

The Director General

Maisons-Alfort, 9 March 2020

OPINION **of the French Agency for Food, Environmental** **and Occupational Health & Safety**

on an urgent request to assess certain risks associated with COVID-19

ANSES undertakes independent and pluralistic scientific expert assessments.

ANSES's public health mission involves ensuring 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 9 March 2020 shall prevail.

On 2 March 2020, ANSES received an urgent request from the French Directorate General for Food 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 traced to a seafood and live animal market 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 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, imported cases of COVID-19 from China to other countries were observed from the beginning of the epidemic in Wuhan, and have intensified since mid-February (source: French High Council for Public Health, HCSP).

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:

www.santepubliquefrance.fr). 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, 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 on 6 March 2020 and sent to ANSES's General Directorate.

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).

3. ANALYSIS AND CONCLUSIONS OF THE GECU

1. Potential role of domestic animals in SARS-CoV-2 virus transmission

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

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

Coronaviruses are classified into four genera: alpha (α CoV), beta (β CoV), gamma (γ CoV), and the recently discovered delta (δ CoV) (de Groot *et al.* 2012). They are responsible for infections in multiple species of birds (γ CoV, δ CoV) and mammals (α CoV, β CoV, γ CoV), including human beings. They can cause a wide range of diseases, but mainly affect the respiratory and digestive systems.

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).

Furthermore, *Betacoronaviruses* belong to a viral genus that is 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
Embecovirus	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)	
Sarbecovirus	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)
	Severe acute respiratory syndrome Coronavirus SARS-CoV-2	<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)
Merbecovirus	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)
Hibecovirus	Bat Hp-BetaCoV	<i>Hipposideros pratti</i>	Wu <i>et al.</i> (2016)
Nobecovirus	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 related 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* found in domestic animals.

In light of the above, and based on the phylogenetic analyses undertaken, the experts underline that no viruses belonging to the sub-group of SARS-CoV-2 (*Sarbecovirus*) have been detected in domestic animals (livestock animals or pets) and that there is no direct genetic relationship between SARS-CoV-2 and the strains of *Betacoronavirus* 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 the genome 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 diversification of coronaviruses currently described as “SARS-like” viruses, whose origin probably dates back to the 1990s. Several homologous recombination events between a *Betacoronavirus* in this “SARS-like” group and other *Sarbecovirus Betacoronaviruses* (detected in horseshoe bats and pangolins) seem to have contributed to the current SARS-CoV-2 genome.

