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Begeleidingsformulier aanvraag dierproef DEC- UM

Versie 2006

Herziene versie

DECNR: 2011-068

Ontvangen: 16-06-2011

DEC datum goedkeuring#	Type aanvraag [2]
17-06-2011	Pilot + experiment

VROM/GGONR[3]

LNV/CBDNR[4]

Hoofdproject	CARIM	NUTRIM	Hersenen en gedrag	GROW	biomaterialen	**Ander UM**	Geen UM
Deelproject						**X**	

Financieel beheerder	

Budgetnummer	7290 (kostenplaatsnummer

Titel van het onderzoek:

Ventilation through a small-bore catheter; conventional jet ventilation or EVA?

startdatum 1-8-2011 einddatum [9] 1-12-2011 *Duur van de proef[10]:* *1 dag*

	Naam	Tel (+ Tel privé enkel VO, VVO en VM)	E-mailadres	Bevoegdheid[5]	Cap. groep /afdeling
1.Verantwoordelijk onderzoeker (VO)				Art.9	
2. Vervanger VO (VVO)				Art.9	
3. Verantwoordelijk medewerker (VM) GGO[7]					
4. overige uitvoerenden				Art. 12	
5.	Medewerker CPV			Art.9/12[8]	CPV
				Anders[6]:	

Diergroep	1		.	.	.	.	.
ctrl/exp/sham	exp						
Diersoort	pig						
Stam							
Construct / mutatie ?	-						
Herkomst (leverancier) *	03						
Aantal	6						
Geslacht	f/m						
Dieren immuuncompetent ?	ja[8]		ja/nee[8]	ja/nee[8]	ja/nee[8]	ja/nee[8]	ja/nee[8]
Leeftijd/gewicht	ca 40 kg						
Doel van de proef *	37						
Belang van de proef *	01						
Toxicologisch onderzoek *	01						
Bijzondere technieken *	01						
Anesthesie *	04						
Pijnbestrijding *	04						
Mate ongerief *	02						
Toestand dier einde exp*	01						

* VHI-coderingen zie bijlage

Verantwoording

Aanvraag dierproef DEC-UM

Titel: *Ventilation through a small-bore catheter; conventional jet ventilation or EVA?*

1. Doel van de proef

An acute infection, external trauma, edema or a growing tumour can result in narrowing of the upper airway and suffocation of the patient. In such emergency situations often only a small-bore catheter can be placed in the airway. To achieve adequate ventilation through a small-bore catheter is challenging as a decrease in inner diameter of an airway catheter results in an increase in resistance to gas flow [Dworkin, 1990]. A catheter with an inner diameter of less than 3 mm has such a high resistance that conventional ventilation is impossible. To assure adequate oxygen insufflation a high-pressure oxygen source is used and so called jet ventilation is applied. Jet ventilation is shown to be effective and safe in experienced hands [Jacquet, 2006]. As passive outflow of gas via a small-bore catheter is inadequate, an open upper airway is mandatory for the egress of gas when applying jet ventilation. Several case reports, however, illustrate the risk of hyperinflation leading to barotrauma and hemodynamic instability or even circulatory collapse when the outflow of gas in not secured [Craft, 1990; Cook, 2006].

In the last two decades several techniques have been proposed to augment the exhalation by applying suction to a small-bore airway catheter during the expiratory phase [Schapera, 1994; Garry, 1998; Meissner, 2008]. Until recently these expiratory-assisted ventilation techniques have been impracticable and/or their efficacy has been disappointing.

developed and studied a simple, portable ventilation system, , supporting the expiration by suction using Bernoulli's principle. In a mechanical lung model achieves a minute volume of 7 $L \cdot min^{-1}$ (sufficient for adequate ventilation of an adult) through a short catheter with an inner diameter of 2 mm even in a completely obstructed upper airway. Although in a pilot study the principle of expiratory ventilation assistance (EVA) by applying suction seems promising, further evaluation of this technique regarding efficacy in a partially obstructed and open airway is necessary.

