



The Director General

Maisons-Alfort, 14 April 2020

## **Supplemented<sup>1</sup> OPINION of 9 March 2020 of the French Agency for Food, Environmental and Occupational Health & Safety**

**on an urgent request related to certain risks associated with Covid-19**

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*ANSES undertakes independent and pluralistic scientific expert assessments.*

*ANSES primarily ensures environmental, occupational and food safety as well as assessing the potential health risks they may entail.*

*It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.*

*It provides the competent authorities with the necessary information concerning these risks as well as the requisite expertise and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).*

*Its opinions are made public.*

*This opinion is a translation of the original French version. In the event of any discrepancy or ambiguity the French language text dated 14 April 2020 shall prevail.*

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On 2 March 2020, ANSES received an urgent request from the Directorate General for Food (DGAL) to assess certain risks associated with Covid-19.

### **1. BACKGROUND AND PURPOSE OF THE REQUEST**

On 31 December 2019, the Chinese authorities informed the World Health Organization (WHO) of an outbreak of clustered cases of pneumonia, the first confirmed cases of which were connected to a market selling live animals and seafood products in the city of Wuhan (Hubei province), China.

On 9 January 2020, a novel emerging virus was identified by the WHO as being responsible for these clustered cases of lung disease in China. It was a coronavirus, temporarily named 2019-nCoV virus (Novel Coronavirus) by the WHO. Later, on 11 February 2020, the WHO officially named it severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for Coronavirus Disease 2019 (Covid-19).

On 30 January 2020, in light of the scope of the epidemic, the WHO declared it a Public Health Emergency of International Concern (PHEIC). Indeed, imports of Covid-19 cases from China to other

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<sup>1</sup> Cancels and replaces the Opinion of 9 March 2020. For the tracking of changes, see Annex 6 of this Opinion.

countries were observed from the start of the epidemic in Wuhan and have intensified since mid-February (source: French High Council for Public Health, HCSP).

SARS-CoV-2 is mainly transmitted from person to person, by direct or indirect contact or through the air, via the inhalation of infectious micro-droplets produced when a patient sneezes or coughs (Bernard Stoecklin *et al.*, 2020; Guan *et al.*, 2020).

At a time when France is in stage 2 of managing the epidemic, and under the terms of the formal request, ANSES has been asked to give its opinion regarding:

- *The potential role of domestic animals (livestock animals and pets) in the spread of the SARS-CoV-2 virus;*
- *The potential role of food in the transmission of the virus.*

## 2. ORGANISATION OF THE EXPERT APPRAISAL

ANSES entrusted the examination of this formal request to the “Covid-19” Emergency Collective Expert Appraisal Group (GECU). Its expert appraisal was therefore conducted by a group of experts with complementary skills. The expert appraisal was carried out in accordance with French Standard NF X 50-110 “Quality in Expert Appraisals - General Requirements of Competence for Expert Appraisals (May 2003)”.

The “Covid-19” GECU urgently convened on 4 March 2020 and adopted its conclusions at its meeting. Based on these conclusions, a draft of the GECU's analysis and conclusions was written by the scientific coordination team. It was reread in electronic form by the GECU and sent to ANSES's General Directorate. An initial version of the opinion was sent to the DGAL on 9 March 2020.

New scientific evidence related to Covid-19 and domestic animals was made available after that date, leading the GECU to meet again on 8 April to supplement its opinion.

This supplemented opinion takes into account the latest information on natural infections with the SARS-CoV-2 virus identified for a few animals (domestic animals and carnivores in captivity) as well as the scientific studies made available to the GECU as of 8 April 2020.

ANSES analyses interests declared by experts before they are appointed and throughout their work in order to prevent risks of conflicts of interest in relation to the points addressed in expert appraisals.

The experts' declarations of interests are made public via the ANSES website ([www.anses.fr](http://www.anses.fr)).

## 3. ANALYSIS AND CONCLUSIONS OF THE GECU

### 1. Potential role of domestic animals in transmitting the SARS-CoV-2 virus

#### 1.1 Genetic relationship between SARS-CoV-2 and other viruses in the genus *Betacoronavirus*

Coronaviruses (CoVs) are viruses in the family *Coronaviridae* that belong to the order *Nidovirales*. They are pleomorphic-enveloped viruses that can range from 60 to 220 nm in size. They have a positive, single-stranded RNA genome (directly translated) associated with the nucleocapsid protein. Coronaviruses owe their name to their appearance in electron microscopy: the structural proteins of the envelope form a crown (“*corona*” in Latin) around the viral particles.

Coronaviruses are classified into four genera: alpha ( $\alpha$ CoV), beta ( $\beta$ CoV), gamma ( $\gamma$ CoV), and the recently discovered delta ( $\delta$ CoV) (de Groot *et al.* 2012). They are responsible for infections in multiple species of birds ( $\gamma$ CoV,  $\delta$ CoV) and mammals ( $\alpha$ CoV,  $\beta$ CoV,  $\gamma$ CoV), including humans. They can cause a wide range of diseases in humans and domestic animals, although they mainly affect the respiratory and digestive systems.

The main coronaviruses usually encountered in domestic animals are as follows:

- In pigs, four porcine coronaviruses belonging to the genus *Alphacoronavirus* are associated with diseases:
  - porcine epidemic diarrhoea virus (PEDV), transmissible gastroenteritis virus (TGEV), and swine acute diarrhoea syndrome coronavirus (SADS-CoV), associated with digestive disorders;
  - porcine respiratory coronavirus (PRCV), a TGEV mutant, associated with respiratory disorders.

Porcine hemagglutinating encephalomyelitis virus (PHEV), responsible for vomiting and wasting disease, belongs to the genus *Betacoronavirus* (see Table 1). Porcine deltacoronavirus, another porcine coronavirus belonging to the genus *Deltacoronavirus*, also causes digestive disorders.

- Birds are mainly infected with *Gammacoronaviruses*: in chickens, infectious bronchitis coronavirus (IBV) is a highly infectious avian pathogen that affects the respiratory system, digestive system, kidneys and reproductive system.

Two other similar viruses have been isolated in other Galliformes: turkey coronavirus (TCoV), involved in a multifactorial enteric disease in turkeys, and guinea fowl coronavirus (Gf-CoV), involved in fulminating disease.

- In cats, feline coronavirus (FCoV), which causes feline infectious peritonitis, belongs to the genus *Alphacoronavirus*.
- In dogs, two coronaviruses have been described: canine enteric coronavirus (CCoV), which causes digestive disorders and belongs to the genus *Alphacoronavirus*, and canine respiratory coronavirus, which belongs to the genus *Betacoronavirus* (see Table 1).
- Bovine coronavirus (BCoV) is a *Betacoronavirus* that causes neonatal diarrhoea in calves, winter dysentery in adults, and respiratory symptoms at all ages (see Table 1).

The human coronaviruses known to date belong to the genera *Alphacoronavirus* (HCoV-229E and HCoV-NL63) and *Betacoronavirus* (HKU1, HCoV-OC43, SARS-CoV, MERS-CoV and SARS-CoV-2).

*Betacoronaviruses* make up a viral genus that is also highly represented in the animal population. A non-exhaustive list of the animal species currently known as being prone to infection with these viruses is given in Table 1. The genus *Betacoronavirus*, which includes SARS-CoV-2, is itself divided into five sub-genera, according to the International Committee on Taxonomy of Viruses (ICTV): *Embecovirus*, *Hibecovirus*, *Merbecovirus*, *Nobecovirus*, and *Sarbecovirus*.

Table 1: Non-exhaustive list of the *Betacoronaviruses* identified to date and their host species

Sub-genus	Viral species	Host species	References
<b>Embecovirus</b>	Bovine and bovine-like coronaviruses (BCoV, bovine-like CoV)	<i>Bovidae</i> <i>Bos frontalis</i> , <i>Kobus ellipsiprymnus</i> and <i>Hippotragus niger</i> <i>Odocoileus virginianus</i> , <i>Cervus unicolor</i> and other <i>Cervidae</i>	Alekseev <i>et al.</i> (2008) Rajkhowa <i>et al.</i> (2007)
	Gi CoV OH3	<i>Giraffa camelopardalis</i>	Hasoksuz <i>et al.</i> (2007)
	ECoV	<i>Equus caballus</i>	Davis <i>et al.</i> (2000)
	PHEV	<i>Sus scrofa domesticus</i>	Greig <i>et al.</i> (1962)
	CrCoV	<i>Canis lupus familiaris</i>	Erles <i>et al.</i> (2003)
	RbCoV HKU14	<i>Oryctolagus cuniculus</i>	Lau <i>et al.</i> (2012)
	ACoV	<i>Vicugna pacos</i>	Jin <i>et al.</i> (2007)
	HCoV-OC43	<i>Homo sapiens</i>	Hamre <i>et al.</i> (1966)
	HCoV-HKU1	<i>Homo sapiens</i>	Woo <i>et al.</i> (2005)
	Murine coronavirus MHV	<i>Mus musculus</i>	Coley <i>et al.</i> (2005)
	Rat coronavirus RCV/SDAV and sialodacryoadenitis virus	<i>Rattus rattus</i>	Easterbrook <i>et al.</i> (2008) Miura <i>et al.</i> (2007)
<b>Sarbecovirus</b>	Severe acute respiratory syndrome Coronavirus SARS-CoV	<i>Homo sapiens</i>	Poutanen <i>et al.</i> (2003)
	Civet SARS-related-coronavirus	<i>Nyctereutes procyonoides</i> , <i>Paguma larvata</i>	Woo <i>et al.</i> (2005)
	<b>Severe acute respiratory syndrome Coronavirus SARS-CoV-2</b>	<i>Homo sapiens</i>	Zhou <i>et al.</i> (2020)
	Bat SARS-related-CoVZC45	<i>Rhinolophus pusillus</i>	Hu <i>et al.</i> (2018)
	Bat SARS-related-CoVZXC21	<i>Rhinolophus pusillus</i>	Hu <i>et al.</i> (2018)
<b>Merbecovirus</b>	HKU5 Pi-BatCoV HKU5	<i>Pipistrellus sp.</i>	Woo <i>et al.</i> (2006)
	Dromedary MERS-CoV	<i>Camelus dromedarius</i>	Ferguson <i>et al.</i> (2014)
	Hedgehog CoV	<i>Erinaceus europaeus</i>	Corman <i>et al.</i> (2014)
	MERS-CoV	<i>Homo sapiens</i>	Zaki <i>et al.</i> (2012) van Boheemen <i>et al.</i> (2012)
<b>Hibecovirus</b>	Bat Hp-BetaCoV	<i>Hipposideros pratti</i>	Wu <i>et al.</i> (2016)
<b>Nobecovirus</b>	Ro-BaCoV HKU9	<i>Rousettus leschenaulti</i>	Woo <i>et al.</i> (2007)

