



CHAPTER 18

THE DESIGN AND DEVELOPMENT OF A LOW-COST HIGH FLOW NASAL OXYGEN DEVICE: A FUNCTIONAL ANALYSIS

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ABSTRACT

High Flow Nasal Oxygen (HFNO) medical devices are utilised to non-invasively oxygenate Coronavirus disease 2019 (COVID-19) and acute respiratory distress syndrome (ARDS) patients with mechanisms of clinical benefit. Most recently, HFNO has proven to be effective against hypoxemic symptoms by providing a range of oxygen concentration levels (FiO_2) and aims to improve patient compliance and comfort with heating and humidification of inspiratory gases. HFNO has been shown in studies to be feasible in resource-constrained settings, relying on an affordable solution to drive an increased number of supplied devices to healthcare facilities to effectively treat patients independently of intensive care units (ICU). Therefore, a Proof of Concept was developed under an iterative design approach. A full cost summary of materials was R8 100, compared to at least R45 000 for current South African market competitors. Additionally, the solution was functionally tested to determine levels of verification in technical specifications and validation in addressing clinician and patient needs. The solution achieved associated 10 - 60 l/min flow rates; stable FiO_2 from 50 - 100% (with a minimum of 40%); and inspiratory gas temperatures and humidity of up to 40 °C and 90% relative humidity (RH). Further design and development need to be conducted to output a high-performing and safe medical device as guided by ISO 80601-2-90.

Keywords: HFNO, COVID-19, ARDS, resource-constrained, low-cost, affordable, ICU, Proof of Concept, medical device

NOMENCLATURE

FiO_2	-	Device oxygen and air concentration level
SpO_2	-	Patient oxygen saturation level
VFR	m^3/s	Volumetric flow rate
C	-	Discharge coefficient for partial fluid viscosity
ΔP	Pa	Differential pressure

A_1	m^2	Upstream venturi cross-sectional area
A_2	m^2	Downstream venturi cross-sectional area
ρ	kg/m^3	Fluid density
VFR_{oxygen}	m^3/s	Volumetric flow rate of oxygen gas
VFR_{air}	m^3/s	Volumetric flow rate of ambient air

INTRODUCTION

Patients with COVID-19 and ARDS experience symptoms related to respiratory failure. These include hypoxemic or low oxygen saturation levels (SpO_2) and require intervention in oxygenation treatments. HFNO has been extensively used to treat COVID-19 patients, or patients with similar respiratory failure. The reason for this relates to the non-invasive characteristic of the treatment because patients do not need to be intubated, consequently improving chances for patients tolerating treatment without sedation.

- HFNO provides mechanisms of clinical benefit that relate to the following: (Slain et al., 2017; Vega & Pisani, 2021; WHO, 2021)
- Stable inspiratory oxygen flow at high flows.
- Nasal cannulas reduce breathing effort. Open-flow systems promote carbon dioxide washout.
- Continuous positive airway pressures result in positive end-expiration pressure (PEEP) effect reaching up to $7cmH_2O$.
- Active heating and humidification attenuate discomfort, sinus pains, and drying of mucosa.

Studies have shown that the use of HFNO mitigates risks involved in treating patients with more invasive mechanical ventilators, as associated mortality rates for these devices can be high. The use of HFNO to treat initial acute hypoxemic symptoms allows for patients to be weaned off ventilation treatments before reaching invasive mechanical ventilation (Calligaro et al., 2020).

