ANSES Opinion
Request no. 2022-SA-0110
Related request no. 2022-SA-0102

The Director General

Maisons-Alfort, 24 June 2022

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

on "Recommendations for reducing the risk of transmission of monkeypox virus (MPXV) through the handling and consumption of food"

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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 all necessary information concerning these risks as well as the requisite expertise and scientific 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 published on its website. This opinion is a translation of the original French version.
In the event of any discrepancy or ambiguity the French language text dated 24 June 2022 shall prevail.

On 14 June 2022, ANSES received a request from the Directorate General for Health (DGS) and the Directorate General for Food (DGAL) to carry out the following assessment: recommendations for reducing the risk of transmission of monkeypox virus through the handling and consumption of food.

1 BACKGROUND AND PURPOSE OF THE REQUEST

Monkeypox (MPX) is an infectious disease caused by a virus (Monkeypox virus - MPXV) of the *Poxviridae* family and the *Orthopoxvirus* genus, an enveloped DNA virus. In France, infections by this virus are subject to permanent surveillance through the mandatory reporting system.

French Agency for Food, Environmental and Occupational Health & Safety
14 rue Pierre et Marie Curie 94701 Maisons-Alfort Cedex - France
Tél +33 (0)1 49 77 13 50 — www.anses.fr

Since the beginning of May 2022, numerous local cases of monkeypox virus (MPXV) infection have been reported in several non-endemic countries. The first case of Monkeypox virus infection in France was confirmed on 19 May 2022 in the Île-de-France region[1].

As of 21 June 2022, 2,746 human cases have been confirmed in the European Union/European Economic Area (EU/EEA)[2]. As of 22 June, 3,308 confirmed cases worldwide have been reported in 42 countries, including 426 cases outside the EU/EEA[3]. In France, as of 23 June 2022, 330 cases of Monkeypox have been confirmed[4]. 52 of the 287 cases investigated by Santé publique France, the French public health agency, are secondary cases. To date, in Europe, these cases have occurred without any history of contact with an animal imported from an endemic and enzootic zone, in persons who do not report having travelled to an area where the virus usually circulates, and in the context of an outbreak with only human-to-human transmission to date.

ANSES was asked for the first time on 3 June 2022 about recommendations for reducing the risk of dissemination of the monkeypox virus to animals in France (request no. 2022-SA-0102).

In this second request, ANSES is asked to assess the risk of transmission of MPXV through food during its handling and consumption, and to issue recommendations for this risk.

2 ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with the French standard NF X 50-110 "Quality in Expert Appraisals - General requirements of Competence for Expert Appraisals (May 2003)".

The collective expert appraisal was carried out by the emergency collective expert appraisal group (GECU) "Monkeypox - Food".

The GECU held an emergency meeting to address the request, and adopted its conclusions on 20 June 2022. Based on these conclusions, a draft of the GECU's analysis and conclusions was prepared by the Scientific Coordination team, which was reviewed and validated by the GECU electronically on 23 and 24 June 2022.

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

The experts' declarations of interests are made public via the website: https://dpi.sante.gouv.fr/

A systematic literature search was conducted on the PubMed database, queried by pairing the terms "monkeypox" or "monkey pox" with terms related to food or food transmission[5]. This first search was conducted on 10 June 2022 and identified 30 references. The references were exported to EndNote and were selected on the basis of the following inclusion criteria: study

[1] https://www.santepubliquefrance.fr/presse/2022/un-premier-cas-confirme-de-monkeypox-sur-le-territoire-national
[2] https://www.ecdc.europa.eu/en/monkeypox-outbreak
[3] https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html
[4] https://www.santepubliquefrance.fr/les-actualites/2022/cas-de-variole-du-singe-point-de-situation-au-23-juin-2022
[5] Food-related and food transmission terms: "*bread, dairy products, eggs, fast foods, flour, fruit, meal, meat, raw foods, salads, vegetables, food, digestive tropism, gastrointestinal, intestine, digestive, feces, stool, fecal*" Hyperlink to PubMed query

on MPXV, description of cases with suspicion or evidence of transmission through food, lesion or replication in the digestive system.

This initial bibliographical search was supplemented by searching other databases (Scopus), other keywords or combinations such as "*pox and food"*, "*monkeypox and bushmeat",* etc.), by the "snowball" method and by elements of the grey literature (reports, scientific communications, etc.).

The following elements were taken into account in carrying out this assessment:

- the request;
- the elements of the expert opinion of the request no. 2022-SA-0102 (Anses 2022);
- the bibliographic data listed in this expert opinion.

3 ANALYSIS AND CONCLUSIONS OF THE EMERGENCY COLLECTIVE EXPERT APPRAISAL GROUP

3.1 Overview of Monkeypox Disease (MPX)

3.1.1 Monkeypox virus and disease in humans

Monkeypox (MPX) is an infectious disease caused by a virus (Monkeypox virus - MPXV) of the family *Poxviridae* (poxvirus) and the genus *Orthopoxvirus*, an enveloped DNA virus.

Monkeypox virus infection is a localised or systemic infection, which may be associated with fever, headache, body aches and asthenia. The vesicular rash may be present at the beginning, may appear after the general signs, or may be isolated. One or more flare-ups may be observed. The initial papular lesions most often evolve into vesicular forms, followed by drying, crusting and then scarring after the crusts fall off. Scarring may sometimes occur before vesicles form. The bullous lesions are mostly concentrated on the face, palms and soles of the feet. The mucous membranes are also affected (mouth or ano-genital region). Ano-genital lesions are the most frequent in this non-African outbreak[6] .

The incubation period of the disease is estimated to be 5-21 days. The fever phase lasts about 1 to 3 days. The disease is usually mild and usually clears spontaneously after 2 to 3 weeks. A sick person is contagious as soon as symptoms appear and until the injured skin has completely healed. Transmission in the absence of symptoms has never been documented (Grant *et al.* 2020).

Poxviridae are characterised by a marked tissue tropism for skin and mucous membranes. MPXV can be transmitted directly, through skin or mucosal contact with an infected individual, as well as through droplets contaminated by mucosal lesions (saliva, sneezes, sputum, kissing, etc.). The May 2022 outbreak also assumes transmission through intimate and sexual contact, but transmission through seminal fluid or semen has not been established to date (Otu *et al.* 2022).

[6] https://www.santepubliquefrance.fr/presse/2022/un-premier-cas-confirme-de-monkeypox-sur-le-territoire-national

Another direct transmission route for MPXV is the respiratory route, which is also known for variola virus (VARV) and other poxviruses (Diaz 2021). There is possible maternal-foetal-perinatal transmission with severe forms in the newborn (Mbala *et al.* 2017).

MPXV can also be transmitted indirectly via the environment contaminated by the patient (bedding, clothing, crockery, bathroom linen, etc.). Thus, the first local case identified in 2018 in the United Kingdom involved a care assistant who was most likely contaminated by the bed sheets of a patient with MPX (Aisling Vaughan *et al.* 2020). Adler *et al.* (2022) also mention three cases in a family cluster in the UK. A systematic review suggests a secondary attack rate of about 8% (range 0-11%) in unvaccinated household contacts (Beer and Rao 2019).

Complications may occur: skin superinfection, keratitis in the case of ocular lesions, pulmonary, digestive and neurological damage, and generalised infection, which can result in death.

3.2 Top-down assessment: evidence of foodborne cases of Monkeypox virus (MPXV) infection in humans (bushmeat)

Analysis of the various MPX outbreaks has identified two sources of infection for humans: animal and human. Outbreaks are classically initiated from an animal source and are followed by human-to-human transmission (Bunge *et al.* 2022). In both situations, a vehicle for transmission may be the ingestion of meat from a contaminated animal.

Contact with animal reservoir(s) and/or intermediate animal hosts (some sciurids, other rodents, or other species, see Annex 2), alive or dead, often during hunting and preparation of bushmeat as food, is a presumed mode of infection with MPXV (Durski *et al.* 2018).