SARS-CoV and SARS-CoV-2 are classified in the same sub-genus *Sarbecovirus* and belong to two sister clades that include several tens of coronaviruses affecting bats of the genus *Rhinolophus* (e.g. Bat SARS-related-CoVZC45 and Bat SARS-related-CoVZXC21, Table 1). Table 1 also shows that SARS-CoV-2 does not belong to the same group of *Betacoronaviruses* usually found in domestic animals.

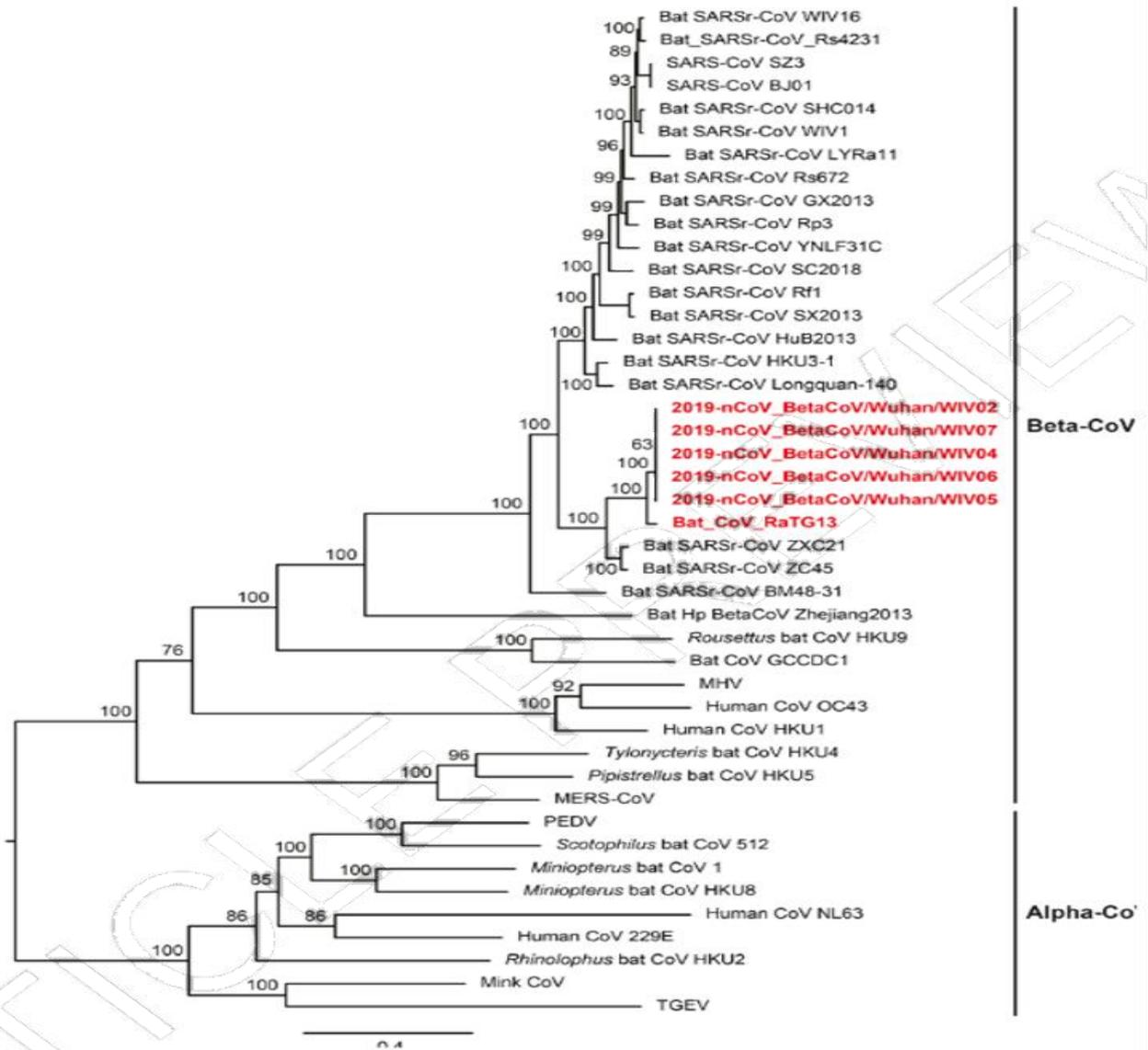
In light of the above, and based on the phylogenetic analyses undertaken, the experts underline that there is no direct genetic relationship between SARS-CoV-2 and the strains of *Betacoronavirus* usually isolated from domestic animals.

## 1.2 Crossing of the species barrier

### 1.2.1 Origin of SARS-CoV-2

The SARS-CoV-2 genome shares 96.3% identity (Paraskevis *et al.*, 2020) with that of the RaTG13/2013 virus (strains marked in red, Figure 1) detected in a bat of the genus *Rhinolophus* in China (Zhou *et al.* 2020). The evolution of *Sarbecoviruses* led to the strong diversification of coronaviruses currently described as “SARS-CoV-like or SARS-CoV-related” viruses in horseshoe bats from Asia (two clades; SARS-CoV and SARS-CoV2), Europe (Ar Gouilh *et al.*, 2018) and Africa (Tong *et al.*, 2009). Their origin probably dates back to the 1980s (M. Le Gouil, personal communication).

The most direct wild ancestor, which is still unknown at this point in time, is the result of a complex evolutionary history involving several recombination events, occurring over the past 50 years, among the numerous *Betacoronaviruses* co-circulating in several Asian horseshoe bat species (M. Le Gouil, personal communication; Boni *et al.*, 2020).



**Figure 1: Phylogenetic tree based on the whole genomes of *Alphacoronaviruses* and *Betacoronaviruses* including the novel SARS-CoV-2 (2019-nCoV in red) (Zhou *et al.*, 2020).**

It is important to take into account the time factor when considering the evolutionary process of coronaviruses. The three most recent evolutionary events that led to the appearance of SARS-CoV in 2002-2003, MERS-CoV in 2012 and SARS-CoV-2 in 2019 testify to this (time intervals of around two decades). Crossing of the species barrier is not a common phenomenon and can require the selection of several events for adaptation to a new host species.

The experts stress that the biology of coronaviruses shows high evolutionary potential: it is entirely possible that SARS-CoV-2 may, over time and as it evolves, acquire new mutations and undergo genetic recombination events. The question is whether these phenomena are likely to enable the human virus to

adapt to other animal species. The experts underline that in light of the current epidemiological situation, SARS-CoV-2 is adapted to humans with effective human-to-human transmission<sup>2</sup>.

**SARS-CoV-2 is of animal origin (bats, *Rhinolophidae*), whether or not an intermediate host was involved. However, in the current context and in light of the points cited, the GECU considers that the transmission of SARS-CoV-2 from humans to a domestic animal species (livestock animals or pets) cannot be completely ruled out (see 1.2.2) but that adaptation to this species currently seems unlikely.**

## 1.2.2 Natural SARS-CoV-2 infections in animal species

### 1.2.2.1 Identified cases of animals testing positive for SARS-CoV-2

- Case of two dogs and one cat in Hong Kong

On 29 February 2020, OIE received an official report from Hong Kong regarding a 17-year-old (Pomeranian) dog that had been quarantined on 26 February after its owner was hospitalised for Covid-19. The animal did not show any specific clinical signs. The five oral and nasal samples successively collected between 26 February and 9 March tested “weak positive” by RT-PCR<sup>3</sup>. The virus could not be isolated from these samples. After negative RT-PCR results were obtained with samples collected on 12 and 13 March 2020, the dog was returned to its owner. It then died on 16 March 2020. The causes of its death are still unknown, since the owner did not consent to an autopsy. However, the authorities in Hong Kong considered that it did not die because of its SARS-CoV-2 infection.