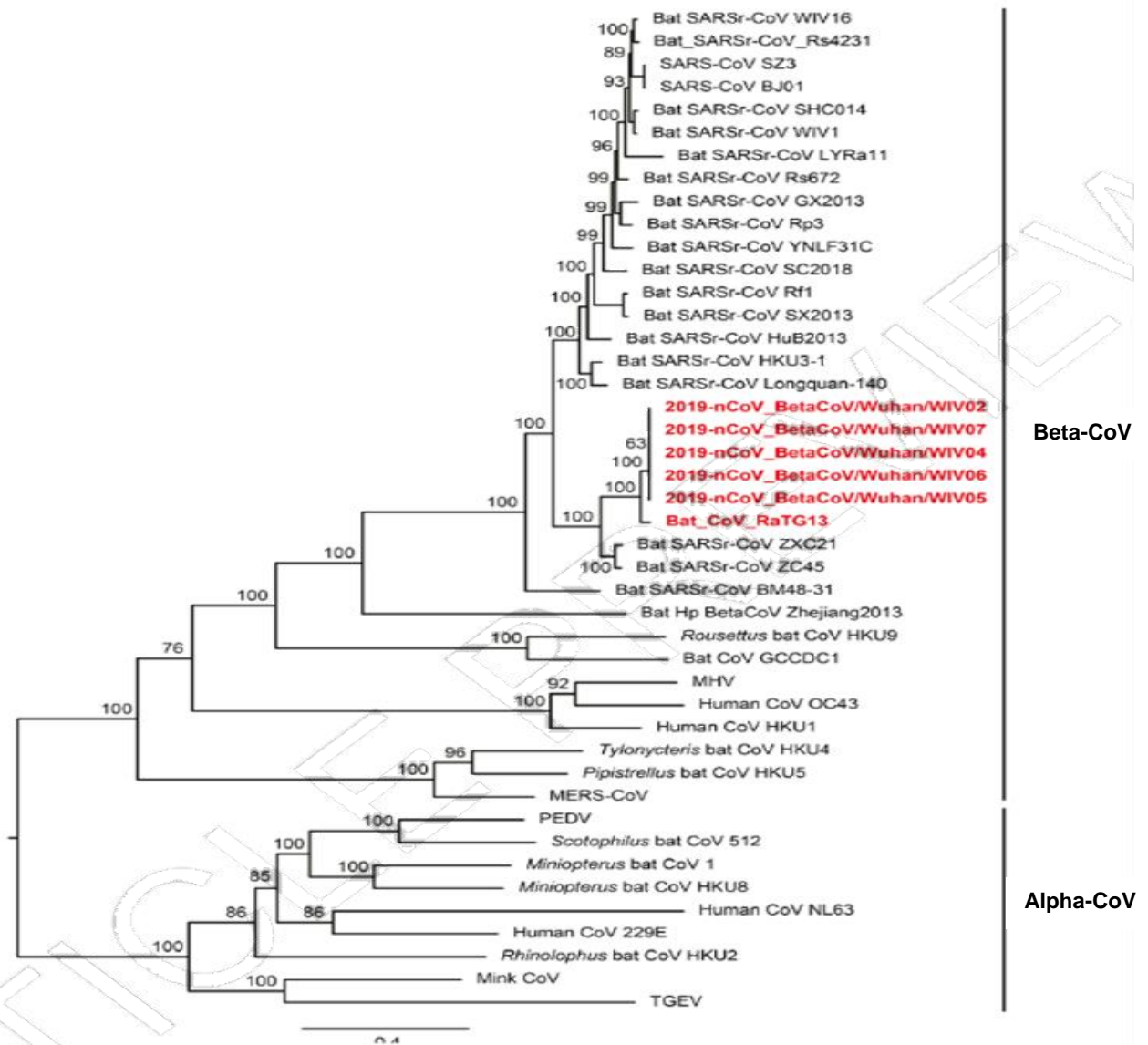


Figure 1: Phylogenetic tree based on the whole genomes of *Alphacoronaviruses* and *Betacoronaviruses* including the novel SARS-CoV-2 (2019-nCoV in red) (Zhou et al. 2020).

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 emergence 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 virus to spread from humans to other animal species in the short term. The experts underline that in light of the current epidemiological situation, SARS-CoV-2 is adapted to humans with effective human-to-human transmission ($R_0 > 1$).

SARS-CoV-2 seems to be of animal origin and probably came from a species of bat, 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 spread of SARS-CoV-2 from human beings to another animal species (domestic in particular) currently seems unlikely.

1.2.2 Animal species deemed susceptible and/or receptive to SARS-CoV-2

With the exception of work on infections undertaken in transgenic mice (Bao *et al.* 2020) expressing the human form of the Angiotensin-Converting Enzyme 2 (ACE2) receptor (the receptor for SARS-CoV and SARS-CoV-2), very few studies have described animals experimentally infected with SARS-CoV-2. Studies are in progress, in particular in Germany¹ and the Netherlands, to study the susceptibility of certain species of livestock animals, including pigs, chickens and cattle, to SARS-CoV-2.

1.2.3 ACE2 receptor

ACE2, the receptor for SARS-CoV-2, 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 are summarised in Table 2.

Table 2: Summary of various studies dealing 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)

¹ In its public note of 5 March, the Friedrich Loeffler Institute (FLI) mentions that the results on this point will not be available before the end of April.

	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 to further knowledge on the possible transmission of infection to other species. However, cross-species transmission 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.

1.3 Case of the dog that tested positive for SARS-CoV-2 in Hong Kong

On 29 February 2020, OIE received an official report from Hong Kong regarding a dog that was placed under quarantine after its owner was hospitalised due to SARS-CoV-2 infection. The animal did not exhibit any specific clinical signs. Three nasal, oral and rectal swabs as well as faecal samples² were collected after the dog was admitted to the quarantine centre. On 26 February, the nasal and oral samples

² Samples taken by two laboratories, one of which was regional and the other national

tested positive for SARS-CoV-2 via RT-PCR. On 28 February, two other nasal and oral samples were taken and tested “weak positive” by RT-PCR. On 2 March, according to the website of Hong Kong's Agriculture, Fisheries and Conservation Department³, new oral and nasal samples were collected. The nasal sample tested “weak positive”. RT-PCR is a test that can only detect viral RNA, and not a living virus. Thus, no evidence of the infectious nature of the samples has been provided to date. Investigations are ongoing to determine whether the animal was infected or whether there was simply external contamination of the nasal cavities. New samples will be collected in the coming weeks.

According to the experts, RNA detection via RT-PCR in the nasal and oral cavities is not sufficient evidence to conclude that the animal was infected. Passive contamination cannot be ruled out. In view of this, the GECU stresses the need to investigate this case further by carrying out additional analyses, and to continue reporting the results to OIE as they are submitted.

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 evidence provided above regarding the potential role of livestock animals in the zoonotic transmission of the virus, the consumption of foodstuffs of animal origin from infected animals was ruled out as a source of infection. Therefore, only the second source of food contamination via a person 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 cases⁴, 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. In addition, proper compliance with

³ According to https://www.afcd.gov.hk/english/publications/publications_press/pr2342.html, consulted on 06/03/2020

⁴ *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) .

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 because 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 control 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 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.