The aim of this study is to compare the effects of conventional jet ventilation and Ventrain on gas exchange, intrathoracic pressures and hemodynamics in an animal-model with a partially obstructed and open upper airway.

2. Maatschappelijke relevantie en/of wetenschappelijk belang

The use of EVA enables ventilation of a patient through a "straw". This might give new possibilities for patients with severe airway stenosis either in emergencies (e.g. obstructing tumor, anatomical distortion) or elective settings (e.g. airway obstruction during laryngeal or tracheal intervention) . Hopefully, it will lead to a decrease in morbidity and mortality both in prehospital and hospital settings.

3. Alternatieven

Replacement

The first part of our project, optimizing the prototype of ' and studying the achievable minute volume, has already been done *in vitro* on a mechanical lung simulator [Hamaekers, 2008]. In the second part of our research we studied the efficacy of EVA on gas exchange in an emergency

situation with hypoxia and hypercarbia. We noticed that the patency of the upper airway had a significant effect on the efficacy of EVA [Hamaekers, 2010]. As an *in vitro* model is too simplistic, animal experiments are necessary to compare the effects of jet ventilation and EVA on gas exchange, intrathoracic pressures and hemodynamics. This cannot be studied in a standardized way in humans. The use of a small animal was considered, but is regarded not suitable as the is designed specifically for adult patients.

Reduction

The number of animals necessary for the experiment is reduced by the fact that every animal will be its own control. Furthermore, there will be two experiments conducted on each pig. Collected data will be analyzed during the experiment.

Refinement

The 8-hour fasting period and the intramuscular injection of the premedication will be stressful for the animal. After induction of anaesthesia there will be no more discomfort for the pig. The animals will be euthanized at the end of the experiment.

4. Ethische afweging

According to the results of the *in vitro* and first *in vivo* studies EVA is a very promising new ventilation technique. However, its efficacy in a partially obstructed and open upper airway still has to be proven and a comparison with current available techniques has to be made. The animals suffering within this study can be justified by the positive results that may be obtained, promising a decrease in morbidity and mortality in patients with severe airway obstruction).

Wetenschap

5. Wetenschappelijke onderbouwing

Safe and efficient ventilation through a small-bore catheter is a topic on debate already for several decades. To achieve an adequate gas flow through a small-bore catheter a high-pressurized oxygen source is needed for insufflation of oxygen, so-called jet ventilation [Bould, 2008]. For the egress of gas a patent upper airway is mandatory, as passive expiration through a small-bore catheter is very slow [Rone, 1982]. In case of complete upper airway obstruction (conventional) jet ventilation will lead to air trapping, when compressed oxygen is injected into the lungs during the inspiratory phase. Insufficient escape of gas during the expiratory phase then results in increased end-expiratory lung pressures and, correspondingly, a rapid decrease in minute volume up to ventilation failure [Craven, 2004] and/or barotrauma and circulatory collapse, respectively [Neff, 1983; Stothert, 1989].

In 1978, Dunlap already suggested properly applied suction following jet injections in order to assist expiration to overcome the problem of hypoventilation and hyperinflation in case of upper airway obstruction. Although in the last three decades several techniques have been proposed to augment expiration, most of these techniques are either not applicable to clinical practice or not efficient enough for ventilating an adult patient [Dunlap, 1978; Schapera, 1994; Meissner, 2008].

developed a simple, portable ventilation system, (figure 1), providing expiratory ventilation assistance (EVA) [Enk, 2007,]. Connected to a (pressure compensated) flowmeter by tubing (at I, figure 2) set to a rate of 15 $L \cdot min^{-1}$ this device allows to efficiently ventilate a patient through a "straw". Oxygen flowing through the device at high speed supports

expiration by suction. This effect is generated by Bernoulli's principle. To activate the on/off-switch (II, figure 2) must be sealed by finger. For inspiration the oxygen flow is redirected to the patient by occluding the outlet (III, figure 2) by finger, intermittent release of the outlet results in assisted expiration.