There is very little evidence linking the preparation or consumption of the food to the onset of the disease (Simpson *et al.* 2020) but several studies suggest that contamination through ingestion of meat from infected animals is possible (Reynolds *et al.* 2019; Yong *et al.* 2020).

Appendix 3 lists cases or outbreaks where the role of contaminated food was suspected. This list was compiled from two systematic reviews (Brown and Leggat 2016; Bunge *et al.* 2022) and literature searches conducted by the GECU. From 1970 to June 2022, 20 outbreaks were identified with possible transmission through contaminated food. Analysis of these data shows that no food, other than bushmeat, has been identified or suspected to be associated with human cases of MPX (Annex 3). In the majority of the studies listed, it is difficult to distinguish the vehicle of contamination, as people may be contaminated by handling dead animals and/or by eating their meat.

None of these references provided robust information to support the possibility of proven foodborne transmission of MPXV, nor its presence in foods other than bushmeat. It can therefore be concluded that foods other than bushmeat have never been identified as being associated with human cases of Monkeypox in any of the reported outbreaks.

However, ingestion of contaminated food cannot be excluded as an exposure route in natural infections, although this has never been directly observed.

3.3 Bottom-up assessment of the risk of Monkeypox virus transmission through food

The GECU adopted a similar approach to that applied by EFSA in the bottom-up risk assessment of a zoonotic virus (European Food Safety Authority 2014). The approach is

shown in Figure 1 and summarises the series of steps required for a single case of MPX to occur from food (other than bushmeat) contaminated with MPXV.

The required chain of events involves many barriers: 1) the raw food must be naturally contaminated with MPXV or contaminated by a food handler; 2) the food must contain viable virus when it reaches the consumer; 3) the person must be exposed to the virus (orally or by contact); and 4) the person must be infected after exposure. The different stages of this pathway are described below. It should be noted that all steps are necessary; if the answer to any of the questions in any of the steps is "no", the probability of the MPX case occurring is zero.

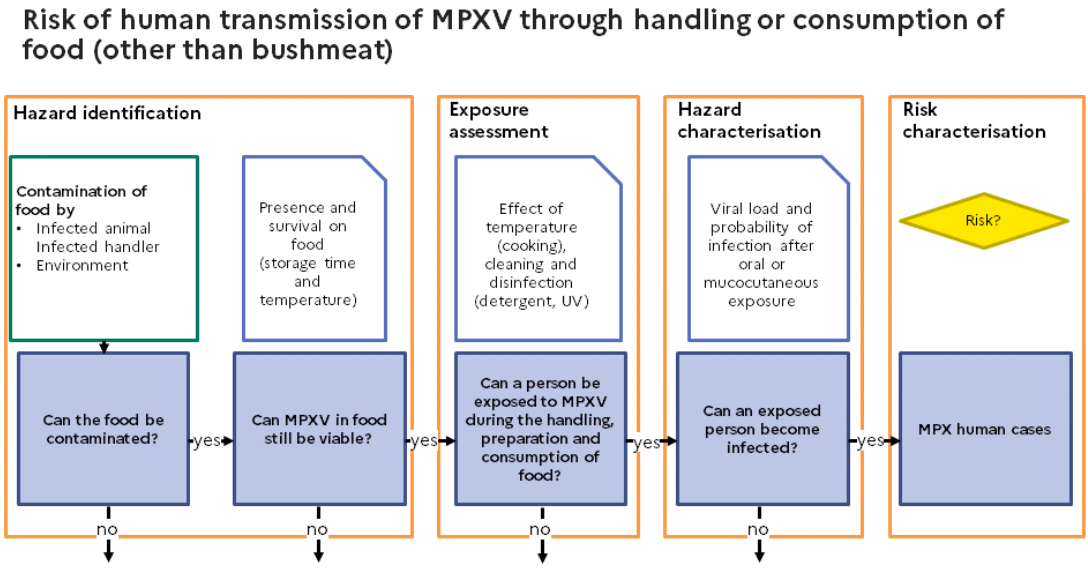

Figure 1. Bottom-up risk assessment approach used to answer the request question.

3.3.1 Potential sources of food contamination with MPXV

The first step in hazard identification is the possibility of food contamination. Food produced in areas where MPXV is circulating (either in wildlife or in the human population, or both) could be contaminated in several ways: at source (infected animal), from the environment (effluent, wildlife), or by an operator processing or preparing food.

3.3.1.1 Food produced from an infected animal

The analysis of the cases (Annex 3) showed that some cases of MPX are attributed to the consumption of wild animals. It is therefore possible that bushmeat may be naturally contaminated with MPXV.

In France, bushmeat consumption is based on illegal introduction. Illegal importation of food of animal origin is either a deliberate or an unintentional act. Illegal imports of small quantities by individuals may be for personal use, while larger quantities could be distributed by retailers or sold in markets for commercial purposes (Jansen *et al.* 2019). Border controls reduce the illegal inflow of food of animal origin into the EU, but cannot totally prevent it. Several studies have shown that among illegally imported food of animal origin, meat from animals that are potential reservoirs of zoonotic viruses was sometimes identified (Bair-Brake *et al.* 2014; Beutlich *et al.* 2015; Smith *et al.* 2012).

Based on 1) the limited number of suspected MPX outbreaks to date in endemic and enzootic areas (Annex 3) (despite the common consumption of bushmeat); 2) the handling of bushmeat in France, which does not involve high-risk practices (such as hunting and butchering (Chastel and Charmot 2004)); 3) preparation techniques (such as long cooking times); and 4) the assumed low overall consumption of bushmeat in France, the GECU experts assume that the potential for introduction and transmission of MPXV through bushmeat in France is currently very low. A better knowledge of the data associated with the importation of bushmeat into France (species involved, geographical origin and volume of bushmeat imported into France) could improve the estimation of this risk.

In the case of livestock, a limited study involved 120 small ruminants in an agroforestry setting where the virus and/or anti-MPXV antibodies had been detected in humans and squirrels, with negative results (Khodakevich *et al.* 1988).

With regard to cattle, the state of knowledge according to Haddad (2022) shows a lack of experimental data on MPXV susceptibility and sensitivity in ruminants, as well as on infection under natural conditions. Therefore, ruminants are to be considered as a hypothetical source of transmission in case of infection.

Rabbits have been shown to be subcutaneously susceptible while recovering if they are adults, except in one study of albino rabbits, in which swelling occurred at the site of inoculation, followed seven days later by a rash with progression to death (Parker and Buller 2013). Newborn rabbits are particularly susceptible to infection. However, no data on the infection of lagomorphs with MPXV under natural conditions are available.

In the absence of knowledge about transmission to livestock, it is recommended to apply preventive measures: sick humans should avoid contact with animals. If this is not possible, personal protective equipment is essential. To limit the possible transfer of MPXV to animals, it is worth recalling that kitchen and table waste (peelings and other food scraps produced during meal preparation, and leftovers from plates after consumption) are considered to be a category 3 animal by-products. Therefore, they cannot be fed directly to animals without treatment (Regulation (EC) No. 1069/2009 Article 10).

Based on current knowledge, the possibility of contamination of food of animal origin from an infected animal has been excluded.

3.3.1.2 Operator processing or preparing a food

In the context of this request, which concerns a virus actively circulating in human populations, one of the potential sources identified is the contamination of food by infected food handlers. It would then be possible for an infected and symptomatic operator involved in food processing or preparation to contaminate food with MPXV. This food could be offered for sale and consumed.

The risk of transmission would depend on the stage of human disease in the infected food handler. Transmission is considered negligible before the onset of symptoms (Grant *et al.* 2020). Prolonged but low-level exposure could result in infection without visible clinical signs (M. G. Reynolds *et al.* 2010).

In humans, the highest levels of viral shedding are found in vesicles and dry scabs, although the amount of virus shed by sick people varies. During this outbreak, initial diagnostic information from recent cases has shown Ct[7] of 20-32 (i.e. $10^{8.3}$ to $10^{5.3}$ genome copies/ml or $10^{6.6}$ to $10^{3.6}$ PFU/ml[8]), in skin lesion samples and in oral and nasopharyngeal samples, confirming shedding via the nasal and oropharyngeal routes.