HFNO has proven to be used in varying application settings. The use of HFNO within resource-constrained settings is feasible (Calligaro et al., 2020). HFNO may be used within ICU's and general pulmonology wards, and to the extent of home use (Calligaro et al., 2020; ResMed, 2021). This results in not requiring ICU facilities which reduces length of stay in ICU for ventilated patients and reduces staffing requirements without compromising patient care (Bice et al., 2013). Additionally, ICU and ventilator expertise are less of a requirement (Liu et al., 2021). Transportation of unstable patients is appropriate with HFNO treatments (Kedzierewicz et al., 2021). Moreover, high flow therapy is limited by the source of oxygen, whereby typical oxygen concentrators for home-use can produce up to 10 l/min (Hardavella et al., 2019). Therefore, hospital wall oxygen provides the most suitable approach for supplying HFNO devices with oxygen for meeting high flow rate benefits. Studies need to be

conducted for HFNO treatment in pre-hospital settings but have been used as a first choice from home to emergency transport. These introduce exceeding battery energies associated with high energy consuming components for heating and humidification, as well as low oxygen delivery times with oxygen tanks like a 4.5-L ME36 cylinder (Kedzierewicz et al., 2021).

HFNO is classified as non-invasive within a high flow nasal oxygen category. The treatment is aimed at providing high flow oxygen delivery with heated humidification. The effectiveness of the treatment is associated with the high-velocity gas expelling from the cannula of a patient interface. Therefore, the system is based off flow rate requirements with maximum flow rates generally delivered between 50 and 70 l/min (WHO, 2021). This provides the necessary airway pressures and advantageous PEEP effect without requiring sealing of a patient interface. Additionally, as enlisted by the World Health Organization (WHO), technical specifications may be adopted to provide a basis for the development of the HFNO proposed solution. (WHO, 2021)

HFNO has many components constituting to the device. These may be broken up into stages described as inspiratory gas flows through the device and consecutively includes: oxygen regulation and mixing, humidification and heating, and the patient interface stages. The oxygen regulation and mixing stage make use of active flow generation in types of air-oxygen blenders or built-in flow generators, whereas passive entrainment systems provide for an additional method of mixing. Oxygen/air mixtures can have a range of FiO_2 from 0.2 to 1.0 and are usually dependent on input or generated flow rates (Nishimura, 2019; WHO, 2021). Dry gas, especially over long-term delivery, may cause mucociliary malfunction, epithelial damage, mucus plugging, ulceration of mucosa, and in this context, ventilator-induced lung injury (VILI) (Cerpa et al., 2015). Therefore, active heated humidifiers are used to primarily provide humidification at high flows. Additionally, a heated patient circuit is used to provide effective gas heating, as well as provide humidity regulation. Finally, a patient interface consisting of a nasal cannula provide an open system connection to the patient. Equipped with high flow rates, HFNO can provide more stable inspiratory flow rates and humidity, since low flow rate systems comparatively provide unmatched device settings due to inspiratory flow rates less than HFNO flow rates (Nishimura, 2019). Existing solutions for HFNO are internationally recognised, imported, and supplied in local supply chains. The cost range in the South African market is between R45 000 and R60 000 (*High-Flow Nasal Cannula Oxygen COVID-19 cases*, 2020). Therefore, the project aims to design and develop a high flow nasal oxygen device that is low-cost for improved accessibility and chance of local manufacturing to address the needs of resource-constrained and low-income settings for healthcare facilities.

DESIGN AND METHODS

Approaching a final concept with iterative design and development, the aim was to prototype an initial Proof of Concept with basic functionality that could be verified

and validated. Therefore, the following requirements and their methods were considered throughout the project:

- *Low cost:* To promote affordable solutions within most resource-constrained and low- to middle-income country (LMIC) settings. Due to premature cost analysis, the bill of materials must not exceed a quarter of the minimum cost margin within South Africa, which requires for the materials to cost a maximum of R11 250.
- *Local manufacturing:* To fulfil the national goal of promoting local economic growth, most of the manufacturing processes were conducted with no tooling and mostly 3D printed using Ender 3 Pro and FormLabs resin printers.
- *Clinical needs:* With collaboration, design features need to provide convenience and effectiveness and solve current challenges wherever possible. Needs will be defined and assessed for the Proof of Concept based on clinical aspects to validate the design methods used.
- *Functional design:* The solution within this initial project scope needs to output a functional solution that is verified and validated within current laboratory facilities. Thus, facilities within the University of Cape Town (UCT) Medical Devices laboratory (MDL) will be utilised to verify technical specifications as guided by WHO (WHO, 2021). Problem needs will be matched against the Proof of Concept in a qualitative manner.