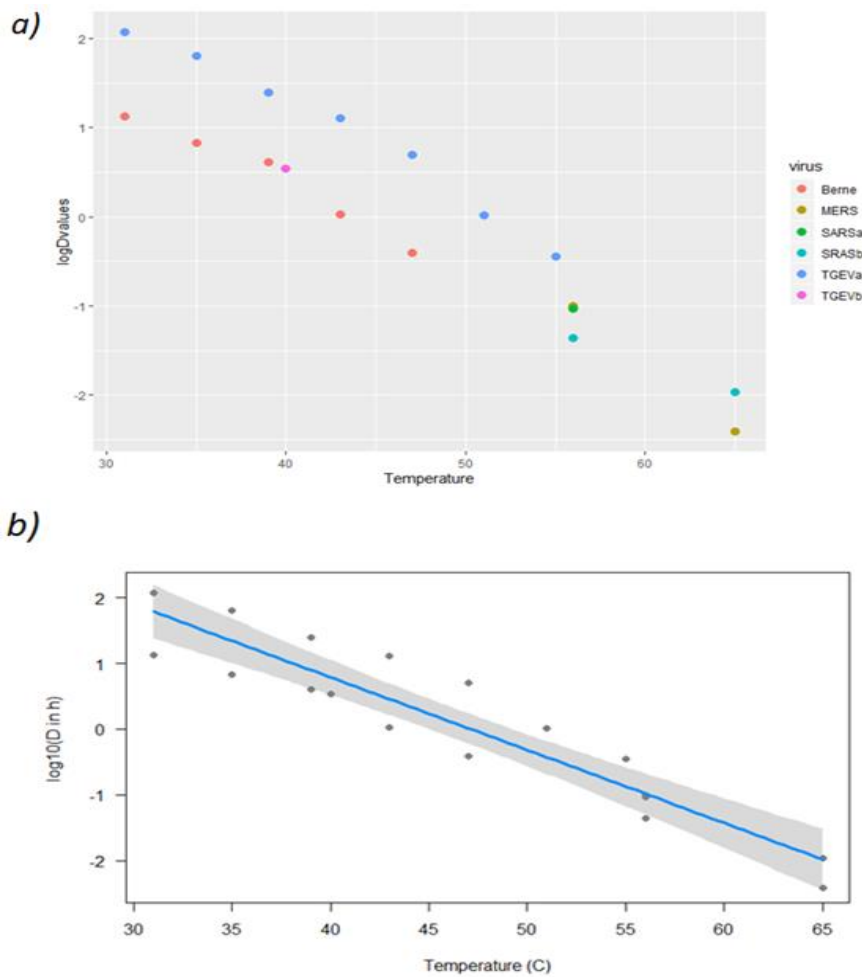
Concerning cooked foods

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 decimal reduction value (D^5) was calculated for each temperature.

Figure 3a below shows the values obtained. A secondary thermal inactivation 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.

⁵ D is the time needed to divide by 10 the initial population of a virus



**Figure 3: (a) Log destruction values (D^6) 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 operator⁷ 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 Dietary 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

⁶ D is the time needed to divide by 10 the initial population of a virus

⁷ 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>

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.

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 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* infecting domestic animals. The epidemiological situation currently observed shows that SARS-CoV-2 is adapted to humans. The spread of SARS-CoV-2 to another animal species (domestic in particular) currently seems unlikely.

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.

Lastly, regarding the specific case of the dog that tested positive for SARS-CoV-2 in Hong Kong, the tests undertaken have only detected viral RNA, not a live virus. Thus, no evidence of the infectious nature

of the samples has been provided to date. Passive contamination of the animal through the oral and nasal cavities cannot be ruled out. Investigations are in progress and the results should be reported to OIE as soon as possible.

In light of the available scientific information (phylogenetics of SARS-CoV-2, epidemiology of COVID-19, *in vitro* studies, etc.), the GECU considers that there is no evidence that domestic animals play a role in the spread of the SARS-CoV-2 virus.

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 food handlers 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” uncertainty⁸ associated with these conclusions, given the limited number of scientific studies on this novel virus. 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 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 Agency endorses the conclusions of the “Covid-19” Emergency Collective Expert Appraisal Group (GECU). In this regard, it stresses the limited number of studies specifically available for this novel *Betacoronavirus*. It notes that these conclusions are consistent with those provided in the communications available to date dealing with these aspects that have yet to be fully investigated (communications of the World Health Organization and World Organisation for Animal Health, and some opinions by health agencies such as the Friedrich Loeffler Institut and BfR). The resulting recommendations are in line with the strict hygiene measures indicated to prevent human-to-human transmission.

⁸ According to ANSES Opinion No 2013-SA-0049

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.

