

Inventaris Wob-verzoek W20-05									
nr.	Meldingsdossier 20209404-1	wordt verstrekt				weigeringsgronden			
		reeds openbaar	niet	geheel	deels	10.1.c	10.2.e	10.2.g	11.1
1	Aanvraagformulier, d.d. 5 november 2020				x		x	x	
2	Toelichting op melding				x			x	
3	Ontvangstbevestiging, d.d. 6 november 2020				x		x	x	



Aanvraag Projectvergunning Dierproeven Administratieve gegevens

- U bent van plan om één of meerdere dierproeven uit te voeren.
- Met dit formulier vraagt u een vergunning aan voor het project dat u wilt uitvoeren. Of u geeft aan wat u in het vergunde project wilt wijzigen.
- Meer informatie over de voorwaarden vindt u op de website www.centralecommissiedierproeven.nl, of in de toelichting op de website.
- Of bel met 0900-2800028 (10 ct/min).

1 Gegevens aanvrager

- 1.1 Heeft u een deelnemernummer van de NVWA?
Neem voor meer informatie over het verkrijgen van een deelnemernummer contact op met de NVWA.

Ja > Vul uw deelnemernummer in
 Nee > U kunt geen aanvraag doen

10.2.g

- 1.2 Vul de gegevens in van de instellingsvergunninghouder die de projectvergunning aanvraagt.

Naam instelling of organisatie

10.2.g

Naam van de portefeuillehouder of diens gemachtigde

10.2.e

KvK-nummer

10.2.g

Straat en huisnummer

Postbus

Postcode en plaats

IBAN

Tenaamstelling van het rekeningnummer

- 1.3 Vul de gegevens van het postadres in.
Alle correspondentie van de CCD gaat naar de portefeuillehouder of diens gemachtigde en de verantwoordelijke onderzoeker.

- 1.4 Vul de gegevens in van de verantwoordelijke onderzoeker.

(Titel) Naam en voorletters

10.2.e

Dhr. Mw.

Functie

Afdeling

Telefoonnummer

E-mailadres

- 1.5 (Optioneel) Vul hier de gegevens in van de plaatsvervangende verantwoordelijke onderzoeker.

(Titel) Naam en voorletters

Dhr. Mw.

Functie

Afdeling

Telefoonnummer

E-mailadres

- 1.6 (Optioneel) Vul hier de gegevens in van de persoon die er verantwoordelijk voor is dat de uitvoering van het project in overeenstemming is met de projectvergunning.

(Titel) Naam en voorletters

Dhr. Mw.

Functie

Afdeling

Telefoonnummer

E-mailadres

- 1.7 Is er voor deze projectaanvraag een gemachtigde?

Ja > Stuur dan het ingevulde formulier *Melding Machtiging* mee met deze aanvraag

Nee

2 Over uw aanvraag

- 2.1 Wat voor aanvraag doet u?

Nieuwe aanvraag > Ga verder met vraag 3

Wijziging op (verleende) vergunning die negatieve gevolgen kan hebben voor het dierenwelzijn

Vul uw vergunde projectnummer in en ga verder met vraag 2.2

Melding op (verleende) vergunning die geen negatieve gevolgen kan hebben voor het dierenwelzijn

Vul uw vergunde projectnummer in en ga verder met vraag 2.3

AVD 10.2.g

- 2.2 Is dit een *wijziging* voor een project of dierproef waar al een vergunning voor verleend is?

Ja > Beantwoord dan in het projectplan en de niet-technische samenvatting alleen de vragen waarop de wijziging betrekking heeft en onderteken het aanvraagformulier

Nee > Ga verder met vraag 3

- 2.3 Is dit een *melding* voor een project of dierproef waar al een vergunning voor is verleend?

Nee > Ga verder met vraag 3

Ja > Geef hier onder een toelichting en ga verder met vraag 6

Het Biomedical Primate Research Centre melding van een voorgenomen aanpassing van het project 'Evaluation of vaccines and antiviral compounds against emerging coronavirus infections'.