Different *in vitro* experiments using an LS800 lung simulator (Dräger Medical AG, Lübeck, Germany) have been conducted to optimize EVA. Early prototypes of 's centerpiece have been tested at different compliances and resistances, representing healthy and compromised lungs [Hamaekers, 2008]. In simulated upper airway obstruction the best prototype achieved a minute volume of 7.5 $L \cdot min^{-1}$ (sufficient for adequate ventilation of an adult) through a short catheter with an inner diameter of 2 mm [Hamaekers, 2009].

After tuning several technical details addressing the results of the *in vitro* experiments, the final design became a product. has been CE-marked already and is now available on the European market.

The efficacy of ' in combination with a partially obstructed and open airway needs to be elucidated and compared to the current golden standard, (conventional) jet ventilation. The ability to oxygenize adequately as well as to remove carbon dioxide sufficiently and the effect on hemodynamics will be studied.

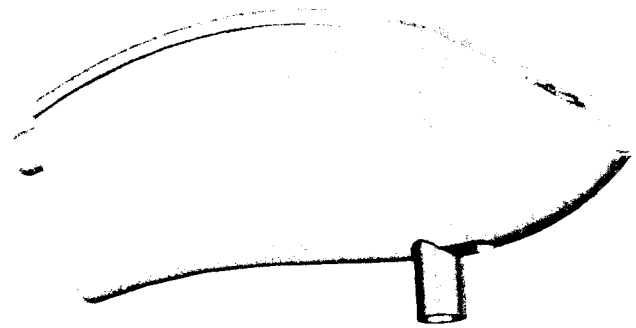

Figure 1

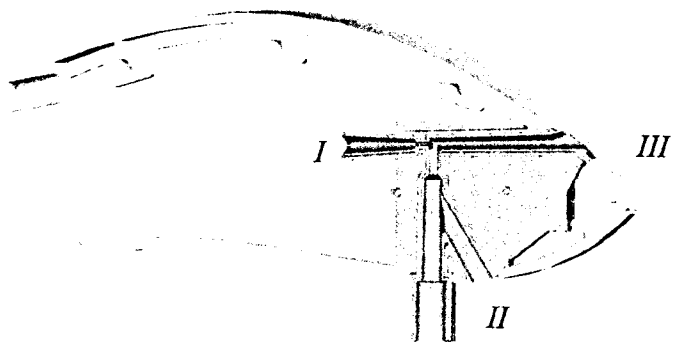

Figure 2

6. Wetenschappelijke beoordeling

This project will be funded by OP-Zuid and has been evaluated for its scientific merit by the scientific board of OP-Zuid. The research project has also been evaluated and approved by (a member of the research committee of the Department (

Proefdier

7. Proefdier keuze

7a. Soort, stam, herkomst, eindbestemming

Pigs with a weight of approximately 40 kg will be obtained from a local breeder.

To extrapolate the results to adult patients it is important that the experiments are conducted on large animals with a minute volume comparable to human adults (approximately 7 $L \cdot min^{-1}$). Experiments to study pulmonary damage are often conducted in pigs. Even though the lobar anatomy differs between humans and piglets there is a big resemblance between the two regarding alveolar structure, gas exchange and the circulatory system. Furthermore, there is a porcine model available [Schaefer, 2007].

At the end of the experiment the animal will be killed.

7b. Sekse

Both female and male pigs will be used for the experiments.

7c. Aantal

To prove equality in efficiency between (conventional) jet ventilation and EVA two cross-over experiments will be performed. Based on the low variability in arterial saturation en $paCO_2$ measurements in our pilot study 6 pigs will be needed overall.