REFERENCES

- Alekseev, K. P., A. N. Vlasova, K. Jung, M. Hasoksuz, X. Zhang, R. Halpin, S. Wang, E. Ghedin, D. Spiro and L. J. Saif. 2008. "Bovine-like coronaviruses isolated from four species of captive wild ruminants are homologous to bovine coronaviruses, based on complete genomic sequences." *Journal of Virology* 82 (24):12422-31. doi: 10.1128/JVI.01586-08.
- ANSES. 2013. "Fiche d'hygiène domestique – saisine 2012-SA-0005."
- ANSES. 2015. "Avis 2013-SA-0089 relatif à une méthode de hiérarchisation des maladies animales exotiques et présentes en France."
- Bao, Linlin, Wei Deng, Baoying Huang, Hong Gao, Jiangning Liu, Lili Ren, Qiang Wei, Pin Yu, Yanfeng Xu, Feifei Qi, Yajin Qu, Fengdi Li, Qi Lv, Wenling Wang, Jing Xue, Shuran Gong, Mingya Liu, Guanpeng Wang, Shunyi Wang, Zhiqi Song, Linna Zhao, Peipei Liu, Li Zhao, Fei Ye, Huijuan Wang, Weimin Zhou, Na Zhu, Wei Zhen, Haisheng Yu, Xiaojuan Zhang, Li Guo, Lan Chen, Conghui Wang, Ying Wang, Xinming Wang, Yan Xiao, Qiangming Sun, Hongqi Liu, Fanli Zhu, Chunxia Ma, Lingmei Yan, Mengli Yang, Jun Han, Wenbo Xu, Wenjie Tan, Xiaozhong Peng, Qi Jin, Guizhen Wu and Chuan Qin. 2020. "The Pathogenicity of SARS-CoV-2 in hACE2 Transgenic Mice." *BioRxiv*:2020.02.07.939389. doi: 10.1101/2020.02.07.939389.
- Bernard Stoecklin, S., P. Rolland, Y. Silue, A. Mailles, C. Campese, A. Simondon, M. Mechain, L. Meurice, M. Nguyen, C. Bassi, E. Yamani, S. Behillil, S. Ismael, D. Nguyen, D. Malvy, F. X. Lescure, S. Georges, C. Lazarus, A. Tabai, M. Stempfelet, V. Enouf, B. Coignard, D. Levy-Bruhl and Team Investigation. 2020. "First cases of coronavirus disease 2019 (COVID-19) in France: surveillance, investigations and control measures, January 2020." *Euro Surveill* 25 (6). doi: 10.2807/1560-7917.Es.2020.25.6.2000094.
- Casanova, Lisa M, Soyoung Jeon, William A Rutala, David J Weber, and Mark D Sobsey. 2010. "Effects of air temperature and relative humidity on coronavirus survival on surfaces." *Applied and Environmental Microbiology* 76 (9):2712-2717.
- Coley, S. E., E. Lavi, S. G. Sawicki, L. Fu, B. Schelle, N. Karl, S. G. Siddell and V. Thiel. 2005. "Recombinant mouse hepatitis virus strain A59 from cloned, full-length cDNA replicates to high titers in vitro and is fully pathogenic in vivo." *J Virol* 79 (5):3097-106. doi: 10.1128/jvi.79.5.3097-3106.2005
- Corman, V. M., R. Kallies, H. Philipps, G. Gopner, M. A. Muller, I. Eckerle, S. Brunink, C. Drosten and J. F. Drexler. 2014. "Characterization of a novel betacoronavirus related to middle East respiratory syndrome coronavirus in European hedgehogs." *J Virol* 88 (1):717-24. doi: 10.1128/jvi.01600-13.
- Danchin, Antoine, Tuen Wai Patrick Ng and Gabriel Turinici. 2020. "A new transmission route for the propagation of the SARS-CoV-2 coronavirus." *Preprint medRxiv*. doi: 10.1101/2020.02.14.20022939.
- Darnell, Miriam ER, Kanta Subbarao, Stephen M Feinstone, and Deborah R Taylor. 2004. "Inactivation of the coronavirus that induces severe acute respiratory syndrome, SARS-CoV." *Journal of Virological Methods* 121 (1):85-91.
- Davis, E., B. R. Rush, J. Cox, B. DeBey and S. Kapil. 2000. "Neonatal enterocolitis associated with coronavirus infection in a foal: A case report." *Journal of Veterinary Diagnostic Investigation* 12 (2):153-156.
- de Groot, Raoul J, SC Baker, R Baric, Luis Enjuanes, AE Gorbalenya, KV Holmes, S Perlman, L Poon, PJM Rottier and PJ Talbot. 2012. "Family coronaviridae." *Virus Taxonomy*:806-28.

