The Ventilator Challenge, 2 years on; the HEV and HPLV response

**Part 2: High Performance Low Cost Ventilator, from prototype towards certification**

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on behalf of the HPLV collaboration

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CERN Knowledge Transfer seminar
How do we get to the industry stage?

- Taking a medical prototype device to the stage of production and commercialisation is a long, complex and costly process.
- Company must prove device compliance with a range of norms and follow procedures.
  - Electrical and software tests.
  - Risk analysis.
  - Safety and efficacy, usability.
  - Medical certification of device by regulatory authority.
  - Product registration procedure.
  - Documentation, ...

Examples from Brazilian regulatory body ANVISA
The High Performance Low Cost Ventilator project

- HPLV builds on the HEV development with **aim of lowering the barrier to industrialisation**.
  - Re-engineer hardware with medically-compatible components, optimised design.
  - Rewrite software and test according to regulations.
  - Adapt device for low and middle-income countries, with Brazil as a target.
- The project was awarded funding from the **UK Research & Innovation council Global Challenges Research Fund / Newton Fund: Agile Response call to address COVID-19**.
  - Targeting low and middle-income countries (from OECD DAC list) likely to be negatively impacted by the pandemic.
  - Project approved in September 2020.
  - Started around the beginning of 2021, ended in April 2022.
- **Multidisciplinary team**: particle physics, engineering, software and medical specialists.
  - Close collaboration with HEV.
The HPLV collaboration

- Project leader Ian Lazarus, Hannah Newton – STFC, UK.
- WP1 – Brazilian implementation, testing and training – UFRJ, Brazil.
  - Gabriel Antão, Cesar Chagas, Vinicius Côrtes, Kristy Godoy, Fernando Guimarães, Katherine Maslova, Irina Nasteva, Carlos Ortiz, Gabriel Rodrigues.
- WP2 – Regulatory compliance, standards and testing.
  - Tom Clutton-Brock, MD-TEC, UK.
- WP3 – Software and microcontroller.
  - Themis Bowcock, Karol Hennessy – U. of Liverpool, UK.
  - Sofia Fuster Almenar, Jim Bannister, Andrew Hill, Matthew Marshall, Sarah Medley, David Meredith, Benjamin Mummery, Tim Nicholls, Joseph Nobes, Tim Powell, Tiago Sarmento – STFC.
- WP4 – Engineering and prototypes.
  - Phil Allport, Karl Dearn, James Glover, Amir Hajiyavand, Juergen Thomas – U. of Birmingham, UK.
- WP5 – Knowledge transfer.
  - Phil Carvil – STFC, Amanda D. Fernandez, Ben Fritsch – CERN.
  - Jan Buytaert, Paula Collins – HEV / CERN.
Brazilian clinical conditions

- Clinical conditions vary locally, however the regulations follow the international standards.
  - Gas and electric connections, $O_2$ consumption, gas pressure.
- Distribution of ICU beds and ventilators is very uneven, with shortages in many regions.
  - Especially in regions of difficult access, where there are few hospitals and ICUs.

1g) Mechanical ventilators per 10,000 inhabitants (macro-regions) – Total
- Mechanical ventilators per 10,000 inhabitants
  - 0.0 [0]
  - 0.2-1.2 [27]
  - 1.2-2.3 [45]
  - 2.3-3.3 [34]
  - 3.3-4.4 [9]
  - 4.4-5.4 [2]

1h) Mechanical ventilators per 10,000 inhabitants (macro-regions) – SUS
- Mechanical ventilators per 10,000 inhabitants
  - 0.0 [0]
  - 0.2-1.2 [35]
  - 1.2-2.3 [57]
  - 2.3-3.3 [22]
  - 3.3-4.4 [2]
  - 4.4-5.4 [NA]

1i) Mechanical ventilators per 10,000 inhabitants (macro-regions) – Private
- Mechanical ventilators per 10,000 inhabitants
  - 0.0 [6]
  - 0.2-1.2 [73]
  - 1.2-2.3 [3]
  - 2.3-3.3 [1]
  - 3.3-4.4 [NA]
  - 4.4-5.4 [NA]

Figure 1 (continued)

NA: not available.