In the crab-eating macaque, viral loads in blood increase rapidly during the course of the disease, from 10^3 to 10^8 genomes/g of tissue within 14 days (Jordan *et al.* 2009). Although viral loads in lesions are higher than in lesion-free skin, the latter still has high genome loads (Table 1). This was also found in goats infected with a *Capripoxvirus* (a different genus of virus in the *Poxviridae* family) (Bowden *et al.* 2008). In control macaques exposed to 10^6 and 10^7 PFU of MPXV intratracheally, viral loads in throat swabs increased rapidly, reaching peak levels at day 11, with loads of approximately 10^3 PFU/ml (Stittelaar *et al.* 2005).

Recently, the MPXV genome has been detected in the stools of patients (Antinori *et al.* 2022), which may suggest faecal shedding. Patrono *et al.* (2020) have already observed such shedding in chimpanzees in a natural infection situation.

Table 1. Viral loads in tissues or secretions of animals infected with two different *Poxviridae* (MPXV and GTPV)

Species	Infecting strain Exposure Measures	Tissue / matrix	Tissue load	Reference
Crab-eating macaque (*Macaca fascicularis*)	MPXV - Zaire 79 Intravenous Dose: $5x10^7$ PFU Measurement 3 days after infection	Blood	$1.1x10^4$ genomes/g tissue	(Jordan *et al.* 2009)
		Skin - Lesion	$1.4x10^7$ genomes/g tissue	
		Skin - Normal	$1.5x10^6$ genomes/g tissue	
	Dose: 10^6 PFU	Throat swab	< 3 log_{10} PFU/ml	(Stittelaar *et al.* 2005)
	Dose: 10^7 PFU		~3 log_{10} PFU/ml	
Goat	*Capripoxvirus* (Indian GTPV) Intradermal Dose $10^{4.4}$ $TCID_{50}$ Measurements between 4 and 13 days after inoculation (control animals)	Skin - Normal	Between 2.7 and 4.4 log_{10} $TCID_{50}$/g	(Bowden *et al.* 2008)
		Skin - Lesion (Macule)	< 2.7 log_{10} $TCID_{50}$/g	
		Skin - Lesion (Papule)	Between 5.2 and > 7.2 log_{10} $TCID_{50}$/g	
		Nasal mucosa	Between < 2.7 and 3.2 log_{10} $TCID_{50}$/g	

Contamination of foods by a sick food handler cannot be excluded. A human shedding the virus may contaminate food by contact with soiled hands (e.g. in the presence of lesions) or in the case of poor hygiene practices (oro- or nasopharyngeal excretion). Possible faecal contamination with MPXV cannot be excluded.

The GECU experts point out that there is a lack of data on the viral loads shed by different tissues, and that in view of the data in animals, there is uncertainty about shedding through the skin of a sick human without visible lesions. The lack of knowledge about possible shedding of MPXV in pre- or post-symptomatic individuals, and the possible existence of asymptomatic cases, are also limitations to this analysis.

[7] The Ct value is a relative measure of the concentration of the viral target. It corresponds to the number of qPCR cycles required to reach a threshold. Thus, Ct values are inversely proportional to viral loads.

[8] PFU: plaque-forming unit

3.3.1.3 Environment

A study showed that MPXV genetic material could be found in the regurgitation/defecation products of flies that landed or fed on the faeces of naturally infected chimpanzees (including one sample with infectious virus) (Patrono *et al.* 2020).

The good hygiene practices usually in place (insect and pest control) are sufficient to avoid theoretical contamination of food from this source.

The GECU experts assume that contamination of the environment (in the food industry, catering industry or at home) can only occur through shedding by infected persons, especially through contact with lesions, scabs and nasal or oropharyngeal secretions.

3.3.1.4 Conclusion on sources of food contamination by MPXV

Based on current knowledge, the possible contamination of food of animal origin from an infected animal has been excluded. The usual pest control measures (insects, rodents) are able to control the very hypothetical risk of contamination of the environment and food by insects.

Contamination of food by a sick food handler cannot be excluded. A human shedding the virus can contaminate food by contact with soiled hands (e.g. in the presence of lesions) or in the case of poor hygiene practices (oral or nasopharyngeal excretions). The GECU experts do not exclude the possibility of faecal contamination in the event of insufficient hand hygiene.

Environmental contamination in the food industry or catering industry can only occur through infected persons (e.g. through scabs and oral or nasopharyngeal secretions). Confirmed cases must self-isolate at home, and may be given time off work for a period of 3 weeks from the date of onset of clinical signs[9] .

The GECU experts recall that good hygiene practices in food processing or catering imply that people with infected skin symptoms (lesions, skin disease) or symptoms of gastroenteritis should not handle food (DILA 2015). In the current context, any person with symptoms suggestive of MPX[10] (including lesions, papules etc.) should not handle food, should consult a medical/healthcare professional and be tested[11], and in the event of a positive result should follow the current recommendations.

In its opinion of 24 May 2022, the French High Council for Public Health (HCSP) states that contacts are considered to be free of infection in the absence of symptoms (Haut Conseil de la Santé Publique 2022). The experts of the GECU consider that contact persons working in the restaurant or food industry should be made aware of the symptoms suggestive of MPX and should be advised to follow the current recommendations issued by the HCSP.

New knowledge on the quantification of viral loads shed by symptomatic persons without lesions, and on the possible shedding of MPXV in presymptomatic, asymptomatic and post-

[9] See case definitions: https://www.santepubliquefrance.fr/media/files/maladies-a-declaration-obligatoire/definition-de-cas-cat-monkeypox

[10] See link https://www.coreb.infectiologie.com/UserFiles/File/monkeypox/fichedermatomkp-v9-juin22.pdf

symptomatic persons, could extend the scope of these recommendations to infected persons without lesions who are in contact with food.

3.3.2 Presence and survival of MPXV in food

The presence and survival of MPXV in food depends on the location of the virus (surface or internal), the initial viral load and the storage conditions.

No information is available on the potential of MPXV to survive on the surface or inside food. There are no quantitative data on the initial viral loads of MPXV that could be found in food (see section 3.3.1). In 2003, supported by epidemiological analyses, the CDC assumed that MPXV could remain infectious in bushmeat (Food and Drug Administration & Centers for Disease Control and Prevention 2003).

Regarding storage conditions, MPXV remains stable under refrigerated conditions (4°C) in laboratory media. By extrapolation, MPXV could remain viable in contaminated food stored under refrigeration.

In the absence of data on the survival of MPXV in food, the survival of other viruses of the *Poxviridae* family was explored.

3.3.2.1 Survival of other viruses of the Poxviridae family in food matrices

Data on several viruses of the *Poxviridae* family show that infectious viruses remain stable over long periods at refrigeration temperatures. Essbauer *et al.* (2007) characterised the survival of *vaccinia virus* (VACV) and *variola virus* (VARV) in several food matrices (bread, sausage and salad). Both viruses showed stable infectivity over 166 days at 4.5°C.

In milk, VACV remains stable in milk after 48 h of storage at 4°C (De Oliveira *et al.* 2010). In cheeses, it was shown that this virus was partially inactivated during ripening, but infectious viruses were found in cheeses even after 60 days of ripening (Rehfeld *et al.* 2017). De Oliveira *et al.* (2010) showed that freezing did not affect the infectivity of the viruses (milk samples at - 20°C).

Data on *sheep pox virus* (SPPV) and *goat pox virus* (GTPV) show that they are stable under freezing conditions (ILSI Europe Expert Group on Animal-Borne Viruses 2009).

Thus, some of the examples presented above suggest the presence and survival of *Poxviridae* in foods after storage. The persistence of viruses depends on their location (surface or internal), initial viral load and storage conditions (e.g. duration, temperature or exposure to ultraviolet radiation from sunlight). In addition, upstream food preparation steps (e.g. peeling, rinsing) could also influence virus survival in the food or finished product.

In conclusion, the initial viral loads of MPXV that could be found on food are not known. Data on individual viruses of the *Poxviridae* family show that they can remain stable in several food matrices under refrigeration conditions (4°C).