Onder de huidige vergunning zijn 48 dieren aangevraagd voor de bepaling van de farmakinetiek van antivirale middelen tegen CoV (proef 3.4.4.3), en 100 dieren voor de bepaling van de werkzaamheid van deze middelen (proef 3.4.4.4).

Vanwege de grote vraag naar studies met makaken voor het vaccinonderzoek tegen CoV, willen wij 24 apen van 3.4.4.3 en 40 apen van 3.4.4.4 overzetten naar proef 3.4.4.2. 'Vaccine evaluation in nonhuman primates'.

De aanpassing zal niet resulteren in veranderingen in de procedures zoals beschreven in de bijlagen beschrijving dierproeven en zal niet leiden tot een toename van het aantal dieren of een verandering in het ongerief.

De aanpassing is voorgelegd aan de IvD van het instituut en daar besproken en akkoord bevonden.

3 Over uw project

- 3.1 Wat is de geplande start- en einddatum van het project?

Startdatum 17 - 03 - 2020

Einddatum 16 - 03 - 2025

- 3.2 Wat is de titel van het project?

Evaluation of vaccines and antiviral compounds against emerging coronavirus infections

3.3 Wat is de titel van de niet-technische samenvatting?

Onderzoek naar de werkzaamheid van vaccins en antivirale middelen tegen nieuwe coronavirussen

3.4 Wat is de naam van de Dierexperimentencommissie (DEC) aan wie de instellingsvergunninghouder doorgaans haar projecten ter toetsing voorlegt?

Naam DEC	DEC
Postadres	Postbus 10.2.g
E-mailadres	dec@10.2.g

4 Betaalgegevens

4.1 Om welk type aanvraag gaat het? Nieuwe aanvraag Projectvergunning € Lege

Wijziging € 818 Lege

4.2 Op welke wijze wilt u dit bedrag aan de CCD voldoen. Via een eenmalige incasso

Na ontvangst van de factuur

Bij een eenmalige incasso geeft u toestemming aan de CCD om eenmalig het bij 4.1 genoemde bedrag af te schrijven van het bij 1.2 opgegeven rekeningnummer.

5 Checklist bijlagen

5.1 Welke bijlagen stuurt u mee?

Verplicht

Projectvoorstel

Niet-technische samenvatting

Overige bijlagen, indien van toepassing

Melding Machtiging

6 Ondertekening

6.1 Print het formulier uit, onderteken het en stuur het inclusief bijlagen via de beveiligde e-mailverbinding naar de CCD of per post naar:

Centrale Commissie
Dierproeven
Postbus 20401
2500 EK Den Haag

Ondertekening door de instellingsvergunninghouder of gemachtigde (zie 1.7). De ondergetekende verklaart:

- dat het projectvoorstel is afgestemd met de Instantie voor Dierenwelzijn.
- dat de personen die verantwoordelijk zijn voor de opzet van het project en de dierproef, de personen die de dieren verzorgen en/of doden en de personen die de dierproeven verrichten voldoen aan de wettelijke eisen gesteld aan deskundigheid en bekwaamheid.
- dat de dieren worden gehuisvest en verzorgd op een wijze die voldoet aan de eisen die zijn opgenomen in bijlage III van richtlijn 2010/63/EU, behalve in het voorkomende geval de in onderdeel F van de bijlage bij het bij de aanvraag gevoegde projectvoorstel gemotiveerde uitzonderingen.
- dat door het ondertekenen van dit formulier de verplichting wordt aangegaan de leges te betalen voor de behandeling van de aanvraag.
- dat het formulier volledig en naar waarheid is ingevuld.

Naam

10.2.e

Functie

Plaats

Datum

05 - 11 - 2020

Handtekening

10.2.e



Appendix Description animal procedures

- This appendix should be enclosed with the project proposal for animal procedures.
- A different appendix 'description animal procedures' should be enclosed for each type of animal procedure.
- For more information, see our website (www.centralecommissiedierproeven.nl).
- Or contact us by phone (0900-2800028).