K. Noronha et. al., https://doi.org/10.1590/0102-311X00115320
Brazilian end-user needs

- Produced and analysed a **survey** of 29 Brazilian experienced intensive-care therapists on ventilator use and **essential** / **desirable** / **optional** functionality:
  - Many of the functions, modes and characteristics are already implemented in HEV.
  - Most of the remaining functions can be implemented in software/firmware.
  - All requested monitored parameters and alarms are implemented.
  - Good and intuitive user interface, and keeping historical log of the patient are requested.
  - Oxygen consumption should not be very high.
  - Battery autonomy of 2 hours pointed out as vital – choice of new battery in HPLV.
Brazilian end-user needs

- Produced and analysed a survey of 29 Brazilian experienced intensive-care therapists on ventilator use and essential / desirable / optional functionality:
  - In agreement with medical experts worldwide about the importance of high-quality ventilation, with reliable delivery of high-flow pressure controlled breaths, measurement of the delivered volume, precise synchronisation with the patient breathing, and control of the oxygen mixture of the delivered breaths.
Brazilian regulations

• Brazilian agency ANVISA (National Agency for Sanitary Monitoring) regulates the registration of any medical devices to be employed in the country.
  • Signatory of the International Medical Device Regulators Forum (IMDRF).
  • Also adopts the Medical Device Single Audit Program (MDSAP).
  • Most ANVISA resolutions follow the internationally adopted ones.
• After initially implementing emergency procedures for regularisation of devices during COVID-19, ANVISA later went back to its full requirements.
  • Note on pulmonary ventilators (May 2020).
  • Guide of Medical Device Cybersecurity (Sep 2020, based on IMDRF).
  • Technical Note on Software for Health products (2012).
  • ABNT PR 1003:2020 – Recommended practice on Pulmonary ventilators for critical care.
Regulatory compliance

- All development followed clinical advice on regulatory aspects and applicable standards.
  - List of Essential Requirements based on identified needs and norms.
  - RMVS / WHO and Brazilian requirements.
- Continuous feedback to engineering and software development, as well as documentation.
- Clinical and regulatory advice guided the in depth Risk Analysis process and tests.

MD-TEC ventilator testing facility

Risk Traceability Matrix
• Design was **re-engineered for manufacturing**.
  • Repackaging of prototype to reduce size and weight.
  • Ergonomic casing design with smooth corners and edges.
  • Separate electronic and pneumatic sections.
  • Relocation of the outlet exhale line and inhale guarantee allowing better accessibility.
  • Integrated touch screen and robust handle.
HPLV mechanical components

- **Biocompatibility** of choice of materials in compliance with regulations.
  - All materials in contact with gases are oxygen-, biocompatible and non-toxic.
- Use of **medical-grade** pneumatic parts and valves.
  - When not immediately available, an equivalent valve was used that can be certified.
- **Alternative designs** of air buffer to reduce weight and cost.
  - High-density polyethylene, lighter than 1 kg and several times cheaper.
- An alternative **Bill of Material with locally sourced components in Brazil**.

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**LIST OF IMPROVEMENTS**

1. Reductions in weight and cost of the air reservoir.
   - Prototype: HEV Prototype III
   - Upgrade: HPLV
     - Component: Festo CRVZS-10
     - Material: High-alloy stainless steel, High-density polyethylene
     - Dimensions: Ø251.8 x 326.8 mm, 427 x 206 mm
     - Capacity: 10 l, 10 l
     - Weight: 6.5 kg, 0.7 kg
     - Cost: £331.21, £41.13

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**Dimensions**

- High Density Polyethylene
  - Ø251.8 x 326.8 [mm]
- Polypropylene
  - Ø180 x 570 [mm]
Supply chain database

- Software database for sourcing equivalent parts in different regions of the world.
- Investigated the available suppliers in 7 representative countries.
- Searchable bill of material with detailed info and links to suppliers.
Redesigned electronics

• The electronics were redesigned for medical compatibility, safety and compliance with norms.
  • Microcontroller: safety-critical TI Hercules.
  • Single-board computer: Asus Tinkerboard.
  • PCB motherboard: redesigned for new components.
• Powered via a medical-grade Uninterrupted Power Supply.
  • Onyx UPower Pro-22 with 2 batteries of 90 Wh each.
  • 2 hour autonomy and software access to battery data.
Redesigned electronics

- The electronics were redesigned for medical compatibility and compliance with norms.
  - Microcontroller, Single-board computer, motherboard, medical-grade UPS.
Software

- The software organisation follows that of HEV.
  - The microcontroller controls the operation of valves, monitors sensors, and controls the breathing functions.
  - The single-board computer runs the user interface client and server, connected to a touch screen for receiving input and displaying information.
Microcontroller software

- Controls the operation of valves, monitoring of sensors, and the breathing functions.
  - 3 independent loops: breathing, safety/alarms and user interface.
  - Semi-independent final-state machines with exchange of information.
  - Continues cycling even if contact lost with user interface.
- The microcontroller code was ported to the TI Hercules.
  - Safety-grade and triplicate redundancy.
- The code was rewritten and tested to comply with regulations.
  - Modularity: hardware abstraction, wrapper and higher level.
User interface software