3.3.3 Exposure assessment

This stage concerns the survival of MPXV during the preparation of dishes made with contaminated food, as well as exposure to MPXV (probability and number of infectious viruses by contact or ingested), during handling and preparation (both by consumers and staff handling food in kitchens immediately prior to consumption), as well as through the consumption of contaminated food.

There are no data on MPXV to answer this question. However, it is likely that the survival of the virus depends on how and for how long food is transported and stored, how it is handled, and how the food is prepared. With regard to the latter, adequate cooking should inactivate MPXV, but good hygiene practices should be applied to avoid recontamination after cooking (by a sick food handler). Conversely, MPXV could survive in products consumed without further cooking (i.e. leafy vegetables eaten raw). Certain practices, such as drying/dehydration, washing or peeling of fruits and vegetables, could also reduce the degree of exposure to MPXV. In addition, the risk of cross-contamination should be taken into account.

In the absence of data on MPXV, the GECU experts reviewed the available data on the *Poxviridae* family.

3.3.3.1 Heat treatment efficiency

Analysis of the scientific literature identified several studies quantifying the impact of temperature on the inactivation of *Poxviridae* (Annex 4). The raw data from these studies were digitised and the decimal reduction values (D) (i.e. the time required to divide the infectious load by 10) were adjusted for 36 kinetics over a temperature range of 30-65°C. Figure 2 shows the 36 values of $\log_{10}$(D) as a function of temperature.

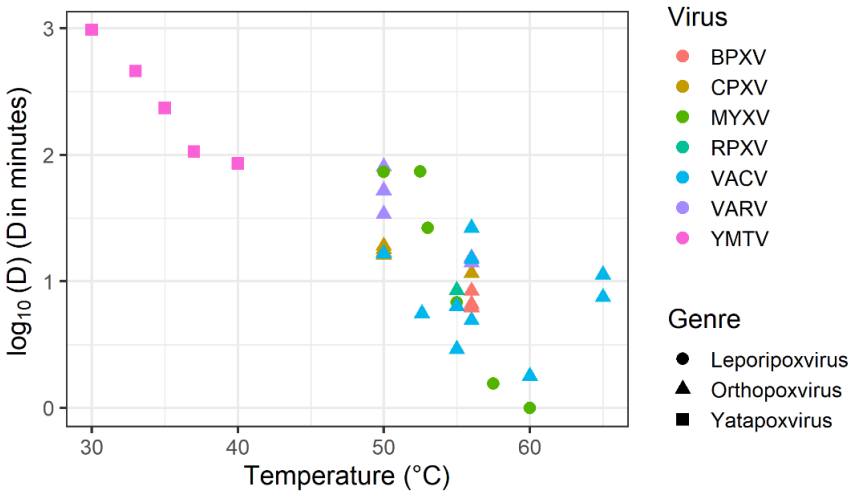

Figure 2. Overview of data on decimal reduction values (D) observed at different temperatures for three genera of viruses of the *Poxviridae* family. *The associated studies are detailed in the table in Annex 4. Example of reading: for Yatapoxvirus (YMTV, pink square symbol), at a temperature of 40°C, a duration of 2 $\log_{10}$ min (i.e. 100 minutes) is required to reduce the infectious load of the virus by a factor of 10.*

Figure 3 shows the fit of the secondary decimal reduction time model (Bigelow model). It quantifies the impact of temperature on the D values. The fitted parameter values predict the inactivation of viruses of this family for different temperatures.

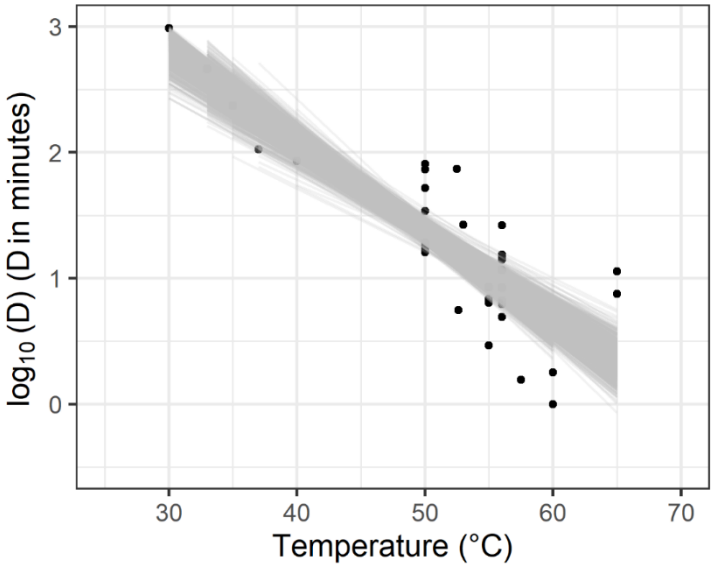

Figure 3. Observed (dots) and fitted Bigelow model (grey lines corresponding to bootstrap resampling) values of decimal reduction time (logarithmic scale in minutes) as a function of temperature for viruses belonging to the *Poxviridae* family.

For a targeted performance criterion, i.e. the definition of a number of decimal reductions to be achieved, it is possible from the developed model to specify the time-temperature pair to be applied to achieve the target. Table 2 provides several examples of time-temperature pairs that achieve a 4-6 log_{10} reduction in viruses belonging to the *Poxviridae*.

Table 2. Time required (in minutes) at different temperatures to achieve decimal reduction targets of 4-6 log_{10}. Values were calculated from the Bigelow secondary model with log_{10} D70=0.287 and Z=14.9°C

Temperature	4 log_{10}	5 log_{10}	6 log_{10}
50°C	169 min	211 min	253 min
65°C	16.8 min	20.9 min	25.1 min
70°C	7.8 min	9.7 min	11.6 min
80°C	1.7 min	2.1 min	2.5 min

3.3.3.2 Efficiency of other processes

Enveloped viruses are among the easiest to inactivate, as detergents damage their lipid envelope. *Poxviridae are* sensitive to common disinfectants. ECDC[12] states that cleaning can be done with ordinary products, followed by disinfection with sodium hypochlorite (NaClO) solution[13] (*European Centre for Disease Prevention and Control 2022)*.

In its opinion of 24 May 2022, the HCSP specifies several recommendations concerning hand hygiene and cleaning procedures. For surfaces, standard household cleaners/disinfectants can be used in accordance with the manufacturer's instructions. Regarding utensils, it is specified that dishes and other kitchen utensils should not be shared. It is not necessary for the infected person to use dedicated utensils if they are properly washed, either in a

[12] European Centre for Disease Prevention and Control
[13] For example, by diluting 1:25 using household bleach (usually at an initial concentration of 2.6% in France)

dishwasher or by hand with warm water and detergent (Haut Conseil de la Santé Publique 2022).

The usual measures for cleaning and disinfecting equipment and premises (especially hygiene rooms for staff) are effective against MPXV when the doses and action times required to achieve virucidal activity are applied.

The GECU experts point out that some materials that may come into contact with sick people may be difficult to clean and disinfect (e.g. leather gloves for handling hot serving dishes), and are likely to be used by several people. It is therefore recommended that these materials not be used. They can be replaced by materials that can be easily machine washed or soaked in disinfectant solutions (e.g. cloths, silicone potholders).

Washing utensils and dishes in a dishwasher (> 60°C) and clothes in a washing machine (> 60°C) will eliminate the virus.

In addition, and in general, UV has an effective virucidal action on food-borne viruses: it alters their genetic material. UV treatment of clear liquids (or opaque liquids in turbulent flow) is particularly effective. For solid foods, the irregularity of the surface limits inactivation (Gómez-López *et al.* 2021). Regarding the effectiveness of UV, *Orthopoxviruses* are very sensitive to UV light (Centers for Disease Control and Prevention 2022).

3.3.3.3 Conclusions on exposure assessment

In conclusion, cooking (12 minutes at 70°C[14]) could be considered effective in inactivating MPXV in food. Thus, contaminated food that has not had sufficient heat treatment (temperature and duration) or that is cooked but not protected against recontamination after cooking may be a source of exposure. Cleaning and disinfection procedures, if properly applied, can be considered sufficient to limit cross-contamination through surfaces.