Dierproef

8. Experiment

The aim of the experiment is to compare (conventional) jet ventilation and EVA in the presence of a (partially) obstructed and open upper airway. The primary outcome is paO_2, $paCO_2$ and oxygen saturation in the arterial blood during 30 minutes ventilation. Secondary outcomes are other arterial blood gas parameters, central venous pressure, cardiac output, mean arterial blood pressure and intratracheal and intrathoracic pressures, respectively.

Detailed experimental set-up

The pigs will be premedicated with an i.m. injection of tiletamine/zolazepam (6 $mg \cdot kg^{-1}$, Zoletil®) and atropine (0.05 $mg \cdot kg^{-1}$) to allow placement of an 18 G catheter in an ear vein. Prior to induction continuous electrocardiogram and pulse oxymetry monitoring will be placed. Anaesthesia will be induced with propofol 4-8 $mg \cdot kg^{-1}$ and sufentanil 0.4 $mcg \cdot kg^{-1}$. After the trachea has been intubated with a 9 mm ID (inner diameter) cuffed endotracheal tube pancuronium (0.15 $mg \cdot kg^{-1}$) will be administered. The pigs will be mechanically ventilated with intermitted positive pressure ventilation (IPPV) with an FiO_2 of 0.40 and a positive endexpiratory pressure (PEEP) of 5 cm H_2O. The tidal volume will be set to 10 $ml \cdot kg^{-1}$ and respiratory frequencies will be adjusted to achieve a normal arterial $paCO_2$ of 40-45 mm Hg. Gas flow and airway pressures will be measured at the proximal

end of the endotracheal tube (ETT) with a standard monitor for ventilation measurements. During the whole experiment the pigs will stay in supine position.

Anaesthesia will be maintained by continuous infusions of sufentanil (8 $mcg \cdot kg^{-1} \cdot h^{-1}$), propofol (9 $mg \cdot kg^{-1} \cdot h^{-1}$) and pancuronium (0.3 $mg \cdot kg^{-1} \cdot h^{-1}$). During the experiment the animals will receive 10 $ml \cdot kg^{-1} \cdot h^{-1}$ body warm isotonic saline. The body temperature will be monitored and controlled by thermo convection. A Swan-Ganz (SG) thermodilution catheter and a single lumen central venous catheter will be inserted via the right external jugular vein. The balloon tip of the SG will be placed in the pulmonary artery for cardiac output and pulmonary artery (occlusion) pressure measurements, respectively. The pigs will receive a left femoral arterial catheter for continuous arterial pressure measurements and arterial blood sampling. Intratracheal pressure will be measured continuously using a catheter connected to a manometer positioned 2 cm above the carina. As a surrogate for intrapleural pressure, oesophageal pressure will be measured with a balloon catheter.

A jet catheter will be placed through the endotracheal tube. Under visual control by a fiberscope the tip will be placed 3 cm above the carina.

The workflow of the experimental protocol is presented in figure 3. Pigs will be randomized either to the (conventional) jet ventilation or the EVA group. After recording stable hemodynamic parameters for 30 minutes baseline hemodynamics, ventilation, pressure recordings and gas exchange data will be determined. Then the tube will be disconnected from the ventilator and (conventional) jet ventilation or EVA will be initiated through the small-bore catheter. This will be done in a randomized order.

The following cardiopulmonary and respiratory variables will be collected/recorded at baseline, at T5, T10, T15, T20, T25, and T30: cardiac output, heart rate (HR), mean arterial pressure (MAP), and mean pulmonary artery pressure (MPAP), central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), intratracheal and intrathoracic pressures, arterial and mixed venous blood gases.

After 30 minutes conventional jet ventilation or EVA will be stopped and the pig will be mechanically ventilated using IPPV. There will be a washout period of at least 30 minutes before the second experiment begins. Data collection will be the same as in the first experiment.

