



gondo mastutik <gondomastutik@fk.unair.ac.id>

# **Submission Confirmation**

1 message

Veterinary World <noreply@ejmanager.com> Reply-To: Veterinary World <editorveterinaryworld@gmail.com> To: gondomastutik@fk.unair.ac.id Tue, Oct 19, 2021 at 8:53 PM

Dear Gondo Mastutik,

Your submission entitled **Experimental and Evidence of Natural SARS-CoV-2 Infection in Pets, Wildlife, and Farm Animals: A Review** (Manuscript Number: VETWORLD-2021-10-575) has been received by **Veterinary World**.

You could follow status of your manuscript by login to your author account at www.ejmanager.com.

Thank you for submitting your work to our journal.

Best regards,

Editor Veterinary World http://www.veterinaryworld.org

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JOURNAL CONTACT EMAIL: editorveterinaryworld@gmail.com

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http://www.ejmanager.com



# Your article waiting for Revision

1 message

**noreply@ejmanager.com** <noreply@ejmanager.com> Reply-To: noreply@ejmanager.com To: gondomastutik@fk.unair.ac.id Mon, Jan 3, 2022 at 5:25 PM

This is an automatic email. DO NOT REPLY TO THIS EMAIL Send your emails to to journal editor (editorveterinaryworld@gmail.com).

Dear Gondo Mastutik,

You have article(s) waiting for revision in http://my.ejmanager.com/vetworld/

Please login to your account by using your username and password in order to COMPLETE your article(s) waiting for your revision.

If you want to withdraw your article you need to send an email to journal editor (editorveterinaryworld@gmail.com).

Your Username: gondomastutik@fk.unair.ac.id

Your Password: 46989

Journal: Veterinary World

http://my.ejmanager.com/vetworld/

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JOURNAL CONTACT EMAIL: noreply@ejmanager.com

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# Request additional time for revision manuscript [Ms.Nr. VETWORLD-2021-10-575]

3 messages

**gondo mastutik** <gondomastutik@fk.unair.ac.id> To: editorveterinaryworld@gmail.com Tue, Jan 4, 2022 at 8:54 AM

#### Dear Editors,

We are very pleased and grateful for your email regarding the results of the reviewer's review and comments from the editor on our manuscript entitled "Experimental and Evidence of Natural SARS-CoV-2 Infection in Pets, Wildlife, and Farm Animals: A Review\" (Ms.Nr. VETWORLD-2021-10-575.

However, we are having problems revising the manuscript as we received it almost at the end of the year. We have revised our manuscript and have received a reply from the copy-editing service ENAGO. Currently, we are asking the approval from our co-author from Spain but it looks like will be a little late because there are currently a Christmas and New Year's holiday until January 9, 2022, in Spain.

Based on this, we hereby request additional time to revise our manuscript. We hope that the Editor understands our condition and is willing to give us a long deadline for reviewing our manuscript. We hope that the editor will grant our request. Thank you very much.

Best Regards, Gondo Mastutik, PhD.

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Gondo Mastutik

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Universitas Airlangga, Surabaya, Indonesia.

St. Prof. Dr. Moestopo No 47, Surabaya 60132, Indonesia, Phone: +62-31-5020251 ext 151.

Mobile: +6281 231 071 818

E-mail: gondomastutik@fk.unair.ac.id, gondomastutik@gmail.com

**Veterinary World** <editorveterinaryworld@gmail.com> To: gondo mastutik <gondomastutik@fk.unair.ac.id> Tue, Jan 4, 2022 at 10:56 AM

Dear Gondo Muastutik,

The time to submit the revised manuscript is 4 weeks; however, the system sends the reminder periodically to the authors to speed up the process.

We sent the article revision letter to you before 16 days and you have almost 2 weeks time to submit the revised manuscript. So, do not worry about the deadline for the submission of the revised manuscript.

# NEWS:

Dr. Anjum Sherasiya, Editor-in-Chief of Veterinary World is appointed as Crossref Ambassador.

-----Best Regards,

Dr. Anjum Sherasiya Editor-in-Chief, Veterinary World Crossref - Ambassador Star, Gulshan Park, NH-8A, Chandrapur Road, Wankaner - 363621, Dist. Morbi (Gujarat), India. Website: www.veterinaryworld.org, onehealthjournal.org E-mail: editorveterinaryworld@gmail.com



# **Article Revision Letter for Authors - (VETWORLD-2021-10-575)**

14 messages

Veterinary World <noreply@ejmanager.com> Reply-To: Veterinary World <editorveterinaryworld@gmail.com> To: gondomastutik@fk.unair.ac.id Sun, Dec 19, 2021 at 5:03 AM

Dear Gondo Mastutik,

Your manuscript entitled \"Experimental and Evidence of Natural SARS-CoV-2 Infection in Pets, Wildlife, and Farm Animals: A Review\" (Ms.Nr. VETWORLD-2021-10-575) was reviewed by reviewers of the Veterinary World. As initial decision, your manuscript was found interesting but some revisions have to be made before it can reach a publishable value. Please refer comments given at bottom.

You should send your revised manuscript via the online system of ScopeMed on https://ejmanager.com/my/vetworld/.

Sincerely yours,

Editor-Veterinary World Star, Gulshan Park, NH-8A, Chandrapur Road, Wankaner-363621, Dist. Morbi, Gujarat, India www.veterinaryworld.org

COMMENTS for Authors:

#### EDITORIAL COMMENTS:

- Highlight all corrections/additions in red color font in revised manuscript.

- Please answer all the comments below point-by-point in an accompanying response letter to your revised submission and include your responses at appropriate paragraphs in the revised word file.

- Include all authors name, affiliation, ORCID and email address in revised Word file as per format and style of Veterinary World. Please check latest article from www.veterinaryworld.org for format of this section.

- All reference no. in the text must be in continuous no. as per style of Veterinary World and amend the reference section accordingly if you have not done it.

- Please divide the introduction into 3 paragraphs if you have already not done. Introduction must be divided into 3 paragraphs i.e., 1. introduction 2. significance of the study and 3. aim of the study.

- Include authors\' contributions (refer just below the conclusion section in latest article from www.veterinaryworld.org for format of this section) if you have not added.

- Include Acknowledgements along with source of fund for this study if you have not included.

- All journal names in references must be as per standard journal abbreviation.

- If you will not revise strictly as per suggestion then there will be chance of rejection. So, revise carefully. If you have any query then please email to Editor-in-Chief.

=> Reviewer # 1

The article was well written, but it was better to explain the transmissions of this pandemic between animals. Citing references is well done. Article classification can be slightly improved. But overall the manuscript is very good

=> Reviewer # 2

Please check the title for the correct English.

Shorten the Conclusion section with inclusion of only important things rather than long description.

Editor\'s comment:

Get professional copyediting from ENAGO or Editage [keep all corrections in track changes (language as well as editorial and reviewers) and paste the certificate in the revised word file] or ask Veterinary World in answer letter for copyediting service (with extra payment) as your manuscript needs extensive copyediting.



# A message from Editor (Veterinary World)

1 message

Veterinary World <noreply@ejmanager.com> Reply-To: Veterinary World <editorveterinaryworld@gmail.com> To: gondomastutik@fk.unair.ac.id Mon, Jan 24, 2022 at 8:35 PM

Dear Gondo Mastutik,

Article Title: Experimental and Natural Infections of SARS-CoV-2 in Pets and in Wild and Farm Animals

Mns Id: VETWORLD-2021-10-575

We have received the payment in our PayPal account. We will issue the signed acceptance letter once the payment will be credited to our bank account. This process may take up to 3-5 days.

Editor-Veterinary World Star, Gulshan Park, NH-8A, Chandrapur Road, Wankaner-363621, Dist. Morbi, Gujarat, India www.veterinaryworld.org

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JOURNAL CONTACT EMAIL: editorveterinaryworld@gmail.com

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# Decision Letter to Authors - Acceptance - (VETWORLD-2021-10-575)

1 message

Veterinary World <noreply@ejmanager.com> Reply-To: Veterinary World <editorveterinaryworld@gmail.com> To: gondomastutik@fk.unair.ac.id Tue, Jan 25, 2022 at 6:15 PM

Dear Gondo Mastutik

I am pleased to inform you that your manuscript titled as "Experimental and Natural Infections of SARS-CoV-2 in Pets and in Wild and Farm Animals" (Manuscript Number: VETWORLD-2021-10-575 is accepted for publication in the Veterinary World.

- We have received the revised manuscript as per reviewers suggestions.

- We have received the payment.

- You will receive the signed acceptance letter within 2 days by email. Please check your inbox/spam folder for the same.

Sincerely yours,

Editor-Veterinary World Star, Gulshan Park, NH-8A, Chandrapur Road, Wankaner-363621, Dist. Morbi, Gujarat, India www.veterinaryworld.org

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JOURNAL CONTACT EMAIL: editorveterinaryworld@gmail.com

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# Gondo Mastutik and co-authors: Acceptance letter

1 message

**Veterinary World - Publisher** <veterinaryworldpublisher@gmail.com> Thu, Jan 27, 2022 at 11:33 AM To: gondomastutik@fk.unair.ac.id, alirohman@fst.unair.ac.id, ritishom@fk.unair.ac.id, irarrondo@riojasalud.es, deblas@unizar.es

Cc: Anjum Sherasiya <editorveterinaryworld@gmail.com>

#### Dear Authors,

I am attaching herewith the acceptance letter of your article.

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Best Regards,

Nazir Editorial Assistant Veterinary World Star, Gulshan Park, NH-8A, Chandrapur Road, Wankaner, Dist. Morbi, Gujarat India www.veterinaryworld.org www.onhealthjournal.org

Bondo Mastutik - 40.pdf



# Notification for Status Change of your Article

11 messages

Veterinary World <noreply@ejmanager.com> Reply-To: Veterinary World <editorveterinaryworld@gmail.com> To: gondomastutik@fk.unair.ac.id Sun, Jan 23, 2022 at 1:18 AM

Dear Gondo Mastutik,

VETWORLD-2021-10-575

As we declared in "Instructions for Authors", you need to contribute to Veterinary World for your provisionally accepted article.

For this purpose you should pay the following amount: \$500. The amount should be paid within 15 days.

In order to make payment, login to your account at http://www.scopemed.org or https://ejmanager.com/my/vetworld/ ---> open Status of my Articles ---> find Articles waiting for Payment and make your payment by your credit/debit card or your PayPal account.

If you want to send the payment by bank then bank details are as follows : Amount: USD 500 (sender/intermediate bank charges must be bear by the sender, so, inform your bank to select Details of charges as "OUR" among "OUR/BEN/SHA" ) Bank Name: AXIS Bank Account/Beneficiary name: Veterinary World Account Type: Current/Business Account No.: 915020046954469 Swift code: AXISINBB662 (Morbi) Branch Name: Wankaner, Dist. Morbi(Gujarat), India Purpose for remittance: Subscription to newspaper/scientific journal Please send us the scan copy of bank slip by an email.

Best Regards Editor-Veterinary World Star, Gulshan Park, NH-8A, Chandrapur Road, Wankaner-363621, Dist. Morbi, Gujarat, India www.veterinaryworld.org

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**gondo mastutik** <gondomastutik@fk.unair.ac.id> To: Ali Rohman <alirohman@gmail.com> Sun, Jan 23, 2022 at 6:31 AM

Assalammu alaikum wr wb

Pak..alhamdulillah accepted. Untuk pembayarannnya, menopo saget dipun bantu Pak? Matur nuwun



# Gondo Mastutik and co-authors: Proof for corrections

14 messages

**Veterinary World - Publisher** <veterinaryworldpublisher@gmail.com> Sat, Feb 12, 2022 at 2:07 PM To: gondomastutik@fk.unair.ac.id, alirohman@fst.unair.ac.id, ritishom@fk.unair.ac.id, irarrondo@riojasalud.es, deblas@unizar.es

Cc: Anjum Sherasiya <editorveterinaryworld@gmail.com>

#### Dear Authors,

I am attaching herewith copy-edited word file proof for corrections. Please read the instructions given in the attached file "Instructions for proof corrections" and correct the proof accordingly and send it back to me through the corresponding author's email.

-----

Best Regards,

Nazir Editorial Assistant Veterinary World Star, Gulshan Park, NH-8A, Chandrapur Road, Wankaner, Dist. Morbi, Gujarat India www.veterinaryworld.org www.onhealthjournal.org

#### 2 attachments

Instructions for proof corrections.docx 15K

Gondo Mastutik.docx 504K

**gondo mastutik** <gondomastutik@fk.unair.ac.id> To: Veterinary World - Publisher <veterinaryworldpublisher@gmail.com>

Dear Editor,

Thank you very much for sending me a proof file. I would like to ask the additional time (around 5 days), because I have already been out of the hospital to accompany my son from COVID-19 and now I have COVID-19 too (but I have light symptoms). But I will try to finish it soon as possible. I hope you will understand my condition. Thank you very much.