The final concept subsystem units are divided into the following: oxygen regulation and mixing unit, heating and humidification unit, and the patient interface. The final prototype is shown in Figure 1.



Figure 1: Proof of Concept prototype solution developed.

i. Oxygen regulation and mixing unit

The oxygen regulation and mixing unit incorporates a manual analog control solution whereby input oxygen and ambient air flow rates may be controlled in a low-cost manner. The unit utilises a Venturi entrainment device to entrain ambient air from the hospital wall oxygen outlet. Oxygen and air flow rates were determined by separate Venturi chambers that generate differential pressures across a decrease in diameters along the gas flow path. This differential pressure is measured, and Bernoulli's equation is used to calculate volumetric flow rates. The form of Bernoulli's equation

used is shown in Equation 1. With the user able to control flow rates of oxygen and air, the FiO_2 is manually controlled. There is a relationship between these two flow rates that calculate the output FiO_2 , referred to in Equation 2 (Ely & Clapham, 2003). The nomenclature provides reference to the use and units of these equations.

$$VFR = C \sqrt{\frac{2\Delta P}{\rho}} \frac{A_1}{\sqrt{\left(\frac{A_1}{A_2}\right)^2 - 1}} \quad (1) \quad | \quad FiO_2 = \frac{VFR_{oxygen} + 0.2VFR_{air}}{VFR_{oxygen} + VFR_{air}} \quad (2)$$

The testing of this unit involved the use of a portable tank compressor equipped with filters to provide compressed air at a maximum of 2.2 bars. The device would internally regulate the pressure between 0 and 4 bar, simulating the conditions from hospital oxygen wall supplies (SARAO, 2020). The MPX5100DP and the MPX5010DP differential pressure sensors were procured to provide analog measurement readings. These sensors are inexpensive, coupled with the Venturi chamber to produce affordable flow meters. Signal filtering techniques were used to mitigate noisy sensor measurements, particularly for differential pressure, volumetric flow rates, and calculated outputs which include total flow rate and FiO_2 . These techniques involved digital low-pass filtering, passive laminar inducing components, and running averages. The flow rates were verified with the highly accurate Sensirion SFM3000 flow meter in the UCT MDL. A basic Liquid Crystal Display (LCD) was used to present all required measurements and calculations. This allowed for accurate usability and display of measurements. Ultimately, results were captured for the controlled oxygen and entrained ambient air flow rates, as well as the calculated summated total flow rate and FiO_2 percentages. A custom control valve for the entrained air was developed with six different settings: setting "0" referring to the least air entrained and setting "5" referring to the most air entrained. Therefore, a higher setting number will provide for a lower FiO_2 output for a given oxygen flow rate input.

ii. Heating and humidification unit

The method to heat and provide humidity to the inspiratory gases requires active heater element components. The mechanical design was developed to transport gas from the oxygen regulation and mixing unit to the patient interface efficiently, with the procured water chamber by Inspira and heated breathing circuit by BMC. Two sensing units, at chamber-end and patient-end, were incorporated to measure relative humidity and temperature; and monitor effectiveness of active humidification of the water chamber and heating regulation of the breathing circuit. By applying air flow through the unit and allowing for the chamber water and heat exchanger to warm up, results show the characteristics of heating and humidification along the path to the patient. With the use of a basic control system, Pulse Width Modulated (PWM) triggers were utilised to control average voltages supplied to the water chamber and heated breathing circuit power elements. This will be controlled via a user menu implemented with a rotary encoder. Moreover, two DHT22 temperature and humidity sensors were used for chamber-end and patient-end measurements. Additionally, a temperature

sensor is placed in the chamber heater element to prevent overheating. All voltages and sensor measurements are presented on an LCD as the unit's user interface.

iii. Patient interface

A patient interface was developed to deliver inspiratory gases through a nasal cannula. The nasal cannula provides high-velocity gas deliverance into the nostrils of a patient. Throughout testing, the patient interface was only demonstrated and not connected to any person with the device on. Nevertheless, the interface provides adjustable fitment around the face with comfortable padding to insulate frontal sinuses. Additionally, a removable face shield may be placed onto the interface to minimise aerosolization effects associated with HFNO, standard oxygen masks and nasal cannula; and limit infectious spreading of respiratory-related diseases (Li et al., 2020).