According to the website of Hong Kong's Agriculture, Fisheries and Conservation Department, the serological analysis of a blood sample taken from this dog on 3 March 2020 had provided an initial negative result. New serological analyses of this same sample were then undertaken at the OIE Reference Laboratory in Hong Kong. The result ended up being positive on 27 March 2020, enabling the Hong Kong authorities to conclude that this dog had been infected with SARS-CoV-2<sup>4</sup>. The press release also specified that the viral sequence obtained from the dog was very similar<sup>5</sup> to that of the virus isolated from the infected owner (Sit *et al.*, 2020).

A second dog, whose owner had contracted Covid-19, tested positive for SARS-CoV-2<sup>6</sup>. This two-year-old German Shepherd dog was sent for quarantine on 18 March 2020 with another four-year-old mixed-breed dog. The oral and nasal swabs collected from the German Shepherd on 18 and 19 March tested positive for SARS-CoV-2 by RT-PCR. The virus was isolated from one of the samples on 25 March. Seroconversion of this animal was confirmed on 3 April 2020 (OIE Notification of 7/4/2020). No positive samples were obtained from the mixed-breed dog, and neither of the two dogs showed any clinical signs of the disease.

<sup>2</sup> Only the Chinese data (duration of contagiousness) currently enable an R0 value to be calculated ( $1.4 < R_0 < 3.9$ ) (Sun *et al.*, 2020). This value is therefore specific to the epidemic and context in China. Regarding the estimation of an R(t) value, i.e. the R0 value at a given time, for the situation in France, hospitalisation figures can be used (thus reflecting the near-current state of the epidemic). Using this approach, the R0 value in France fell below 2 on 22 March 2020 and has been below 1 since 1 April 2020. It is highly likely that this improvement is due to the lockdown measures taken (personal communication of Samuel Alizon, [http://alizon.ouvaton.org/Rapport5\\_R.html](http://alizon.ouvaton.org/Rapport5_R.html)).

<sup>3</sup> Samples collected on 26/2, 28/2, 2/3, 5/3 and 10/3/2020

<sup>4</sup> <https://www.info.gov.hk/gia/general/202003/26/P2020032600756.htm>, consulted on 8/4/2020

<sup>5</sup> It differed at three nucleotide positions, two of which resulted in amino acid substitutions

<sup>6</sup> <https://www.info.gov.hk/gia/general/202003/19/P2020031900606.htm>, consulted on 8/4/2020.

On 30 March 2020, Hong Kong's Agriculture, Fisheries and Conservation Department reported that a cat living with its owner, infected with Covid-19, had tested positive for SARS-CoV-2, based on oral, nasal and rectal samples collected on 30 March and 1 April 2020. The cat is currently in quarantine and shows no clinical signs of the disease<sup>7</sup> (OIE Notification of 3/4/2020)<sup>8</sup>.

On 31 March 2020, a cohort of 27 dogs and 15 cats, in close contact with Covid-19 patients and quarantined by the Hong Kong authorities, was monitored for the SARS-CoV-2 virus. Only two dogs and one cat showed positive RT-PCR results (Thiry, 2020).

- Case of a cat in Belgium

On 18 March 2020, a cat belonging to an individual infected with Covid-19 tested positive for SARS-CoV-2. SARS-CoV-2 viral RNA was detected in the faeces and vomit of the cat, which showed digestive and respiratory clinical signs. SARS-CoV-2 infection was confirmed by high-throughput sequencing (AFSCA, 2020). The general condition of the cat improved nine days later. The role of SARS-CoV-2 in the clinical signs observed was not formally established.

- Case of a tiger at the Bronx Zoo in New York

On 6 April 2020, OIE received a report regarding a four-year-old tiger (*Panthera tigris*) that had shown respiratory clinical signs on 27 March 2020. The nasal, oropharyngeal and tracheal samples tested positive for SARS-CoV-2 via RT-PCR and sequencing (OIE Notification of 6/4/2020)<sup>9</sup>. By 3 April 2020, three other tigers as well as three lions were showing clinical signs (dry cough and respiratory difficulty). No samples were collected from these felines. By 6 April 2020, their general condition had improved (OIE Notification of 6/4/2020).

#### **1.2.2.2 Serological investigation of cats tested in Wuhan**

This study undertaken by Chinese scientists (Zhang *et al.*, 2020) is available as a preprint on the bioRxiv portal. The investigation focused on serum samples collected from cats before (n=39) and after (n=102) the start of the SARS-CoV-2 epidemic. The results showed that 15/102 sera collected after the start of the epidemic were positive for the receptor binding domain (RBD) of the spike protein by specific indirect ELISA. By seroneutralisation, 11 of the 15 cats tested positive with titres ranging from 1/20 to 1/1080. The GECU notes that the three cats that had significantly high titres (from 1/360 to 1/1280) corresponded to those clearly identified as having had close contact with Covid-19 patients. RT-PCR based on the nasopharyngeal and rectal swabs of all the tested cats gave negative results. These results show that in a context of high pressure in terms of viral infection, cats can be infected with SARS-CoV-2. However, the authors do not indicate the proportion of cats showing a seronegative result out of all those having been in close contact with owners infected with Covid-19.

<sup>7</sup> [https://www.news.gov.hk/eng/2020/03/20200331/20200331\\_220128\\_110.html?type=ticker](https://www.news.gov.hk/eng/2020/03/20200331/20200331_220128_110.html?type=ticker), consulted on 8/4/2020

<sup>8</sup> [https://www.oie.int/wahis\\_2/public/wahid.php/Reviewreport/Review?page\\_refer=MapFullEventReport&reportid=33832&newlang=en](https://www.oie.int/wahis_2/public/wahid.php/Reviewreport/Review?page_refer=MapFullEventReport&reportid=33832&newlang=en), consulted on 8/4/2020

<sup>9</sup> [https://www.oie.int/wahis\\_2/public/wahid.php/Reviewreport/Review?page\\_refer=MapFullEventReport&reportid=33885](https://www.oie.int/wahis_2/public/wahid.php/Reviewreport/Review?page_refer=MapFullEventReport&reportid=33885), consulted on 8/4/2020

### **1.2.2.3 Serological and virological investigation undertaken with cats and dogs of students at the National Veterinary School of Maisons-Alfort (ENVA)**

This study, conducted by scientists from the ENVA and *Institut Pasteur*, is available as a preprint on the bioRxiv portal. It dealt with a cohort of 12 dogs and nine cats living in close contact with their owners, i.e. 20 students of veterinary medicine. Two of the owners had tested positive for Covid-19, while 11 others had shown highly evocative signs of Covid-19 infection. Nasal and rectal swabs were collected from each animal to test for SARS-CoV-2, and serological analyses were conducted. None of the RT-PCR or serological tests showed positive results. The authors suggest that in natural conditions, SARS-CoV-2 has a low level of transmission from humans to pets (Temmam *et al.*, 2020).

### **1.2.2.4 IDEXX study**

A study undertaken by the IDEXX veterinary diagnostic laboratory between 14 February and 13 March 2020 investigated more than 4000 samples<sup>10</sup> collected from horses, cats and dogs<sup>11</sup> in the United States (mainly from geographic areas where human Covid-19 cases had been identified) and South Korea. The samples were analysed using an RT-PCR test developed by the company that targets a nucleic acid sequence specific to the SARS-CoV-2 virus responsible for the current pandemic. No positive results were obtained with any of the samples in this study. The assay design and its analytical validation are explained in detail on the company's website (source: IDEXX<sup>12</sup>). According to IDEXX, “the IDEXX SARS-CoV-2 (COVID-19) RealPCR Test met all analytic validation requirements [in the United States]. Specificity studies showed no cross-reactivity with the new PCR test against common veterinary coronaviruses affecting companion animals”. Moreover, “specimens were also tested in parallel with three assays from the Centers for Disease Control and Prevention (CDC)”.

**In conclusion, the experts underline that very few cases of pets contaminated by and/or infected with SARS-CoV-2 have been reported up to now. These cases of contamination and infection remain sporadic and isolated in view of the high level of virus circulation in humans and the scale of the pandemic at the present time. The investigated cases suggest that the virus can be transmitted from humans to animals. The GECU stresses that there is little information regarding the proportion of animals testing negative for the virus that have been in close contact with people infected with Covid-19. The experts also reiterate that RNA detection by RT-PCR is not strongly associated with the presence of infectious viral particles or with productive infection; therefore, it does not provide sufficient evidence to conclude that the animal was infected. Passive contamination cannot be ruled out.**

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<sup>10</sup> 77% were respiratory, and 23% were faecal

<sup>11</sup> 55% of the specimens were from canines, 43% were from felines, and 4% were from equines

<sup>12</sup> <https://www.idexx.com/en/veterinary/reference-laboratories/overview-idexx-sars-cov-2-covid-19-realpcr-test/>

### 1.2.3 Experimental infections

#### 1.2.3.1 ACE2 receptor

Angiotensin-converting enzyme 2 (ACE2), the receptor for SARS-CoV-2 (and for SARS-CoV), is necessary in order for the virus to enter cells. It is expressed in various types of cells, such as those of the upper oesophagus, lungs, kidneys and testicles, as well as the intestinal epithelial cells (small intestinal enterocytes, Gao *et al.*, 2020). This receptor seems to be well conserved in other animal species (mammals, birds, reptiles and amphibians).

