the tests for accuracy of controls and systems. It covers 36 tests each for changing lung compliance, airway resistance, O$_2$ setting, tidal volume and PIP. However, the MHRA specification does not cover tests for trigger signals. Further requirements for PDVs are also covered in the MHRA specifications.

| PDV test protocol | MHRA recommendation |
|-------------------|---------------------|
| **Testing**       |                     |
| **Accuracy of controls and systems** | 33 tests (volume control) | 36 tests (volume control – compliance) |
|                   | 33 tests (pressure control) | 36 tests (volume control – resistance) |
| **Trigger signals** | Testing of pressure drop, time to pressure minimum, trigger delay time and pressure time product | not included |
| **O$_2$ dynamics** | Testing of t$_{90}$, high pressure O$_2$ accuracy and low pressure O$_2$ efficiency | O$_2$ accuracy test included in tests of accuracy of controls and systems |
| **Pressure relief test** | no | Tests confirmation that the pressure in the system does not exceed 80cmH$_2$O and alarm is activated |
| **Closed suction test** | no | Tests confirmation that the ventilator returns to default setting after vacuum is applied |
| **Further requirements** |       |
| **General requirements** | n.a. | yes |
| **Gas and electricity** | n.a. | yes |
| **Infection control** | n.a. | yes |
| **Monitoring and alarms** | n.a. | yes |
| **Biological safety** | n.a. | yes |
| **EMC safety** | n.a. | yes |
| **Software safety** | n.a. | yes |
3 Accuracy of Controls and Instruments

3.1 Overview

**Supplementary Table 2** Mean and standard deviation (SD) of the relative error over all experiments and respiratory cycles for RR, PEEP, I:E ratio and PIP or Vt for the pressure-controlled and volume-controlled ventilators, respectively.

| Ventilator / Parameter | Pressure-controlled mode | Volume-controlled mode |
|------------------------|--------------------------|------------------------|
|                        | Hamilton T1 (PCV+)       | GirVent                | HEV CERN     |
|                        | Mean ± SD (%)            | Mean ± SD (%)          | Mean ± SD (%)|
| PIP                    | 0.26 ± 1.12              | -1.89 ± 4.08           | -2.19 ± 3.94|
| Vt                     | -                        | -                      | -            |
| RR                     | 0.02 ± 0.08              | -2.84 ± 1.26           | 0.01 ± 0.09  |
| PEEP                   | -1.15 ± 1.16             | -6.34 ± 1.33           | -19.51 ± 3.04|
| I:E                    | 1.42 ± 1.05              | -8.28 ± 2.91           | 2.55 ± 1.91  |
|                        |                          |                        |              |
| Hamilton T1 ((SCMV+)   | Mean ± SD (%)            | Mean ± SD (%)          |              |
|                        | -                        | -                      |              |
| Breathe                | -4.72 ± 1.63             | 2.27 ± 0.89            |              |
|                        | -0.02 ± 0.17             | -0.89 ± 0.32           |              |
|                        | -0.25 ± 1.44             | -0.73 ± 4.00           |              |
|                        | 1.64 ± 0.93              | 5.76 ± 4.20            |              |
3.2 Pressure-Controlled Ventilators