Best Regard, Gondo Mastutik [Quoted text hidden]

**Veterinary World - Publisher** <veterinaryworldpublisher@gmail.com> To: gondo mastutik <gondomastutik@fk.unair.ac.id> Cc: Anjum Sherasiya <editorveterinaryworld@gmail.com> Tue, Feb 15, 2022 at 12:37 PM

Tue, Feb 15, 2022 at 11:04 AM

Dear Gondo Mastutik,

OK. No problem. Wish you all the best for the better health of you and your family.

De et De wende

Best Regards,

Nazir

# **Reviewer comments**



gondo mastutik <gondomastutik@fk.unair.ac.id>

# Veterinary World: Cover page and Index of March 2022

1 message

**Veterinary World - Publisher** <veterinaryworldpublisher@gmail.com> Cc: Anjum Sherasiya <editorveterinaryworld@gmail.com> Bcc: gondomastutik@fk.unair.ac.id Mon, Apr 4, 2022 at 7:12 PM

Dear Authors,

I am attaching herewith cover page image and Index of March 2022 issue of Veterinary World.

We will send the whole issue to PubMed and PMC in the last week of this month, so you can expect your article in PubMed and PMC up to 15th of next month.

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Best Regards,

Nazir Editorial Assistant Veterinary World Star, Gulshan Park, NH-8A, Chandrapur Road, Wankaner, Dist. Morbi, Gujarat India www.veterinaryworld.org www.onhealthjournal.org

2 attachments

Title-Index-March 2022.pdf 415K

Title-March 2022.pdf 1655K



# **VETERINARY WORLD**

Open access and peer reviewed journal

 Star, Gulshan Park, NH-8A, Chandrapur Road, Wankaner - 363621, Dist. Morbi (Gujarat) India, Website: www.veterinaryworld.org, Email: editorveterinaryworld@gmail.com
 Editor-in-Chief: Anjum V. Sherasiya, Publisher: Veterinary World, EISSN: 2231-0916

SCOPUS: Citescore - 2.6, SJR - 0.550, SNIP - 1.387

# By E-mail

Ref No. VW/Accept/40/2022

Date: 25-01-2022

To, Gondo Mastutik Department of Anatomic Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya 60131, Indonesia. E-mail: gondomastutik@fk.unair.ac.id

# Acceptance of article for publication in Veterinary World

Dear Dr.

I am pleased to inform you that your manuscript titled as -

**Experimental and natural infections of SARS-CoV-2 in pets and wild and farm animals -** Gondo Mastutik, Ali Rohman, Reny I'tishom, Ignacio Ruiz-Arrondo and Ignacio de Blas

is accepted for publication in Veterinary World.

We have received the payment for publication (bill no. 353 dated 25-01-2022). So, you will receive the galley proof within 4-5 weeks. You must have to solve the query, if we point out any in galley proof.

After correction of galley proof, your article will be published online at www.veterinaryworld.org in chronological order.

Thanking You.

Yours Sincerely,

Dr. Anjum V. Sherasiya Editor-in-Chief Veterinary World



Indexed and Abstracted in Academic Journals Database, AGORA, AGRICOLA, AGRIS, CABI, CAS, DOAJ, EBSCO, ESCI- Thomson Reuters, Gale, Google Scholar, HINARI, Index Scholar, Indian Animal Science Abstracts, Indian Science Abstracts, JournalSeek, Open J-gate, ProQuest, PubMed, PubMed Central, SCOPUS, TEEAL







# CERTIFICATE OF EDITING

This is to certify that the paper titled Experimental and Natural Infections of SARS-CoV-2 in Pets and in Wild and Farm Animals commissioned to us by Gondo Mastutik has been edited for English language and spelling by Enago, an editing brand of Crimson Interactive Inc.



Issued by: Enago, Crimson Interactive In 1732, 1st Ave #22627 New York, 10128 Phone: +1-877-712-21770

Disclaimer: The author is free to accept or reject our changes in the document after our editing. However, we do not bear responsibility for revisions made to the document after our edit on December 31, 2021.

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About Crimson:

Crimson Interactive Inc. provides English language editing, transcription, and translation services to individuals and corporate customers worldwide.

# Reviewer comments & Jawabannya

Dear Editor,

Thank you very much for your comment on our manuscript. Herewith we have corrected our manuscript as follows:

# EDITORIAL COMMENTS:

- 1. Highlight all corrections/additions in red color font in revised manuscript. Yes, we did. In red font.
- 2. Please answer all the comments below point-by-point in an accompanying response letter to your revised submission and include your responses at appropriate paragraphs in the revised word file. Yes. Thank you.
- Include all authors name, affiliation, ORCID and email address in revised Word file as per format and style of Veterinary World. Please check latest article from <u>www.veterinaryworld.org</u> for format of this section. Yes. Thank you.
- 4. All reference no. in the text must be in continuous no. as per style of Veterinary World and amend the reference section accordingly if you have not done it. Yes, we did.
- 5. Please divide the introduction into 3 paragraphs if you have already not done. Introduction must be divided into 3 paragraphs i.e., 1. introduction 2. significance of the study and 3. aim of the study. Yes, we did. In Line 35-101.
- Include authors' contributions (refer just below the conclusion section in latest article from <u>www.veterinaryworld.org</u> for format of this section) if you have not added. Yes, we did. In line 626-630.
- 7. Include Acknowledgements along with source of fund for this study if you have not included. Yes, we did. In line 639-640.
- 8. All journal names in references must be as per standard journal abbreviation. Yes, we did.
- 9. If you will not revise strictly as per suggestion then there will be chance of rejection. So, revise carefully. If you have any query then please email to Editor-in-Chief. Yes. Thank you.

# REVIEWER # 1

1. The article was well written, but it was better to explain the transmissions of this pandemic between animals. Yes, we did.

Explanation:

- We have described the transmission between animals.
- Transmission among cats, we describe in line 135-145, 208-211.
- Transmission among dogs, we describe in line 229-233, 267-271.
- Transmission among big cats, we describe in line 283-286.
- Transmission among deer, we describe in line 340-345.
- Transmission among cattle, sheep, pigs, we do not describe because those animals have low susceptibility, therefore no transmission between animals.
- Transmission among minks, we describe in line 455-457, 503-513, 514-522, 523-530.
- Transmission among poultry, we do not describe because those animals have no susceptibility, therefore no infections and transmission between animals.
- Transmission in other animal, we do not describe because there is no data available.

- 2. Citing references is well done. Thank you.
- 3. Article classification can be slightly improved. Yes. Thank You. We revised the title and subtitle.
- 4. But overall the manuscript is very good. Thank you.

# REVIEWER # 2

- Please check the title for the correct English.
   Title before: Experimental and Evidence of Natural SARS-CoV-2 Infection in Pets, Wildlife, and Farm Animals: A Review
   To be: Experimental and Natural Infections of SARS-CoV-2 in Pets and in Wild and Farm Animals
- 2. Shorten the Conclusion section with inclusion of only important things rather than long description. Yes. Thank You. In line 601-624

# EDITOR'S COMMENT:

Get professional copyediting from ENAGO or Editage [keep all corrections in track changes (language as well as editorial and reviewers) and paste the certificate in the revised word file] or ask Veterinary World in answer letter for copyediting service (with extra payment) as your manuscript needs extensive copyediting. YES. I paste the certificate in the last page.

We also revised some parts in manuscript as follows:

- 1. Abstract and all part as ENAGO suggestions.
- 2. Figure 1 (change Gibbon to be Gorilla) and explanation of picture.
- 3. We adjust the number of references in the manuscript, references, and table.

Thank you very much.

I hope you will consider our manuscript to publish in your journal.

Best Regard, Gondo Mastutik and co-authors

## Vet World

# Experimental and Natural Infections of SARS-CoV-2 in Pets and in Wild and Farm Animals

Journal Name :	Veterinary World
Manuscript ID :	VETWORLD-2021-10-575
Manuscript Type :	Review Article
Submission Date :	19-Oct-2021
Abstract :	The severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) has spread globally and has led to extremely high mortality rates. In addition to infecting humans, this virus has also infected animals. This study aims to review experimental (both replication and transmission) in vitro, ex vivo and in vivo studies of SARS-CoV-2 infections in pets and in wild and farm animals, and to provide details on the mechanism associated with natural infection. Experimental studies and natural infections showed that dogs have a low susceptibility to SARS-CoV-2 infection, whereas domesticated cats and other animals in the family Felidae, such as lions, tigers, snow leopards, and cougars, have high susceptibility to viral infections. In addition, wild white-tailed deer, gorillas, and otters have been found to be infected by SARS-CoV-2 infection. The virus appears to spread among minks and generate several new mutations, resulting in increased viral virulence. Furthermore, livestock animals, such as cattle, sheep, and pigs, were found to have low susceptibility to the virus, whereas chicken, ducks, turkeys, quail, and geese did not show susceptibility to SARS-CoV-2 infection. This knowledge can provide insights for the development of SARS-CoV-2 mitigation strategies in animals and humans.
Keywords :	animal disease, COVID-19, infectious disease, pandemic, SARS-CoV-2

For your questions please send message to editorveterinaryworld@gmail.com

# **Reviewer comments**

## 1 Experimental and Natural Infections of SARS-CoV-2 in Pets and in Wild and Farm Animals

2 3 4	Gondo Mastutik <sup>1 https://orcid.org/0000-0002-1681-0222</sup> , Ali Rohman <sup>2 https://orcid.org/0000-0002-8177-5881</sup> , Reny I'tishom <sup>3</sup> https://orcid.org/0000-0002-9971-7786, Ignacio Ruiz-Arrondo <sup>4 https://orcid.org/0000-0001-8198-8118</sup> and Ignacio de Blas <sup>5</sup> https://orcid.org/0000-0002-1204-4356
6	1. Department of Anatomic Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya 60131,
7	Indonesia; 2. Department of Chemistry, Faculty of Science and Technology, Universitas Airlangga,
8	Surabaya 60115, Indonesia; 3. Department of Medical Biology, Faculty of Medicine, Universitas
9	Airlangga, Surabaya 60131, Indonesia; 4. Center for Rickettsioses and Arthropod-Borne Diseases,
10	Hospital Universitario San Pedro–CIBIR, Logroño, Spain; 5. Department of Animal Pathology,
11	Faculty of Veterinary Sciences, Instituto Universitario de Investigación Mixto Agroalimentario de
12	Aragón (IA2), Universidad de Zaragoza, Spain
13	
14	Corresponding author: Gondo Mastutik, e-mail: gondomastutik@fk.unair.ac.id
15	<b>Co-authors:</b> AL: <u>alirohman@fst.unair.ac.id</u> , RI: <u>ritishom@fk.unair.ac.id</u> , IRA:
16	<u>irarrondo@riojasalud.es</u> , IdB: <u>deblas@unizar.es</u>
17	

#### 18Abstract

19 The severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) has spread 20globally and has led to extremely high mortality rates. In addition to infecting humans, this virus has 21also infected animals. This study aims to review experimental (both replication and transmission) *in* 22*vitro, ex vivo and in vivo* studies of SARS-CoV-2 infections in pets and in wild and farm animals, and 23to provide details on the mechanism associated with natural infection. Experimental studies and 24natural infections showed that dogs have a low susceptibility to SARS-CoV-2 infection, whereas 25domesticated cats and other animals in the family Felidae, such as lions, tigers, snow leopards, and 26cougars, have high susceptibility to viral infections. In addition, wild white-tailed deer, gorillas, and 27otters have been found to be infected by SARS-CoV-2. Furry farm animals, such as minks, have a 28high susceptibility to SARS-CoV-2 infection. The virus appears to spread among minks and generate 29several new mutations, resulting in increased viral virulence. Furthermore, livestock animals, such as 30cattle, sheep, and pigs, were found to have low susceptibility to the virus, whereas chicken, ducks, 31turkeys, quail, and geese did not show susceptibility to SARS-CoV-2 infection. This knowledge can 32provide insights for the development of SARS-CoV-2 mitigation strategies in animals and humans.