Various studies have been undertaken, using different methodologies, to assess the ability of ACE2 receptors from animal species to bind to spike protein (S-protein, the main entry protein for coronaviruses) and enable SARS-CoV-2 cell entry. The results of peer-reviewed publications are summarised in Table 2 (preprints have not been taken into account).

**Table 2: Summary of various studies published in 2020 that deal with the ability of SARS-CoV-2 to interact with receptors (ACE2) from various animals**

Animals	Methodology	Observation	Reference
Horseshoe bats	HeLa cells expressing ACE2 homologue, then infection	Cellular infection	Zhou <i>et al.</i> (2020)
	SARS-CoV-2 S-protein pseudotype particles in RhiLu/1.1 (lung) cells	Entry of pseudotype particles	Hoffmann <i>et al.</i> (2020)
	Computer prediction of SARS-CoV-2 S-protein and ACE2 recognition	Likely recognition	Wan <i>et al.</i> (2020)
Daubenton's bats	Pseudotype particles expressing SARS-CoV-2 S-protein in MyDauLu/47.1 (lung) cells	No entry of pseudotype particles	Hoffmann <i>et al.</i> (2020)
Civets	HeLa cells expressing ACE2 homologue, then infection	Cellular infection	Zhou <i>et al.</i> (2020)
	Computer prediction of SARS-CoV-2 S-protein and ACE2 recognition	Likely recognition	Wan <i>et al.</i> (2020)
Monkeys (species not specified)	SARS-CoV-2 S-protein pseudotype particles in Vero (kidney) cells	Entry of pseudotype particles	Hoffmann <i>et al.</i> (2020)
	Computer prediction of SARS-CoV-2 S-protein and ACE2 recognition	Likely recognition	Wan <i>et al.</i> (2020)
Orangutans	Computer prediction of SARS-CoV-2 S-protein and ACE2 homologue recognition	Likely recognition	Wan <i>et al.</i> (2020)
Pigs	HeLa cells expressing ACE2 homologue, then infection	Cellular infection	Zhou <i>et al.</i> (2020)
	Pseudotype particles expressing SARS-CoV-2 S-protein in LLC-PK1 (kidney) cells	No entry of pseudotype particles	Hoffmann <i>et al.</i> (2020)
	Computer prediction of SARS-CoV-2 S-protein and ACE2 homologue recognition	Likely recognition	Wan <i>et al.</i> (2020)
Mice	HeLa cells expressing ACE2, then infection	No cellular infection	Zhou <i>et al.</i> (2020)
	Pseudotype particles expressing SARS-CoV-2 S-protein in NIH/3T3 (embryonic) cells	No entry of pseudotype particles	Hoffmann <i>et al.</i> (2020)
	Computer prediction of SARS-CoV-2 S-protein and ACE2 homologue recognition	Unlikely recognition	Wan <i>et al.</i> (2020)
Rats	Computer prediction of SARS-CoV-2 S-protein and ACE2 homologue recognition	Unlikely recognition	Wan <i>et al.</i> (2020)
Hamsters	SARS-CoV-2 S-protein pseudotype particles in BHK (kidney) cells	No entry of pseudotype particles	Hoffmann <i>et al.</i> (2020)
Cattle	SARS-CoV-2 S-protein pseudotype particles in MDBK (kidney) cells	No entry of pseudotype particles	Hoffmann <i>et al.</i> (2020)

Dogs	SARS-CoV-2 S-protein pseudotype particles in MDCK II (kidney) cells	Entry of pseudotype particles	Hoffmann <i>et al.</i> (2020)
Cats	Computer prediction of SARS-CoV-2 S-protein and ACE2 homologue recognition	Likely recognition	Wan <i>et al.</i> (2020)
Ferrets	Computer prediction of SARS-CoV-2 S-protein and ACE2 homologue recognition	Likely recognition	Wan <i>et al.</i> (2020)

The experts consider that additional studies on the interactions between SARS-CoV-2 and ACE2 homologues from various animal species, as well as studies on the distribution of ACE2 in tissue, are necessary for the advancement of knowledge on the possible transmission of infection to other species. However, the passage of a virus to another species does not rely solely on the presence of the receptor but also on the presence of other cellular factors required for viral replication (see Annex 3). Further studies should also be undertaken to identify these factors.

#### 1.2.3.2 Analysis of investigations of experimental SARS-CoV-2 infections in domestic animals

Studies on experimental infections in domestic animal species were recently undertaken by various research teams. However, on the date when this opinion was written, some of these studies were only available as preprints. The GECU based its analysis on published articles as well as on articles that had not yet been peer-reviewed and even ProMED communications<sup>13</sup> (see Table 3). At this stage of their evaluation, the above do not provide the same level of evidence as articles duly published in peer-reviewed journals. All of the data from these studies are given in Table 3 below.

<sup>13</sup> <https://promedmail.org/> Programme of the International Society for Infectious Disease

**Supplemented ANSES Opinion  
Request No 2020-SA-0037**

**Table 3: Summary of various studies, as of 8 April 2020, dealing with the experimental infection of domestic animals (dpi = days post-inoculation). For presentation reasons, the table's columns are spread out across two pages.**

Article	Article source (journal name if published article, preprint, other)	Animal species	Number of animals	Age	Route of inoculation	Dose (with unit)	Clinical signs
Beer, 2020	ProMed Post (Archive Number: 20200407.7196506)	Ferrets ( <i>Mustela putorius furo</i> )	9 inoculated	Not provided	Intranasal	10 <sup>5</sup> TCID <sub>50</sub>	Not provided
		Pigs ( <i>Sus scrofa domesticus</i> )	9 inoculated	Not provided	Intranasal	10 <sup>5</sup> TCID <sub>50</sub>	Not provided
		Chickens ( <i>Gallus gallus</i> )	17 inoculated	Not provided	Intranasal	10 <sup>5</sup> TCID <sub>50</sub>	Not provided
Kim et al., 2020	<i>Cell Host Microbes</i>	Ferrets ( <i>Mustela putorius furo</i> )	15 inoculated	12-24 months (males and females)	Intranasal	10 <sup>5.5</sup> TCID <sub>50</sub> per animal	Moderate (moderate hyperthermia, listlessness, occasional cough, no mortality)
Shi et al., 2020	<i>Science</i>	Ferrets	5	3-4 months	Intranasal	10 <sup>5</sup> pfu/ml	33% of animals with fever and loss of appetite
		Ferrets	8	3-4 months	Intratracheal	10 <sup>5</sup> pfu/volume?	Not provided
		Cats	2	8 months	Intranasal	10 <sup>5</sup> pfu/volume?	Not provided
		Cats	2	70-100 days	Intranasal	10 <sup>5</sup> pfu/volume?	Death of one cat
		Beagle puppies	5	3 months	Intranasal	10 <sup>5</sup> pfu/volume?	Not provided
		Pigs	5	40 days	Intranasal	10 <sup>5</sup> pfu/volume?	Not provided
		Chickens	5	4 weeks	Intranasal	10 <sup>4.5</sup> pfu/volume?	Not provided
Sia et al., 2020	Preprint natureresearch <a href="https://www.researchsquare.com/article/rs-20774/v1">https://www.researchsquare.com/article/rs-20774/v1</a>	Golden hamsters ( <i>Mesocricetus auratus</i> )	12 inoculated and 3 contact (only males)	4 to 5 weeks	Intranasal	8 · 10 <sup>4</sup> TCID <sub>50</sub>	Weight loss (10%) and ruffled hair coat
		Golden hamsters ( <i>Mesocricetus auratus</i> )	15 inoculated and 8 in contact with 8	6-10 weeks (males and females)	Intranasal	10 <sup>5</sup> pfu in 100 µl DMEM	Lethargy, prostration, ruffled hair coat, weight loss (11%) and polypnoea