**Supplementary Figure 3** Measured PIP error in the Hamilton T1 (PCV+ mode), the HEV and the GirVent: effects of altering PIP (cmH\textsubscript{2}O), RR (bpm), PEEP (cmH\textsubscript{2}O), I:E (ratio), Crs (mL/cmH\textsubscript{2}O) and Raw (cmH\textsubscript{2}O/(L/s)). Base setting indicated by *. The markers and lines denote the mean error and the maximum and minimum errors, respectively. The grayed-out area indicates the acceptable performance (ISO norm).
**Supplementary Figure 4** Measured PEEP error in the Hamilton T1 (PCV+ mode), the HEV and the GirVent: effects of altering PIP (cmH₂O), RR (bpm), PEEP (cmH₂O), I:E (ratio), Crs (mL/cmH₂O) and Raw (cmH₂O/(L/s)). Base setting indicated by *. The markers and lines denote the mean error and the maximum and minimum errors, respectively. The grayed-out area indicates the acceptable performance (ISO norm).
Supplementary Figure 5 Measured RR error in the Hamilton T1 (PCV+ mode), the HEV and the GirVent: effects of altering PIP (cmH₂O), RR (bpm), PEEP (cmH₂O), I:E (ratio), Crs (mL/cmH₂O) and Raw (cmH₂O/(L/s)). Base setting indicated by *. The markers and lines denote the mean error and the maximum and minimum errors, respectively. The grayed-out area defines the acceptable performance (±5%).
**Supplementary Figure 6** Measured I:E error in the Hamilton T1 (PCV+ mode), the HEV and the GirVent: effects of altering PIP (cmH₂O), RR (bpm), PEEP (cmH₂O), I:E (ratio), Crs (mL/cmH₂O) and Raw (cmH₂O/(L/s)). Base setting indicated by *. The markers and lines denote the mean error and the maximum and minimum errors, respectively. The grayed-out area defines the acceptable performance (±10%).
3.3 Volume-Controlled Ventilators

|       | Vt = 350 mL | Vt = 400 mL | Vt = 450 mL |
|-------|-------------|-------------|-------------|
| RR = 10 | *           |             |             |
| RR = 15 | *           |             |             |
| RR = 20 |             |             |             |
| PEEP = 5 |             | *           |             |
| PEEP = 10 |             |             |             |
| PEEP = 15 |             |             |             |
| I:E = 1:1 |             |             |             |
| I:E = 1:2 |             |             |             |
| I:E = 1:3 |             |             |             |
| C_rs = 54 |             |             |             |
| C_rs = 30 |             |             |             |
| C_rs = 15 |             |             |             |
| R_aw = 5 |             |             |             |
| R_aw = 20 |             |             |             |
| R_aw = 50 |             |             |             |

Supplementary Figure 7 Measured V_t error in the Hamilton T1 ((S)CMV+ mode) and the Breathe: effects of altering V_t (mL), RR (bpm), PEEP (cmH_2O), I:E (ratio), C_rs (mL/cmH_2O) and R_aw (cmH_2O/(L/s)). Base setting indicated by *. The markers and lines denote the mean error and the maximum and minimum errors, respectively. The grayed-out area defines the acceptable performance (ISO norm).
Supplementary Figure 8 Measured PEEP error in the Hamilton T1 ((S)CMV+ mode) and the Breathe: effects of altering Vt (mL), RR (bpm), PEEP (cmH2O), I:E (ratio), Crs (mL/cmH2O) and Raw (cmH2O/(L/s)). Base setting indicated by *. The markers and lines denote the mean error and the maximum and minimum errors, respectively. The grayed-out area defines the acceptable performance (ISO norm).
Supplementary Figure 9 Measured RR error in the Hamilton T1 ((S)CMV+ mode) and the Breathe: effects of altering $V_t$ (mL), RR (bpm), PEEP (cmH$_2$O), I:E (ratio), $C_{rs}$ (mL/cmH$_2$O) and $R_{aw}$ (cmH$_2$O/(L/s)). Base setting indicated by *. The markers and lines denote the mean error and the maximum and minimum errors, respectively. The grayed-out area defines the acceptable performance ($\pm 5\%$).
**Supplementary Figure 10** Measured I:E error in the Hamilton T1 ((S)CMV+ mode) and the Breathe: effects of altering V_t (mL), RR (bpm), PEEP (cmH_2O), I:E (ratio), C_\text{rs} (mL/cmH_2O) and R_\text{aw} (cmH_2O/(L/s)). Base setting indicated by *. The markers and lines denote the mean error and the maximum and minimum errors, respectively. The grayed-out area defines the acceptable performance (±10%).
4 Flow profiles

Supplementary Figure 11 Measured flow profiles in the base setting for all ventilators tested (PIP 20cmH₂O or Vt 350mL, RR = 10 bpm, PEEP = 10 cmH₂O, I:E = 1:2). A) Hamilton T1 PCV+ mode, B) HEV Cern, C) GirVent, D) Hamilton T1 (S)CMV mode, E) breathe.
5 Efficiency of oxygen use and response to a change in oxygen supply