1 General information

1.1 Provide the approval number of the 'Netherlands Food and Consumer Product Safety Authority'.

10.2.g

1.2 Provide the name of the licenced establishment.

10.2.g

1.3 List the serial number and type of animal procedure.

Serial number	Type of animal procedure
4	CoV antiviral efficacy study in nonhuman primates

Use the serial numbers provided in Section 3.4.4 of the Project Proposal form.

2 Description of animal procedures

A. Experimental approach and primary outcome parameters

Describe the general design of the animal procedures in relation to the primary outcome parameters. Justify the choice of these parameters.

In order to evaluate the use of antiviral compounds to prevent or treat CoV infection, we will use the following general study set-up for a therapeutic treatment: a group of animals will be experimentally infected with CoV (Appendix 1). Then, the animals will be administered the compound, and nasal and tracheal swab samples are collected at regular time points to determine if the virus load is influenced by the therapeutic administration of the compound. A group of animals will not receive the compound, and will be used as controls. During the study, nasal and tracheal swabs are collected at regular time points and tested for the presence or absence of virus.

The primary outcome parameter for antiviral efficacy will be the reduction of viral load in nasal and tracheal swabs.

Secondary outcome parameters for CoV infection that may be evaluated are:

1. Absence or reduction of fever caused by CoV infection
2. Absence or reduction of clinical symptoms caused by CoV infection
3. Absence or reduction of lung pathology caused by CoV infection

Describe the proposed animal procedures, including the nature, frequency and duration of the treatment. Provide justifications for the selected approach.

A telemetric temperature sensor is surgically placed in the abdominal cavity at least 4 weeks before the first compound administration takes place (prophylactic treatment), or before experimental infection (therapeutic treatment). This timeframe is necessary for full recovery of the animals from the surgery, and

to allow adequate body temperature recording during a two to three-week period to establish normal values before the administration/infection start.

Antiviral study set up:

At the start of the study, the animals will experimentally be infected. The optimal route and inoculum dose are determined in an infection study with this inoculum (Appendix 1). At that same time point, a group of animals that will not receive the compound are also infected, and will act as untreated infection controls in the study. Next, the animals will receive the antiviral compound. The route of administration and the dosage to be used are based on PK studies with this compound performed in NHP (Appendix 3), or are based on studies performed by collaborating institutes. At the same time blood is collected for a zero-value determination. Typically, after infection of the animals, swabs and blood will be collected daily for a period of maximally 14 days to monitor the progress of the viral infection and to control for changes in clinical chemistry and hematology parameters. This intensive sampling is necessary because in this period significant and rapid changes in the amount of virus in the blood may occur in untreated animals. During this period of daily sampling the animals will be given liquid foods by means of a stomach tube because the daily anesthesia necessitates fasting of the animals. In this way, the wellbeing of the animals is affected as little as possible. After this period, the frequency of sample collection will be brought down to maximally once every two days. After the untreated control animals have become virus-negative in the PCR for the first time, the groups may be followed for an extra period of 3-4 weeks to confirm absence of the virus and to monitor for sudden re-activations of virus replication in any of the animals. At the end of the study, maximally 6 weeks after the start, the animals will be humanely euthanized and necropsy will be performed for the collection of tissue samples for histopathological and virus tests. The animals will be monitored daily during the study period for general behaviour, appetite, faeces, etc., and at each time-point when the animals are sedated, body weight will be measured. The application of X-ray or PET-CT scanning to measure lung infiltration will give us insight in the disease progression of the CoV infection, and how this is influenced by the antiviral compound. X-ray or PET-CT scanning will be performed when animals are already sedated for sampling of blood and swabs, and will thus not cause additional discomfort.

The details of each study, including the route of infection, dose used, number of animals used, will be submitted for approval to the AWB.