**Supplemented ANSES Opinion  
Request No 2020-SA-0037**

Article	Article source (journal name if published article, preprint, other)	Animal species	Lesions	Tissue virology	Viral excretion	Serological results	Transmission on contact -, +, ++ or +++
Beer, 2020	ProMed Post (Archive Number: 20200407.7196506)	Ferrets ( <i>Mustela putorius furo</i> )	Not provided	Virus detected in the upper respiratory system (only)	Viral RNA detected in the nasal washes of 8/9 animals between 2 and 8 dpi	Antibodies detected from 8 dpi	Yes (+) (3/3 infected, direct contact)
		Pigs ( <i>Sus scrofa domesticus</i> )	Not provided	Negative	Negative	Negative	-
		Chickens ( <i>Gallus gallus</i> )	Not provided	Negative	Negative	Negative	-
Kim et al., 2020	<i>Cell Host Microbes</i>	Ferrets ( <i>Mustela putorius furo</i> )	Macroscopic lesions: Not provided Microscopic lesions: Acute bronchiolitis	Virus detected (RT-qPCR) and isolated in the nasal turbinates and lungs, detected in the trachea, kidneys and intestines (RT-qPCR, low viral loads)	Detected (RT-qPCR) and isolated in nasal secretions and saliva between D2 and D8 and (with low viral loads) in urine and faeces	Antibodies detected by seroneutralisation 12 days post-infection in all ferrets	Direct contact: +++ Indirect contact: +
Shi et al., 2020	<i>Science</i>	Ferrets	Yes, pulmonary	Virus detected and titrated in upper respiratory tract	Virus detected and isolated in nasal secretions	Positive	No contact
		Ferrets	Not provided	Virus detected by RT-qPCR in upper respiratory tract	Not provided	Not provided	No contact
		Cats	Not provided	Virus detected and titrated in respiratory tract	Yes	Positive	+ (1 in 3)
		Cats	Yes, pulmonary	Virus detected and titrated in respiratory tract	Yes	Positive	+ (1 in 3)
		Beagle puppies	Not provided	No	Virus detected by RT-PCR in stools (2/5)	Positive (2/5)	-
		Pigs	Not provided	No	No	No	-
		Chickens	Not provided	No	No	No	-
		Ducks	Not provided	No	No	No	-
Sia et al., 2020	Preprint natureresearch <a href="https://www.researchsquare.com/article/rs-20774/v1">https://www.researchsquare.com/article/rs-20774/v1</a>	Golden hamsters ( <i>Mesocricetus auratus</i> )	Inflammation of lungs and upper respiratory tract	In lungs and nasal cavities = + cultures / kidneys and faeces = RNA only / duodenal cells = antigen	Max. 2 days post-inoculation in nasal wash and lungs	Seroconversion of all animals	Placed in contact in the same cage 24h after inoculation, so +++ contact and +++ transmission since all were contaminated with the same signs, excretion observed in inoculated animals only
Chan et al., 2020	<i>Clinical Infectious Diseases</i>	Golden hamsters ( <i>Mesocricetus auratus</i> )	Acute tracheitis and severe pneumonia; Intestinal epithelial necrosis	Mean loads in tissues from D2 to D7 for nasal turbinates, lungs, trachea; Viral culture from lung tissue: 10 <sup>5</sup> -10 <sup>7</sup> TCID50/g from D2 to D4; At D4, a small amount in the intestines and low load in the blood and other organs (D2 to D4)	Consistent with tissue virology here	Neutralising antibodies detected in serum on D7 and D14 (mean titres)	Yes (+) (8/8 infected, direct contact)

In conclusion, the GECU reiterates that its expert appraisal, in particular for the updating of the opinion, was partly based on articles that had not yet been peer-reviewed and on ProMED communications.

The experimental infections described in these studies did not show that 40-day-old pigs or four-week-old chickens and ducks were receptive to the SARS-CoV-2 virus, in the conditions of the two trials (Shi *et al.*, 2020; Beer, 2020<sup>14</sup>).

In dogs (three-month-old beagle puppies), the reported study showed viral detection by RT-PCR only in the rectal swabs of two of the four inoculated animals, although no infectious virus was identified. Moreover, a serological response was found in these two animals. However, the dogs in contact with the inoculated animals were not infected. Dogs therefore had low receptivity to the virus in the experimental conditions of the study (Shi *et al.*, 2020).

Regarding cats, the results of the published study show that these animals are receptive to the virus. The inoculated adult cats all developed a serological response, although no clinical signs were reported. However, young animals appeared to be more susceptible than adults in light of the observed pulmonary lesions; furthermore, they all seroconverted. For one of the three contact cats, placed in separate cages adjacent to the initially infected animals, viral RNA was detected in the respiratory tract together with seroconversion, suggesting a transmission event, in the study's conditions. The GECU underlines that the animals were infected with high doses of the virus via direct intranasal inoculation. In this study, the same dose was administered to the kittens, adult cats, ferrets, puppies and 40-day-old pigs (Shi *et al.*, 2020).

Concerning ferrets, three experimental studies showed that these animals are receptive to the virus, with clinical signs and lesions observed in the respiratory tract. Early detection of the virus in contact animals prior to the development of clinical signs clearly suggests the effectiveness of viral transmission in these animals.). The same observation was made for hamsters (*Mesocricetus auratus*) (Beer, 2020; Kim *et al.*, 2020; Shi *et al.*, 2020).

Lastly, there is currently no scientific evidence indicating whether SARS-CoV-2 can be transmitted from an infected domestic animal to a human.

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<sup>14</sup> <https://promedmail.org/promed-post/?id=7196506>, consulted on 8/4/2020

## 2. Potential role of food in transmitting the SARS-CoV-2 virus

Regarding the potential role of food in the transmission of Covid-19, the GECU's experts consider that the two theoretical modes of food contamination by the SARS-CoV-2 virus are associated with 1) infected livestock animals and the transfer of the virus to foodstuffs of animal origin, and 2) the handling of foodstuffs by people infected with this virus.

In light of the information given above regarding the potential role of livestock animals in the zoonotic transmission of the virus, the consumption of foodstuffs of animal origin contaminated by infected animals was ruled out as a source of infection. Therefore, only the second source of food contamination via a human infected with the SARS-CoV-2 virus was investigated.

### 2.1 Food contaminated by an infected human

Generally speaking, general hygiene measures should be adopted when preparing food (this is valid for both consumers and agri-food operators): wash hands frequently, frequently clean and maintain surfaces, materials and utensils, and separate raw and cooked foods. Moreover, people who are sick should be aware of the importance of not handling food if they show symptoms of gastro-enteritis (diarrhoea, fever, vomiting, headaches). In the current context, attention should also be paid to symptoms of flu-like syndrome.

### 2.2 Faecal-oral food contamination

In addition to confirmed and possible cases<sup>15</sup>, there are benign and asymptomatic forms of the disease that are difficult to detect (Bernard Stoecklin *et al.*, 2020). People with mild forms are likely to contaminate foods, theoretically by the faecal-oral route, which is the main route of transmission for foodborne viruses such as noroviruses. SARS-CoV-2 viral RNA has been observed in the stools of patients (Guan *et al.*, 2020). However, although two studies described cultivation of the SARS-CoV-2 virus from stool samples, no cases of faecal-oral transmission of Covid-19 have been reported yet (Zhang *et al.*, 2020; Ong *et al.*, 2020). To demonstrate possible faecal-oral transmission, additional information, such as the infectivity and quantification of viruses detected in stools, would be necessary. Moreover, proper compliance with general daily hygiene rules, such as frequent and systematic hand-washing after using the toilet, can help prevent faecal-oral exposure.

### 2.3 Food contamination via the transfer of droplets

The virus is more likely to pass from an infected person to food as a result of sneezing or coughing or direct contact with soiled hands, when droplets are deposited on the food or on a contact surface or utensils (cutting board, plate, etc.). Washing hands with soap before and during meal preparation is an essential measure. This washing is necessary after any contaminating gesture (after coughing, blowing one's nose, etc.).

On inert surfaces, without any cleaning measures, viruses in the *Coronaviridae* family can persist for up to nine days (Kampf *et al.*, 2020), especially when the temperature and relative air humidity are low (Casanova *et al.*, 2010).

However, given 1) the poor ability of coronaviruses to survive cleaning and disinfection, 2) the lack of data showing that SARS-CoV-2 behaves differently from other coronaviruses (Kampf *et al.*, 2020), and 3) the proper, daily implementation of good hygiene practices and cleaning and disinfection procedures

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<sup>15</sup> *Santé publique France* has provided definitions of a "confirmed case" and "possible case" that are available online. They rely on clinical criteria that will evolve as knowledge is acquired on the virus and the epidemic (*Santé publique France*, 2020) .

in agri-food industry and at home (ANSES, 2013), food contamination by surfaces is controlled in principle.

The GECU then examined the following theoretical scenario: an asymptomatic individual who may have directly or indirectly contaminated a food via the deposition of infectious droplets at one or more stages in the food chain for animal and plant products (processing, preparation, consumption).

In this scenario, the experts identified two possibilities, depending on the food in question:

- 1) Foods that are to be consumed cooked;
- 2) Raw or undercooked animal- or plant-based foods, or prepared foods, consumed as is or used as ingredients in a prepared product not meant to be consumed cooked.

### Concerning cooked foods

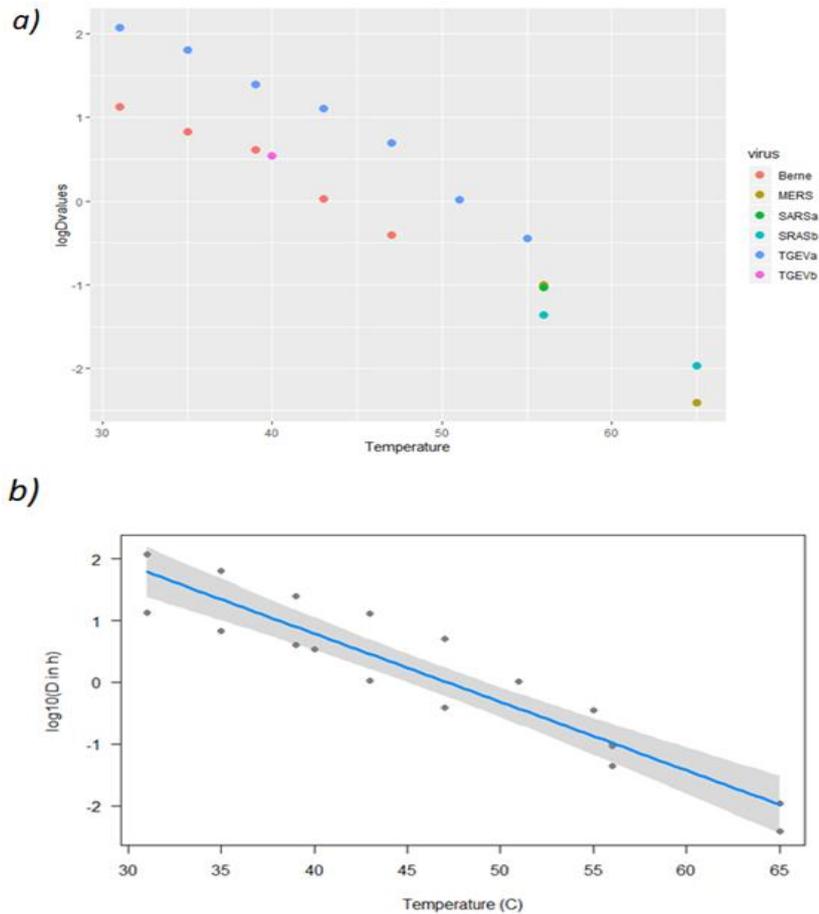
To date, there are no data on the thermal inactivation of the SARS-CoV-2 virus. However, there are data on other zoonotic viruses and viruses involved in animal diseases for the *Coronaviridae* family. The table in Annex 4 lists the various studies that were identified. For each of these studies, the thermal destruction value ( $D^{16}$ ) was calculated for each temperature.