33

34Keywords: animal disease, COVID-19, infectious disease, pandemic, SARS-CoV-2

# 35Introduction

36 In December 2019, an outbreak of a new human infectious respiratory disease was documented 37in Wuhan, Hubei province, China [1]. The disease spread rapidly through human transmission and 38became a global pandemic. The disease had a high health impact, amounting to 241,456,031 cases and 394,913,664 deaths by 18 October 2021 [2]. The causative agent of the disease was identified as a new 40coronavirus strain [1]. As such, the disease was designated by the World Health Organization as the 41coronavirus disease 2019 (COVID-19), and the virus was named as the severe acute respiratory 42syndrome-related coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of 43Viruses [3]. The SARS-CoV-2 genome was 96.2% identical to the bat coronavirus RaTG13, 44Rhinolophus affinis, which was isolated at the Yunnan Province in China [4]. The increased genomic 45similarity and close phylogenetic tree prove that bats were the origin of SARS-CoV-2 [4]. The 46intermediate host appeared to be the Malayan pangolin (Manis javanica), whose genome Pangolin 47CoV is 91% identical to that of the SARS-CoV-2 and is 90.55% identical to that of the BatCoV 48RaTG13 [5]. Snakes and turtles can be considered as intermediate hosts, but this is still controversial 49and requires further investigation [6]. SARS-CoV-2 was then transmitted to humans in Wuhan, China 50[1], and spread worldwide. The first cases of SARS-CoV-2 infections were identified in Australia on 5119 January 2020 [7], in Europe on 24 January 2020 [8], in the Americas on 29 February 2020 [9] and 52in the African continent on 5 March 2020 [10].

53 SARS-CoV-2 belongs to the subgenus *Sarbecovirus* (genus *Betacoronavirus*) in the family 54*Coronaviridae*. It is an enveloped virus, with a single-stranded, positive-sense ribonucleic acid (RNA) 55genome with a nucleotide size of ~30 kb [1, 11]. The SARS-CoV-2 genome encodes four structural 56proteins: the nucleocapsid protein (N), membrane protein (M), envelope protein (E) and surface spike 57protein (S) [1, 11]. The S-protein of SARS-CoV-2 is a glycosylated transmembrane protein that forms 58a homotrimer structure. It protrudes from the viral surface and mediates viral entry into host cells 59[12]. The S-protein of SARS-CoV-2 uses the angiotensin-converting enzyme 2 (ACE2) receptor as its 60binding receptor [13]. The sequence of the receptor-binding domain (RBD) of SARS-CoV-2, which 61includes the receptor-binding motif (RBM) of the S-protein, directly contacts the ACE2 receptor [14-6216]. Human ACE2 is highly expressed in the lungs, heart, kidney, bladder, and gastrointestinal system 63[14, 17]. ACE2 may also be present in mammalian cells. Analyses of the phylogenetic tree of animals 64that come into close contact with humans, such as pets and livestock, and ACE2 homology with the 65human ACE2 in various mammalian cells, showed a high degree of homology similarity [18-21]. *In* 66*silico* studies showed that ACE2 receptors from various domesticated animals, such as *Felis catus* 67(cat) and *Canis lupus familiaris* (dog), are highly homologous. *Felis catus* and *C. lupus familiaris* 68have high degrees of similarities to human ACE2 of the orders of 85.2% and 83.4%, respectively [21]. 69Likewise, livestock, such as *Bos taurus* (cow), *Ovis aries* (sheep) and *Sus scrofa domesticus* (pig), 70exhibit high similarity [18-21]. The interactions between the ACE2 amino acids of the cat, dog, cow, 71sheep, and pig and the RBD and RBM of the SARS-CoV-2 S-protein were predicted to allow the 72binding of SARS-CoV-2 [18, 19]. Analyses of changes in the binding energy (ΔΔG) of the SARS-73CoV-2 S-protein and the ACE2 complexes from cats, dogs, cows, sheep, and pigs showed that these 74animals belong to the risk category of SARS-CoV-2 infections, as indicated by ΔΔG values <3.72 75[22]. Consequently, these findings support the susceptibility of domesticated and livestock animals to 76SARS-CoV-2 infections.

In addition to infecting humans, SARS-CoV-2 has been reported to infect animals. 77 78Experimental infections of SARS-CoV-2 in animals have been reported in cats, dogs, ferrets, and 79poultry (March 2020) [23]. SARS-CoV-2 RNA has also been detected by the reverse transcription 80polymerase chain reaction (RT-PCR) in pets from owners with confirmed COVID-19 infections. The **81**first case was reported in dogs in Hong Kong (February 2020) [24], in cats in Hong Kong [25] and 82Belgium in March 2020 [26] and in France in April 2020 [27]. The serological surveys found 83antibodies against SARS-CoV-2 in cats from Wuhan, China (during January–March 2020) [28] and in 84cats and dogs in Italy (May 2020) [29]. Furthermore, SARS-CoV-2 was detected in wild animals, such 85as lions, and tigers, at the Bronx Zoo in New York City, United States of America (USA) in March 862020 [30, 31]. Recently, antibodies to SARS-CoV-2 were also detected in wild white-tailed deer 87(Odocoileus virginianus) during January–March 2021 in four states in the USA [32]. SARS-CoV-2 88RNA was detected in wastewater in Australia (published online on 18 April 2020) [33] and in the 89USA in January 2021 [34]. Both the SARS-CoV-2 RNA virus and antibodies against SARS-CoV-2 90were also detected in farmed minks. The first case was also detected in the Netherlands during April 91and May 2020 [35]. Furthermore, SARS-CoV-2 was reported to be transmitted from humans to

92minks, which led to the development of zoonotic diseases that have been proved to be transmitted 93back to humans [36]. Many animals, including those with experimentally induced or natural 94infections, are not yet known for their susceptibility to SARS-CoV-2 infections and many cases of 95natural infection have not been reported. Therefore, this review focuses on experimental studies of 96SARS-CoV-2 infections, including *in vitro*, *ex vivo* and *in vivo* studies on viral replication and 97transmission capabilities, in pets and in wild and farmed animals. This explains the evidence of 98natural cases of SARS-CoV-2 infections in domesticated animals, including cats, dogs, and minks, as 99well as in wild animals, such as big cats and wild deer in all continents until October 2021. This 100knowledge can be used to determine policy strategies adopted to mitigate the spread of infectious 101diseases in both animals and humans.

102

## 103SARS-CoV-2 infections in pets

#### 104SARS-CoV-2 infections in cats

Some animals have been known to be experimentally infected with the SARS-CoV-2 virus. 106Additionally, there has been evidence of natural infections in various animals from several countries, 107including China, which was the first country in which human infections were found, and in other 108countries in Asia, Europe, Australia, Africa, and the Americas. Some studies conducted to challenge 109animals against SARS-CoV-2 infection are presented in Table 1, whereas natural infections in 110animals, including domestic animals, farm animals and wild animals, are listed in Table 2, and natural 111infections in the United States are listed in Table 3. Experimental infections and natural cases with the 112presumed sources of infection and their transmission are summarised in Figure 1.

Experimental studies on SARS-CoV-2 replication and transmission have been observed in cats 114[23, 37-40]. The viral replication was investigated in juvenile [23], sub-adult [23, 38-40] and adult 115cats [37]. In juvenile cats, SARS-CoV-2 was efficiently replicated in the upper and lower respiratory 116tracts [23]. In young cats, viral RNA replicated and was detected in nasal or oropharyngeal swabs 117during the first week post infection and peak viral shedding at 4–5 days post infection [38-40]. In sub-118adult cats, the virus replicated efficiently in the upper respiratory tract in the beginning of infection, **119**but some replicated in the lower respiratory tract and in the small intestine [23]. Viral replication and **120**shed viruses were also found both orally and nasally up to days 5 post infection in adult cats [37].

All young and sub-adult cats did not show clinical signs and symptoms of the disease [38-40]. All young and sub-adult cats did not show clinical signs and symptoms of the disease [38-40]. All young and sub-adult cats did not show clinical signs and symptoms of the disease [38-40]. All young and sub-adult cats did not show clinical signs and symptoms of the disease [38-40]. All young and sub-adult cats did not show clinical signs and symptoms of the disease [38-40]. All young and sub-adult cats did not show clinical signs of the respiratory tract [39-40] but tended to persist during the clearance of the virus, during which the lesions tage [39-40] but tended to persist during the clearance of the virus, during which the lesions of the order of the virus, during which the lesions for the order of the virus, during which the lesions of the terms indicated subclinical pathological changes in the upper 128 respiratory tract [37]. Juvenile cats exhibited massive lesions in the upper and lower respiratory tracts, 129 suggesting that young cats are more susceptible to SARS-CoV-2 infections than adult cats [23]. Viral 130 RNA obtained from nasal swabs was not detectable in re-infected animals. Microscopically, the lungs 131 appeared with peribronchial fibrosis and thickening of the alveolar septa [39]. All these experiments 132 revealed that cats were highly susceptible to SARS-CoV-2 infection, in which the virus can replicate 133 efficiently in the respiratory tract, and can then shed nasally and orally, even though the cats did not 134 exhibit any clinical symptoms [23, 37-40].

The transmission of SARS-CoV-2 from inoculated cats to naive-contact cats was observed in 136juvenile, sub-adult, and adult cats [23, 37-40]. In naive co-housed cats, viral RNA was detected in 137rectal swabs and in the upper respiratory tract tissues at days 1–3 post exposure, persisted at 5–9 days 138post exposure, and the shed virus reached the peak at days 4–5 post exposure [23, 37, 38, 40]. Viral 139RNA in the naive co-housed cats was detected in the upper respiratory tract and oesophagus, but not 140in the lung or other organs on day 5 post exposure [37]. The virus was optimally replicated and longer 141in the upper respiratory tract [37-40] compared to that in the lower respiratory tract [39]. 142Subsequently, the virus was excreted and spread from the oral or nasal cavity [37, 38, 40] with 143respiratory droplets to the naive co-housed cats via the airborne route [23]. This suggested that cats 144allowed viral replication and the virus was then transmitted by direct contact (co-housed) to naive 145cats. It is proved the transmission of SARS-CoV-2 from infected cats to other cats [23, 37, 40]. In addition, re-challenges of SARS-CoV-2 infections in cats were observed at 21 days [40] and 14728 days after the first infection [39]. A re-challenge at 21 days showed that the animals were 148asymptomatic, but viral RNA was found high in the upper respiratory tract and gastrointestinal tissue, 149and low in the lower respiratory tract, lymphatic tissues, heart, and olfactory bulb [40]. On the 150contrary, re-infection at 28 days showed no viral RNA detection in nasal, oral and rectal swabs, or in 151the respiratory tract, brain, liver, spleen, kidney, small and large intestines, heart, and eyelid tissues on 152day 3 after re-infection [39]. This may be related to the immunity to SARS-CoV-2. Immunoglobulin 153M bound to the RBD of SARS-CoV-2 was detected on day 7 and reached the peak on day 14, and 154decreased up to day 28, whereas IgG was detected on day 7 post infection and continued to increase 155up to day 28; it then reached a plateau on day 42 post infection [37]. Immunity on day 28 after the 156first infection may have reached its peak to provide the protection effect on the second challenge 157infection [37].

In addition to the proof on experimentally induced SARS-CoV-2 infections, some studies 159reported natural infections in several animals, as summarised in Table 2. In Hong Kong, the natural 160infection with SARS-CoV-2 has been observed in 6 of 50 (12%) quarantined animals from 161households, or from animals that had close contacts with patients with COVID-19 [25]. A serological 162study in cats collected from animal shelters, pet hospitals and households with COVID-19 in Wuhan, 163China, from January to March 2020 showed that 15 of 102 (14.7%) cats were positive to antibodies 164against SARS-CoV-2, but all nasopharyngeal and anal swabs were negative for SARS-CoV-2 viral 165RNA [28]. In Thailand, a serological survey was conducted on cats from April to December 2020 and 166showed that 4 of 1,112 serum antibodies were positive to antibodies against SARS-CoV-2 [41].

Natural SARS-CoV-2 infection was reported in Europe, including Belgium, Spain, France and 168Italy. In Belgium, a cat from the owner with COVID-19 in March 2020 was positive for the SARS-169COV-2 viral RNA and developed neutralising antibodies against SARS-CoV-2 [26]. In La Rioja, 170Northern Spain, a study on 23 asymptomatic animals in quarantine from 8 April to 4 May 2020, 171including eight cats from an owner with COVID-19, found that one of eight cats was positive for 172SARS-CoV-2 viral RNA based on RT-PCR [42]. One of the two cats of the owners who died from 173COVID-19 on 18 March 2020, in Spain, were reported seroconverted to SARS-CoV-2; however, viral 174RNA was detected in the first cat but not in the second cat [43]. In France, a cohort study conducted 175on 22 cats from owners who were infected, or suspected to be infected, showed that a cat was positive 176for viral RNA and with antibodies. This cat had the mild respiratory and digestive signs. Furthermore, 177the genomic analysis of SARS-CoV-2 from this cat revealed a genome resembling the SARS-CoV-2 178genome in most French humans [27]. In addition, another study in France reported that seroprevalent 179antibodies against SARS-CoV-2 were increased in cats and dogs from the confirmed COVID-19 180household cases by 21.3%, and by 2.6% in no confirmed COVID-19 households [44]. In Italy, an 181epidemiological study involving 277 cats living in SARS-CoV-2-positive households, or in the 182geographic areas severely affected by COVID-19, found that several animals developed neutralising 183antibodies, whereas viral RNA was negative in all swab samples [29].