RESULTS AND DISCUSSION

i. Oxygen regulation and mixing unit

The sensor measurements and calculations were captured from a single test whereby total flow rates were stepped in increasing 10l/min flow rates, for each entrained air control valve setting (0 - 5). Figure 2 and Figure 3 illustrate the dependency of total flow rates and FiO_2 for an input oxygen flow rate and each entrainer valve setting.

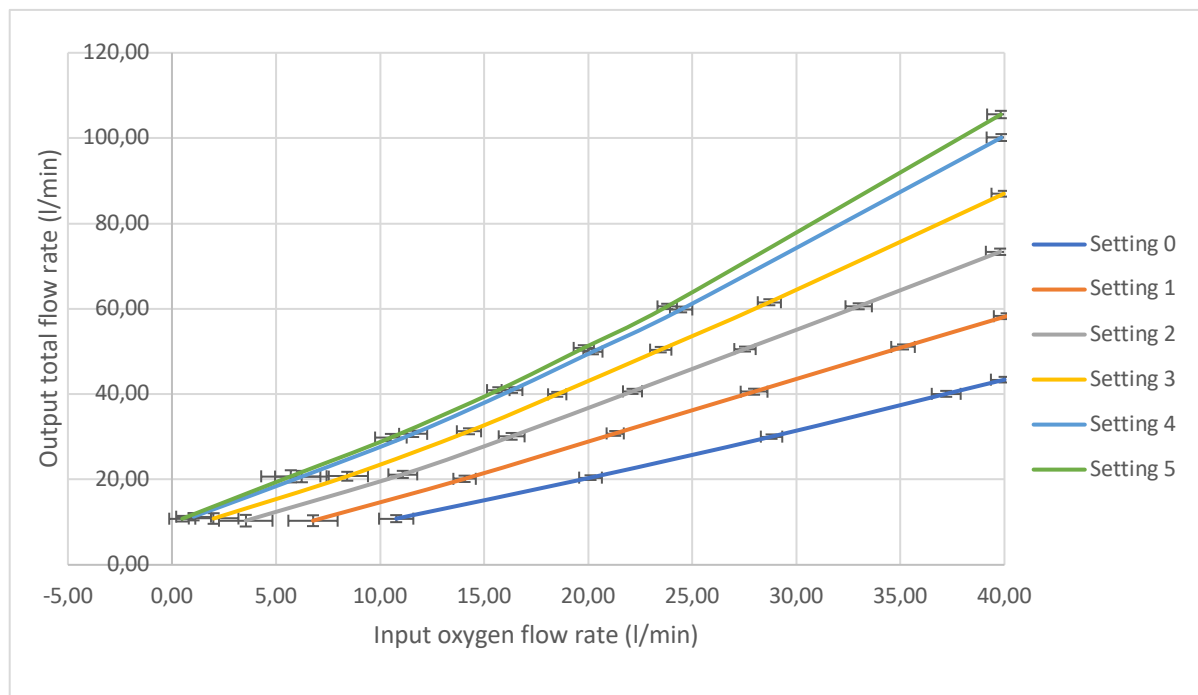


Figure 2: Mean flow rates for input oxygen and total flow for each setting on the entrainer valve, with standard deviation error bars showing measurement precision.