Figure 3a below shows the values obtained. A secondary thermal destruction model was then applied to calculate the impact of the temperature on D values. This model can be used to predict the inactivation of viruses in this family for various temperatures (Figure 3b). According to this analysis, four log reductions ( $4 \log_{10}$ ) in viral titre can be obtained, for example, within four minutes at 63°C (*i.e.* the temperature used when preparing hot food in catering).

**In conclusion, cooking (for four minutes at 63°C) may be considered an effective way to inactivate coronaviruses in foods.**

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<sup>16</sup> D is the time needed to divide by 10 the initial population of a virus



**Figure 3: (a) Log destruction values ( $D^{17}$ ) observed at various temperatures ( $^{\circ}\text{C}$ ) for viruses of the genus *Coronavirus* (the corresponding studies are set out in the table in Annex 4). (b) Linear model fit to  $\log_{10}(D)$  according to temperature.**

### Concerning raw or undercooked prepared foods

The following scenario was investigated by the GECU: a food meant to be consumed as is (without cooking) that may be contaminated by an asymptomatic operator<sup>18</sup> or consumer who does not comply with good hygiene practices. It should be noted that the current data show that coronaviruses seem stable at low and negative temperatures, which means that refrigeration and freezing are not inactivation treatments for this microorganism.

#### 2.3.1 Digestive exposure

Since some Covid-19 patients with respiratory infections sometimes show gastro-intestinal symptoms, the assumption of SARS-CoV-2 transmission via the digestive tract has been considered by several authors (Guan *et al.*, 2020; Gao *et al.*, 2020; Danchin *et al.*, 2020), although it has not been confirmed or ruled out for the time being.

<sup>17</sup> D is the time needed to divide by 10 the initial population of a virus

<sup>18</sup> See the ANSES data sheet for the drafting of a guide to good hygiene practices (GGHP): “Operators as sources or vectors of food contamination” (in French) <https://www.anses.fr/fr/system/files/GBPH2017SA0153.pdf>

ACE2, the receptor for SARS-CoV-2, is necessary in order for the virus to enter cells. ACE2 expression in various types of cells, such as those of the upper oesophagus and lungs as well as intestinal epithelial cells (small intestinal enterocytes), can contribute to multi-tissue infection with the virus (Li *et al.*, 2020; Gao, Chen and Fang, 2020).

SARS-CoV-2 seems to be a coronavirus with primary respiratory tropism whose involvement in the digestive system may essentially be secondary to its spread by viraemia. There can be direct infection of the digestive tract for certain coronaviruses, but these are characterised by S-proteins with the ability to bind to the sialic acid that protects them from gastric juices (Wentworth and Holmes, 2007). To the experts' knowledge, this property has not been studied for SARS-CoV-2.

Thus, according to the current data, the GECU's experts consider that the gastro-intestinal symptoms found in patients are related first and foremost to the virus systemically spreading and affecting the digestive system, and not to direct entry through the digestive tract.

**In light of the above and in the current state of knowledge, the direct digestive transmission of SARS-CoV-2 was ruled out by the GECU's experts.**

### 2.3.2 Respiratory exposure

A risk of the airways becoming infected after ingestion of a contaminated food has not been observed with coronaviruses and therefore seems unlikely. However, considering observations made with other viruses such as the Nipah virus and avian influenza viruses, this risk cannot be completely ruled out (World Health Organization 2008, Food Safety and Inspection Service, Food and Drug Administration and Animal and Plant Health Inspection Service 2010). In these cases, the route of entry for the virus is the respiratory tract during chewing.

## 3. Conclusions of the GECU

SARS-CoV-2 belongs to the genus *Betacoronavirus*. Four other human *Betacoronaviruses* are known to date: two that mainly cause benign respiratory infections (HCoV-OC43 and HKU1), SARS-CoV, responsible for the 2002-2003 epidemic, and MERS-CoV, which emerged in 2012 and continues to circulate at a low level.

The scientific and phylogenetic data suggest that bats (*Rhinolophidae*) act as an animal reservoir for SARS-CoV-2, based on the detection of strains characterised as genetically related to SARS-CoV-2. However, this virus has proven to be different from several *Betacoronaviruses* already known in domestic animals. The epidemiological situation currently observed shows that SARS-CoV-2 is well adapted to humans.

Considering the scale of the current epidemic, very few cases of pets contaminated by and/or infected with SARS-CoV-2 have been reported up to now. These cases of contamination and infection remain sporadic and isolated, even though the virus is widely circulating in the human population.

Regarding the analysis of the experimental infection data, the GECU reiterates that its expert appraisal was partly based on articles that had not yet been peer-reviewed, as well as on ProMED communications. The results of the studies describing experimental infections did not show that pigs and poultry (chickens and ducks) were receptive to SARS-CoV-2, in the conditions of the two trials. As for dogs, they appeared to have low receptivity to the virus in the experimental conditions of the only study that was analysed. Regarding cats, the results of the sole study showed that these animals were receptive to the virus, with

lesions in the respiratory system of young cats and an event involving transmission to contact cats. As for ferrets, the three experimental studies showed that these animals were receptive to the virus and developed clinical signs and respiratory tract lesions, with proven transmission of the virus to contact individuals. The same observation was made for hamsters (*Mesocricetus auratus*).

**In light of the scientific evidence currently available (phylogenetics of SARS-CoV-2, epidemiology of Covid-19, *in vitro*, *in vivo* studies, etc.), and despite the sporadic cases that have been described as well as the experimental infections having shown that a few animal species are receptive to the virus, the GECU considers that there is currently no evidence that domestic animals play an epidemiological role in the spread of SARS-CoV-2; the spread of this virus is the result of effective human-to-human respiratory transmission.**

In this regard, the GECU reiterates the need to apply basic hygiene measures after any contact with a domestic animal, to prevent any risk of the virus spreading (wash hands with soap after touching an animal or after cleaning a litter box, avoid close contact at face level, etc.).

Moreover, to prevent sporadic cases of transmission to domestic animals, the GECU advises people infected with Covid-19 to avoid any close contact with their animals, without endangering their welfare. To this end, the GECU supports the recommendations issued by OIE and by several health agencies (for example, the Friedrich Loeffler Institute in Germany and AFSCA in Belgium), which advise taking preventive and distancing steps in the context of this epidemic.

Concerning the role of food in the transmission of SARS-CoV-2, the experts reiterate that the main route of entry is the respiratory tract. In the current state of knowledge, the possible contamination of foodstuffs of animal origin via an infected animal has been ruled out. Infected humans can contaminate food in the event of poor hygiene practices, such as coughing, sneezing and contact with soiled hands.

To date, there is no evidence to suggest that consumption of contaminated food can lead to infection of the digestive tract; however, the possibility of the respiratory tract becoming infected during chewing cannot be completely ruled out. In all cases, the GECU reiterates that cooking (e.g. for four minutes at 63°C) may be considered an effective way to inactivate coronaviruses in foods. Good hygiene practices, if properly observed when handling and preparing food, prevent food from becoming contaminated by the SARS-CoV-2 virus. The GECU also reiterates that people who are sick should be aware of the importance of not handling food if they show symptoms of gastro-enteritis (diarrhoea, fever, vomiting, headaches) or, in the current context, of flu-like syndrome.

The experts nonetheless underline the “moderate” uncertainty<sup>19</sup> associated with these conclusions. New scientific facts supplementing knowledge of this virus may modify this uncertainty.

## AGENCY CONCLUSIONS AND RECOMMENDATIONS

On 2 March 2020, the French Agency for Food, Environmental and Occupational Health & Safety received a formal request from the Directorate General for Food (DGAL) to assess, within four days, certain risks associated with the SARS-CoV-2 virus (the causal agent for Covid-19), and more specifically

<sup>19</sup> According to ANSES Opinion No 2013-SA-0049

to give an opinion regarding the potential role of domestic animals (livestock animals and pets) in the spread of the SARS-CoV-2 virus as well as the potential role of food in the transmission of the virus.

The emergence of new information and data on the links between the virus and animals led ANSES to supplement its opinion, taking into account the available data in this area, including scientific data that had not yet been peer-reviewed.