After completion of the experiments, a bronchoscopy will be performed. The pigs will be euthanized with a lethal dose of Euthanimal (Pentobarbital 150 $mg \cdot kg^{-1}$). A sternotomy will then be performed to exclude pneumothorax and to harvest lung tissue for microscopic examination.

Preparation	Base line	Run 1	Washout	Run 2	End
Anaesthesia Line insertions Placing catheters	Recording for 30 minutes	EVA in a (partially) obstructed airway or (conventional) jet ventilation in an open airway for 30 minutes	30 minutes	EVA or (conventional) jet ventilation in an open airway for 30 minutes	Bronchoscopy Euthanization Histology

Figure 3: Flow chart of the experiments

9. Experimentele condities

9a. Anesthesie

The pigs will be premedicated with an i.m. injection of tiletamine/zolazepam and atropine and anaesthesia will be induced intravenously with propofol/fentanyl and a muscle relaxant (pancuronium). We will use intravenous anaesthesia, because there will be to much spill of the inhalation anesthetic in case of a (partially) open upper airway. A muscle relaxant is given to eliminate any interference of contractions of the diaphragm on ventilation during the experiment.

9b. Pijnbestrijding

Perioperative pain treatment consists of intravenous administration of sufentanil at 4 $mcg \cdot kg^{-1} \cdot h^{-1}$.

9c. Euthanasie en humane eindpunten

At the end of the experiment all the animals will be killed with Euthanimal. As the experiments are under anaesthesia there are no indications for premature euthanasia during the study. Prior to the experiments the animals will be checked daily. In case of illness or discomfort a veterinarian will be consulted.

Zorg

10a. Ongerief

The animals will be euthanized under general anaesthesia, therefore we estimate the inconvenience of the animals with a SCCI as small/moderate (score 2).

10b. Welzijnsevaluatie

During their stay at the CPV facilities, prior to the experiments, the pigs will be checked daily.

11. Verzorging en huisvesting

After transport, pigs will be kept for a minimum of 7 days in the housing facilities of the CPV to acclimatize. Temperature and humidity will be kept stable and a 12 hours light – 12 hours dark cycles will be maintained. The animals will be housed on straw. There will be toys available (environmental enrichment) and the pigs can be housed in groups of two in a cage. At arrival, pigs will be checked for diseases and a "welfare check" is done daily. Only healthy animals are included in the study.

The pigs will have free access to food and water until 8 hours before the experiment, when the food will be removed. The water will remain *ad libitum*.

The experiments will be conducted at the operating theatre for large animals at the CPV facility.

12. Deskundigheid

Concerning the animals experiments VO and VVO are qualified to perform the interventions

according to article 9 of the "wet op dierproeven". During the experiments assistance of an article 12 person will be requested. The co-worker from the CPV large animal facility has a lot of experiences with inducing anaesthesia and insertion vascular lines.

13. Standard Operation Procedures (SOP)

Anaesthesia conform SOP CPV-3-V

14. Relevante literatuur

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practical aspects. *J Trauma* 1983; 23: 84-90
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Werkschema

Voorbereiding

1. Pre-anesthesthetisch onderzoek zoals beschreven in SOP-CPV-3-V
2. Premedicatie: zoletil 8 mg/kg im. en atropine 0.05 mg/kg im.
3. Plaatsen perifere 18G of 20G canule in oorvene
4. Positioneren in buikligging en aansluiten bewaking bestaande uit ECG, NIBD en pulsoximeter
5. Inductie anesthesie volgens SOP-CPV-3-V:
    - propofol 4-8 mg/kg iv.
    - fentanyl 4 mcg/kg iv.
    - pancuronium 0,15 mg/kg iv.
6. Onderhoud van de anesthesie:
    - Propofol 9 mg/kg/u
    - Sufentanil 8 mcg/kg/u
    - Pancuronium 0,3 mg/kg/u
7. Tracheal intubatie met gecuffte tube 8.5 of 9.0 ID
8. Start kunstmatige ventilatie
9. Basisinfuus NaCl 0.9% 10 mL/kg/u verwarmd
10. Verwarmingsmatras
11. Plaatsen rectale thermometer