SARS-CoV-2 infections in cats were reported in Rio de Janeiro, Brazil. Data were collected 185from June to August 2020 from cats living in a household with owners with confirmed COVID-19 186and stray animals. Interestingly, serum from a stray cat tested positive for antibodies to SARS-CoV-2, 187even though the tests were negative for viral RNA [45]. Another study in the same city showed that 188cats from households with owners positive for COVID-19 showed positive results for viral RNA (3 of 18910 household cats) and developed a neutralising antibody to SARS-CoV-2 (two of four cats) [46].

In the USA, the first infection with SARS-CoV-2 in cats was reported in April 2020 [47, 48]. 191The other cases were reported by the World Organisation for Animal Health (OIE) in the follow-up 192reports, with numbers of 2, 3, 5, 6, 7, 9, 11, 12, 14, 16, 17, 18, 19, 20, 21 and 23 [47-62], as listed in 193Table 3. SARS-CoV-2 infections were confirmed by RT-PCR in a total of 44 suspected cats and 21 194cats [47-62]. In the first case, two cats had clinical signs of respiratory illness from owners with 195COVID-19. Both cats were positive for SARS-CoV-2 RNA and developed antibodies against SARS-196CoV-2 [47, 63]. Recently, in Texas, USA, infection with SARS-CoV-2 was reported in cats of the 197COVID-19 household, which showed 17.6% of the cats were positive for SARS-CoV-2, and 43.8% of 198the cats were found to have neutralising antibodies against SARS-CoV-2 [64].

The susceptibility of animals to SARS-CoV-2 infection was predicted by comparing ACE2 200animal and human [18, 65, 66]. ACE2 is the receptor that interacts with the spike protein of SARS-201CoV-2 that allows viral entry to host cells [18, 65, 66]. Cats ACE2 presented four amino acid changes 202related to Gln24Leu, Asp30Glu, Asp38Glu and Met82Thr [65]. The residue Asp30 in ACE2 was 203negatively charged and forms a salt bridge with Lys417 (positively charged) in the S-protein of 204SARS-CoV-2. This is a stable bridge located in the middle of the surface interaction [65]. The Asp30 205to Glu mutation residue formed more stable bridges than Asp30 residue [65]. His34, located in the 206centre of surface interaction, and the N-glycosylation site at residue Asn90 were still the same as those 207of human ACE2 [18, 65, 66]. This predicted that cat ACE2 was suitable as the attachment site of the 208S-protein of SARS-CoV-2 [18, 65, 66]. The findings of these *in silico* studies were consistent with 209experimental studies [23, 37-40] and with naturally infected cases of SARS-CoV-2 in cats [25, 26, 42, 21043, 64]. This may also explain the susceptibility of cats to SARS-CoV-2 infection [25, 26, 42, 43, 64], 211and the ability of the virus to replicate and transmit between cats [23, 37, 48].

212 SARS-CoV-2 infections in studies in vivo [37-40], and mainly in naturally infected cases, did 213not result in clinical symptoms [67]. Although asymptomatic, thickening of the alveolar septa was 214 found histopathologically, which indicated chronic lung inflammation [39]. Recently, an unusual 215clinical manifestation has been documented, which included severe myocarditis and impaired general 216health in cats infected by the B.1.1.7 variant of SARS-CoV-2 [68]. It was also reported previously in 217human patients that symptoms of acute myocarditis developed in more than 25% of critical cases 218because of SARS-CoV-2 infections [14]. Several studies reported that cats developed variable mild to 219severe respiratory signs, with predominant presentations of sneezing and coughing, gastroenteritis 220(vomit and diarrhoea), diminishing general health status (fever, lethargy, lack of appetite), 221cardiovascular signs (cardiomyopathy, congestive heart failure, ventricular arrythmia) and 222neurological signs [67]. The unusual signs may relate to the accumulation of mutations in the SARS-223CoV-2 genome, which lead to changes in the virulence of the virus and resulted in unusual outcomes 224[68]. Therefore, further research is needed on SARS-CoV-2 mutations in humans and cats and to 225increase awareness and suspicion in natural cases of SARS-CoV-2 infection, especially in 226asymptomatic cats.

227

#### 228SARS-CoV-2 infections in dogs

Experimental studies in dogs found that SARS-CoV-2 replicated in the respiratory tract of dogs, animals may not transmit the virus to other dogs [23, 37]. Several inoculated dogs were positive alfor viral RNA, thus indicating the presence of viral replication, but dogs did not shed the infectious 232virus [23, 37]. In addition, antibodies against SARS-CoV-2 were detected in inoculated dogs but were 233undetectable in naive co-housed dogs [23, 37].

The natural infection of SARS-CoV-2 in dogs was reported in Hong Kong for the first time a household infected with COVID-19. The dogs were found to be positive for viral RNA and Safeseroconverted to SARS-CoV-2 [34]. Interestingly, the SARS-CoV-2 genomes from both dogs were are lated human case [34]. In addition, a serological study in dogs were with Wuhan outbreak showed that 1.69% of the dogs' serum were positive for SARS-CoV-2 safe the viral genome from the owner, a pet hospital and stray animal [69]. The atomic result in Thailand showed that 1.66% of the serum collected from dogs during the outbreak were safe to SARS-CoV-2 antibodies [41].

In Italy, an epidemiological survey on SARS-CoV-2 infection in dogs reported that viral RNA 243was not detected, but several dogs with COVID-19 positive or negative owner found positive for 244SARS-CoV-2 neutralising antibodies [29]. In France and Croatia, the seroprevalence of SARS-CoV-2 245in dogs with COVID-19 positive owners was 15.4% [48] and 43.9% [70], respectively, whereas in the 246United Kingdom from the unknown owner status was 1.4% [71].

Several cases of SARS-CoV-2 infection in dogs were also reported in Rio de Janeiro, Brazil, 248from a household with a confirmed COVID-19 infection [46] and from a stray dog [45]. As many as 24931% of dogs from households with patients with positive COVID-19 were positively infected with 250SARS-CoV-2, and some showed positive outcomes for antibodies to SARS-CoV-2 [46].

The first confirmed case of SARS-CoV-2 in a dog in the USA was announced on 2 June 2020. 252A German shepherd dog, which lived with another dog and the owner who was COVID-19 positive, 253developed the symptoms of respiratory illness and tested positive for viral RNA and neutralising 254antibodies to SARS-CoV-2 [72, 73]. In addition, several SARS-CoV-2 infection cases were reported 255by the OIE in follow-up reports with the numbers of 4, 8, 9, 10, 11, 12, 13, 14, 16, 17, 18, 20 and 23 256[52-60, 62, 73-86]. In Texas was found 1.7% of dogs from infected COVID-19 households were 257positive for the viral RNA, and 11.9% were positive for neutralising antibodies to SARS-CoV-2 [64]. 258A serological study in Minnesota during April to June 2020 showed that 0.98% of dogs were 259seropositive for the N-protein SARS-CoV-2 [77].

The S-protein of SARS-CoV-2 interacted with the ACE2 of dogs. The analysis of canine ACE2 261compared with human ACE2 contained five amino acid changes. These same amino acid changes also 262occurred in pig ACE2. These included the residues Gln24Leu, Asp30Glu, His34Tyr, Met82Thr and 263Asp38Glu [65]. Changes in Gln24Leu and His34Tyr resulted in failure of hydrogen bond formation 264and in the weakening of the stability of the interaction between ACE2 and the S-protein of SARS-265CoV-2 [78], whereas the replacement of Asn90 residues with Asp resulted in a lack of N-glycosylation 266at position 90 [18, 65, 66]. *In silico* studies found the low susceptibility of dogs to SARS-CoV-2 267infections [18, 65, 66]. In addition, no viral transmission was documented from inoculated animals to 268naive, close contact animals [23, 37]. In the cases of natural infections, there was no confirmed 269evidence of COVID-19 transmission among dogs [24]. This suggests that dogs may be infected with 270SARS-CoV-2, but they have low susceptibility and have not transmitted the virus to other dogs [23, 27124].

272

## 273SARS-CoV-2 infections in wild animals

## 274SARS-CoV-2 infections in big cats

Natural infections of SARS-CoV-2 in big cats have been reported in the tiger (*Panthera tigris*) 276[30, 31, 79-82], lion (*Panthera leo*) [30, 31, 79, 80], snow leopard (*Panthera uncia*) [81, 82] and 277cougar (*Puma concolor*) [83]. The first confirmed SARS-CoV-2 case was reported in the Bronx Zoo, 278New York City, USA, in tigers on 4 April 2020, and in lions on 15 April 2020 [79, 80]. Tigers and 279lions showed clinical signs, such as dry cough and some wheezing, but no respiratory distress. All 280animals with clinical signs improved and recovered. The sources of infection were assumed to be 281transmissions from the zookeepers who had no clinical signs (asymptomatic) [79, 80]. Epidemiologic 282and genomic data from the tiger and lion showed a different genotype of SARS-CoV-2, which 283indicated human-to-animal transmission from two different sources [30, 31]. Furthermore, the viral 284RNA shedding was found in faeces and respiratory secretions of infected animals and persisted in the

**285**faeces for >4 weeks [30, 31]. Based on the infection timeline, it was assumed that the virus was **286**transmitted from zookeepers to animals, and subsequently to other animals in the same cage [30, 31].

Another case in Tennessee, USA, found that 3 Malayan tigers (*P. tigris tigris*) exhibited clinical 288signs, including mild coughing, lethargy, and inappetence; all tigers were confirmed positive for 289SARS-CoV-2. It seems that the tigers were infected by the transmission of SARS-CoV-2 from an 290infected human. All tigers recovered [81, 82]. In addition, other natural infection cases of SARS-CoV-2912 in big cats and in the snow leopard at the Louisville Zoo, USA, were detected in December 2020 292[83] and at the San Diego Zoo, USA, in July 2021 [84]; additionally, there was a cougar case in Texas, 293USA, in February 2021 [85]. In mid-September 2021, three tigers and six lions at the Smithsonian 294National Zoo, USA, were presumed positive for SARS-CoV-2 after they presented mild respiratory 295symptoms, such as coughing and sneezing, lethargy, and decreased appetite [86].

296 Natural cases of SARS-CoV-2 in Katanga lions (*P. leo bleyenberghi*) were reported in the 297Barcelona Zoo (Catalonia, Spain) from November–December 2020 [87]. These four lions had 298respiratory symptoms, such as sneezing, coughing and nasal discharge, and developed antibodies 299against SARS-CoV-2 [87].

Recently, in Indonesia, two Sumatran tigers (*P. tigris sumatrae*) at Ragunan Zoo Jakarta were 301confirmed positive for SARS-CoV-2 by RT-PCR, on 15 July 2021. These big cats presented with mild 302respiratory symptoms, such as lethargy, sneezing, shortness of breath, mucus secretion from the nose 303and decreased appetite [88, 89]. In India, nine lions [90] and three [91] Asiatic lions (*P. leo persica*) 304were reported to be positive to SARS-CoV-2 Delta variant in the B.1.617.2 lineage during May–June 3052021 [90, 91].

The susceptibility of the tiger, lion, leopard, and puma were analysed by *in silico* studies by 307comparing the ACE2 of these animals with the human ACE2. ACE2 receptors from the tiger, cougar, 308and leopard (*Panthera pardus*) identified four amino acids changes, which were Gln24Leu, 309Asp30Glu, Asp38Glu and Met82Thr and had His34 and N-glycosylated Asp90, the same as those for 310humans and cats [65, 78, 92]. By contrast, in lions, apart from having the same four amino differences 311as cats, there was a mutation of Asn90 to Asp that resulted in the loss of N-glycosylation at site 90 312[69]. Furthermore, a mutation was reported in His34 to Ser was also reported [65]. The His34 residue 313was considered a critical residue associated with the susceptibility of lions and tigers to SARS-CoV-2 314infections [78]. The His34 to Ser mutation was predicted to decrease the binding stability between 315ACE2 and the SARS-CoV-2 S-protein [78]. This suggested that animals with His34Ser mutations had 316a lower susceptibility than animals with His34 [78].