The Agency endorses the conclusions of the “Covid-19” Emergency Collective Expert Appraisal Group (GECU). In this regard, it stresses that knowledge is still limited for this novel *Betacoronavirus*. It notes that these conclusions are consistent with those provided in the communications available to date dealing with these animal health and food hygiene aspects (communications of the World Health Organization and World Organisation for Animal Health, and some opinions by health agencies such as AFSCA, the Friedrich Loeffler Institut and BfR).

The resulting recommendations are in line with the strict hygiene measures indicated to prevent human-to-human transmission.

ANSES will remain attentive to future information and studies that may lead it to modify this assessment.

Dr. Roger Genet

#### **MOTS-CLÉS / KEYWORDS**

SARS-CoV-2, COVID-19, chauve-souris, coronavirus, transmission, aliments, animaux domestiques.

SARS-CoV-2, Covid-19, bats, coronavirus, transmission, food, domestic animals.

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## ANNEX 1

### Presentation of the participants

**PREAMBLE:** The expert members of the Expert Committees and Working Groups or designated rapporteurs are all appointed in a personal capacity, *intuitu personae*, and do not represent their parent organisation.

### EMERGENCY COLLECTIVE EXPERT APPRAISAL GROUP (GECU)

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#### Chair

Ms Sophie LE PODER – Professor, Alfort National Veterinary School – Virology, Immunology, Vaccinology

#### Members

Mr Paul BROWN – Head of research into avian metapneumoviruses and coronaviruses, ANSES Ploufragan – Virology, Avian metapneumoviruses and coronaviruses

Mr Meriadeg LEGOUIL – University Hospital Assistant, Caen University Hospital-Virology – Ecology and evolution of microorganisms, zoonotic and emerging viruses circulating in bats

Ms Sandra MARTIN-LATIL – Scientific Project Leader, Laboratory for Food Safety, ANSES Maisons-Alfort – Food virology, Cellular cultures, Diagnostic and detection tools, Food hygiene

Mr François MEURENS – Professor, ONIRIS – Veterinary School of Nantes – Virology, Immunology, Vaccinology, Swine diseases

Mr Gilles MEYER – Professor, National Veterinary School of Toulouse – Virology, Immunology, Vaccinology, Ruminant diseases

Ms Elodie MONCHATRE-LEROY – Director of the Laboratory for Rabies and Wildlife, ANSES Nancy – Virology, Epidemiology, Risk assessment, Wildlife

Ms Nicole PAVIO – Research Director – Laboratory for Animal Health, ANSES Maisons-Alfort – Food virology, Cellular cultures, Diagnostic and detection tools, Food hygiene

Ms Gaëlle SIMON – Deputy Head of Unit, Pig Immunology and Virology Unit, ANSES Ploufragan-Plouzané-Niort – Virology, Immunology, Diseases of monogastric animals

Ms Astrid VABRET – University Professor - Hospital Practitioner, Caen University Hospital – Human medicine, Virology, Zoonoses

## **ANSES PARTICIPATION**

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### **UERSABA scientific coordination**

Ms Charlotte DUNOYER – Head of the Unit for the assessment of risks related to animal health, nutrition and welfare – ANSES

Ms Florence ETORE – Deputy Head of the Unit for the assessment of risks related to animal health, nutrition and welfare – ANSES

Ms Elissa KHAMISSE – Scientific Coordinator – Unit for the assessment of risks related to animal health, nutrition and welfare – ANSES

### **UERALIM scientific coordination**

Ms Estelle CHAIX – Scientific Coordinator – Unit for the assessment of biological risks in foods – ANSES

Mr Laurent GUILLIER – Scientific Project Leader – Unit for the assessment of biological risks in foods – ANSES

Mr Moez SANAA – Head of the Unit for the assessment of biological risks in foods – ANSES

### **Administrative secretariat**

Angélique LAURENT – Risk Assessment Department – ANSES

ANNEX 2 REQUEST LETTER



2020-SA-0037

MINISTÈRE DE L'AGRICULTURE ET DE L'ALIMENTATION

LE DIRECTEUR GÉNÉRAL DE L'ALIMENTATION

**Direction générale  
de l'alimentation**

251 rue de Vaugirard  
75 732 Paris cedex

À

Agence nationale de sécurité sanitaire (ANSES)  
14, rue Pierre et Marie Curie  
94700 MAISONS-ALFORT

à l'attention de M. Roger Genet, directeur général.

Paris, le 2 mars 2020

**Objet : saisine urgente de l'Agence sur certains risques liés au virus COVID-19**

Conformément au code de la santé publique, j'ai l'honneur de saisir l'Agence dans le but d'apporter en situation d'urgence des éléments de réponse aux deux questions suivantes :

- Rôle potentiel des **aliments** dans la transmission de la maladie liée au COVID-19 ;
- Rôle potentiel des **animaux domestiques** dans la propagation du virus. Les animaux domestiques visés sont les animaux de compagnie (chiens, chats) et les animaux de rente.

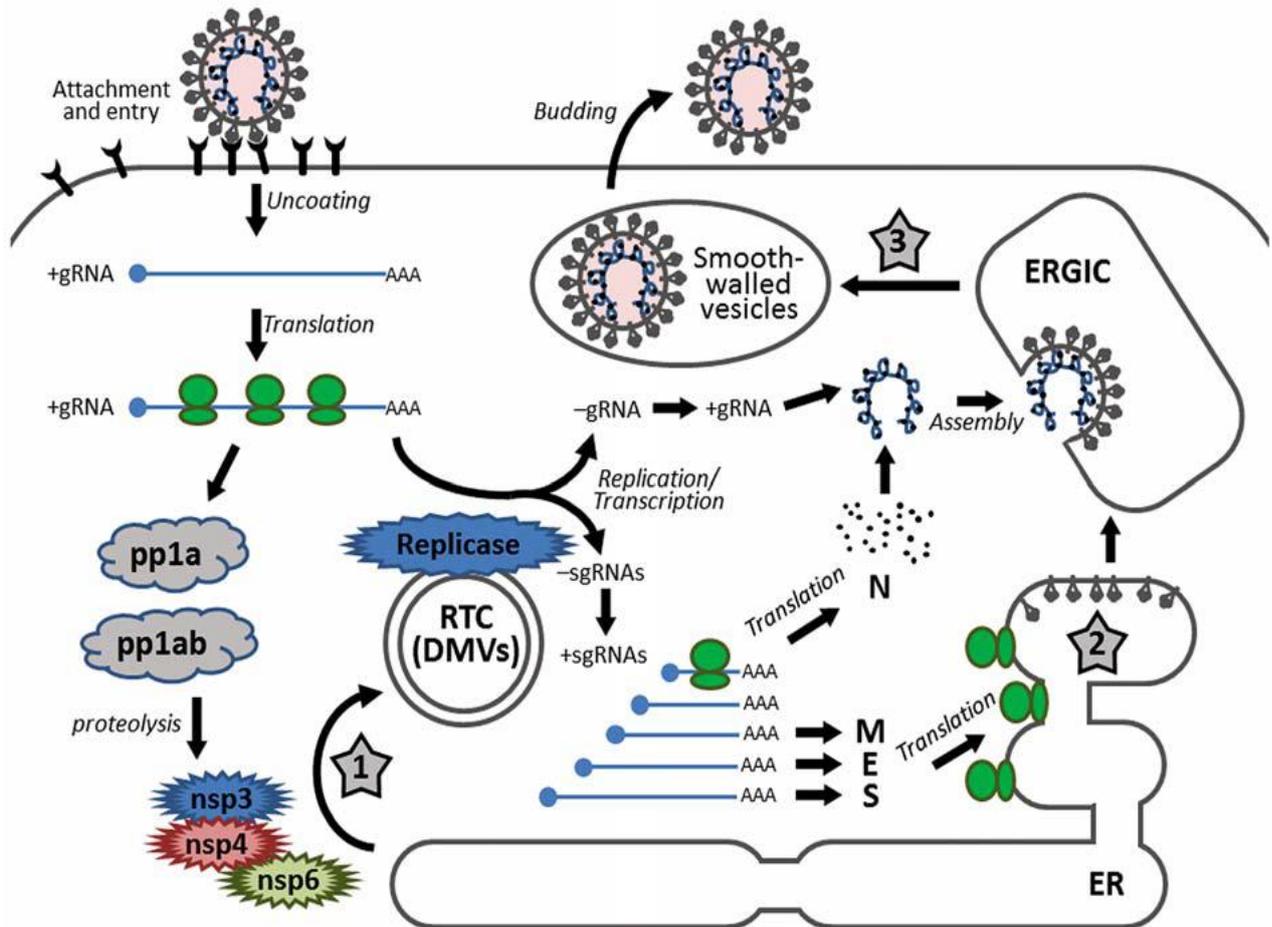
Une réponse de synthèse basée sur les observations épidémiologiques documentées et sur les conclusions du HCSP sur la faible résistance du virus notamment sera un appui suffisant pour cette demande qui vise à obtenir des éléments de réassurance indépendants, face aux questions qui ne vont pas manquer au moment où la France est entrée en phase 2 de la gestion épidémique.

Je vous remercie par avance de répondre à cette saisine **au plus tard le vendredi 6 mars**.