Als het dier onder narcose is, wordt er gestart met het plaatsen van:

1. de arterielijn in de arterie femoralis bdz. (zie SOP 1)
2. een Swan-Ganz thermodilutie catheter (zie SOP 2)
3. drukballon in de oesophagus

Na calibratie van de drukmodules en controle van de anesthesiediepte en volume status wordt er gestart met opslaan van de uitgangsgegevens middels het IDEEQ systeem. Gedurende 30 minuten worden de volgende parameters zowel digitaal als op papier (zie bijlage "registratieformulier") geregistreerd: pols, saturatie, arteriele druk, centraal veneuze druk, pulmonale druk, cardiac output, beademingsparameters, tracheale druk en intrathoracale druk. Tevens worden bloedgasanalyses gedaan.

Indien het varken hemodynamisch en respiratoir stabiel blijft tijdens deze basisregistratie wordt er gestart met het eerste experiment. De beademing wordt los gekoppeld en door de tube wordt een jetcatheter geplaatst. Er wordt gestart beademing middels EVA of klassieke jet ventilatie. Gedurende 30 minuten wordt er door de dunne jet catheter geventileerd. Op T5, T10, T15, T20, T25 en T30 worden cardiac output, hartfrequentie, bloeddruk, pulmonale drukken, intrathoracale druk en saturatie genoteerd. Deze parameters worden tevens continu geregistreerd middels IDEEQ. Op de bovengenoemde meetpunten worden ook arteriele bloedmonsters afgenomen voor bepaling.

Na de eerste run is er wash out van minimaal 30 minuten. De tweede run zal starten nadat de hemodynamische, respiratoire en bloedgas waarden weer genormaliseerd zijn. Na de tweede run wordt er een bronchoscopy verricht waarna het varken gedood wordt (SOP 3).

Onderstaand diagram geeft het verloop van het gehele experiment aan.

Preparation	Base line	Run 1	Washout	Run 2	End
Anaesthesia Line insertions Placing catheters	Recording for 30 minutes	EVA in a partially obstructed airway or (conventional) jet ventilation in an open airway for 30 minutes	30 minutes	EVA or (conventional) jet ventilation in an open airway for 30 minutes	Bronchoscopy Euthanization Histology

SOP 1 Cannulatie van de arterie femoralis bij het varken

Narcose: zoals beschreven in SOP-CPV-3-V

Als het varken onder narcose is:

- Varken op de rug positioneren
- Lies scheren
- Lies desinfecteren
- Percutaan aanprikken van a.femoralis middels een 18 G seldinger systeem
- Catheter fixeren middels hechtdraad
- Aansluiten aan druk module en systeem nullen

Arterial catheterization set 18G
Arrow REF: FA-04018

SOP 2 Plaatsen Swan Ganz Thermodilutie catheter

Narcose: zoals beschreven in SOP-CPV-3-V

Als het varken onder narcose is:

- Varken op de rug positioneren
- Nek scheren
- Nek desinfecteren
- Percutaan aanprikken van v. jugularis rechts middels een 18G introducer naald
- Voerdraad opvoeren
- Dilatatie huid en plaatsen 9 Fr. sheath
- Sheath fixeren
- 8 Fr. Swan Ganz thermodilutie catheter door sheath opvoeren en ogv drukcurves tip positioneren in wedge
- Centrale veneuze bloedgas afnemen en Swan Ganz calibreren

Percutane sheath introducer kit
Arrow REF: AH-09801

Swan Ganz CCOmbo CCO/SvO2/VIP thermodilutie catheter
Edwards Lifesciences REF: 746HF8

SOP 3 Euthanasie varken

Narcose: zoals beschreven in SOP-CPV-3-V

Als het experiment ten einde is:

1. intraveneuze toegang controleren
2. Pentobarbital 100-200 mg per kg intraveneus toediening als bolus injectie. *Voor een dier van 60-70 kg Euthanimal® (200 mg/ml Pentobarbitalnatrium) 40 tot 70 ml iv. toedienen.*
3. Controleer of varken overleden is (vlak ECG, geen cortonen)
4. Koppel beademing en bewaking los.