- Easterbrook, J. D., J. B. Kaplan, G. E. Glass, J. Watson and S. L. Klein. 2008. "A survey of rodent-borne pathogens carried by wild-caught Norway rats: a potential threat to laboratory rodent colonies." *Lab Anim* 42 (1):92-8. doi: 10.1258/la.2007.06015e.
- Erls, K., C. Toomey, H. W. Brooks and J. Brownlie. 2003. "Detection of a group 2 coronavirus in dogs with canine infectious respiratory disease." *Virology* 310 (2):216-23. doi: 10.1016/s0042-6822(03)00160-0.
- Ferguson, N. M. and M. D. Van Kerkhove. 2014. "Identification of MERS-CoV in dromedary camels." *Lancet Infect Dis* 14 (2):93-4. doi: 10.1016/s1473-3099(13)70691-1.
- Food Safety and Inspection Service, Food and Drug Administration and Animal and Plant Health Inspection Service. 2010. "Interagency Risk Assessment for the Public Health Impact of Highly Pathogenic Avian Influenza Virus in Poultry, Shell Eggs, and Egg Products." Available at: http://www.fsis.usda.gov/wps/wcm/connect/955e7a9a-24f8-4b31-9826-56485c06eab7/HPAI_Risk_Assess_May2010.pdf.
- Fung, To S. and Ding X. Liu. 2014. "Coronavirus infection, ER stress, apoptosis and innate immunity." *Frontiers in Microbiology* 5 (296). doi: 10.3389/fmicb.2014.00296.
- Gao, Q. Y., Y. X. Chen and J. Y. Fang. 2020. "2019 novel coronavirus infection and gastrointestinal tract." *Journal of Digestive Diseases*. doi: 10.1111/1751-2980.12851.
- Greig, A. S., D. Mitchell, A. H. Corner, G. L. Bannister, E. B. Meads and R. J. Julian. 1962. "A Hemagglutinating Virus Producing Encephalomyelitis in Baby Pigs." *Can J Comp Med Vet Sci* 26 (3):49-56.
- Guan, W. J., Z. Y. Ni, Y. Hu, W. H. Liang, C. Q. Ou, J. X. He, L. Liu, H. Shan, C. L. Lei, D. S. C. Hui, B. Du, L. J. Li, G. Zeng, K. Y. Yuen, R. C. Chen, C. L. Tang, T. Wang, P. Y. Chen, J. Xiang, S. Y. Li, J. L. Wang, Z. J. Liang, Y. X. Peng, L. Wei, Y. Liu, Y. H. Hu, P. Peng, J. M. Wang, J. Y. Liu, Z. Chen, G. Li, Z. J. Zheng, S. Q. Qiu, J. Luo, C. J. Ye, S. Y. Zhu, N. S. Zhong and China Medical Treatment Expert Group for Covid-19. 2020. "Clinical Characteristics of Coronavirus Disease 2019 in China." *New England Journal of Medicine*. doi: 10.1056/NEJMoa2002032.
- Hamre, D. and J. Procknow (1966). "A new virus isolated from the human respiratory tract." *Proceedings of the Society for Experimental Biology and Medicine* 121(1): 190-193
- Hasoksuz, M., K. Alekseev, A. Vlasova, X. Zhang, D. Spiro, R. Halpin, S. Wang, E. Ghedin and L. J. Saif. 2007. "Biologic, antigenic, and full-length genomic characterization of a bovine-like coronavirus isolated from a giraffe." *Journal of Virology* 81 (10):4981-90. doi: 10.1128/JVI.02361-06.
- Hoffmann, Markus, Hannah Kleine-Weber, Nadine Krüger, Marcel A Mueller, Christian Drosten and Stefan Pöhlmann. 2020. "The novel coronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells." *BioRxiv*.
- Horzinek, Marian C and Hans Lutz. 2009. "An update on feline infectious peritonitis." *Veterinary Sciences Tomorrow* 2001.
- Hu, D., C. Zhu, L. Ai, T. He, Y. Wang, F. Ye, L. Yang, C. Ding, X. Zhu, R. Lv, J. Zhu, B. Hassan, Y. Feng, W. Tan and C. Wang. 2018. "Genomic characterization and infectivity of a novel SARS-like coronavirus in Chinese bats." *Emerg Microbes Infect* 7 (1):154. doi: 10.1038/s41426-018-0155-5.
- Jin, L., C. K. Cebra, R. J. Baker, D. E. Mattson, S. A. Cohen, D. E. Alvarado and G. F. Rohrmann. 2007. "Analysis of the genome sequence of an alpaca coronavirus." *Virology* 365 (1):198-203. doi: 10.1016/j.virol.2007.03.035.