Describe which statistical methods have been used and which other considerations have been taken into account to minimise the number of animals.

The number of animals will be based on statistical power analysis. Calculations account for the number of animals needed to measure statistically significant reduction in virus load in relation to untreated controls. In addition, calculations are performed to establish the number of animals needed to obtain a significant reduction in virus load in the trachea between the treated groups and the untreated control group. Only the minimum number of animals needed will be used. Since historical data are available on infection in untreated animals (Appendix 1), usually less animals can be used in the control group than in the antiviral-treated groups.

B. The animals

Specify the species, origin, estimated numbers, and life stages. Provide justifications for these choices.

The experiments will be performed in NHP (rhesus macaques, and/or cynomolgus macaques, adult, M/F, maximally n=100. All NHP are purpose bred at our institute, or incidentally they will be obtained from a certified supplier. Both mature male and female animals can be used.

Rhesus macaques (*Macaca mulatta*), and cynomolgus macaques (*Macaca fascicularis*) are susceptible to an array of (emerging) human coronaviruses (5-9), and have already been used in coronavirus antiviral research (1-4). The decision to use a specific macaque species will be based on currently ongoing infection studies with the recently emerged SARS-CoV-2, and studies already performed with SARS and MERS CoVs in NHP. The decision which species will be used, will be submitted for approval to the AWB.

The calculated number of animals assumes that each study will contain 1 treatment group and 1 control group, with max. 10 animals per group. The group size will be determined per experiment, and will be based on power calculations using reduction of virus load as primary outcome measure. As stated above,

probably fewer animals will be needed in the non-vaccinated challenge control groups. In all, we anticipate performing 5 such studies over a 5-year period with $5 \times 20 =$ maximally 100 animals. Since historical data are available on infection in untreated animals (Appendix 1), usually less animals can be used in the non-treated control group than in the groups treated with antiviral compound.

References:

1. Falzarano, D., de Wit, E., Rasmussen, A. L., Feldmann, F., Okumura, A., Scott, D. P., et al. (2013). Treatment with interferon- α 2b and ribavirin improves outcome in MERS-CoV-infected rhesus macaques. *Nature Medicine*, 19(10), 1313–1317.
2. Haagmans, B. L., Kuiken, T., Martina, B. E., Fouchier, R. A. M., Rimmelzwaan, G. F., van Amerongen, G., et al. (2004). Pegylated interferon- α protects type 1 pneumocytes against SARS coronavirus infection in macaques. *Nature Medicine*, 10(3), 290–293.
3. Sheahan, T. P., Sims, A. C., Graham, R. L., Menachery, V. D., Gralinski, L. E., Case, J. B., et al. (2017). Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. *Science Translational Medicine*, 9(396), eaal3653.
4. Tang, Q., Li, B., Woodle, M., & Lu, P. Y. (2008). Application of siRNA against SARS in the rhesus macaque model. *Methods in Molecular Biology (Clifton, NJ)*, 442, 139–158.
5. Totura, A. L., & Bavari, S. (2019). Broad-spectrum coronavirus antiviral drug discovery. *Expert Opinion on Drug Discovery*, 14(4), 397–412.
6. Gong, S.-R., & Bao, L.-L. (2018). The battle against SARS and MERS coronaviruses: Reservoirs and Animal Models. *Animal Models and Experimental Medicine*, 1(2), 125–133.
7. Sutton, T. C., & Subbarao, K. (2015). Development of animal models against emerging coronaviruses: From SARS to MERS coronavirus. *Virology*, 479–480, 247–258.
8. Yu, P., Xu, Y., Deng, W., Bao, L., Huang, L., Xu, Y., et al. (2017). Comparative pathology of rhesus macaque and common marmoset animal models with Middle East respiratory syndrome coronavirus. *PLoS One*, 12(2), e0172093.
9. Greenough, T. C., Carville, A., Coderre, J., Somasundaran, M., Sullivan, J. L., Luzuriaga, K., & Mansfield, K. (2005). Pneumonitis and multi-organ system disease in common marmosets (*Callithrix jacchus*) infected with the severe acute respiratory syndrome-associated coronavirus. *The American Journal of Pathology*, 167(2), 455–463.