Almost all animals had respiratory tract symptoms, with or without general symptoms of Almost all animals had respiratory tract symptoms, with or without general symptoms of Alloisease, such as lethargy or loss of appetite [30, 31, 79-85, 88, 89]. In addition, up to 96.5% of Alganimals had a cough and 79% of animals had sneezing symptoms [67]. The appearance of the clinical algosigns may be explained by the ACE2 expressions in the ciliated bronchial epithelium cells from tigers all and lions, and in the endothelial blood vessels within the alveolar septa in tigers [93]. In view of the algosigns of ACE2 in the respiratory tracts of big cats [93], the increasing number of natural algosigns of SARS-CoV-2 in these animals and the transmission of the virus from asymptomatic algosignes [30, 31, 79-86, 88, 89], a SARS-CoV-2 vaccination programme should be implemented in algosithese big cats, and there should be more concern about SARS-CoV-2 surveillance in wild animals to algominimise the spread of SARS-CoV-2 within the animal population.

#### 327

#### 328SARS-CoV-2 infections in deer

The susceptibility of deer to the virus was investigated in studies *in vitro* and *in vivo*, as well as 330*in silico*. An *in vitro* study was performed in deer lung cells infected with SARS-CoV-2 isolate 331TGR/NY/20 [94] and human/USA/WA1/2020 [99]. It was found that SARS-CoV-2 replicated in 332white-tailed deer (*Odocoileus virginianus*) and mule deer (*Odocoileus hemionus*) lung cells [94, 95], 333whereas the virus did not replicate in elk (*Cervus canadensis*) lungs cells [91].

Furthermore, in an *in vivo* study, SARS-CoV-2 replicated in white-tailed deer fawns [94] and 335adult deer [95] and both groups of animals experienced subclinical viral infections [94, 95]. Viral 336RNA was detected in nasal secretions and faeces in fawns for periods longer than those in adult deer 337[94, 95], in fawns during days 1–21 post infection [94] and in adults during days 1–10 post infection 338[95]. The virus replicated in the upper respiratory and gastrointestinal tracts and was shed from nasal, 339oral and rectal swabs [95]. Viral transmission occurred from inoculated animals to indirect contact animals [94, 95]. Viral 341RNA was detected in nasal, oral or rectal swabs of co-housed animals [95]. Infectious viruses were 342detected in nasal secretions and in the faeces from indirect contact animals at days 2–7 post infection 343[94]. Both inoculated and non-inoculated deer developed neutralising antibodies [94]. Furthermore, 344despite the horizontal transmission between inoculated animals and indirect contact animals, the 345vertical transmission from the adult female deer to the foetus was also reported [95].

*In vitro* and *in vivo* studies showed a high susceptibility of deer to SARS-CoV-2 infections [94]. 347Recently, a serological survey during January–March 2021 in the USA (Michigan, Pennsylvania, 348Illinois and New York states) has found SARS-CoV-2 antibodies in 40% of the wild white-tailed deer 349population [26]. In addition, antibodies against SARS-CoV-2 were detected in one and three serum 350samples in 2019 and 2020, respectively; however, these samples show low percent inhibition values 351[32]. Currently, the first confirmation of SARS-CoV-2 in the wild white-tailed deer was announced in 352Ohio, USA, on 27 August 2021 [96].

White-tailed deer, reindeer (*Rangifer tarandus*) and Père David's deer (*Elaphurus davidianus*) 354were predicted to have a high susceptibility to SARS-CoV-2 infections [92]. Homology analyses of 355deer ACE2 revealed high similarities to humans ACE2 [92]. It showed four different amino acid 356residues (Asp30Glu, Leu79Met, Met82Thr and Asn322His) and a Lys31Asn residue for Père David's 357deer [92]. In addition, analyses of the interaction between ACE2 of these three species of deer and 358RBD of SARS-CoV-2 exhibited a high-binding score and indicated high susceptibility to viral 359infection [92]. Considering these *in silico* studies [92], the high susceptibility and transmissibility to 360SARS-CoV-2 infection [94, 95], the high seroprevalence of SARS-CoV-2 in the wild white-tailed deer 361population [32] and the first confirmed SARS-CoV-2 infection case in wild deer in the world, it is 362necessary to monitor the deer, its predators and other wildlife populations [32].

363

#### 364SARS-CoV-2 infections in farm animals

# 365SARS-CoV-2 infections in cattle and sheep

366 In cattle (*Bos taurus*), an *in vitro* study was performed in the bovine cell line, including 367turbinate, trachea normal, pulmonary artery, foetal bovine lung and foetal bovine kidney cells. Cell 368lines were infected with SARS-CoV-2 isolate TGR/NY/20. This indicated that SARS-CoV-2 did not 369replicate [97]. However, another *ex vivo* study in organ cultures of respiratory tract cells demonstrated 370that SARS-CoV-2 replicated in lung and trachea cells. The respiratory tract was also shown to the be 371immunoreactive to the polyclonal antibody of ACE2 [98].

An *in vivo* study of SARS-CoV-2 infection in cattle showed that the virus replicated but was 373not transmitted [97, 98]. Six-week-old calves exhibited mild symptoms, such as a high temperature 374and mild cough. The virus replicated, but viral shedding was not found. The calves developed 375neutralising antibodies against SARS-CoV-2, but this antibody titre did not persist for more than 21 376days [97]. Another study in older calves revealed that the virus replicated, but the calves did not shed 377the virus and there were no clinical signs [99].

Homogenetic analyses of ACE2 of the family Bovidae, including cattle (*Bos taurus*), water 379buffalo (*Bubalus bubalis*), wild goat (*Capra aegagrus*), goat (*Capra hircus*) and sheep (*Ovis aries*), 380with human ACE2 exhibited high similarity. This analysis identified four amino acid residues 381different from those of human ACE2: Asp30Glu, Leu79Met, Met82Thr and Asn322Tyr. Furthermore, 382the evaluation of the binding contact between ACE2 of those animals with RBD in the S-protein of 383SARS-CoV-2 predicted medium susceptibility to SARS-CoV-2 infection, at the same level as that 384documented in the cat [92]. In addition, ACE2 receptors were expressed in the bronchiole epithelia of 385cattle and sheep, but not in the nasal mucosa and alveoli [93]. By contrast, ACE2 receptors in cats 386were expressed in alveoli and type I pneumocytes [93]. However, an *in vivo* study found that the 387infectious virus was not detected in cattle. This may indicate that cattle had low susceptibility to 388SARS-CoV-2 infections [97, 99].

389 The susceptibility of sheep to SARS-CoV-2 infection was investigated in *ex vivo* organ cultures 390of respiratory tract cells infected with SARS-CoV-2 with D614 and SARS-CoV-2 with D614G. The 391results demonstrated that sheep lung and trachea cells exhibited ACE2 receptors, and thus supported 392the replication of both SARS-CoV-2 variants [98]. This indicates that SARS-CoV-2 can infect sheep, 393but further *in vivo* studies are needed to confirm the susceptibility of sheep to SARS-CoV-2 infection. 394Likewise, research on the susceptibility of other ruminant groups to SARS-CoV-2 infections still 395requires further *in vitro* and *in vivo* research studies.

#### 397SARS-CoV-2 infections in pigs

The susceptibility of pigs to SARS-CoV-2 infections was investigated *in vitro* using swine cell 399lines. Swine testicular cells and swine kidney cells (SK-6 and PK-15) [100, 101] supported SARS-400CoV-2 replication. In contrast, SARS-CoV-2 did not replicate in *ex vivo* respiratory organ cultures 401from pigs [98].

In vivo studies in domesticated pigs (*Sus scrofa domesticus*) found no viral replication and 403transmission of SARS-CoV-2 from inoculated animals to contact-naive animals [23, 100-102]. Viral 404RNA was not detectable in oropharyngeal and rectal swabs from pigs inoculated with  $10^5$  PFU of 405CTan-H or naive animals at all time points, and there were no antibodies to SARS-CoV-2 [23]. Pigs 406infected with  $10^5$  TCID<sub>50</sub> of 2019\_nCoV Muc-IMB-1 yielded the same results [100]. Inoculated and 407naive-contact animals had no clinical signs. Viral RNA, antibodies and organ lesions after necropsy 408were also not detected [100]. Both those studies challenged pigs intra-nasally [23, 100]. Another study 409that carried out the challenge via the intranasal, oral and intratracheal routes simultaneously obtained 410the same results, despite the fact that the dose was higher (dose  $10^6$  TCID<sub>50</sub> of SARS-CoV-2) [101]. 411Meanwhile, pigs inoculated with  $10^{5.8}$  TCID<sub>50</sub> of SARS-CoV-2 intravenously and intramuscularly 412were shown to have low levels of anti-SARS-CoV-2 antibodies, despite the fact that they did not show 413clinical signs, and viral RNA was not detected in nasal or rectal swabs [102].

Although previous studies that challenged pigs with SARS-CoV-2 via intranasal, intratracheal, Although previous studies that challenged pigs with SARS-CoV-2 via intranasal, intratracheal, intramuscular, and intravenous routes showed that pigs were not susceptible to SARS-CoV-2 Al6infections [23, 100-102], but there were two research groups reported different results [103, 104]. Al7First, pigs aged 8 weeks were challenged with 10<sup>6</sup> PFU/animal of SARS-CoV-2 isolate hCoV-Al819/Canada/ON-VIDO-01/2020 via the nasal and pharynx routes. It was the first study that detected Al9low-level viral RNA in nasal washing and oral fluids after inoculation, but it was not detectable in A20other swab samples (oral, nasal, and rectal swabs). The study also found neutralising antibodies A21against SARS-CoV-2 at low levels in two pigs. One pig presented cough and mild depression A22symptoms from day 1 to 4 post infection, and the infectious virus was detected in this pig in the A23submandibular lymph node at day 13 post infection [103]. A second study on pigs involved infections 424with  $6.8 \times 10^6$  TCID<sub>50</sub> of the SARS-CoV-2 isolate TGR/NY/20 via the intratracheal, intranasal, and 425intravenous routes. Viral RNA in nasal/oral and rectal swabs, and neutralising antibodies against 426SARS-CoV-2 from all groups of administration routes were detectable, but transient. Furthermore, 427some tissues (tonsils, mandibular lymph node, tracheobronchial lymph node) from inoculated animals 428showed weak positivity for viral RNA, but the infectious viruses were not isolated successfully. That 429study proved that inoculation of the virus through these routes could not produce the infectious virus, 430and there were no viral transmissions from inoculated animals to naive-contact animals [104].

Several studies predicted the susceptibility of pigs to SARS-CoV-2 infections based on 432comparisons of pig ACE2 with human ACE2. These studies found five amino acid changes in pig 433ACE2 and an Asn90Thr mutation that prevented N-glycosylation. There were mutations of Asn30 to 434Glu, Leu79 to Ile and Met89 to Thr [92]. In addition, mutations of Gln24 to Leu and His34 to Leu led 435to the failure of hydrogen bond formation between the SARS-CoV-2 S-protein and porcine ACE2 436receptors [92]. Based on these *in silico* studies, pigs and dogs exhibited low susceptibility to SARS-437CoV-2 infections together with dogs [92], but dogs were naturally infected with SARS-CoV-2 [24, 44, 43845, 46, 72, 73].

*Ex vivo* [98] and *in vivo* studies [23, 100-102] in swine respiratory tract cells found no SARS-440CoV-2 replication. On the contrary, infection with higher doses showed weak positive viral RNA in 441swabs [103-104], and SARS-CoV-2 RNA and protein of inoculated animals were undetectable in 442respiratory tract cells [98, 101, 103]. The distribution of ACE2 protein on the tissues showed no 443expression in the upper and lower respiratory tract cells [93, 98], but the mRNA type was found to be 444weakly expressed [104]. However, it was overexpressed in the small intestine [93] and kidney [98, 445104]. This may explain the fact that SARS-CoV-2 replicated in kidney cells [100, 101] but not in the 446respiratory tract cells of pigs [98, 100, 101, 104]. Those experimental studies were consistent with *in* 447*silico* predictions and indicated that pigs have a low susceptibility to SARS-CoV-2 infections [92].

#### 449SARS-CoV-2 infections in minks

450 The first case of natural infection of SARS-CoV-2 in minks (*Neovison vison*) was reported in 451two farms in the Netherlands in April 2020 [35]. These animals revealed severe respiratory diseases 452and increased mortality. The clinical signs included breathing difficulties and nasal exudate. SARS-453CoV-2 viral RNA and viral antigen were detected in the upper and lower respiratory tracts [35]. 454Histopathological features included the thickening and degeneration of alveolar septa, which indicated 455acute severe interstitial pneumonia or diffuse alveolar damage [35, 105]. Before the SARS-CoV-2 456outbreak occurred in the mink farm, a worker in the farm tested positive for SARS-CoV-2 indicating 457the probable transmission from the human to mink [35].

In addition, SARS-CoV-2 infected minks were reported in Denmark around June 2020 [106]. 459Similar findings were reported in several countries in Europe, which included Spain in July 2020 460[107, 108], Italy in August 2020 [107, 108], Sweden in October 2020, Greece, France, Poland and 461Lithuania in November 2020, a second infection in a mink farm in Poland on 30 January 2021, and in 462Latvia in April 2021 [107, 108, 109]. In the Netherlands and Denmark, the virus spread rapidly among 463minks and resulted in respiratory diseases and increased mortality [36, 106].