Copie : DGS, ANSP, DGCCRF

Le directeur général adjoint de l'alimentation  
Chef du service de la gouvernance  
et de l'international  
CVO  
Loïc EVAÏN

ANNEX 3 DIAGRAM SHOWING THE VIRAL CYCLE OF A CORONAVIRUS (FUNG ET AL., 2014)



Description of the diagram: The virus enters by attaching to its cellular receptor. This is the first stage in the cycle, but the diagram also shows the other stages necessary for the full cycle and the formation of new viral particles (replication of the genome, transcription and translation of the viral proteins, assembly and release of the new viral particles). Cellular proteins will be necessary for each of these stages. The adaptation of a virus to a new host species thus requires the ability to use a new cellular receptor and use the cellular proteins required for the other stages in the cycle.

**ANNEX 4: LIST OF STUDIES INVESTIGATING THE THERMAL INACTIVATION OF VIRUSES IN THE GENUS CORONAVIRIDAE**

Virus	Strain	Measurement	Temperatures (°C)	Conditions associated with heat treatment	Study reference	Key
<b>Berne virus</b>	P138/72	Cellular infectivity in EMS cells	31, 35, 39, 43, 47°C	Cell culture supernatant	(Weiss <i>et al.</i> 1986)	Berne
<b>TGEV</b>	D52	Cellular infectivity in RPtg cells	31, 35, 39, 43, 47, 51 and 55°C	In solution at pH 7	(Laude 1981)	TGEVa
<b>TGEV</b>	-	Cellular infectivity in ST cells	40°C	Stainless steel surface with 80% humidity	(Casanova <i>et al.</i> 2010)	TGEVb
<b>SARS-CoV</b>	FFM-1	Cellular infectivity in Vero cells	56°C	Cell culture supernatant without FBS (foetal bovine serum)	(Rabenau <i>et al.</i> 2005)	SARSa
<b>SARS-CoV</b>	Urbani	Cellular infectivity in Vero cells	56, 65°C	DMEM (Dulbecco's modified Eagle's medium)	(Darnell <i>et al.</i> 2004)	SARSb
<b>MERS-CoV</b>	FRA2	Cellular infectivity in Vero cells (TCID-50)	56°C	Cell culture supernatant	(Leclercq <i>et al.</i> 2014)	MERS

**ANNEX 5: CALCULATION OF THE THERMAL DESTRUCTION VALUE ACCORDING TO THE TABLE IN ANNEX 4. (SHOWN IN FIGURE 3 OF THE OPINION; A BETTER RESOLUTION IS PROVIDED HERE)**

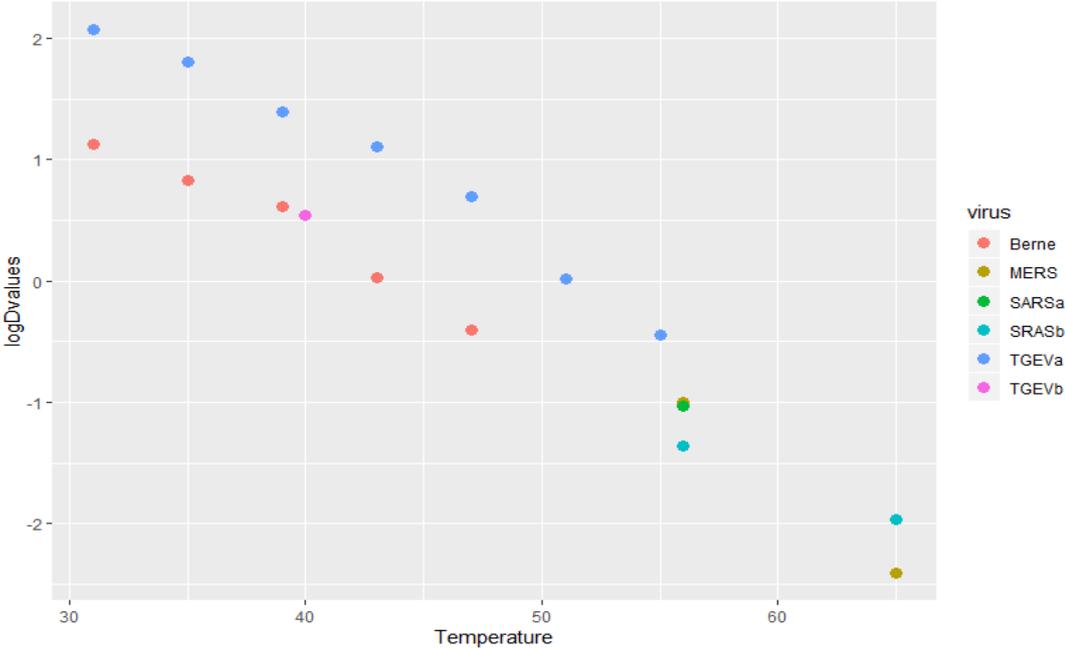


Figure 3(a): Log destruction values (D) observed at various temperatures for viruses of the genus *Coronavirus* (the corresponding studies are set out in the table in Annex 4).

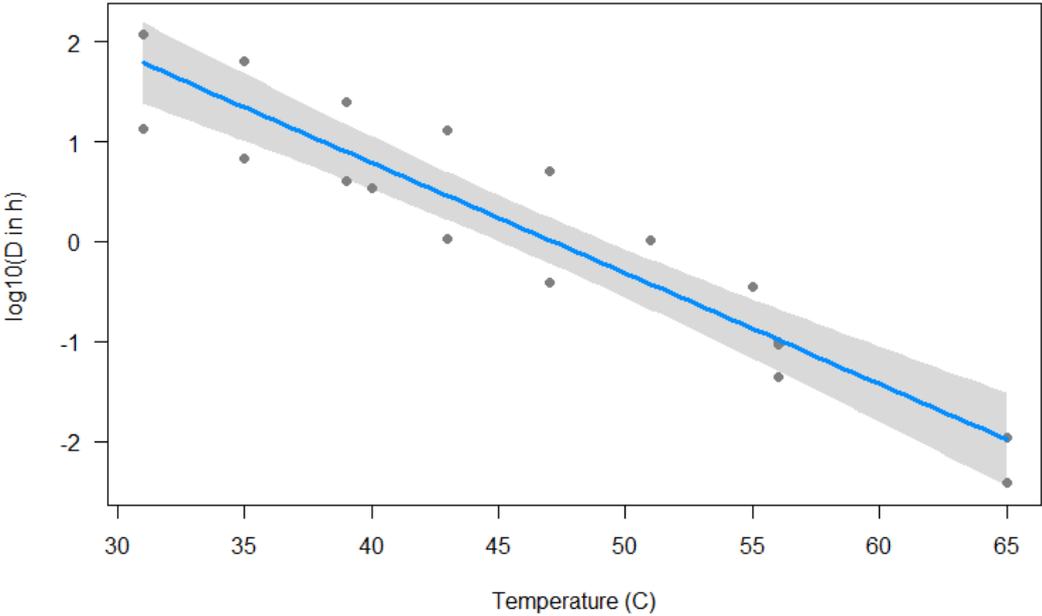


Figure 3(b): Linear model fit to log<sub>10</sub>(D) according to temperature

**ANNEX 6: TRACKING OF CHANGES TO THE OPINION**

Section	Description of the change
Background and purpose of the request	Deletion of “As of 4 March 2020, 77 countries had reported 93,076 confirmed cases, including 3202 deaths (3.4%). In France, on the same date, 285 cases had been confirmed, including four deaths (source: <a href="http://www.santepubliquefrance.fr">www.santepubliquefrance.fr</a> )”
1.1	Addition of a section on coronaviruses found in pigs, poultry, cattle and cats Modification of the conclusion
1.2.1	Modification of the first paragraph of this section and addition of new information on the evolution of <i>Sarbecoviruses</i> For the second paragraph that starts with “It is important to take into account the time factor”, addition of “enable the human virus to <u>adapt</u> to other animal species”. Addition also of a footnote on R0 Modification of the conclusion for this section
1.2.2	Deletion of §1.2.2 initially entitled “Animal species deemed susceptible and/or receptive to SARS-CoV-2”. This section was replaced with another entitled “Natural SARS-CoV-2 infections in animal species”, with four sub-sections: 1.2.2.1 Identified cases of animals testing positive for SARS-CoV-2 1.2.2.2 Serological investigation of cats tested in Wuhan 1.2.2.3 Serological and virological investigation undertaken with cats and dogs of students at the National Veterinary School of Maisons-Alfort (ENVA) 1.2.2.4 IDEXX study New conclusion for this section
1.2.3	New title of this section: “Experimental infections” The initial section “1.2.3. ACE2 receptor” was moved to sub-section “1.2.3.1” and addition of a statement “The results of peer-reviewed publications are summarised in Table 2 (preprints have not been taken into account)” Addition of sub-section 1.2.3.2 “Analysis of investigations of experimental SARS-CoV-2 infections in domestic animals” New conclusion for this section
1.3	Deletion of this section
3	Modification of the GECU's conclusion for the part on animal health
Agency conclusions and recommendations	Addition of “The emergence of new information and data on the links between the virus and animals led ANSES to supplement its opinion, taking into account the available data in this area, including scientific data that had not yet been peer-reviewed”; “knowledge is still limited for this novel Betacoronavirus”; “aspects that have yet to be fully investigated” replaced with “these animal health and food hygiene aspects” Addition of “AFSCA” in the examples of health agencies
Annex 1	Addition of the following experts: Mr François MEURENS, Mr Gilles MEYER and Ms Gaëlle SIMON