C. Re-use

Will the animals be re-used?

No, continue with question D.

Yes > Explain why re-use is considered acceptable for this animal procedure.

Animals that will be used in these experiments, have possibly been used in previous experiments. Animals that have been involved in previous CoV studies or that have pre-existing antibodies against CoVs are not suitable because of possible immunological cross-reactivity between the different CoVs. In view of the long life of the animals of this species reuse of animals will take place within the limitations described in art 1e of the Wet op de Dierproeven.

Are the previous or proposed animal procedures classified as 'severe'?

No

Yes > Provide specific justifications for the re-use of these animals during the procedures.

D. Replacement, reduction, refinement

Describe how the principles of replacement, reduction and refinement were included in the research strategy, e.g. the selection of the animals, the design of the procedures and the number of animals.

Replacement

Before compounds are evaluated for its efficacy in NHP, they have been tested extensively for efficacy and toxicity in *in vitro* assays. If possible, *in silico* modeling of the pharmacokinetics has been applied. (Rajoli 2015). This computer-simulation may result in a drastic decrease of the number of animals necessary, or even make *in vivo* PK studies superfluous. It is not yet known which antivirals will be investigated, and if *in silico* modeling is achievable for all compounds, but before *in vivo* PK studies will be performed, all other options, including *in silico* PK, will be investigated and the results will be presented to the AWB. Only if a compound is positively tested, it will be examined for its efficacy against CoV infection in NHP.

Although animal models for CoV infection, other than nonhuman primates (NHP), are also in use in research for CoV, NHP are the animal model that best mimic infection and pathogenesis in humans. Equally, in contrast to other animal species that are used in biomedical research, like rodents, NHP have the great advantage that their body surface area/mass ratio, drug metabolism, pharmacokinetics, and anatomical structure are highly comparable to that of humans. As a consequence, drugs are metabolized in a similar way in NHP as in humans, and also exert their mode of action similarly. This, in combination with the fact that CoV infection of NHP mimics infection and pathogenesis in humans, renders them preclinical animal models of choice to investigate the efficacy of potential anti-CoV compounds for human use.

Reduction

This study involves the efficacy testing of antiviral compounds in the CoV infection model in NHP. Because the variability in viral replication kinetics in the NHP will only become available after the completion of the infection studies, the exact number of animals to be used in the studies cannot be provided at this point. Under A we have described the statistical analyses that will be performed on basis of the infection studies. Only the minimum number of animals needed will be used. If possible, studies will be combined. In such a case, one control group will suffice and the total number of animals will be reduced.

Refinement

Supplementary nutritious and calorie-rich diet is administered when the animals are daily sedated for blood sampling. This eliminates the possible negative effects of fasting for the purpose of frequent sedation. Infection and bleeding take place under sedation, and at the same time the animals will be weighed and examined. The animals are trained to work as much as possible voluntarily on invasive biotechnological actions such as giving anaesthesia or virus infection. In consultation with our collaborators, the number of blood samplings, and the collected volumes of blood will be reduced to a minimum.

The use of telemetric temperature sensors makes it possible to record the body temperature 24/7, and to monitor the body temperature in real-time. We have designed a method that allows very precise calculation of fever induction caused by the infection (5). With this method we have observed a significant reduction in fever by some vaccine candidates (4). Such precise measurements are not possible with the traditional rectal temperature measurement. Placement of the telemetric temperature sensor will require a small surgery, which will be done under anaesthesia. Subsequently, animals will receive analgesics as long as required. The use of imaging (X-ray or PET-CT scan) will provide us with data regarding lung pathology.