In the USA, the first case was reported in August 2020 in two commercial mink farms. The 465clinical findings included respiratory signs and sudden death. It was assumed that a mink was infected 466from SARS-CoV-2 infected people who contacted the mink and the virus spread it among minks in 467these farms [110]. A total of 177,357 suspected minks and the deaths of 16,130 minks due to SARS-468CoV-2 infections were reported in mink farms in Utah, Michigan, Wisconsin and Oregon, from June 469to October 2020, as OIE reported in the follow-up reports No. 15, 16, 19, 20, 21, 22, 25, 26 [56, 59-47061, 82, 110-112].

The SARS-CoV-2 genome in the mink farm in the Netherlands had a high diversity [36]. There 472were five clusters, among which three clusters (A, C, E) contained the mutation of aspartate 614 to 473glycine (D614G) that was found in general human populations and in cases related to minks [36]. In 474Denmark, mutations that occurred in the ORF 1b gene were mutations of threonine 730 to isoleucine 475(T730I) and proline 314 to leucine (P314L), whereas in the ORF3a gene, there was a mutation of 476histidine 182 to tyrosine (H182Y). Finally, in the nucleoprotein gene, there were mutations of arginine 477203 to lysine (R203K) and glycine 204 to arginine (G204R) [106]. In addition, D614G and Y453F 478mutations occurred in the spike gene [106]. The SARS-CoV-2 variant T730I was found in humans 479and in the mink population in Jutland, Denmark, and in one sequence from New Zealand [106]. A 480H182Y mutation within ORF3a appeared in all minks in Denmark and in human cases related to the 481mink. Even if it was a rare mutation, it was also found in a mink farm in the Netherlands [106]. 482Recently, the new variant of SARS-CoV-2 that contained the deletions of histidine 69 (H69) and 483valine 70 (V70) has been reported. Some mutations developed in mink farms and in 12 humans with 484COVID-19 who lived around the mink farms in Jutland included Y453F, D614G, isoleucine 692 to 485valine (I692V), and methionine 1229 to isoleucine (M1229I) [113]. The deletion of H69 and V70 486within the spike gene occurred in mink farms probably as an adaptation of the virus to increase its 487binding ability to the receptor [114]. The same finding was revealed in Poland [115]. Mutations 488occurred in the spike gene, which resulted in alterations of the amino acids glycine 75 to valine 489(G75V), methionine 177 to threonine (M177T), cysteine 1247 to phenylalanine (C1247F), and 490contained the amino acid mutation Y453F [115], as previously reported in the mink farm in Denmark 491[106, 113].

D614G and Y453F are two interesting mutations in the S-protein of SARS-CoV-2. These are 493specific mutations found in the mink and are related to the mutations found in humans on the mink 494farm [36, 106]. Mutations of D614G in S-protein was found predominantly in the human population, 495in the mink farm in Denmark and in the Netherlands [36, 106]. Furthermore, Y453F mutation was 496found in mink farms in the Netherlands and was related to human cases in a mink farms in Denmark 497[106]. The change of aspartate residue at position site 614 to glycine, and the change of tyrosine 498residue at position site 453 to phenylalanine were a form of virus adaptation to allow the virus to entry 499into host cells; this efficiently increased ACE2 binding in minks and humans [116]. In addition, the 500mutation of Y453F reduced the efficiency of antibody therapy and convalescent serum/plasma therapy 501from patients with COVID-19, and thus reduced the success of therapy and increased the risk of death 502in patients [116].

503 The SARS-CoV-2 genome obtained from the mink samples was found to have high similarity 504with humans associated with mink farms in the Netherlands and Denmark [36, 106], indicating viral 505transmissions from the mink workers to the animals [36]. Subsequently, spreading of the virus among 506minks in the farms occurred by inhalation of spray droplets from sneezing and coughing or inhalation 507of aerosol microparticles ( $<5 \mu m$ ) that contained infectious viruses [117, 118]. This has been proven 508by finding viral RNA in dust samples collected using stationary air sampling (over 5-6-h periods) in 509the mink farm during the outbreak [35]. Furthermore, based on genomic and epidemiological studies, 510it appeared that SARS-CoV-2 was transmitted from humans to minks and spread among minks 511following the appearance of several new mutations; it was then transmitted back to humans, as was 512also observed in the Netherlands and Denmark [36, 106], making it possible to transfer the virus to 513other sites [107].

The spread of SARS-CoV-2 from the mink to the surrounding environment or to other animals 515that live at the farms is also possible [107, 119]. This is based on the finding of viral RNA in airborne 516dust collected at locations 2–3 m from farms, in fur and straw from infected farms, and in the feet of 517seagulls that often forage on mink farms in Denmark, thus making it possible to transfer the virus to 518other sites [107]. The dogs and cats on the farm were also positive for viral RNA, and some dogs and 519cats had antibodies to SARS-CoV-2 [107]. A study from the Netherlands [119] reported that viral 520RNA was identified in stray cats that lived near farm sites, as well as in cats and dogs that lived on the 521farm [119]. The authors presumed that the stray cats were infected by the minks, but the source of 522viral infections in dogs has not been determined [119].

523 SARS-CoV-2 transmission from humans to minks, minks to minks, and minks to humans or 524other animals was found [36, 106, 107, 119]. In addition, indirect transmission through dust or objects 525around the mink farm that contain the active virus [109, 119]. There was evidence of the possibility of 526emergence of new strains because of new mutations or accumulations of mutations in the viral 527genome in the mink group, which were faster and more virulent [106, 113, 115, 116]. Hence, it is 528necessary to consider mitigation strategies to manage outbreaks in animals and humans globally, 529especially those related to transmission cases among animals and from animals to humans, and vice 530versa. It is also crucial to protect stray animals and wild animals around mink farms.

531

#### 532SARS-CoV-2 infections in poultries

533 To evaluate poultries susceptibility to SARS-CoV-2 infection, several experimental studies 534have been conducted, including in chickens (*Gallus gallus domesticus*), turkeys (*Meleagris* 535*gallopavo*), pekin ducks (*Anas platyrhinchos domesticus*), Japanese quails (*Coturnix japonica*) and in 536white Chinese geese (*Anser cygnoides*) [23, 100, 120]. These domesticated fowl were infected intra-537nasally or oculo-oronasally and later introduced to naive animals. All studies reported that viral RNA 538was not detected in any oropharyngeal and cloacal swabs collected from inoculated animals or naive 539animals. In addition, all these birds were seronegative for SARS-CoV-2 [23, 100, 120]. All animals 540also showed no clinical signs during the study, and any lesion was detected at necropsy [100, 120]. 541Similarly, embryonated chicken eggs (ECEs) were usually used for isolation, and the laboratory host 542system in the vaccine production exhibited no viral replication in ECEs [100, 120]. All these studies 543on poultry and ECEs showed that the viral RNA cannot be replicated and transmitted among birds 544[23, 100, 120].

545 Despite experimental studies, it was found that chicken that had indirect contact with the mink 546farm outbreak were negative for SARS-CoV-2 viral RNA [107, 119]. It was also reported that wild 547birds trapped in the mink farms affected, including hundreds of seagulls with other birds, including 548one hooded crow (Corvus cornix), a jackdaw (Corvus monedula) and a common kestrel (Falco 549tinnunculus), were found negative for SARS-CoV-2 RNA [107]. This was in accordance with the 550predictions of in silico studies [65]. The class Aves, including chickens and ducks, had ACE2 551receptors that did not match the S-protein of SARV-CoV-2 [65]. Analyses conducted to compare the 552chicken and duck ACE2 receptors with human ACE2 receptors showed that the receptors of these 553avian species contained ten amino acids changes and lacked the N-glycosylation at position site 90 554[65]. These changes affected the amino acid residue involved in the binding of ACE2 to the SARS-555CoV-2 S-protein, in chicken including Gln24Glu, His34Val, Leu79Asn and Met82Arg, and 556Gly354Asn, and in ducks was His34Val, Leu79Asn, Met82Asn, and Gly354Asn [65]. This change 557also occurred in Tyr83Phe, which resulted in the failure of hydrogen bond formation, and in 558Asp30Ala, which resulted in the lack of salt bridge formation [65]. Therefore, these findings may 559explain the inability of ACE2 receptors in the bird group to bind to the S-protein of the SARS-CoV-2. 560These findings suggest that poultry are not susceptible to SARS-CoV-2 infections [23, 100, 120].

561

562SARS-CoV-2 infections in other animals

SARS-CoV-2 infection has been reported in several animals. Gorillas (*Gorilla gorilla*) at the 564San Diego Zoo, USA, were found positive for SARS-CoV-2 on 11 January 2021. Despite appearing to 565have a mild cough, stuffy nose and lethargy symptoms, they recovered [121]. Confirmation of 566COVID-19 was reported in Asian small-clawed otters (*Aonyx cinereus*) in Georgia, USA, in April 5672021 [122]. These otters which includes in the family Mustelidae that the same family with minks. 568showed clinical signs, such as sneezing, runny noses, mild lethargy, and coughing [122]. Recently, 569several animals have been reported to be infected with SARS-CoV-2, including animals at a zoo in 570Illinois, USA, that was a binturong (*Arctictis binturong*) and a fishing cat (*Prionailurus viverrinus*) on 5715 October 2021 [123] and a coati (coatimundi) on 14 October 2021 [124]. Furthermore, two hyenas at 572Denver Zoo in Colorado, USA [125] were tested positive for SARS-CoV-2 with other animals in the 573zoo, including lions and tigers on 5 November 2021 [125]. Then, there were two hippos at a zoo in 574Antwerp, Belgium that were positive for SARS-CoV-2 infections on 6 December 2021 [126].

Animals from infected mink farms, such as chicken, rabbits, and horses, tested negative for 576SARS-CoV-2 [107]. PCR-negative outcomes for SARS-CoV-2 were also found in a group of wild 577animals collected in the areas around the infected mink farms from October to November 2020 in 578Denmark, including red foxes (*Vulpes vulpes*), badgers (*Meles meles*), least weasel (*Mustela nivalis*), 579polecats (*Mustela putorius*), otter (*Lutra lutra*), beech martens (*Martes foina*) and raccoon dogs 580(*Nyctereutes procyonoides*), as well as in feral mink (*N. vison*) [107]. SARS-CoV-2 infections has not 581been reported in other wild animals, pets and farm animals that have close contact with humans, such 582as horses, goats, camels, and buffaloes, have not been reported. This requires further investigation in 583terms of both the detection of viral RNA and serological surveys.

Recently, there have been many reported cases of COVID-19 in animals. To prevent SARSsesCoV-2 infections in various animals, both pets and wild and farm animals, vaccines have been seddeveloped, including a vaccine from Zoetis company, Carnivac-Cov, and the LinearDNA<sup>™</sup> COVIDser19 vaccine [127, 128]. Zoetis has developed a subunit recombinant vaccine for the SARS-CoV-2 Ssesprotein for wild animals. It has been used to vaccine some species of wild animals in several zoos and seysanctuaries in the USA and Canada, including orangutans, bonobos, hyenas, chimpanzees, and lions sey0[127, 129]. Thus, Russia have developed Carnivac-Cov, an inactivated vaccine, and have been on 591clinical trials in dogs, cats, foxes, and minks [[127]. The Linear DNA<sup>™</sup> COVID-19 vaccine has been 592developed by Applied DNA Sciences (United States) and EvviVax (Italy) for use in domestic felines 593[128]. The safety and immunogenicity of this vaccine in cats showed to be well tolerated and induced 594high titers of SARS-CoV-2 neutralizing antibodies [130], while the safety and immunogenicity in 595minks are currently in progress of research [131]. Furthermore, successful immunization of animals 596could protect animals from SARS-CoV-2 infections and prevent virus transmission among animals 597and cross-species. Therefore, it leads to reducing the risk of the emergence of new mutations of 598SARS-CoV-2 [127, 128].

### 599

## 600Conclusions

The susceptibility of animals to SARS-CoV-2 is very different depending on the family. Felines 602including both domestic cats and big cats are susceptible species where transmission of the virus 603between animals has also been detected. Other wild animals that were found to be infected as natural 604infections in the zoos were gorillas, otters, a binturong, a fishing cat, a coatimundi, hyenas, and 605hippos. Livestock, such as cattle, sheep, and pigs, have a low susceptibility to SARS-CoV-2 606infections, whereas poultries have been shown to be less susceptible to SARS-CoV-2 infection.