- The single-board computer runs the **user interface client and data server**.
  - Connection to a touch screen for display and receiving input.
  - Handling of alarms.
  - Interface to UPS battery for display and alarms.
- Code ported to the Asus Tinkerboard, migrated to Python with Qt library.
- Communications, logic, and layout are largely separate to facilitate development.
- Usability improvements, based on clinical guidance.
- Multi-language capability implementation.
User interface

- User interface in English and Portuguese.
- **Language option** as modularity in the code, any language can be added easily.
User interface

- User interface in English and Portuguese.
- **Language option** as modularity in the code, any language can be added easily.
User interface

- User interface in English and Portuguese.
- Ventilation mode and parameter settings, patient information.
User interface

- User interface in English and Portuguese.
- **Alarms** list, table and limit settings.
Software tests

- Software testing implemented alongside the development following ISO/IEC: 62304.
  - **Software Test Plan** based on IEEE 829-2008 (Software and system test documentation) to cover compliance with BS EN 62304 (Medical device software).
- 3 types of tests: Software unit implementation and verification, Software integration testing, and Software system testing.
- 3 Test Case Specifications: HPLV Alarms, HPLV Control, and HPLV Monitor.
- Software of Unknown Provenance (SOUP) anomaly list evaluation, IEC 62304:2006.
Risk analysis

- A comprehensive risk analysis was performed based on the HPLV Essential Requirements.
- Literature review of the standards for risk analysis for medical devices.
Risk analysis

- A comprehensive risk analysis was performed based on the HPLV Essential Requirements.
- **Risk Traceability Matrix** divided by hardware, software, and Brazilian implementation.
- Risk Analysis, Risk Evaluation, Risk Control and Testing Results.

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<th>User Requirement</th>
<th>Risk Level</th>
<th>Next Step</th>
<th>Proposed Risk Control Measure</th>
<th>Category of Risk Control Measure</th>
<th>Practicality of Risk Control Measure</th>
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- Risk Traceability Matrix:**

  - Hardware
  - Software
  - Brazilian implementation

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- Risk Analysis:**

  - Risk Evaluation
  - Risk Control
  - Testing Results.
Prototypes

- Prototypes were developed in parallel in Birmingham and Rio de Janeiro.
  - Bench top prototype and aesthetic prototype in Birmingham.
  - Bench top prototype in Brazil, later integrated into a full prototype.

Oxygen input valve
Air inlet

Exhale line
Inhale line

PEEP valve
Exhale valve
Inhale valve
Pressure relief valve

Purge valve
Exhale
Exhale

Inhale
Inhale

Exhale
Exhale

Oxygen inlet
Air inlet

Bench top prototype in Rio de Janeiro
Prototype integration and tests

- The integration of the mechanics, electronics and software was done on the Rio prototype.
  - Hardware testing and improvements of electronic board.
- Tests of the prototype operation and functionalities with a SmartLung test lung.
  - Debugging, tests of functions and optimisation of microcontroller and UI software.
- Next steps: tests with a ventilator analyser, training materials for users (in Portuguese).
HPLV engagement

- CERN-STFC working group on Knowledge Transfer advises on IP considerations.
  - Organised online event The Ventilator Challenge - One year on (11 May 2021), bringing together learnings from other projects including the HEV and HPLV.
  - Commissioned market study for Indian Market on Ventilator Need in 2021.
  - Hosted large scale event Growing Innovation and Investment for Pandemic Resilience with partners in the UK (10-11 Feb 2022) – showcasing HPLV to over 100 attendees.
- Will continue to offer license opportunities for HEV and from HPLV developments.
HPLV results summary

- HEV and HPLV apply technology developed in fundamental science research to an innovative medical application.
- Design led by user requirements and in compliance with regulations.
- Focus on safety, functionality and performance.
- A re-engineered HPLV ventilator that meets end-user requirements in Brazil and international regulatory norms for medical devices.
  - Medical-grade components and electronics.
  - Software rewritten and tested according to standards.
  - User interface with multi-language capability.
- A pre-regulatory documentation pack / technical file:
  - Bill of material and supply chain database for different regions.
  - Technical drawings of components and assembly.
  - In depth Risk Analysis documentation.
  - Software Technical File with description, test results and plans.

These technological developments and documentation can enable a company to rapidly take the device through regulatory approval to manufacture and deployment.
Interested in using one of these technologies?

HEV is available for licensing from CERN

HPLV will be made available soon

For more information please contact:

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