Reference:

Rajoli RKR, Back DJ, Rannard S, *et al.* In Silico Dose Prediction for Long-Acting Rilpivirine and Cabotegravir Administration to Children and Adolescents. *Clin Pharmacokinet.* 2018;57(2):255–266. doi:10.1007/s40262-017-0557-x

Explain what measures will be taken to minimise 1) animal suffering, pain or fear and 2) adverse effects on the environment.

Animals will be socially housed with a socially compatible animal, whenever possible. There is an extensive program for environmental enrichment in our institute.

All experimental procedures will be performed under sedation. Each time an animal is sedated, the animal will be weighed, and the animal will be closely examined. Our institute uses a customized database that documents all individual animals in the institute. General observations like behaviour, appetite and stool are part of this database. This database thus facilitates early recognition of minor changes in these general parameters. During the study, care will be taken to avoid pain. In case an animal suffers from pain, a veterinarian will be informed, and the animal will receive analgesics to relieve the pain, if necessary.

During the first 2 weeks of the infection the animal will receive tube feeding. This is necessary, because the daily sedations of the animals necessitate fasting of the animals, and the food intake during this period would otherwise be very limited.

Regular analysis of haematological and clinical chemistry parameters is part of the experiment. During these experiments, the virus load in plasma will also be analysed as primary indicator of infection. These data will also be consulted to determine if changes in behaviour, appetite or stool are clinically relevant. If necessary, judged by the veterinarian, measures will then be taken to treat the animal.

The studies will be performed according the Dutch laws, and will cause no adverse effects on the environment.

Repetition and duplication

E. Repetition

Explain what measures have been taken to ensure that the proposed procedures have not already been performed. If applicable, explain why repetition is required.

Not applicable

Accommodation and care

F. Accommodation and care

Is the housing and care of the animals used in experimental procedures not in accordance with Annex III of the Directive 2010/63/EU?

No

Yes > If this may adversely affect animal welfare, describe how the animals will be housed and provide specific justifications for these choices.

G. Location where the animals procedures are performed

Will the animal procedures be carried out in an establishment that is not licenced by the NVWA?

No > Continue with question H.

Yes > Describe this establishment.

Provide justifications for the choice of this establishment. Explain how adequate housing, care and treatment of the animals will be ensured.

Classification of discomfort/humane endpoints

H. Pain and pain relief

Will the animals experience pain during or after the procedures?

No > Continue with question I.

Yes > Will anaesthesia, analgesia or other pain relieving methods be used?

No > Justify why pain relieving methods will not be used.

X Yes > Indicate what relieving methods will be used and specify what measures will be taken to ensure that optimal procedures are used.

After placing the telemetric temperature sensor in the abdomen, the animals will receive analgesics for as long as necessary, typically 3 days. In previous studies we have observed that animals can experience some fever during the first days after insertion of the temperature recording device, but have recovered very well within 1 week after the operation. In case of symptoms caused by CoV infection, this can result in pain. For this purpose, oral or parenteral analgesia will be administered after consultation with the veterinarian.

I. Other aspects compromising the welfare of the animals

Describe which other adverse effects on the animals' welfare may be expected?

1. Discomfort because of insertion of the telemetric temperature sensor.
2. Discomfort due to compound and food administration via gavage
3. Discomfort due to lung lavages
4. Discomfort due to virus inoculation
5. Stress because of sedation
6. Reduced food intake due to repeated daily sedations
7. Disease symptoms due to the infection

Explain why these effects may emerge.

1. The surgery needed for insertion of the telemetric temperature sensor will cause pain and some local inflammation.
2. Insertion of the tube may cause local irritation
3. For the lung lavages a bronchoscope is used. Insertion will cause irritation
4. Intravenous inoculation can cause mild irritation. When virus is given intra-bronchially a bronchoscope is used and this will cause irritation.
5. Animals will be repeatedly sedated for blood sampling and virus inoculation. Nausea can sometimes be observed during recovery from the sedation.
6. Animals will be sedated daily during the first phase of the infection. This will have influence of the appetite
7. Coronavirus infections can cause fever, coughing, sneezing, nose discharge, laboured breathing, loss of appetite, loss of weight, inactivity.