- Kampf, G., D. Todt, S. Pfaender and E. Steinmann. 2020. "Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents." *Journal of Hospital Infection*. doi: 10.1016/j.jhin.2020.01.022.
- Lau, S. K., P. C. Woo, C. C. Yip, R. Y. Fan, Y. Huang, M. Wang, R. Guo, C. S. Lam, A. K. Tsang, K. K. Lai, K. H. Chan, X. Y. Che, B. J. Zheng and K. Y. Yuen. 2012. "Isolation and characterization of a novel Betacoronavirus subgroup A coronavirus, rabbit coronavirus HKU14, from domestic rabbits." *J Virol* 86 (10):5481-96. doi: 10.1128/jvi.06927-11.
- Laude, H. 1981. "Thermal inactivation studies of a coronavirus, transmissible gastroenteritis virus." *Journal of General Virology* 56 (2):235-240.
- Leclercq, India, Christophe Batejat, Ana M Burguière, and Jean-Claude Manuguerra. 2014. "Heat inactivation of the Middle East respiratory syndrome coronavirus." *Influenza and Other Respiratory Viruses* 8 (5):585-586.
- Li, J. Y., Z. You, Q. Wang, Z. J. Zhou, Y. Qiu, R. Luo and X. Y. Ge. 2020. "The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious diseases in the future." *Microbes Infect.* doi: 10.1016/j.micinf.2020.02.002.
- Miura, T. A., J. Wang, K. V. Holmes and R. J. Mason. 2007. "Rat coronaviruses infect rat alveolar type I epithelial cells and induce expression of CXC chemokines." *Virology* 369 (2):288-98. doi: 10.1016/j.virol.2007.07.030.
- Ong, Sean Wei Xiang, Yian Kim Tan, Po Ying Chia, Tau Hong Lee, Oon Tek Ng, Michelle Su Yen Wong and Kalisvar Marimuthu. 2020. "Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomatic Patient." *JAMA*. doi: 10.1001/jama.2020.3227.
- Paraskevis, Dimitrios, Evangelia Georgia Kostaki, Gkikas Magiorkinis, Georgios Panayiotakopoulos, G Sourvinos and S Tsiodras. 2020. "Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event." *Infection, Genetics and Evolution* 79:104212.
- Poutanen, Susan M, Donald E Low, Bonnie Henry, Sandy Finkelstein, David Rose, Karen Green, Raymond Tellier, Ryan Draker, Dena Adachi and Melissa Ayers. 2003. "Identification of severe acute respiratory syndrome in Canada." *New England Journal of Medicine* 348 (20):1995-2005.
- Rabenau, HF, J Cinatl, B Morgenstern, G Bauer, W Preiser, and HW Doerr. 2005. "Stability and inactivation of SARS coronavirus." *Medical Microbiology and Immunology* 194 (1-2):1-6.
- Rajkhowa, S, C Rajkhowa and GC Hazarika. 2007. "Serological evidence of coronavirus infection in mithuns (*Bos frontalis*) from India."
- Santé publique France. 2020. "Définition de cas d'infection au SARS-CoV-2 (COVID-19) - Updated on 3 Mars 2020."
- van Boheemen, S., M. de Graaf, C. Lauber, T. M. Bestebroer, V. S. Raj, A. M. Zaki, A. D. Osterhaus, B. L. Haagmans, A. E. Gorbalenya, E. J. Snijder and R. A. Fouchier. 2012. "Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans." *mBio* 3 (6). doi: 10.1128/mBio.00473-12.
- Wan, Yushun, Jian Shang, Rachel Graham, Ralph S Baric and Fang Li. 2020. "Receptor recognition by novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS." *Journal of Virology*.
- Weiss, M, and MC Horzinek. 1986. "Resistance of Berne virus to physical and chemical treatment." *Veterinary Microbiology* 11 (1-2):41-49.

- Wentworth, David E and Kathryn V Holmes. 2007. "Coronavirus binding and entry." *Coronaviruses: Molecular and Cellular Biology. Caister Academic Press, Norfolk, United Kingdom*:3-32.
- Woo, P. C., S. K. Lau, C. M. Chu, K. H. Chan, H. W. Tsoi, Y. Huang, B. H. Wong, R. W. Poon, J. J. Cai, W. K. Luk, L. L. Poon, S. S. Wong, Y. Guan, J. S. Peiris and K. Y. Yuen. 2005. "Characterization and complete genome sequence of a novel coronavirus, coronavirus HKU1, from patients with pneumonia." *J Virol* 79 (2):884-95. doi: 10.1128/jvi.79.2.884-895.2005.
- Woo, P. C., S. K. Lau, K. S. Li, R. W. Poon, B. H. Wong, H. W. Tsoi, B. C. Yip, Y. Huang, K. H. Chan and K. Y. Yuen. 2006. "Molecular diversity of coronaviruses in bats." *Virology* 351 (1):180-7. doi: 10.1016/j.virol.2006.02.041.
- Woo, P. C., M. Wang, S. K. Lau, H. Xu, R. W. Poon, R. Guo, B. H. Wong, K. Gao, H. W. Tsoi, Y. Huang, K. S. Li, C. S. Lam, K. H. Chan, B. J. Zheng and K. Y. Yuen. 2007. "Comparative analysis of twelve genomes of three novel group 2c and group 2d coronaviruses reveals unique group and subgroup features." *J Virol* 81 (4):1574-85. doi: 10.1128/jvi.02182-06.
- World Health Organization. 2008. "Viruses in food: scientific advice to support risk management activities: meeting report."
- Wu, Z., L. Yang, X. Ren, J. Zhang, F. Yang, S. Zhang and Q. Jin. 2016. "ORF8-Related Genetic Evidence for Chinese Horseshoe Bats as the Source of Human Severe Acute Respiratory Syndrome Coronavirus." *J Infect Dis* 213 (4):579-83. doi: 10.1093/infdis/jiv476.
- Zaki, A. M., S. van Boheemen, T. M. Bestebroer, A. D. Osterhaus and R. A. Fouchier. 2012. "Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia." *N Engl J Med* 367 (19):1814-20. doi: 10.1056/NEJMoa1211721.
- Zhang, Yong, Cao Chen, Shuangli Zhu, Chang Shu, DonFgyan Wang, Jingdong Song, Yang Song, Wei Zhen, Zijian Feng, Guizhen Wu, Jun Xu and Wenbo Xu. 2020. "Isolation of 2019-nCoV from a Stool Specimen of a Laboratory-Confirmed Case of the Coronavirus Disease 2019 (COVID-19)." *2* (8):123-124.
- Zhou, Peng, Xing-Lou Yang, Xian-Guang Wang, Ben Hu, Lei Zhang, Wei Zhang, Hao-Rui Si, Yan Zhu, Bei Li and Chao-Lin Huang. 2020. "A pneumonia outbreak associated with a new coronavirus of probable bat origin." *Nature*:1-4.