3.3.4 Hazard characterisation and tropisms of MPXV

This step assesses the probability of a person becoming infected as a result of preparing or handling contaminated food or eating a meal prepared with such food.

The most susceptible populations, i.e. those with a higher than average probability of developing symptoms or severe clinical forms of MPX after exposure to MPXV, are immunocompromised individuals, pregnant women and young children (Santé publique France 2022; Jezek *et al.* 1986; Doshi *et al.* 2019). Children are known to have more severe forms than adults (Huhn *et al.* 2005; Nakoune *et al.* 2017). This higher susceptibility of neonates and young people is found in animals experimentally infected with MPXV (Parker and Buller 2013).

In the literature, the secondary attack rate (or the probability of transmitting MPXV to people living with an infected person) is in the order of 10%, with no indication of the exposure routes

[14] Or any other value equivalent to the 6 $\log_{10}$ reduction shown in Table 2

involved (Beer and Rao 2019). The GECU experts consider that this secondary attack rate is probably not applicable to the current outbreak.

In this section, the oral route of exposure (the primary route of exposure in the case of contamination by food) will be considered. The mucocutaneous route of exposure will also be considered, thus treating the food as an inert surface.

3.3.4.1 Route of exposure through the digestive system

While bushmeat is mentioned in investigations of MPX cases, the digestive tropism of MPXV is not clearly established. The GECU experts' analysis of the literature shows that viable or replicating virus particles can be found in the digestive tract of sick humans or infected animals with or without clinical signs (Table 3).

Table 3 - Identification of viable or replicating virus particles in tissues, organs or matrices of the digestive system in sick humans or naturally infected animals (with or without clinical signs)

Species	Tissues or samples from the digestive system	Description	Year	Reference
Human	Liver	9-month-old girl with various symptoms including hepatosplenomegaly, diarrhoea, vomiting. Post-mortem analysis of the liver and spleen by electron microscopy showed huge amounts of mature virus particles in the cytoplasm and intercellular spaces of the liver (no virus-free liver cells could be detected, and different stages of morphogenesis were observed, indicating virus replication). Virus particles were also present in the spleen. MPXV was isolated from these tissues by Vero cell culture.	1987	(Müller *et al.* 1988)
Chimpanzee *(Pan troglodytes verus)*	Faecal matter	Viral DNA was detected in 12.6% of the faeces of 19 individuals (7 symptomatic, 12 asymptomatic); viable viral particles (Vero cell) were found in one sample (out of 10 analysed), suggesting that faeces could be a source of infectious MPXV.	2020	(Patrono *et al.* 2020)
Prairie dog (*Cynomys* sp.)	Mouth, trachea, lips, tongue, oesophagus, stomach, intestine, colon, liver, kidney	Lesions in the digestive system included oral ulcers and multifocal plaques in the gastrointestinal wall, numerous ulcers of varying size on the tongue, tongue surface and on the hard palate. Multifocal necrotic lesions were also present in the trachea, lips, tongue, oesophagus, stomach, jejunum, cecum, colon, liver and kidneys. Ultrastructural examination of the intestine revealed aggregates of mature, non-enveloped, free-living virus particles in the cytoplasm of scattered degenerative cells.	2004	(Langohr *et al.* 2004)

More generally, in patients, lesions may appear on the tissues of the digestive system. For example, Meyer *et al.* (2002) reported lesions in the mouths of three children (1, 8 and 9 years) and one adult. In the context of the re-emergence of MPXV in 2017, oral ulcers are mentioned in about 36% of the 122 cases between 2017 and 2018 (Yinka-Ogunleye *et al.* 2019). Patients sometimes mention specific symptoms of the digestive system. In the 2003 US outbreak, patients presented with gastrointestinal symptoms (Huhn *et al.* 2005). In the current outbreak (May-June 2022), gastrointestinal symptoms are not particularly mentioned[15].

Lesions in the digestive system have been specifically reported in experimental studies of MPXV inoculation in animals. A review of natural and experimental infections in animals between 1958 and 2012 was conducted by Parker and Buller (2013). Clinical signs related to the digestive system are mentioned after intravenous inoculation in rhesus macaques (*Macaca mulatta*). Lesions were found in various tissues of the digestive system, notably in the crab-eating macaque (*Macaca fascicularis*), in the stomach, intestine or liver, after exposure by

[15] based on data from Santé publique France and information at https://www.santepubliquefrance.fr/les-actualites/2022/cas-de-variole-du-singe-point-de-situation-au-21-juin-2022

aerosol, or in the stomach, small intestine, colon, rectum and liver after subcutaneous exposure.

In addition to this review, the GECU also identified additional experimental studies in rodents that also show lesions in the digestive system (Table 4).

Table 4 - References to lesions in the digestive system in experimental rodent inoculation studies with MPXV

Species	Exposure	Comment	Year	Reference
Black-tailed prairie dog (*Cynomys ludovicianus*)	Intranasal route MPXV WA strain (MPXV-USA-2003-044) Dose: $4.3x10^4$ PFU/10 µL; 5 µL per nostril	*In vivo* pathogenesis was characterised by imaging. MPXV was visualised in several organs, including the tongue, spleen, stomach, kidney, bladder, small and large intestine.	2019	(Weiner *et al.* 2019)
African rope squirrel (*Funisciurus* sp.)	Intranasal (IN) and intradermal (ID) Central African MPXV strain Dose 10 µL to 10^6 PFU	Viral replication and shedding monitored by *in vivo* bioluminescent imaging, viral culture and real-time PCR, viability by TCID50/Vero cells Viral replication in the oral and nasal areas (up to 18^{th} day pi.) Multiple histological lesions including some on the lips and tongue. No MPXV-related lesions were observed in the liver, small and large intestine, or pancreas	2017	(Falendysz *et al.* 2017)

A few experimental studies have also investigated the inoculation of animals with MPXV by the oral route (Table 5). Guinea pigs, golden hamsters and adult rabbits did not show any apparent signs of disease. Rabbits, white mice and common squirrels developed signs of disease with up to 100% lethality.

Table 5 - Experimental studies of MPXV inoculation in animals by the oral route (from Hutson and Damon (2010))

Species	Exposure	Comment	Year	Reference
Guinea pig	Strain: MPXV Copenhagen Unknown dose	Orally, guinea pigs, despite high doses of virus, show no apparent signs of disease (lack of sensitivity).	1976	(Marennikova and Seluhina 1976)
Golden hamster	Strain: MPX Copenhagen Dose: 1.5 - $5.7x10^7$ PFU / 2 mL	Orally, golden hamsters, despite high doses of virus, show no apparent signs of disease (lack of sensitivity).		
Rabbit	Strain: MPXV Copenhagen Dose: $1.4x10^9$ PFU / 2 mL	Adult rabbits showed no observable signs of disease after oral administration of MPXV (whereas acute disease and a generalised rash were observed intravenously). Ten-day-old rabbits infected with a virus dose of approximately 10^6 -10^7 PFU per ml developed an acute generalised illness with rash.		
White mice	Strain: MPXV Copenhagen Unknown dose	Twelve-day-old mice infected *per os* were ill and died in 14% of cases.		
Common squirrel (*Sciurus vulgaris*)	Strain: MPXV Z-249 Dose: 10^6 PFU	Disease occurred earlier in animals infected orally or intranasally than in those infected by scarification. Infection was lethal in 100% of cases at 7-8 days after infection, regardless of the route of inoculation.	1989	(Marennikova *et al.* 1989)

When contaminated food is ingested and enters the gastrointestinal tract, MPXV should be inactivated by the acidic pH of the stomach. The effect of acidic conditions on the stability of

MPXV was tested: a decrease of the order of 4 $\log_{10}$ was reported in tissue cultures at pH 2 ($<10^1$ PFU/ml compared to $3.5x10^5$ PFU/ml at pH 7) (Rouhandeh *et al.* 1967). The pH of the stomach may vary depending on the presence or absence of food intake. Food may nevertheless provide protection against inactivation of the virus by gastric acids.