5.1 Overview

Supplementary Table 3 Mean, minimum and maximum measured FiO₂ at three O₂ flow rates (2 L/min, 4 L/min and 6 L/min) for the ventilators with low-pressure O₂ supply. Mean, minimum and maximum O₂ concentration are depicted over the last 30s of steady state.

| Ventilator | O₂ supply (L/min) | 2 | 4 | 6 |
|------------|------------------|---|---|---|
| Hamilton T1 | Min | Mean | Max | Min | Mean | Max | Min | Mean | Max |
| GirVent-LP1 | 41.5 | 51.8 | 57.7 | 64.0 | 73.7 | 80.3 | 74.8 | 83.0 | 88.3 |
| GirVent-LP2 | 27.0 | 27.3 | 28 | 32.8 | 33.3 | 34.7 | 38.1 | 38.9 | 41 |
| Breathe | 24.5 | 25.5 | 29.5 | 28.3 | 30 | 35.6 | 32.1 | 37.3 | 53.8 |

Supplementary Table 4 Measured O₂ concentrations of the Hamilton T1 and HEV (high-pressure port) at set concentrations in the UI ((40%, 60%, 80% and 100%).

| Ventilator | O₂ set (%) | 40 | 60 | 80 | 100 |
|------------|------------|---|---|---|---|
| Hamilton T1 | Min | Mean | Max | Min | Mean | Max | Min | Mean | Max | Min | Mean | Max |
| HeV Cern | 39.1 | 39.6 | 40.4 | 60.1 | 60.7 | 61.8 | 78.6 | 79.5 | 81.3 | 100 | 100 | 100 |
| HEV Cern | 58 | 59.6 | 60.7 | 75.7 | 77 | 78.4 | 92 | 94.7 | 97 | 100 | 100 | 100 |

Supplementary Table 5 FiO₂,₉₀ and t₉₀ at O₂ flow rate of 12 L/min (low-pressure) or a set O₂ concentration of 100% (high-pressure) of each ventilator.

| Parameter | O₂ supply / setting | Low-pressure | | High-pressure | |
|-----------|---------------------|---------------|---|---------------|---|
|           |                     | FiO₂,₉₀ [%] | t₉₀ [s] | FiO₂,₉₀ [%] | t₉₀ [s] |
| Hamilton T1 | 12 (L/min) | Mean | 88.9 | 135.9 | 92.1 | 125.3 |
| GirVent – LP1 | 12 (L/min) | Mean | 50.9 | 105.9 | - | - |
| GirVent – LP2 | 12 (L/min) | Mean | 42.6 | 123.4 | - | - |
| Breathe | 12 (L/min) | Mean | 92.1 | 260.8 | - | - |
| HEV | 100 (%) | Mean | 92.1 | 213.3 |
5.2 **O₂ High-Pressure Port**

**Supplementary Figure 12** Oxygen dynamics tests for the Hamilton T1 (high pressure port). The results are based on the last 30s before changing the O₂ supply or setting (time window indicated). Left: FiO₂ measured at different O₂ concentration set in the ventilator user interface (40%, 60%, 80% and 100%). Right: measurement of the t₉₀ time of the high-pressure port with an O₂ setting of 100% in the user interface.

**Supplementary Figure 13** Oxygen dynamics tests for the HEV (high pressure port). The results are based on the last 30s before changing the O₂ supply or setting (time window indicated). Left: FiO₂ measured at different O₂ concentration set in the ventilator user interface (40%, 60%, 80% and 100%). Right: measurement of the t₉₀ time of the high-pressure port with an O₂ setting of 100% in the user interface.
5.3 O₂ Low-Pressure Port

**Supplementary Figure 14** Oxygen dynamics tests for the Hamilton T1 (low pressure port). The results are based on the last 30s before changing the O₂ supply or setting (time window indicated). Left: FiO₂ measured of the low-pressure port at an oxygen supply flow rate of 2L/min, 4L/min and 6L/min. Right: measurement of the t₉₀ time of the low-pressure port with an O₂ supply of 12L/min.