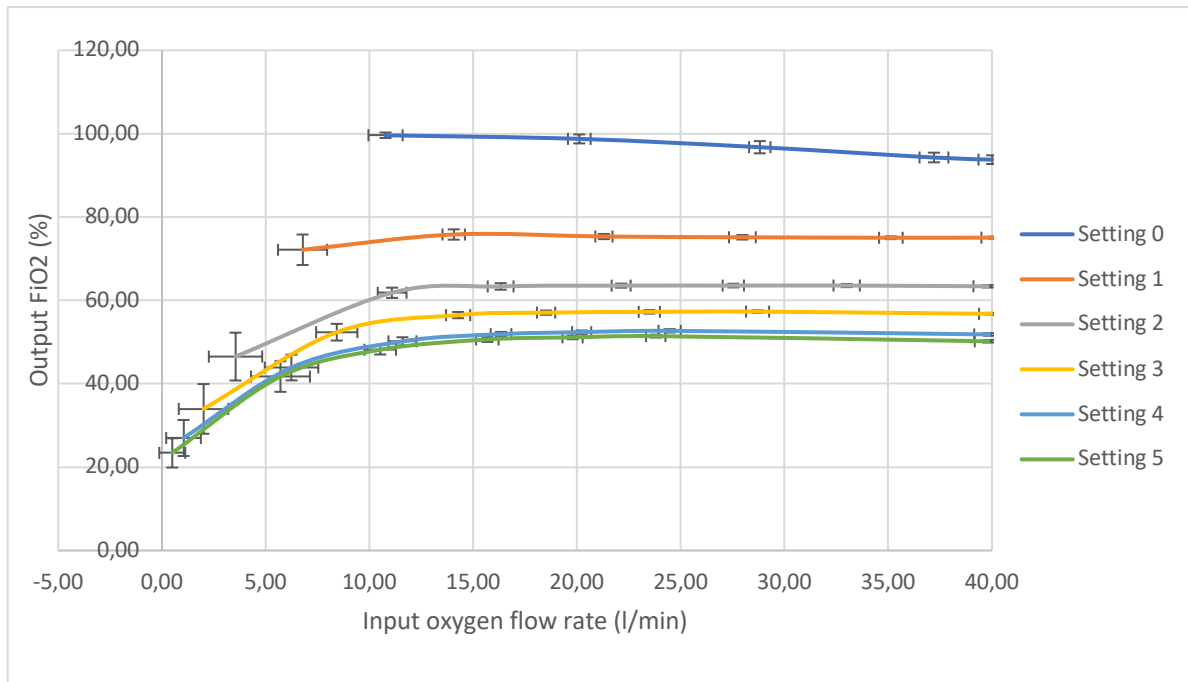


Figure 3: Mean input oxygen flow rates and output FiO_2 for each setting on the entrainer valve, with standard deviation error bars showing measurement precision.

The following aspects of the results for the unit are discussed:

- *Noisy low flow rate measurements:* Large standard deviations were recorded for FiO_2 percentages, whereby a $\pm 5.96\%$ was captured for Setting 3 at 10.86 l/min total flow. This was due to the noisy conditions of the differential pressure sensors where, at low flow rates, differential pressures seemed to have fluctuating characteristics. Although all efforts were made to limit this, the current setup with the chosen sensors or the Venturi chambers may need to be re-investigated. Therefore, the technical specification was limited to 10 l/min. Moreover, the entrained air flow rates were captured with lower standard deviations compared to the oxygen flow rates.
- *Entrainer valve trends:* Across the spectrum of settings 0 to 5, a non-linear FiO_2 trend may be shown, as referred to in Figure 3. The air inlet is shaped with a T-shaped cross-section, allowing to mitigate this effect and linearize the air flow per setting rotation. This has not seemed to work to the full effect.
- *Entrainment performance:* Referring to Figure 2, for an increasing setting number, the total flow rate increasingly deviates from the input oxygen flow rate. This illustrates good functionality with respect to the summation of entrained air and oxygen flow rates as the entrainer valve is opened. Furthermore, due to the high-velocity Venturi nozzle within the Venturi entrainer, the entrained air may exceed the oxygen inlet flow rates, allowing for excessively large flow rates of up to 105 l/min. This is at the inlet oxygen condition of 2.2 bar gauge pressure and may be regulated to limit flow rates for low FiO_2 settings. Moreover, leakages do occur, as shown in the Setting 0 at higher flows, whereby the total flow rate and oxygen flow rate deviate to a mean value of 3.39 l/min. Although PTFE thread tape and O-rings were used, as well as 3D printing the entrainer

valve in highly accurate resin, a more ductile material should be investigated to provide a compression fit in attempt to limit leakages.