University Maastricht

Faculty of Health, Medicine and Life Sciences

Dierexperimenten Commissie

DEC

Aan:

, voorzitter
p/a Secretariaat DEC-UM
Postbus 616
NL-6200 MD Maastricht
Telefoon: 043

Uw referentie:

Onze referentie : f

Maastricht, 31-05-2011

Geachte Onderzoeker,

Uw projectaanvraag: "*Ventilation through a small-bore catheter; conventional jet ventilation or EVA?*", is op de DEC vergadering van 27 mei 2011 besproken.

De DEC heeft een aantal vragen en opmerkingen:

- De DEC verzoekt het doel van de proef op het voorblad aan te passen in code 37.
- Bij punt 6 verzoekt de DEC toe te voegen dat dit DEC protocol wetenschappelijk beoordeeld en **goedgekeurd** is door, enzovoort.
- Bij punt 7a wenst de DEC de motivering voor alleen vrouwelijke dieren en of de gewichtsgrenzen niet iets ruimer gesteld moeten worden?
- Bij punt 12 verzoekt de DEC aan te geven wat de ervaring is van de biotechnici en of er nog andere biotechnici met ervaring gaan meewerken aan dit experiment.
- De DEC verzoekt de SOP's toe te voegen.

Gelieve eventuele vragen te beantwoorden in **een brief en indien noodzakelijk Uw project aan te passen en duidelijk de aanpassingen grijs te markeren.**
Uw project staat bij de DEC geregistreerd onder nummer **2011-068**, gelieve dit nummer in verdere correspondentie te vermelden.

Hoogachtend,

Voorzitter DEC-UM

Maastricht, 3 juni 2011

Betreft: aanpassing DEC protocol 2011-068

Geachte leden van de DEC,

Naar aanleiding van uw brief hebben we de volgende zaken in het protocol aangepast:

- Het doel van de proef op het voorblad is veranderd in code 37.
- Bij punt 6 is toegevoegd dat het protocol wetenschappelijk beoordeeld en **goedgekeurd** is.
- De gewichtsgrenzen zijn iets ruimer gesteld en zowel mannelijke als vrouwelijke dieren mogen geincludeerd worden
- Bij punt 12 is de ervaring van de biotechnici die gaan meewerken aan dit experiment beschreven.
- De SOP zijn in de bijlage toegevoegd.

Hopende u voldoende geinformeerd te hebben.

Met vriendlijke groet,

Maastricht University

Faculty of Health, Medicine and Life Sciences

Aan:

Ons kenmerk	*Doorkiesnummer*	*Maastricht*
	043-	23-06-2011

Project: *Ventilation through a small-bore catheter: conventional jet ventialtion or EVA?*

Verantwoordelijk onderzoeker (VO):

Hierbij delen wij U mede dat voornoemd project aan de ethische toetsingscriteria voor proefdiergebruik voldoet.
De DEC maakt geen bezwaar tegen uitvoering van dit project zoals aangevraagd en geeft een **positief advies.**

Projectnummer:	**2011-068**
Diersoort:	**varken**
Aantal dieren:	**6**
Einddatum:	**17-06-2015**

Uw project staat bij de DEC en CPV geregistreerd onder bovenstaand nummer. Gelieve dieren, die voor dit project bestemd zijn, ook onder dit nummer aan te vragen.

Voorzitter DEC-UM

Vice-Voorzitter DEC-UM

DEC-UM
Voorzitter DEC-UM

p/a secretariaat DEC-UM

Secretariaat DEC-UM
T (043)

Bezoekadres

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