**Supplementary Figure 15** Oxygen dynamics tests for the GirVent (low pressure port 1). The results are based on the last 30s before changing the O₂ supply or setting (time window indicated). Left: FiO₂ measured of the low pressure port at an oxygen supply flow rate of 2L/min, 4L/min and 6L/min. Right: measurement of the t₉₀ time of the low pressure port with an O₂ supply of 12L/min.
Supplementary Figure 16 Oxygen dynamics tests for the GirVent (low pressure port 2). The results are based on the last 30s before changing the O₂ supply or setting (time window indicated). Left: FiO₂ measured of the low-pressure port at an oxygen supply flow rate of 2L/min, 4L/min and 6L/min. Right: measurement of the t₀₀ time of the low-pressure port with an O₂ supply of 12L/min.

Supplementary Figure 17 Oxygen dynamics tests for the Breathe (low pressure port). The results are based on the last 30s before changing the O₂ supply or setting (time window indicated). Left: FiO₂ measured of the low-pressure port at an oxygen supply flow rate of 2L/min, 4L/min and 6L/min. Right: measurement of the t₀₀ time of the low-pressure port with an O₂ supply of 12L/min.
6 Ventilator Trigger Signals

**Supplementary Table 6** Mean values and standard deviation (SD) of trigger signals pressure drop (PD), trigger delay time (TDT), time to pressure minimum (TPM) and pressure time product during trigger (PTP) of each ventilator in assisted breathing at a patient breathing gradient of 2 cmH₂O/100 ms.

| Trigger signals | PD (cmH₂O) Mean ± SD | TPM (s) Mean ± SD | TDT (s) Mean ± SD | PTP (cmH₂O*s) Mean ± SD | PC300 (%) Mean ± SD | PC500 (%) Mean ± SD |
|-----------------|-----------------------|-------------------|-------------------|------------------------|---------------------|---------------------|
| Hamilton T1     | 1.20 ± 0.10           | 0.09 ± 0.01       | 0.24 ± 0.03       | 0.17 ± 0.03            | 51.58 ± 7.04        | 67.66 ± 4.55        |
| GirVent         | 3.68 ± 0.47           | 0.26 ± 0.02       | 0.33 ± 0.02       | 0.69 ± 0.09            | 40.46 ± 3.61        | 52.84 ± 3.83        |
| Breathe         | 5.80 ± 0.17           | 0.28 ± 0.01       | 0.49 ± 0.02       | 1.28 ± 0.07            | 9.64 ± 0.94         | 15.67 ± 0.92        |
| HEV             | 1.74 ± 0.08           | 0.11 ± 0.01       | 0.17 ± 0.01       | 0.15 ± 0.01            | 24.72 ± 1.20        | 42.00 ± 1.00        |

**Supplementary Table 7** Mean values and standard deviation (SD) of trigger signals pressure drop (PD), trigger delay time (TDT), time to pressure minimum (TPM) and pressure time product during trigger (PTP) of each ventilator in assisted breathing at a patient breathing gradient of 4 cmH₂O/100 ms.

| Trigger signals | PD (cmH₂O) Mean ± SD | TPM (s) Mean ± SD | TDT (s) Mean ± SD | PTP (cmH₂O*s) Mean ± SD | PC300 (%) Mean ± SD | PC500 (%) Mean ± SD |
|-----------------|-----------------------|-------------------|-------------------|------------------------|---------------------|---------------------|
| Hamilton T1     | 4.23 ± 0.19           | 0.28 ± 0.01       | 0.32 ± 0.01       | 0.90 ± 0.03            | 69.48 ± 0.87        | 80.17 ± 0.68        |
| GirVent         | 7.35 ± 0.29           | 0.28 ± 0.02       | 0.35 ± 0.01       | 1.50 ± 0.06            | 51.17 ± 1.63        | 64.07 ± 1.40        |
| Breathe         | 11.56 ± 0.11          | 0.28 ± 0.00       | 0.51 ± 0.00       | 2.69 ± 0.06            | 5.48 ± 0.32         | 10.85 ± 0.37        |
| HEV             | 5.77 ± 0.04           | 0.28 ± 0.00       | 0.32 ± 0.00       | 0.96 ± 0.01            | 61.72 ± 0.45        | 72.53 ± 0.40        |