

The Director General

Maisons-Alfort, 5 August 2011

OPINION

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

on an assessment of the risks related to the consumption of raw sprouts, in light of developments in the health context following several cases of haemolytic-uraemic syndrome (HUS) observed in France in June 2011

ANSES conducts independent and pluralistic scientific expertise.

ANSES's public health mission involves ensuring environmental, occupational and food safety as well as assessing the related potential health risks.

It also helps to protect the health and well-being of animals and plant health and assesses the nutritional properties 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 published.

1. REVIEW OF THE REQUEST

In an email received on 2 August 2011, the French Agency for Food, Environmental and Occupational Health & Safety received an emergency request from the Directorate General for Food (DGAL) and the Directorate General for Health (DGS), as well as from the Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF), for an Opinion regarding an assessment of the risks related to the consumption of raw sprouts, in light of developments in the health context following several cases of haemolytic-uraemic syndrome (HUS) observed in France in June 2011.

2. BACKGROUND AND PURPOSE OF THE REQUEST

In May and June 2011, two outbreaks caused by enterohaemorrhagic *Escherichia coli* (EHEC) O104:H4 were observed respectively in Germany and France, resulting in nearly fifty deaths and affecting several thousand people. Epidemiological field investigations and traceability surveys identified contaminated sprouts as the causal agent.

Consequently, in a press release dated 28 June 2011, as a preventive measure, the French authorities advised consumers not to consume raw sprouts. This recommendation was also issued in the other European Union countries that had been affected by these events (Germany, Netherlands, Belgium, United Kingdom, etc.).

Monitoring plans were implemented in establishments in France that produce seeds for sprouting and sprouts, with systematic sampling (NS DGAL/SDQPV/N2011-8154¹ and TN 2011-2T-32DJ²). To date and according to the French authorities, all of these monitoring results have proven satisfactory. Moreover, sprout producers in France have informed the public authorities that they have strengthened their microbiological monitoring plans.

The European Food Safety Authority (EFSA), in its report of 5 July 2011³, indicated, on the basis of investigations undertaken by the Member States, that batches of fenugreek seeds imported from Egypt and intended for sprout production, were the most likely source of contamination.

However, as of 4 August 2011, *E. coli* O104:H4 could not be found in any sprouted seeds or seeds for sprouting that were analysed in Germany or in France. To date, the bacterium has been found in Germany not only in the packet that contained the sprouts, taken from the dustbin of a patient, but also in various foods found in the patients' refrigerator, suggesting contamination by the patient himself.

The European Commission made a decision on 6 July 2011 to withdraw from the market and then analyse and destroy all of the batches of fenugreek seeds that had been imported to Europe by an Egyptian exporter from 2009 to 2011. This Decision also included suspending the importation of Egyptian seeds and beans intended for sprouting until 31 October 2011 (including seeds, fruits and spores for sowing, leguminous vegetables, shelled or unshelled, fresh or chilled, fenugreek, dried leguminous vegetables, shelled, husked or broken, soybeans, whole or crushed, seeds and nuts, whole or crushed)⁴.

Further to this decision, the French authorities ordered the withdrawal, from all points of sale and distribution, and destruction of all batches of fenugreek seeds, whether sprouted or intended for sprouting, found in France, and prohibited the marketing of all other seeds and beans listed by this European Decision (work orders intended for the decentralised authorities⁵ and French Order of 12 July 2011⁶). These measures were implemented (see RASFF notification no. 2011-0842 updated on 22 July 2011⁷).

In its Opinion of 7 July 2011⁸, ANSES issued recommendations for consumers and operators, considering first the main information available on the pathogen involved and the epidemiological data related to it, and secondly, the specificity of the sprout production process and possible contamination sources during critical stages.

Moreover, on 19 July 2011, the French Institute for Public Health Surveillance (InVS) concluded that this outbreak of haemolytic-uraemic syndrome and bloody diarrhoea due to *E. coli* O104:H4 that

¹ Memorandum DGAL/SDQPV/N2011-8154 of 27 June 2011 related to the strengthening of 'Hygiene Package' inspections in sprout-producing establishments

² TN 2011-2T-32DJ: Monitoring plan for the microbiological quality of raw sprouts to be consumed fresh and seeds for sprouting

³ European Food Safety Authority; Tracing seeds, in particular fenugreek (*Trigonella foenum-graecum*) seeds, in relation to the Shiga toxin-producing *E. coli* (STEC) O104:H4 2011 Outbreaks in Germany and France. Question No EFSA-Q-2011-00817, issued on 05 July 2011.

<http://www.efsa.europa.eu/en/supporting/pub/176e.htm>

⁴ Commission Implementing Decision of 6 July 2011 on emergency measures applicable to fenugreek seeds and certain seeds and beans imported from Egypt [notified under document C(2011) 5000]

⁵ Memorandum DGAL/SDQPV/N2011-8163 of 8 July 2011 regarding the procedure for the withdrawal and destruction of Egyptian fenugreek seeds in sprout-producing establishments.