The evidence presented above suggests a possible spread of MPXV in the different organs of the digestive system in animals. It is not possible to quantitatively characterise the hazard of oral exposure to MPXV (lack of data such as the viral load shed by sick people or the initial load introduced in food, or lack of knowledge of the dose-response[16] by the oral route). Data suggesting a digestive tropism of MPXV in humans are scarce, however the GECU experts do not exclude the possibility of oral transmission of MPXV.

3.3.4.2 Exposure through mucocutaneous contact

Epidemiological evidence suggests that human-to-human transmission is based on mucocutaneous tropism following direct contact with the skin (which may include microlesions) or mucosal sites as entry points for initiating infection in humans.

Epidemiological observations show that MPXV can be transmitted indirectly via objects contaminated by the patient (such as bedding, clothing, dishes, bath towels, etc.). In view of the elements presented above, contaminated food can be equated to inanimate surfaces. This concerns in particular prepared food (raw or undercooked), or cooked food that may have been contaminated by an operator or consumer who fails to comply with good hygiene practices.

ECDC recommends avoiding sharing any household items with others. If total isolation is not possible, then good hygiene practices should be rigorously applied: MPXV is able to survive on surfaces or other fomites for long periods (days to months) (European Centre for Disease Prevention and Control 2022).

Based on the current state of knowledge, the GECU experts cannot exclude transmission of the virus through food contaminated with MPXV via the mucosal route.

The experts underline a lack of data that prevents characterisation of the hazard by cutaneous exposure, in particular with regard to the viral load shed by sick people, the initial viral load on surfaces in contact with the sick persons (and in food in particular) or the dose-response[18] by the cutaneous route. Outside the context of food preparation, these elements are essential to assess transmission indirectly, through inert surfaces.

The GECU experts emphasise the need to insist on the application of the control measures and good hygiene practices mentioned above to limit contamination of food during preparation (see elements of Section 3.3.1).

[16] For a given effect, the relationship between the dose and the response, i.e. the probability of the effect occurring, in the population

3.3.4.3 Conclusion on hazard characterisation

In conclusion, when humans ingest raw food contaminated with MPXV, it is possible that infection is initiated by contact of the virus with oropharyngeal tissues, depending on the amount of infectious virus absorbed, and the presence of pre-existing mucosal lesions.

However, the GECU experts point out that other routes of infection (skin, mucous membranes, etc.) appear to be much more effective than the oral route.

The experts also emphasise that there is a lack of data to better characterise the hazard by oral or dermal exposure. In particular, the dose-response relationship[18] of MPXV by the oral route is not known.

3.3.5 Risk characterisation

The purpose of this step is to estimate the probability of at least one human case of MPXV infection occurring in France due to its transmission through contaminated food (other than bushmeat). The scope of the assessment was limited to the risk of transmission of MPXV to humans resulting from the handling and preparation (by consumers or food handlers immediately prior to consumption) and consumption of contaminated food for which cases of MPXV infection have been confirmed.

The lack of data and knowledge at all stages of the bottom-up assessment leads to a very high degree of uncertainty, the sources of which are summarised in Table 6. For example, it is not possible to estimate the risk of foodborne transmission of MPXV through consumption of these foods, or even whether this mode of transmission can occur.

Table 6 - Analysis of sources of uncertainty in the steps of the bottom-up risk assessment of MPXV transmission through food

Risk assessment phase	Sources of uncertainty	Choice made	Information available explaining the choice	Magnitude of impact on outcome (minor, strong or unqualifiable)	Direction (over/ underestimated or unqualifiable)
Potential sources of food contamination	Transmission via a food vehicle is not proven but only suspected. The viral loads shed by a sick person are unknown. Unknown information on possible pre- or post-symptomatic shedding. Uncertainty about the presence of asymptomatic people	The GECU considered that MPXV was potentially transmissible through food, despite the lack of evidence to this effect	Annex 3 lists studies that suggest the possible foodborne transmission of MPXV	Strong	Overestimation
Exposure assessment	Lack of specific data on the behaviour of MPXV (on the new strain in particular) in food (under food storage or preparation conditions).	The GECU explored data on other viruses belonging to the family *Poxviridae*	In microbiological risk assessment, it is usual to consider data from micro-organisms similar to the one being assessed	Not quantifiable	Not quantifiable
Hazard characterisation	No dose-response relationship available for MPXV by oral or mucocutaneous routes	The GECU pointed out the available data on MPXV that showed an oral exposure hazard.	Experimental studies listed in section 3.3.4	Strong	Not quantifiable
Risk characterisation		The GECU remained with a qualitative risk assessment	Impact of the other three components of the risk assessment	Strong	Overestimation

However, the expert opinion reveals that there is no evidence to support the mode of infection with MPXV through food: in humans, no cases have been documented apart from suspicions linked to the consumption of bushmeat.

The chain of events required (Figure 1) to arrive at a case has many conditions:

1) the food must be contaminated with MPXV;
2) the food must contain viable virus when it reaches the handler or consumer;
3) the person must be exposed to the virus and;
4) the person must be infected after exposure.

Each of these steps is necessary for a case of disease to occur.

If foodborne transmission of MPXV were to be confirmed in the future, the risk of becoming infected with the MPXV through handling or consumption of contaminated food would be considered higher if food were produced or consumed under conditions that increase the likelihood of contamination, for example:

- sick MPXV-shedding personnel who handle or prepare food;
- poor hygiene practices;
- contact with MPXV-contaminated bushmeat and/or known susceptible species;
- plants harvested in areas inhabited by infected and shedding wild animals;
- consumption of raw or undercooked contaminated food, and in particular for vegetables, if unwashed or unpeeled;
- storage times and temperatures favourable to the survival of the virus along the food chain.

However, a few measures and the application of good hygiene practices can preventively limit contamination of food in food-production areas or at home (see Table 7).

Table 7 - Examples of preventive measures according to different scenarios of MPXV contamination of foods in France

Scenario	Probability of the scenario	Preventive measures
Contamination of foods from an infected wild animal (bushmeat)	Possible	Bushmeat import ban
Contamination of foods from an infected production animal in France (passage from human to production animal).	Unlikely	Confirmed cases, especially persons working in contact with animals on farms, should not have contact with animals while they are symptomatic (isolation, sick leave, notifiable disease) Raise awareness among contact persons working with animals and presenting with symptoms suggestive of MPX
Contamination of foods by symptomatic infected staff (waiters, cooks, caterers, butchers, pastry cooks, cheese makers, food industry staff, maintenance workers in this sector, etc.)	Possible	Confirmed and probable cases in the kitchen or food industry must not be in contact with food or the food production environment (isolation, sick leave, notifiable disease) Raise awareness among contacts with symptoms suggestive of MPX Medical staff should pay attention to confirmed cases and contact persons working in catering and food industries (suggestion to update the COREB* sheet) For suspected cases, contacts, or undiagnosed persons, good hygiene practices (hand hygiene, wearing masks and gloves when handling food, use of non-shared utensils, cleaning and disinfection of equipment and premises, and pest control) can limit the risk of transmission. Cooking (e.g. 70°C, 12 min) destroys the MPXV. Targeted information for kitchen staff, particularly those working in nurseries and classes for young children, should be provided by the public authorities (departmental directorates for the protection of the population (DDPP), training organisations, analysis laboratories) (suggestion to update the COREB* sheet). Kitchen and table waste[17] must be disposed of in accordance with the regulations. It is forbidden to feed this waste to animals.
Contamination of food by a symptomatic infected person (preparation and consumption at home or consumption of meals outside)		Confirmed cases should isolate themselves (no communal meals) They should avoid preparing meals for other people and should preferably arrange for a replacement. If this is not possible, extra vigilance is needed on hand hygiene, wearing masks and gloves, and clothing that covers lesions. Prefer individual portions and limit self-service. Do not touch food with your hands and use utensils for serving. Dishes and other kitchen utensils should not be shared, and should be washed thoroughly (dishwasher or by hand with warm water and detergent) Kitchen and table waste[9] must be disposed of in accordance with the regulations. It is forbidden to feed this waste to animals.