Most cases infection of SARS-CoV-2 in animals are through close contact with humans, 608including in domesticated animals, big cats, and other wild animals in zoos. This also occurred in 609white-tailed deer and minks. In white-tailed deer, the virus can transmit to other deer that are in close 610contact, or to its foetus experimentally. Furthermore, it is suspected that SARS-CoV-2 may have 611spread to the white-tailed deer population naturally with the finding that the seroprevalence of SARS-612CoV-2 in the deer population was quite high. In minks, the virus infections were be transmitted 613from humans and be spread among minks and then undergone adaptation and spreads back to 614humans. Presumably, the virus in minks and white-tailed deer were also possible to be transmitted to 615other animals because of the large number of infected animals and the high seroprevalence rate in 616these two animal species. When infecting humans or animals, viruses generate several mutations and accumulate; then 618the mutation will be transmitted to other humans or animals. Some mutations increase the level of 619viral virulence, and some cause resistance to antibodies or convalescent plasma therapy. Therefore, it 620is necessary to increase the awareness of rapidly mutating viruses and prepare various forms of 621appropriate therapies and treatments. Not only do vaccines need to be developed, but research related 622to the development of antivirals and therapeutic management, as well as comprehensive strategies for 623mitigating infectious and dangerous diseases are also necessary. This knowledge may contribute to the 624management of the SARS-CoV-2 pandemic in humans and animals.

625

## 626Authors' Contributions

GM: concepting ideas, drafting, submitting, and editing the manuscript. GM, AR, and RI: 628 references collecting. AR and RI: the partial editing of the manuscript. IRA and IdB: the concepting 629 ideas, references sources, reviewing the manuscript. All authors read and approved the final 630 manuscript.

631

## 632Competing interest

633 The authors declare no competing of interest.

634

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## 1095

1096**Figure 1:** Experimental and natural infections of the severe acute respiratory syndrome-related 1097coronavirus 2 (SARS-CoV-2) in pets and wild and farm animals. SARS-CoV-2 was assumed to 1098originate in the bat species, and the virus was then transmitted from them to humans via an 1099intermediate animal host, that is, pangolins. Indeed, the spread of this virus among humans and many 1100animals has been reported widely. These animals include domestic cats, dogs, wild Felidae families, 1101such as tigers, lions, snow leopards and cougars, as well as gorilla. It was confirmed that the animals 1102acquired viral infection from humans infected with SARS-CoV-2. The virus spread among these

1103group animals in the same cage. Another wild animal susceptible to SARS-CoV-2 infection is the 1104white-tailed deer. Experimentally, SARS-CoV-2 has been shown to replicate *in vitro* and transmit *in* 1105*vivo* among these animals and vertically to the foetus. In natural infections, white-tailed deer were 1106found positive for the SARS-CoV-2 infection and had high seroprevalence, although the source of 1107transmission from human or nature is still unclear. Minks were naturally infected with SARS-CoV-2 1108from humans, and subsequently spread the virus among them, and the virus was transmitted back to 1109humans. It is not clear whether minks can transmit the virus to other animals, such as dogs, cats, 1110seagulls, chickens, horses, and rabbits in farms. Experimentally, SARS-CoV-2 cannot infect poultries, 1111such as chickens, ducks, geese, turkeys, and quails. The virus was reported to infect several livestock 1112animals experimentally, including cattle, sheep, and pigs, but natural infections have not been 1113reported.

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## Table 1. Experimental SARS-CoV-2 infection in animals

Species	Method	Age	Route and Dose	Virus Isolation	Clinical Sign	Replicatio n virus	Antibod y to SARS- CoV-2	Trans mission	Susce ptibili ty	Referen ces
Cat (Felis catus)	In vivo	70-100 days.	Intranasal with 10 <sup>5</sup> PFU of CTan-H	SARS-CoV- 2/CTan/human/2020/Wuha n (CTan-H)	N/A	Yes, and shed virus	Yes	Yes	High	[23]
	In vivo	5–18- week-old	Intranasal, oral, intratracheal, ocular by 5.2 x 10 <sup>5</sup> PFU	UT- NCGM02/Human/2020/To kyo	No	Yes, and shed virus	Yes	Yes	High	[38]
	In vivo	6-9 months	Intranasal with 10 <sup>5</sup> PFU of CTan-H	SARS-CoV- 2/CTan/human/2020/Wuha n (CTan-H)	N/A	Yes, and shed virus	Yes	Yes	High	[23]
	In vivo	5-8 years	Nares (500 $\mu$ L/nare) for a total volume of 1 mL (3.0 x 10 <sup>5</sup> PFU)	SARS-CoV-2 virus strainWA1/2020WY96	No	Yes, and shed virus	Yes	Yes	High	[37]
	In vivo	15–18- week-old)	Intranasal, oral, intratracheal, ocular by 5.2 x 10 <sup>5</sup> PFU	UT- NCGM02/Human/2020/To kyo	No	Yes, and shed virus	Yes	Yes	High	[39]
	In vivo	4.5 – 5 months	Intranasal and oral with 1 × 10 <sup>6</sup> TCID <sup>50</sup> /mL	SARS-CoV-2 USA- WA1/2020 strain	No	Yes, and shed virus	Yes	Yes	High	[40]
Dog (Canis lupus)	In vivo	3 months	Intranasal with 10 <sup>5</sup> PFU of CTan-H	SARS-CoV- 2/CTan/human/2020/Wuha n (CTan-H)	N/A	Yes, but not shed virus	Yes	No	Low	[23]
	In vivo	5-6 years	Nares (500 $\mu$ L/nare) for a total volume of 1 mL (1.4 x 10 <sup>5</sup> PFU)	SARS-CoV-2 virus strainWA1/2020WY96	No	Yes, but not shed virus	Yes	N/A	Low	[37]
Cattle (Bos taurus)	In vitro: bovine turbinate (BT), Bos taurus trachea normal (EBTr (NBL- 4)), cow pulmonary artery epithelial (CPAE), primary	N/A	Multiplicity of infection of 1 or 0.1 (MOI = 1 or 0.1)	SARSCoV-2 isolate TGR/NY/20	N/A	Not replicate	N/A	N/A	N/A	[97]

	fetal bovine lung (FBL), and fetal bovine kidney (FBK) cells									
	<i>Ex vivo</i> : Respiratory <i>ex vivo</i> organ cultures	18 months	Infected with 10 <sup>3</sup> TCID <sub>50</sub> /mL	SARS-CoV-2/INMI1- Isolate/2020/Italy (D614); SARS-CoV- 2/IZSAM/46419 (D614G)	N/A	Yes	N/A	N/A	N/A	[98]
	In vivo	6 weeks	Intratracheal or intravenous, 5 ml each respective route	SARSCoV-2 isolate TGR/NY/20	High temp & mild caught	Yes, but not shed virus	Yes	N/A	Low	[97]
	In vivo	<1 year	Intranasal with 1 x 10 <sup>5</sup> 50% tissue culture infectious dose of SARS-CoV-2	SARS-CoV-2 Strain 2019_nCoV Muc-IMB-1	N/A	Yes, but not shed virus	Yes	No	Low	[99]
Sheep (Ovis aries)	<i>Ex vivo</i> : Respiratory <i>ex vivo</i> organ cultures	10 months	Infected with 10 <sup>3</sup> TCID <sub>50</sub> /mL	SARS-CoV-2/INMI1- Isolate/2020/Italy (D614); SARS-CoV- 2/IZSAM/46419 (D614G)	N/A	Yes	N/A	N/A	Low	[98]
White tail deer (Odocoileus virginianus)	<i>In vitro</i> : Deer lung (DL) cells	N/A	Inoculated multiplicities of infection (MOI) of 0.1 and 1	SARS-CoV-2 isolate TGR/NY/20	N/A	Yes	N/A	N/A	N/A	[94]
	<i>In vitro</i> : lung cells isolated from white- tailed deer, mule deer and elk	N/A	Infected at approximately 0.1 MOI	SARS-CoV-2 lineage A WA1 strain	N/A	Yes, in white- tailed deer, mule deer lung cells	N/A	N/A	N/A	[95]
	In vivo	6 weeks	Intranasal with 5 ml (2.5 ml per nostril) of a virus suspension containing $10^{6.3}$ TCID <sub>50</sub> /mL	SARS-CoV-2 isolate TGR/NY/20	Subclinic al viral infection	Yes, and shed virus	Yes	Yes	High	[94]
	In vivo	2 years	Intranasal and oral with 2 ml dose of $1 \times 10^6 \text{ TCID}_{50}$ per animal	1:1 titer ratio of lineage A WA1 and the alpha VOC B.1.1.7 strain	Subclinic al viral infection	Yes, and shed virus	Yes	Yes, and vertical	High	[95]
Pig (Sus scrofa domesticus)	<i>In vitro</i> : Porcine kidney (PK-15), swine kidney (SK-6),	N/A	Inoculated with 10 <sup>5</sup> TCID <sub>50</sub> SARS-CoV-2	SARS-CoV-2 2019_nCoV Muc-IMB-1	N/A	Yes, in SK-6 and ST	N/A	N/A	N/A	[100]

	and swine testicle (ST)									
	<i>In vitro</i> : ST and PK- 15 cell lines	N/A	0.05 MOI of passage 3 of the VeroE6-passaged SARS-CoV-2	SARS-CoV-2 USA- WA1/2020 isolate	N/A	Yes, in ST and PK-15	N/A	N/A	N/A	[101]
	<i>Ex vivo</i> : Respiratory <i>ex vivo</i> organ cultures	12 months	Infected with 10 <sup>3</sup> TCID <sub>50</sub> /mL	SARS-CoV-2/INMI1- Isolate/2020/Italy (D614); SARS-CoV- 2/IZSAM/46419 (D614G)	N/A	Not detected	N/A	N/A	N/A	[98]
	In vivo	5 weeks	Oral, intranasal, intratracheal with 1 x10 <sup>6</sup> TCID <sub>50</sub> of SARSCoV-2	SARS-CoV-2 USA- WA1/2020 isolate	No	Not detected	Not detected	No	No	[101]
	In vivo	N/A	Intranasal with 10 <sup>5</sup> PFU of CTan-H	SARS-CoV- 2/CTan/human/2020/Wuha n (CTan-H)	N/A	Not detected	Not detected	No	No	[23]
	In vivo	9 weeks	Intranasal with 10 <sup>5</sup> TCID <sub>50</sub> SARS-CoV-2	SARS-CoV-2 2019_nCoV Muc-IMB-1	No	Not detected	Not detected	N/A	No	[100]
	In vivo	5 – 6 weeks	Intranasal, intratracheal, intramuscular and intravenous 10 <sup>5.8</sup> TCID <sub>50</sub>	SARS-CoV-2 isolate (GISAID ID EPI_ISL_510689)	No	Yes, but not shed virus	Yes, at IM, IV route	N/A	No	[102]
	In vivo	8 weeks	Intranasal and pharynx routes of 10 <sup>6</sup> PFU/animal	SARS-CoV-2 isolate hCoV-19/Canada/ON- VIDO-01/2020	No, but an animal yes)	Yes, but not shed virus		No	Low	[103]
	In vivo	3 weeks	Intravenous, intratracheal, and intranasal. $6.8 \times 10^6 \text{TCID}_{50}/\text{mL}$	SARS-CoV-2 isolate used in our study (TGR1/NY/20)	No	Yes, but not shed virus	Yes, but not sustained	No	Low	[104]
Chickens (Gallus gallus domesticus)	<i>In vivo:</i> Embryonating chicken eggs (ECE)	N/A	Yolk sac, chorio-allantoic sac, and chorio-allantoic membrane	USA-WA1/2020 isolate of SARS-CoV-2 (BEI NR- 58221)	N/A	Not detected	Not detected	N/A	No	[120]
	In vivo: ECE	N/A	Inoculated SARS-CoV-2 in ECE	SARS-CoV-2 2019_nCoV Muc-IMB-1	N/A	Not detected	N/A	N/A	No	[100]
	In vivo	5 weeks	Oculo-oronasal with 10 <sup>5</sup> TCID <sub>50</sub> SARS-CoV-2	SARS-CoV-2 2019_nCoV Muc-IMB-1	No	Not detected	Not detected	Not	No	[100]
	In vivo	N/A	Challenged with SARS-	USA-WA1/2020 isolate of	No	Not	Not	N/A	No	[120]