Indicate which measures will be adopted to prevent occurrence or minimise severity.

1. Surgery will be done under anaesthesia and after surgery analgesics will be applied.
2. Insertion of the tube will be done by experience caretakers. In case irritation occurs, this will be mild and no extra measures need to be taken
3. For the lung lavages animals are first deeply sedated and receive a muscle relaxant.
4. If irritation occurs, this will be mild. It will therefore not be necessary to take additional measures.
5. Recovery of the animals is monitored and the veterinarian will intervene if animals do not recover fast enough.
6. Animals will receive tube feeding via gavage. This is applied during sedation for blood collection.
7. Animals are monitored twice daily and a weighed clinical scoring list is used to record the clinical symptoms. When a certain pre-determined clinical score is reached the animal will be humanely euthanized and a full necropsy will be performed to establish the cause of the disease and viral distribution over the respiratory organs

J. Humane endpoints

May circumstances arise during the animal procedures which would require the implementation of humane endpoints to prevent further distress?

No > Continue with question K.

X Yes > Describe the criteria that will be used to identify the humane endpoints.

Animals are monitored twice daily and a weighed clinical scoring list is used to record the clinical

symptoms. When a certain pre-determined clinical score is reached the animal will be humanely euthanized. Individual scores are added and decision is based on the total daily score. Symptoms that lead to an immediate endpoint are: open mouth breathing or cyanosis, lethargy as defined by minimal response to human approach.

Indicate the likely incidence.

After CoV infection each animal may become seriously ill. Thus, the percentage is 100%

K. Classification of severity of procedures

Provide information on the expected levels of discomfort and indicate to which category the procedures are assigned ('non-recovery', 'mild', 'moderate', 'severe').

Discomfort is caused by the implantation of the telemetric temperature sensor. By using this device, the animals can be continuously monitored for body temperature. In combination with frequent observations by animal caretakers, this will facilitate the appropriate intervention by veterinarians at the earliest time-point, and will preclude progression to serious disease that may be caused by coronavirus infection. Therefore, the cumulative discomfort will be moderate

End of experiment

L. Method of killing

Will the animals be killed during or after the procedures?

No

X Yes > Explain why it is necessary to kill the animals during or after the procedures.

Animals will be euthanized in case they show signs of disease symptoms in order to avoid severe discomfort. To investigate the presence of virus in tissues and organs, and for the investigation of possible tissue damage caused by CoV or by the compounds, it is necessary to euthanize the animals at the end of the study

Is the proposed method of killing listed in Annex IV of Directive 2010/63/EU?

No > Describe the method of killing that will be used and provide justifications for this choice.

X Yes

Van: info@zbo-ccd.nl
Aan: 10.2.e
Cc:
Onderwerp: Ontvangstbevestiging Melding projectvergunning dierproeven AVD 10.2.g
Datum: vrijdag 6 november 2020 11:41:20

Geachte 10.2.e,

Wij hebben op 05-11-2020 een melding ontvangen op uw projectvergunning dierproeven. Het gaat om uw project "Evaluation of vaccines and antiviral compounds against emerging coronavirus infections" met aanvraagnummer AVD 10.2.g, waarvoor op een vergunning is afgegeven. Uw melding is bij ons geregistreerd onder aanvraagnummer AVD 10.2.g

U geeft aan dat zowel het ongerief voor de dieren als het aantal dieren niet toeneemt.

Meer informatie

Heeft u vragen, kijk dan op www.centralecommissiedierproeven.nl. Of neem telefonisch contact met ons op: 0900 28 000 28 (10 ct/minuut).

Met vriendelijke groet,
Centrale Commissie Dierproeven

10.2.e

www.centralecommissiedierproeven.nl

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.....

T: 0900 2800028
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