* COREB: Operational coordination of epidemic and biological risk

3.3.6 Conclusions of the GECU Monkeypox - Food

In this assessment, the 'top-down' (the episode monitoring approach) and 'bottom-up' (following the agent through the food chain to assess the risk to human health) approaches were combined.

The conclusions of the top-down and bottom-up approaches are consistent and suggest that the risk of transmission of MPXV through food (other than bushmeat) is still only hypothetical and that such an occurrence has never been reported. Thus, the relationship between food consumption and MPX transmission has never been demonstrated. Nevertheless, the GECU experts draw attention to the lack of data to quantitatively assess the risk of MPXV transmission through food.

[17] Kitchen and table waste refers to the peelings and scraps of food produced during meal preparation, as well as the "leftovers" on plates after consumption.

The "top-down" approach first concluded that bushmeat was suspected as a source of MPXV in human cases of MPX. Food (other than bushmeat) has never been identified as being associated with human cases of MPX in any of the recorded cases.

The "bottom-up" approach then concluded that the chain of events required for a human case to become ill after handling or consuming food involves several conditions, namely that 1) the raw food is contaminated with MPXV; 2) the food contains viable virus when it reaches the handler or consumer; 3) the person is exposed to the virus; and 4) the person is infected after exposure.

The GECU experts recall that the isolation measures for confirmed human cases, as well as the application of good hygiene practices, decrease the probability of occurrence of these conditions favouring the transmission of MPXV through food. Cooking (*e.g.* 12 min at 70°C) could be considered effective in inactivating MPXV in food.

Due to the lack of data and knowledge, which leads to a very high degree of uncertainty, it is not possible to quantify the risk of MXPV transmission from handling or eating contaminated food. New scientific facts, which will add to the knowledge about this virus, may change this uncertainty.

It is also emphasised that good hygiene practices in the restaurant or food industry are also based on the health status of the operators. Anyone who is ill should be aware of the importance of not handling food if they have symptoms of gastroenteritis (diarrhoea, fever, vomiting, headache) but also of any case of infected skin symptoms (lesions, skin disease, etc.). In the current context of the MPX outbreak, raising awareness of symptoms suggestive of MPX among contact persons working in the catering and food industry could limit the initial contamination of the food.

4 AGENCY CONCLUSIONS AND RECOMMENDATIONS

The French Agency for Food, Environmental and Occupational Health & Safety endorses the conclusions of the GECU "Monkeypox - Food".

The risk of transmission of the monkeypox virus through food, although never observed to date (except for bushmeat from contaminated animals), cannot be excluded. Limiting this risk requires both individual and collective measures.

Anyone who is ill should be aware of the importance of not handling food intended for others if they have symptoms of gastroenteritis (diarrhoea, fever, vomiting, headache) and, in the current context, symptoms suggestive of Monkeypox. Contact persons should be particularly vigilant about the appearance of any symptoms in order to limit the transmission of the virus, including through the handling of foods that could be consumed by a third person. On this point, it would appear necessary to raise awareness among employers and employees in the restaurant and food-processing sector, with the support of the prevention and occupational health services or preventive medicine services, so that everyone can implement their obligations under the provisions of the French Labour Code, and so that appropriate preventive measures can be put in place.

Given the persistence of *Poxviridae* in the environment but their high sensitivity to common detergents and disinfectants, the application of good hygiene, cleaning and disinfection practices for equipment and premises is sufficient to limit contamination in environments that may have been frequented by infected persons.

This expert appraisal has shown the need to acquire data useful for assessing the risk of transmission of the Monkeypox virus, in particular through foods. The acquisition of these data is based in particular on experimental studies requiring the use of the virus under appropriate safety conditions.

Dr Roger Genet

KEYWORDS

Monkeypox (MPX), virus Monkeypox (MPXV), denrées alimentaires, aliments, transmission, recommandations

Monkeypox, Monkeypox virus, food, transmission, recommendations

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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 "MONKEYPOX – FOOD"

Chair

Ms Nadia HADDAD - Professor, Alfort National Veterinary School - Regulated diseases, epidemiology, zoonoses

Members

Mr Stéphane BERTAGNOLI - Professor, Toulouse National Veterinary School - Virology, Poxvirus, research, laboratory diagnosis

Mr Mickaël BONI - French Armed Forces Biomedical Research Institute (IRBA), Chief Veterinary Officer - Head of Unit - Microbiology, Hygiene, Food Safety and Quality, Food and Water Safety, Food Safety Inspection, Treatment and Sanitary Control of drinking water

Mr Olivier FERRARIS - *Institut de recherche biomédicale des armées*, Researcher in charge of analysis, metrology and quality at the Orthopoxivirus national centre of reference - Biology, infectiology, virology, Orthopoxivirus

Ms Alexandra MAILLES - Epidemiologist in charge of the project concerning the surveillance and investigation of zoonosis outbreaks, emerging diseases in Enteric, Foodborne and Zoonotic Diseases Unit, *Santé publique France* - Epidemiology, surveillance, zoonoses

Mr Jean-Claude MANUGUERRA - Research Director, Head of the Laboratory for Urgent Response to Biological Threats (CIBU), Head of the Infectious and Environmental Risks Unit, Director of the OIE Collaborating Centre. Institut Pasteur - Virology, emerging pathogens, MPX, infectious diseases

Ms Sandra MARTIN-LATIL - ANSES, Laboratory for Food Safety, Scientific Project Leader - Virology, detection methods.

ANSES PARTICIPATION

The scientific coordination of the project was led by the Food Risk Assessment Unit (UERALIM) under the supervision of Ms Hélène GAYON (head of the unit).

Coordination and scientific contribution

Ms Estelle CHAIX - Scientific Coordinator - Food Risk Assessment Unit - Risk Assessment Department

Scientific contribution

Mr Laurent GUILLIER - Scientific Project Leader - Food Risk Assessment Unit - Risk Assessment Department

Administrative Secretariat

Ms Angélique LAURENT - Risk Assessment Department

ANNEX 2

Table 8 - List of possible animal host species for MPXV (non-exhaustive) according to Silva *et al.* (2021).

Order/Family	Species	Investigation method *	Association with human infection
Primates/ *Hominidae*	Human (*Homo sapiens*)	Viral isolation	Exp. infec.
	Orangutan (*Pongo pygmaeus*)	Viral isolation	Exp. infec.
	Chimpanzee (*Pan troglodytes*)	Viral isolation	not
Primates/ *Cercopithecidae*	Sooty mangabey *(Cercocebus atys*)	PCR/ Viral isolation	not
	Crab-eating macaque (*Macaca fascicularis*)	Viral isolation	Exp. infec.
Primates/ *Callithrichidae*	White-tufted marmoset (*Callithrix jacchus*)	Exp. infec.	not
Rodents/*Chinchillidae*	Rabbit (*Oryctolagus cuniculus*)	Exp. infec.	not
Rodents/*Muridae*	Inbred mice (*Mus musculus*)	Exp. infec.	not
Rodents/*Cricetidae*	Hamster	Exp. infec.	not
Rodents/*Nesomyidae*	Giant-pouched rat (*Cricetomys* sp.)	PCR/ Viral isolation	not
Rodents/*Gliridae*	African dormice (*Graphiurus* sp.)	PCR/ Viral isolation	not
Rodents/*Sciuridae*	Rope squirrel (*Funisciurus* sp.)	PCR/ Viral isolation	Exp. infec.
	Black-tailed prairie dog (*Cynomys ludovicianus*)	PCR	Exp. infec.
	Woodchuck (*Marmota monax*)	PCR/ Viral isolation	not
Rodents/ *Dipodidae*	Jerboa (*Jaculus* sp.)	PCR/ Viral isolation	not
Rodents/*Hystricidae*	Porcupine (*Atherurus africanus*)	PCR/ Viral isolation	not
Pilosa/*Macroscelididae*	Ant-eater (*Myrmecophaga tridactyla*)	Viral isolation	not
Didelphimorphs/ *Didelphidae*	Southern opossum (*Didelphis marsupialis*)	PCR/ Viral isolation	not
	Short-tailed opossum (*Monodelphis domestica*)	PCR/ Viral isolation	not
Erinaceomorphs / *Erinaceidae*	African hedgehog (*Atelerix* sp.)	PCR/ Viral isolation	not

- * Method of investigation: viral infection demonstrated by molecular test (PCR) or viral isolation using samples obtained from naturally infected animals;
- Exp. infec.: Susceptibility to infection by MPXV has been observed in experimental laboratory studies.
- ** Transmission to humans already reported in the literature.