- *Pressure regulation:* Due to the large pressure drop requirements needed to reach desirable high flow at high FiO₂ percentages, pressures must be regulated to prevent excessively exceeding output target total flow rates. It was found that a maximum of 40 l/min requires 2.2 bar gauge pressure input for the given Venturi needle diameter. On the other extreme, a 1 bar pressure input is required to reach the 60 l/min target total flow rates for Setting 5.

ii. Heating and humidification unit

Initial tests showed that it was beneficial to allow the water chamber to heat up before applying flow rates. The temperature read from the chamber temperature sensor displayed to settle at the point flow was introduced to the system. Therefore, preliminary tests at intermittent 30 l/min total flow were introduced throughout the entire device. The results are shown in Figure 4 with the following aspects to be discussed:

- *Water chamber:* The heater element can reach 85°C as a maximum temperature after a warm-up cycle. The element is concealed well within a heat exchanger to transfer heat to the water chamber. When flow was off, relative humidity values reached just over 90%. However, there is minimal transfer of heat from the water chamber to the inspiratory gas, only slowly reaching 22°C at the end of the test. With flow rate turned on, relative humidity drops to approximately 55%.
- *Heated circuit:* The circuit regulates humidity and temperatures inversely, as shown by the patient-end humidity and temperature measurements. When flow is turned off, humidity is stable at 42% whereas temperature is poorly transmitted to the gas and across the sensors, reaching approximately 26°C. In contrast, when the flow is turned on, the relative humidity drops to 30% and the temperature reaches 40°C. The results show that flow is important for heat transfer to inspiratory gases, but the prototype needs a more sophisticated control method to increase relative humidity at desired gas temperatures.

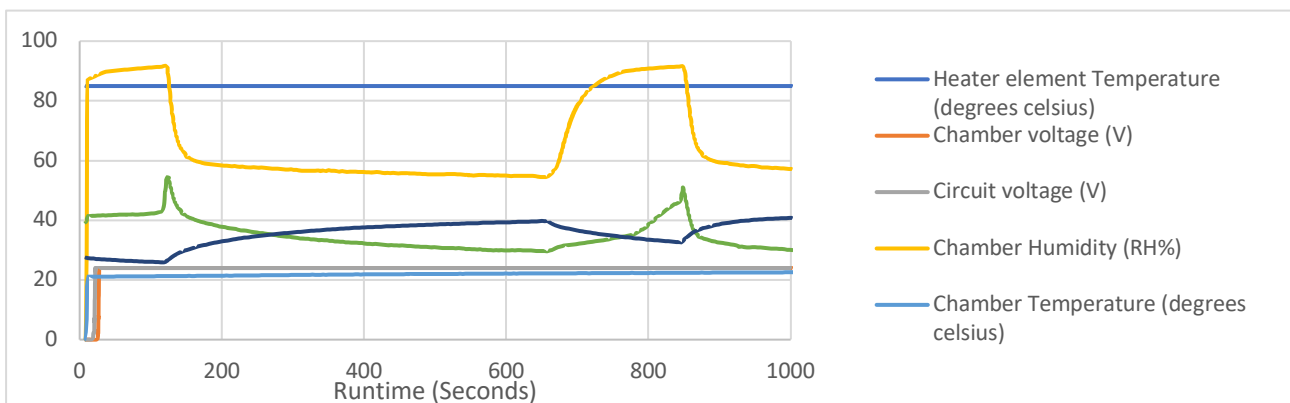


Figure 4: Results showing measurement responses from temperature and humidity sensors for intermittent 30 l/min total flow rates.

iii. Patient interface

The patient interface is demonstrated in Figure 5, depicting the fitment onto the patient's face, as well as the position and connections of all components relative to the patient.