⁶ French Order of 12 July 2011 on emergency measures applicable to fenugreek seeds and certain seeds and beans imported from Egypt

⁷ Rapid Alert System for Food and Feed, foodborne outbreak suspected (verotoxin-producing *E. coli* O104:H4) to be caused by fenugreek seeds for sprouting from Egypt, packaged in the United Kingdom, via the Netherlands and via Germany

<https://webgate.ec.europa.eu/rasff-window/portal/index.cfm?event=notificationsList>

⁸ ANSES Opinion of 7 July 2011 on the current state of scientific knowledge and information available for making recommendations, following the onset of several cases of haemolytic-uraemic syndrome (HUS) observed in France in June 2011 and suspected of being related to the consumption of sprouts <http://www.anses.fr/Documents/MIC2011sa0158.pdf>

had broken out in southwest France in June 2011 was over, after a period that was sufficient to cover case declaration time, time for human-to-human transmission, and the disease's incubation time⁹.

Finally, several countries recently revised their restrictions on the consumption of raw sprouts, the most recent of which were Germany¹⁰, the country that was the most affected by this outbreak, and the United Kingdom¹¹.

In this context, the French ministries in charge of implementing risk management and communication measures aimed at consumers asked ANSES to update its previously issued recommendations, in light of recent developments.

3. ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with the French standard NFX50-110 "Quality in Expert Appraisal Activities – General Requirements of Competence for Expert Appraisals (May 2003)".

The expert appraisal was conducted internally, with the support of experts from the '*Escherichia coli* O104:H4 / sprouts' emergency collective expert assessment group, set up to issue the first ANSES Opinion of 7 July 2011 in response to Request 2011-SA-0158¹².

4. DISCUSSION

4.1. Review of the French epidemiological situation

On 22 June 2011, two hospitals in Bordeaux reported six cases of bloody diarrhoea and two cases of haemolytic-uraemic syndrome (HUS) to the Regional Epidemiological Centre (CIRE) of the Aquitaine region. An epidemiological investigation was immediately undertaken to identify the source of this outbreak of grouped cases and take appropriate control measures (Gault, Weill et al. 2011).

The epidemiological and microbiological investigations have now been completed. In all, fifteen epidemic cases were identified: nine cases of HUS, four cases of bloody diarrhoea and two cases of simple diarrhoea. Eleven patients were hospitalised, none of whom died. The 15 cases included 10 females and 5 males. Their ages ranged from 3 to 64 years (median: 37 years). The dates of symptom onset were spread out from 11 June to 27 June 2011 (Figure 1). All of the patients lived in Bègles (in the Gironde *département*) or nearby.

Thirteen patients had consumed sprouts served as part of the buffet for the open house day that took place on 8 June 2011 in a recreation centre for young children (CLPE) in Bègles. Two cases involving non-consumers of sprouts were secondary cases caused by human-to-human transmission of people in contact with a patient who had consumed sprouts. All of the cases identified were either directly or indirectly related to the CPLPE.

⁹ Final update on the grouped cases of enterohaemorrhagic *Escherichia coli* infection in the Gironde *département*, 26 July 2011 <http://www.invs.sante.fr/Dossiers-thematiques/Maladies-infectieuses/Risques-infectieux-d-origine-alimentaire/Syndrome-hemolytique-et-uremique/Actualites>

¹⁰ Recommendations of the German BfR, BVL and RKI of 21 July 2011: http://www.bfr.bund.de/en/press_information/2011/23/ehc_bfr_bvl_and_rki_issue_specified_consumption_recommendations_for_uncooked_sprouts_and_shoots_germ_buds_-106086.html

¹¹ Recommendations of the British FSA of 21 July 2011: <http://www.food.gov.uk/news/newsarchive/2011/jul/ecoliupdate2107>

¹² ANSES Opinion of 7 July 2011 on the current state of scientific knowledge and information available for making recommendations, following the onset of several cases of haemolytic-uraemic syndrome (HUS) observed in France in June 2011 and suspected of being related to the consumption of sprouts

Twelve cases of infection with EHEC O104:H4 were confirmed. The strain was characterised at the National Centre of Reference (CNR) for *E. coli* and in its affiliated laboratory. These analyses showed that the strain isolated in the cases that occurred in France was genetically similar to the strain that had caused the outbreak in Germany in May-June 2011.

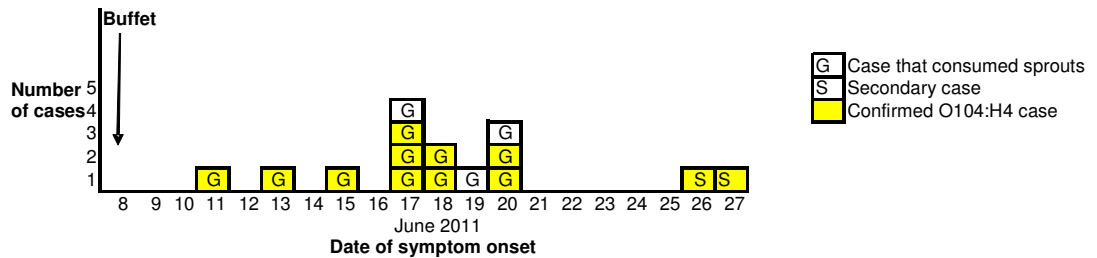


Figure 1: Distribution of epidemic cases according to the date of symptom onset. Grouped cases of infection with EHEC O104:H4, Bègles, June 2011.