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)

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

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

ANSES PARTICIPATION

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.

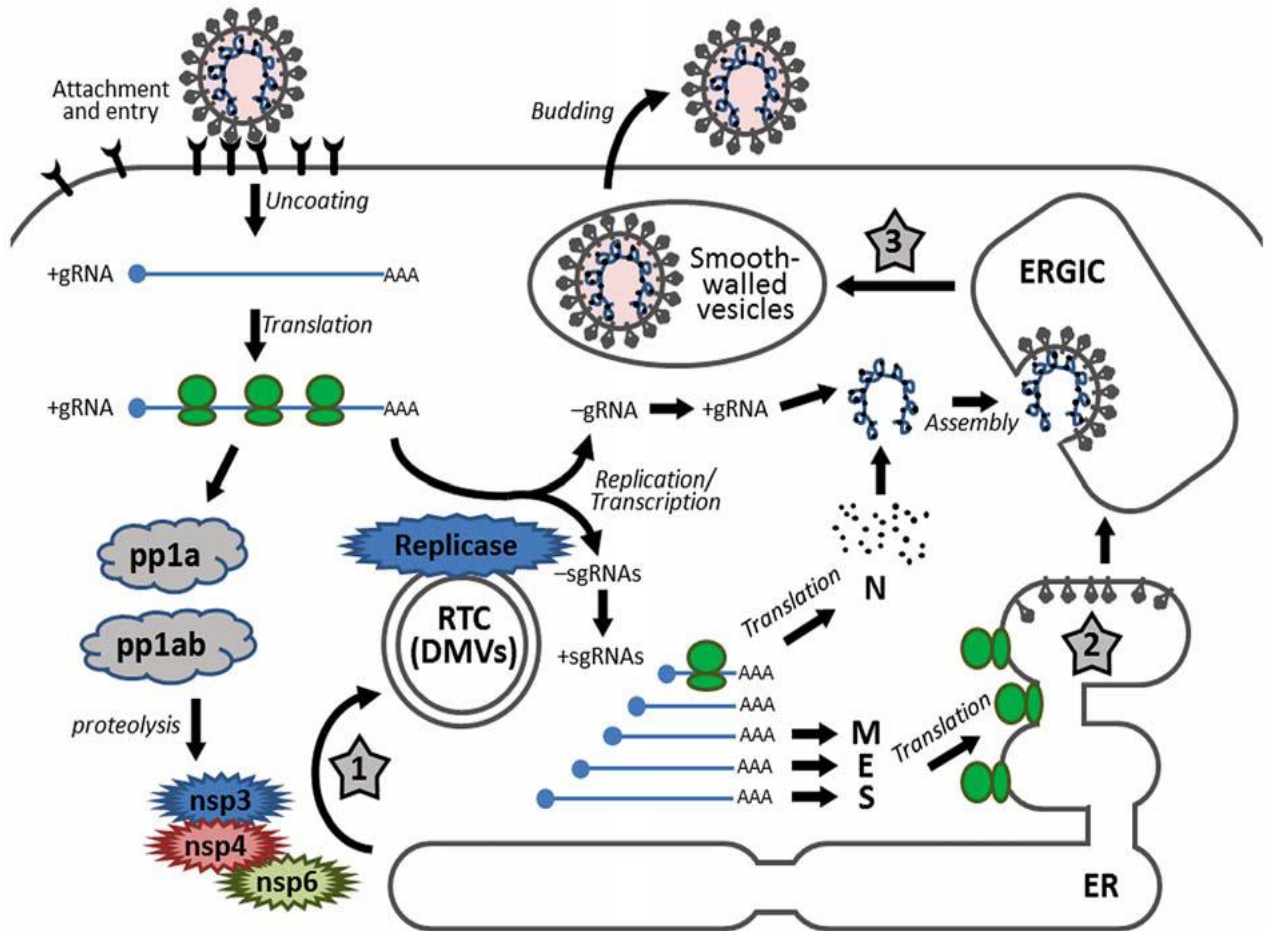
Une réponse de synthèse basée sur les observations épidémiologiques documentées et sur les conclusions du HCSP sur la faible résistance du virus notamment sera un appui suffisant pour cette demande qui vise à obtenir des éléments de réassurance indépendants, face aux questions qui ne vont pas manquer 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
Berne virus	P138/72	Cellular infectivity in EMS cells	31, 35, 39, 43, 47°C	Cell culture supernatant	(Weiss <i>et al.</i> 1986)	Berne
TGEV	D52	Cellular infectivity in RPtg cells	31, 35, 39, 43, 47, 51 and 55°C	In solution at pH 7	(Laude 1981)	TGEVa
TGEV	-	Cellular infectivity in ST cells	40°C	Stainless steel surface with 80% humidity	(Casanova <i>et al.</i> 2010)	TGEVb
SARS-CoV	FFM-1	Cellular infectivity in Vero cells	56°C	Cell culture supernatant without FBS (foetal bovine serum)	(Rabenau <i>et al.</i> 2005)	SARSa
SARS-CoV	Urbani	Cellular infectivity in Vero cells	56, 65°C	DMEM (Dulbecco's modified Eagle's medium)	(Darnell <i>et al.</i> 2004)	SARSb
MERS-CoV	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)