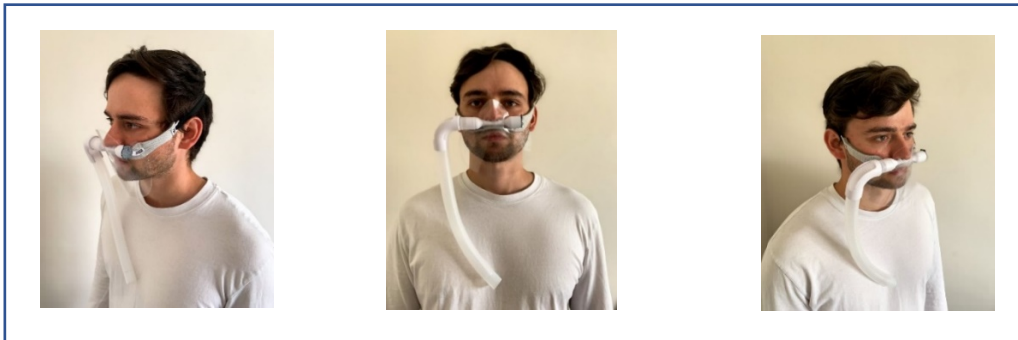


Figure 5: Demonstration of patient fitment and components of the patient interface.

iv. Validation discussion

The general technical specifications for the target Proof of Concept (based on WHO technical specifications and similar device specifications) and the tested prototype is presented in Table 1.

Table 1: Technical specifications and comparison between Proof of Concept and initial final concept.

Unit	Specification	Test condition	Prototype Value	Concept Target	Unit
Oxygen regulation and mixing	Minimum total flow output	@2.2 Bar	10	5	L/min
	Maximum total flow output	@2.2 Bar Entrainer setting 5	105	60	L/min
	Maximum Oxygen concentration	@2.2 Bar Entrainer setting 0	99	100	%
	Minimum oxygen concentration (FiO ₂)	Total VFR > 20 l/min	40	40	%
Humidification and heating	Max Patient end Temperature	@ 30 l/min	40	37	°C
	Max Patient end humidity	@ 0 l/min, 28 °C	55	100	%
		@ 30 l/min, 22 °C	48		

The prototype may be validated to the intended use of the device as well as the top needs defined. This is summarized in Table 2.

Table 2: Validation methods used for the overall outputs of intended use and needs of the Proof of Concept.

Criteria	Description	Validation
Intended use	Oxygenation effect to patient	Device can provide suitable ranges similar to predicate devices. WHO technical specifications for non-invasive ventilation (WHO, 2021).
	Flow rate outputs to patient	
	Heating and humidification active components	Mechanisms of benefits associated with HFNO active patient comfort provision.
Top Needs	Low cost and affordable treatment	Bill of materials approximately R8100.00. Manual control reduces overall costs but is technically limited.
	Components should not inhibit patient comfort in any reasonable physical manner.	Comfortable and adjustable nasal patient interface to deliver treatments minimally and directly. (Similar to predicate devices)
	Manual control of oxygen regulation.	Manually controlled safety valve, oxygen flow rate valve, and air entrainer control valve.
	A safe and reliable solution.	Additional risk management processes (ISO 14971)

CONCLUSION

The project in its current state of development was able to show the feasibility of a low-cost and affordable High Flow Nasal Oxygen solution, both quantitatively and qualitatively. It is well equipped to meet the current requirements and needs of a resource-constrained setting, using a combination of manual analog and digital control. Further design and development processes should be considered to improve the solution's performance in terms of accuracy, usability, safety, and general quality management. Verification in terms of ISO 80601-2-90:2021 should be considered to achieve basic safety and performance (ISO, 2021). Further optimisation and refinement with standardised testing in the laboratory and clinical settings will be conducted.

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