			CoV-2	SARS-CoV-2 (BEI NR- 58221)		detected	detected			
	In vivo	N/A	Intranasal with 10 <sup>5</sup> PFU of CTan-H	SARS-CoV- 2/CTan/human/2020/Wuha n (CTan-H)	N/A	Not detected	Not detected	No	No	[23]
Turkeys (Meleagris gallopavo)	In vivo	N/A	Challenged with SARS- CoV-2	USA-WA1/2020 isolate of SARS-CoV-2 (BEI NR- 58221)	No	Not detected	Not detected	N/A	No	[120]
Ducks (Anas platyrhynchos domesticus)	In vivo	N/A	Intranasal with 10 <sup>5</sup> PFU of CTan-H	SARS-CoV- 2/CTan/human/2020/Wuha n (CTan-H)	N/A	Not detected	Not detected	No	No	[23]
	In vivo		Challenged with SARS- CoV-2	USA-WA1/2020 isolate of SARS-CoV-2 (BEI NR- 58221)	No	Not detected	Not detected	N/A	No	[120]
Quail (Coturnix japonica)	In vivo	N/A	Challenged with SARS- CoV-2	USA-WA1/2020 isolate of SARS-CoV-2 (BEI NR- 58221)	No	Not detected	Not detected	N/A	No	[120]
Geese (Anser cygnoides)	In vivo	N/A	Challenged with SARS- CoV-2	USA-WA1/2020 isolate of SARS-CoV-2 (BEI NR- 58221)	No	Not detected	Not detected	N/A	No	[120]

PFU: plaque-forming units

# Table 2. Natural infections of SARS-CoV-2 in pet, wild and farm animals

Species	Location	Sample Sources	Total sample	Total Positive	Clinical Sign	RNA Virus Detected	Antibody to SARS-CoV-2	References
Cat (Felis catus)	Wuhan (China)	Animal shelters, pet hospital, and Households confirmed COVID-19	102	15	N/A	Negative	Positive	[28]
	Hong Kong (China)	Households confirmed COVID-19	7	0	Asymptomatic	Negative	Negative	[24]
	Hong Kong (China)	Households confirmed COVID-19	50	6	Asymptomatic	Positive	Positive	[25]
	Spain	Households confirmed COVID-19	8	1	Asymptomatic	Positive	N/A	[42]
	Spain	Households confirmed COVID-19	1	1	Feline hypertrophic cardiomyopathy, but the animal was also infected by SARS-CoV-2	Positive	Positive	[43]
	Belgium	Households confirmed COVID-19	1	1	Mild gastrointestinal and respiratory signs	Positive	Positive	[26]
	France	Households confirmed COVID-19	22	1	Mild respiratory and digestive signs.	Positive	Positive	[27]
	Italy	Households confirmed COVID-19 or living in geographic areas that were severely affected by COVID-19	191	11	Not clearly explained	Negative	Positive	[29]
	Rio de Janeiro (Brazil)	Households confirmed or not confirmed COVID-19 and stray animals	49	1	N/A	Negative	Positive	[45]
	Rio de Janeiro (Brazil)	Households confirmed COVID-19	10	4	Unspecified, mild, reversible signs, respiratory or gastrointestinal signs	Positive	Positive	[46]
	New York (USA)	Households confirmed COVID-19	2	2	Sneezing, clear ocular discharge, and mild lethargy	Positive	N/A	[63]
Tiger (Panthera	New York (USA)	Bronx Zoo	5	4	Mild respiratory signs	Positive	Positive (tiger 1) & N/A	[30]
tigris)	Jakarta	Ragunan Jakarta Zoo	2	2	Mild respiratory signs and	Positive	N/A	[8 <b>8, 89</b> ]

	(Indonesia)				general symptoms			
Lion (Panthera leo)	New York (USA)	Animals Zoo	3	3	Mild respiratory signs	Positive	N/A	[30]
	Catalonia (Spain)	Barcelona Zoo	12	3	Mild respiratory signs	Positive	Positive	[87]
	Tamil Nadu (India)	Arignar Anna Zoological Park in Chennai	11	9	Mild respiratory signs and general symptoms	Positive	N/A	[90]
	Uttar Pradesh and Rajasthan (India)	Lion Safari Park, Etawah and Nahargarh Biological Park	3	12	Mild respiratory signs and general symptoms	Positive	Positive	[91]
Snow leopard (Panthera	Louisville (USA)	Louisville Zoo	3	3	Mild respiratory signs	Positive	N/A	[83]
uncia)	San Diego (USA)	San Diego Zoo	1	1	N/A	Positive	N/A	[84]
Cougar (Puma concolor)	Texas (USA)	Texas animals	1	1	Mild respiratory signs	Positive	N/A	[85]
Dog (Canis lupus	Hong Kong (China)	Quarantine animal from households with confirmed COVID-19	15	2	Asymptomatic	Positive	Positive	[24]
familiaris)	Spain	Households confirmed COVID-19	12	0	Asymptomatic	Negative	N/A	[42]
	France	Households confirmed COVID-19	11	0	Mild respiratory and digestive signs	Negative	Negative	[27]
	Italy	Households confirmed COVID-19 or living in geographic areas that were severely affected by COVID-19	451	15	Not clearly explained	Negative	Positive	[29]
	Rio de Janeiro (Brazil)	Households confirmed or not confirmed COVID-19 and stray animals	47	1	N/A	Negative	Positive	[45]
	Rio de Janeiro (Brazil)	Households confirmed COVID-19	29	9	Unspecified, mild, reversible signs, respiratory or gastrointestinal signs	Positive	Positive	[46]
White tail deer ( <i>Odocoileus</i> <i>virginianus</i> )	Michigan, Pennsylvania, Illinois, New	Wild white-tailed deer population	385	152	N/A	N/A	Positive	[32]

	York (USA)							
Mink (Neovison	The Netherlands	Mink farm	16 mink farms	N/A	Mild to severe respiratory distress	Positive	N/A	[35, 36, 105]
vison)	Denmark	Mink farm	1147 mink farms	290 mink farms	N/A	Positive	N/A	[113]
	Poland	Mink farm	28 mink farms	1 mink farm	N/A	Positive (70% sample)	Positive (30% sample)	[109]
Guinea pig (Cavia porcellus)	Spain	Households confirmed COVID-19	1	1	Asymptomatic	Negative	N/A	[42]
Rabbit (Oryctolagus cuniculus)	Spain	Households confirmed COVID-19	1	2	Asymptomatic	Negative	N/A	[42]

Species	No. Follow-up report	Location	Date of outbreak	Suspect	Case	Death	Clinical signs	Reference s
Domestic	No. 2 & 3	Nassau County, Nassau, New York,	01/04/2020	1	1	-	Respiratory signs	[47, 48]
cat (Felis catus)	No. 2 & 3	Orange County, Orange, New York	06/04/2020	2	1	-	Respiratory signs	[47, 48]
cutusj	No. 5	Carver County, Carver, Minnesota	20/05/2020	1	1	-	Respiratory signs	[49]
	No. 6 & 7	Cook County, Cook, Illinois	19/05/2020	1	1	-	Respiratory signs	[50, 51]
	No. 9	Orange County, Orange, California	26/06/2020	1	1	1	Respiratory & cardiac signs	[52]
	No. 9	Orange County, Orange, California	27/06/2020	1	1	-	Asymptomatic	[52]
	No. 11	Brazos County, Brazos, Texas	28/06/2020	1	1	-	Asymptomatic	[53]
	No. 11	Maricopa County, Maricopa, Arizona	10/07/2020	1	-	-	N/A	[53]
	No. 12	Brazos County, Brazos, Texas	17/07/2020	1	1	-	Asymptomatic	[54]
	No. 14	Brazos County, Brazos, Texas	29/07/2020	3	1	-	Asymptomatic	[55]
	No. 16	Coweta County, Coweta, Georgia	14/07/2020	1	1	-	Respiratory signs	[56]
	No. 16	Hartford County, Hartford, Maryland	10/08/2020	5	1	-	Respiratory signs	[56]
	No. 16	Contra Costa County, Contra Costa, California	13/08/2020	1	1	-	Respiratory signs	[56]
	No. 17	Rapides Parish, Rapides, Louisiana	17/08/2020	4	1	-	Respiratory signs	[57]
	No. 18	Brazos County, Brazos, Texas	11/08/2020	1	1	-	Asymptomatic	[58]
	No. 18	Somervell County, Somervell, Texas	12/08/2020	9	1	-	Asymptomatic	[58]
	No. 18	Brazos County, Brazos, Texas	21/08/2020	1	1	-	Asymptomatic	[58]
	No. 19	Fayette County, Fayette, Kentucky	06/09/2020	3	1	-	Respiratory signs	[59]
	No. 20	Brazos County, Brazos, Texas	11/09/2020	1	1	-	Asymptomatic	[60]
	No. 21	Lee County, Lee, Alabama	25/09/2020	4	2	1	Respiratory signs	[61]
	No. 23	Cumberland County, Cumberland, Pennsylvania	02/10/2020	1	1	-	Respiratory signs	[62]
		1	Total	44	21	2		
Domestic	No. 4	Richmond County, Richmond, New York	15/04/2020	2	1	-	Respiratory signs	[72]
dogs ( <i>Canis</i>	No. 8	Berrien County, Berrien, Georgia	22/06/2020	3	1	-	Neurological signs	[73]
lupus	No. 9	Orange County, Orange, California	28/06/2020	1	1	-	Asymptomatic	[52]

# Table 3. Natural infection of SARS-CoV-2 in USA reported by OIE

familiaris)	No. 10	Charleston County, Charleston, South Carolina	26/06/2020	3	1	-	Respiratory signs	[75]
	No. 11	Brazos County, Brazos, Texas	28/06/2020	2	-	-	Asymptomatic	[53]
	No. 11	Maricopa County, Maricopa, Arizona	10/07/2020	3	1	-	Respiratory signs	[53]
	No. 12	Brazos County, Brazos, Texas	17/07/2020	2	-	-	N/A	[54]
	No. 13	Livingston Parish, Livingston, Louisian	22/07/2020	2	1	-	N/A	[76]
	No. 14	Brazos County, Brazos, Texas	28/07/2020	1	1	-	Asymptomatic	[55]
	No. 14	Moore County, Moore, North Carolina	04/08/2020	2	1	1	Respiratory signs & cardiac arrest	[55]
	No. 16	Hartford County, Hartford, Maryland	10/08/2020	1	-	-	N/A	[56]
	No. 17	Rapides Parish, Rapides, Louisiana	17/08/2020	1	-	-	N/A	[57]
	No. 18	Brazos County, Brazos, Texas	11/08/2020	1	1	-	Respiratory signs	[58]
	No. 18	Brazos County, Brazos, Texas	12/08/2020	2	1	-	Respiratory signs	[58]
	No. 18	Somervell County, Somervell, Texas	12/08/2020	2	-	-	Asymptomatic	[58]
	No. 18	Brazos County, Brazos, Texas	21/08/2020	1	-	-	N/A	[59]
	No. 18	Brazos County, Brazos, Texas	21/08/2020	1	1	-	Asymptomatic	[58]
	No. 20	Brazos County, Brazos, Texas	14/09/2020	1	1	-	Respiratory signs	[60]
	No. 23	Brazos County, Brazos, Texas	01/10/2020	2	1	-	Respiratory signs	[62]
	•		Total	33	13	1		
Domestic	No. 15	Utah, Utah	26/06/2020	20,000	N/A	3,524	Respiratory signs & death	[110]
American Mink	No. 15	Utah, Utah	02/08/2020	8,983	N/A	1,451	Respiratory signs & death	[110]
(Neovison	No. 16	Utah, Utah	03/08/2020	6,326	N/A	1,554	Respiratory signs & death	[56]
vison)	No. 16	Utah, Utah	05/08/2020	3,643	N/A	1,119	Respiratory signs & death	[56]
	No. 16	Utah, Utah	05/08/2020	1,705	N/A	205	Respiratory signs & death	[56]
	No. 19	Utah, Utah	08/09/2020	1,500	N/A	59	Respiratory signs & death	[59]
	No. 20	Utah, Utah	07/09/2020	600	N/A	146	Respiratory signs & death	[60]
	No. 20	Utah, Utah	20/09/2020	14,000	N/A	247	Respiratory signs & death	[60]
	No. 21	Michigan, Michigan	27/09/2020	17,000	N/A	2,000	Respiratory signs & death	[61]
	No. 21	Wisconsin, Wisconsin	30/09/2020	14,600	N/A	1,800	Respiratory signs & death	[61]
	No. 22	Utah, Utah	29/09/2020	300	N/A	126	Respiratory signs & death	[62]

No. 25	Utah, Utah	08/10/2020	3,000	N/A	373	Respiratory signs & death	[80]
No. 25	Wisconsin, Wisconsin	19/10/2020	22,500	N/A	2,200	Respiratory signs & death	[80]
No. 25	Utah, Utah	22/10/2020	13,200	N/A	585	Respiratory signs & death	[80]
No. 25	Utah, Utah	25/10/2020	38,000	N/A	739	Respiratory signs & death	[80]
No. 26	Oregon, Oregon	22/10/2020	12,000	N/A	2	Respiratory signs & death	[110]
·		Total	177,357		16,130		