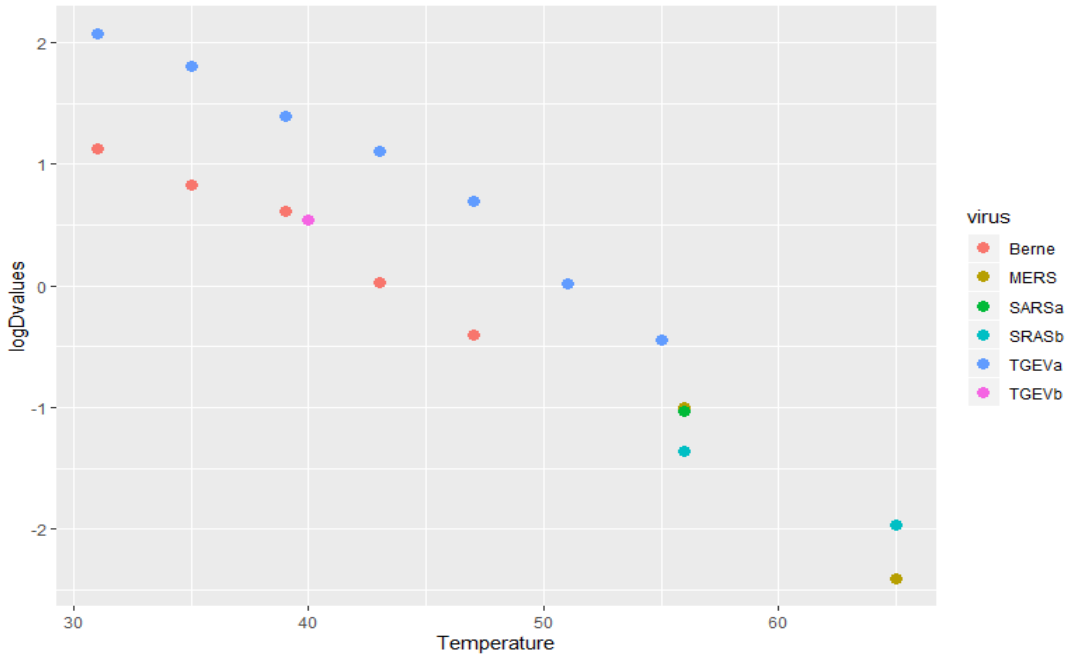


Figure 3(a): Log destruction values (D) observed at various temperatures for viruses of the genus *Coronavirus* (the corresponding studies are set out in the table in Annex 4).

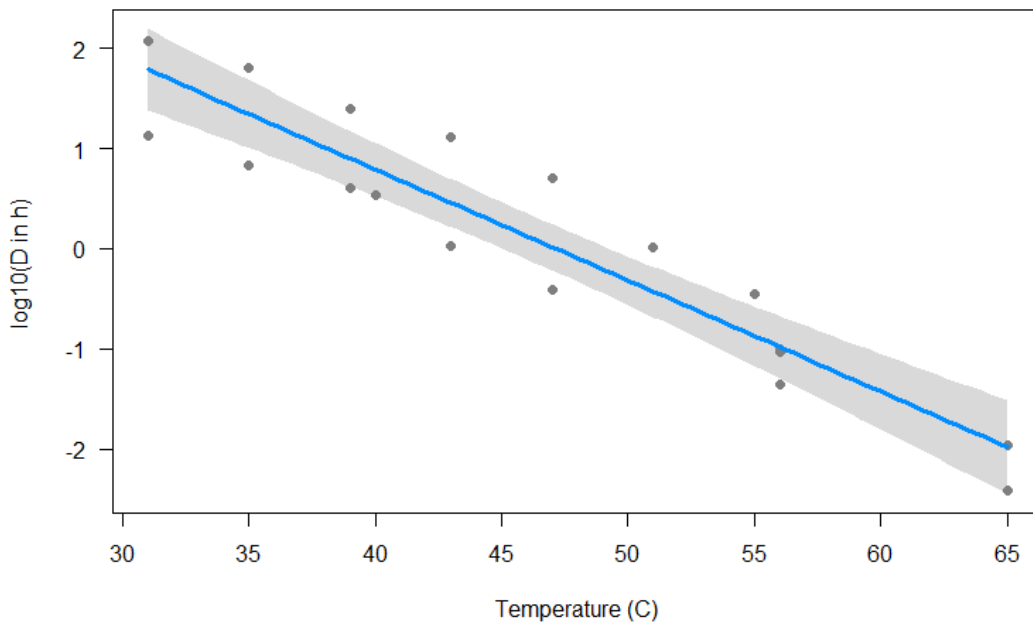


Figure 3(b): Linear model fit to log₁₀(D) according to temperature