ANNEX 3

Table 9 - List of outbreaks in which food consumption was suspected. All references identify only bushmeat consumption.

Country	Year	Mode of transmission	Reference
Liberia	1970	No evidence of consumption, mention of a case of MPX in a child (9 years) who occasionally consumes monkey.	(Foster *et al.* 1972)
Liberia	2017	Suspected consumption: two cases of MPX, one confirmed and one suspected. The confirmed case was an 8-year-old boy. His mother (one suspect/primary case) was a farmer married to a hunter. There was no clear information that the mother had been exposed to bushmeat. The mother and her child had not travelled outside their area of residence.	(Larway *et al.* 2021)
Nigeria	2017-2018	Of the 122 confirmed cases, 2 patients reported contact with an unspecified wild animal and also reported eating bushmeat.	(Yinka-Ogunleye *et al.* 2019)
Nigeria	2017	A total of 172 suspected and 61 laboratory-confirmed cases were reported from 14 states in Nigeria. The authors state that MPX in Nigeria may be linked to a lack of food safety and hygiene, as most people who consume wild animal meat as a "delicacy" have little knowledge of the virus (especially of hygienic meat preparation methods).	(Okareh and Morakinyo 2018)
Central African Republic	1984	In a Pygmy community, 6 cases in two families: five children and a young woman. The head of the family had hunted a monkey with pustules on its body, and an antelope with the same type of lesions, whose flesh had been shared between the different families of the clan.	(Chastel and Charmot 2004)
Central African Republic	2001	The authors report an episode (2 cases) observed in a family a few days after eating a dead monkey	(Nakouné and Kazanji 2012)
Central African Republic	2010	Two cases where lesions developed after hunting and eating a wild rodent	(Berthet *et al.* 2011)
Central African Republic	2016	The index case was a hunter and breeder. The consumption of squirrel meat (*Xerus erythropus*) found dead in the forest could be the source of contamination.	(Kalthan *et al.* 2018)
Democratic Republic of Congo	2011-2012	Of the three cases: - Case 1 also noted contact with bushmeat before the onset of the disease. - Case 2 handled monkeys killed by local hunters and stored and ate monkey meat for his trip.	(McCollum *et al.* 2014)
Democratic Republic of Congo	2014-2015	The index cases of the two outbreaks investigated had consumed bushmeat. The index cases had consumed meat from river hog (*Potamochoerus porcus)* and duiker *(Cephalophus).* For both species, the presence of MPXV was characterised in animals collected in the region.	(Laudisoit *et al.* 2016)
Democratic Republic of Congo	1983	Five cases (two of which allegedly ate a monkey and a Gambian rat) and their respective families.	(Jezek *et al.* 1986)
Democratic Republic of Congo	2001	The identified source of infection of 4 cases may have been a monkey found dead in the forest that was handled and eaten by the family members concerned	(Meyer *et al.* 2002)

Table 9 (continued)

Country	Year	Mode of transmission	Reference
Democratic Republic of Congo	2017	22 cases with three distinct clusters (Eyelle, Dongou and Impfondo). In the Impfondo district, the first case was preparing bushmeat. The other three were family members.	(Doshi *et al.* 2019)
Democratic Republic of Congo	2017	Risk factors determined by the study of two population groups, following an analysis of questionnaires (n=39) The authors indicate that populations frequently reporting risk factors for MPX, such as hunting and butchering of bushmeat and frequent contact with wildlife, are more exposed to sylvatic zoonoses than the general population (IgM antigenic comparison).	(Guagliardo *et al.* 2020)
Sierra Leone	1970	No evidence of consumption, mention of one case of MPX (24 years old) who occasionally consumes monkey.	(Foster *et al.* 1972)
Sierra Leone	2014	1 case (child) with no identity contact with people with monkeypox-like illness or animals in the two weeks prior to onset of illness. Parents reported regular preparation and consumption of wild animal meat. Another potential lead is small rodents that may be present in the home.	(Mary G Reynolds *et al.* 2019)
Sierra Leone	2017	The patient had been hunting and eating squirrels for about 10 days before falling ill	(Ye *et al.* 2019)
Singapore (contracted in Nigeria)	2019	Ingestion of barbecued bushmeat that could have been contaminated. The patient did not handle raw meat and was not exposed to wild animals or their products, had no contact with rodents or people with smallpox-like diseases.	(Yong *et al.* 2020)
United Kingdom	2018	The case reported contact with a person with an MPX-like rash at a large family event and also consumption of bushmeat while visiting a rural area in Nigeria.	(A. Vaughan *et al.* 2018)
Zaire	1972 - 1985	Transmission through food is mentioned as the main source of infection, the authors state that one of the factors of infection is "the method of food preparation". In the Bumba area, 107 human cases of MPX were recorded from 1972 to 1985, while no cases were reported in the entire western region (Bas-Zaïre). The eating habits of the Bumba and Ikela areas differ from those of Tshela. In the first one, rodents, which are caught by children from the age of 5-6 years, account for 60-85% of all wild animals caught by the rural population and are sometimes eaten without cooking. After the age of 9-10 years, children copy their parents and cook the meat. In Bas-Zaïre, on the other hand, children start hunting wild animals at the age of 12-13 and small mammals are relatively rare targets. In addition, the consumption of raw meat is unusual.	(Khodakevich *et al.* 1988)

ANNEX 4

Table 10 - Summary of literature data (used or not used) to establish the effectiveness of heat treatments on *Poxviridae*

Virus	Temperature	Inclusion or Exclusion Criteria	References
Buffalopox virus (BPXV) (4 strains)	56°C	**Inclusion**	(Baxby and Hill 1971)
Capripoxvirus	56, 60°C	No data retained: there is insufficient information for determining the values in the kinetics (only wide ranges are available)	(Wolff *et al.* 2020)
Cowpox virus (CPXV)	56°C	**Inclusion**	(Baxby and Hill 1971)
Cowpox virus (CPXV) - 2 strains	50°C	**Inclusion**	(Elzein 1983)
Myxomatosis virus (MYXV)	50; 55; 52.5; 53; 57.5 and 60°C	**Inclusion**	(Bronson and Parker 1943)
Rabbitpox virus (RPXV)	55°C	Inclusion of only kinetics with the initial strain	(Fenner 1962)
Variola virus (VARV)	40, 45, 50, 55 and 56°C	Data at pH 4.6 were not included (to avoid including data influenced by pH, as all other studies were conducted under near-neutral conditions).	(Hahon and Kozikowski 1961)
Vaccinia virus (VACV)	56°C	**Inclusion**	(Baxby and Hill 1971)
Vaccinia virus (VACV)	56°C	Insufficient information for other temperatures (only equations are proposed for 40, 45, 50, and 55°C and not the raw data) Fowlpox data were not retained due to inconsistencies between the figure and the text of the table	(Chambers *et al.* 2009)
Vaccinia virus (VACV)	65°C	Study not retained (data with LOQ censoring)	(Lelie *et al.* 1987)
Vaccinia virus (VACV)	65°C	**Inclusion**	(De Oliveira *et al.* 2010)
Vaccinia virus (VACV)	40, 75, 85 and 95°C	Study not retained (dry heat on surfaces)	(Sauerbrei and Wutzler 2009)
Vaccinia virus (VACV)	50; 52.5; 55 and 60°C	**Inclusion**	(Kaplan 1958)
Yaba monkey tumor virus (YMTV)	30, 33, 35, 37 and 40°C	**Inclusion**	(Yohn *et al.* 1966)