A cohort study undertaken of 169 participants in the CLPE's open house days, from 29 June to 1 July 2011 in Bègles, showed a strong and significant relationship between consumption of sprouts during the buffet at the open house day and occurrence of the disease [RR=4.2, 95%CI 1.5-11.3]. Consumption of other foods and participation in the activities proposed during the open house day were not significantly linked to the disease. None of the people who had helped prepare the buffet had reported diarrhoea in the month preceding the event or had recently travelled to Germany or had contacts with a sick person who had visited Germany.

Finally, on 19 July 2011, **the InVS considered that the outbreak was over**, after a period that was sufficient to cover case declaration time, time for human-to-human transmission and the disease's incubation time.

The collected data indicate that this epidemic had the same epidemiological, clinical and microbiological characteristics as the epidemic caused by *E. coli* O104:H4 in Germany in May-June 2011. In particular, it had the same predominance of adult women among the cases, an abnormally high proportion of HUS cases in the identified possible cases, a longer than expected median incubation period for cases of shiga toxin-producing *E. coli* infection, and an identical *E. coli* O104:H4 strain (Gault, Weill et al. 2011).

4.2. Review of epidemiological investigations into the source of contamination of the batches of fenugreek seeds imported from Egypt and suspected as being the cause of the outbreaks

The European Union asked the Egyptian authorities for further information in order to improve the investigation of the epidemic which led to the cases in Germany and France. However, the Egyptian authorities have not yet responded. The European Union does not have any additional information that would allow it to determine the source of the contamination and consequently its scope, duration and location, or to assess the likelihood that it will reoccur in this type of product or any other product.

4.3. Review of management measures taken in response to the outbreak that occurred in France in June 2011

4.3.1. Consumer recommendations

In a press release dated 28 June 2011¹³, as a preventive measure, the French authorities advised consumers not to consume raw sprouts. This recommendation was also issued in the other countries of the European Union that had been affected by these events (Germany, Netherlands, Belgium, United Kingdom, etc.).

4.3.2. Controls and analyses

Monitoring plans were implemented in establishments that produce seeds for sprouting and sprouts, with systematic sampling (NS DGAL/SDQPV/N2011-8154 and TN 2011-2T-32DJ).

- Results of controls undertaken in application of Memorandum DGAL/SDQPV/N2011-8154 of 27 June 2011: All establishments producing sprouts or seeds for sprouting had to be inspected. The inspectors were asked to take one sample of sprouts and one sample of seeds for sprouting (3 specimens for each sample, minimum 100g). The samples were to be sent to laboratories identified on a list appended to the Memorandum, for the following analyses:

- o detection of *Salmonella* spp.
- o detection of the virulence genes *stx1*, *stx2* and *eae* of shiga toxin-producing *Escherichia coli* (STEC).

All of the results available to date, according to the information sent to the Agency and dated 28 July 2011, indicate that nothing was found in either of the two analyses. However, as of 28 July 2011, about half of the results were not yet available (15/38 for *Salmonella*, 17/38 for *Escherichia coli*). Moreover, sampling limits should be taken into consideration when interpreting the results.

- Results of the controls performed in the framework of TN 2011-2T-32DJ on 1 July 2011: a plan for monitoring the microbiological quality of fresh ready-to-consume sprouts and seeds for sprouting was drawn up and implemented across France. Samples were taken of the following:

- o sprouts from legumes, cereal grains, vegetables, etc. The sprouts were fresh, intended to be consumed raw, whether they were sold pre-packaged or in bulk or were intended to be incorporated into various preparations such as salads. Thus, sprouts sold deep-frozen or in cans and mixed salads were excluded.
- o Seeds for sprouting.

The samples were to be taken:

- o for sprouts: during production and distribution (retail stores, hypermarkets and supermarkets, specialised organic food stores, markets, traditional restaurants, fast-food restaurants). For sampling during distribution, urban areas were to be preferred, since they show the highest consumption of this type of product.
- o for seeds for sprouting: in their initial marketing phase (importers, wholesalers, packagers).

The following analyses were to be performed:

- o detection of *Salmonella* spp.
- o detection and enumeration of *Listeria monocytogenes* under the following conditions: detection in each 25 gram sample and direct enumeration of *Listeria monocytogenes* (limit of detection $1.0 \cdot 10^1/g$).
- o enumeration of β -glucuronidase-positive *E. coli* in sprout samples only.

¹³ http://www.economie.gouv.fr/files/recom_graines.pdf

- detection of STECs: detection of virulence genes *stx1* and/or *stx2* and *eae*. In cases of STEC detection, the serotype of the detected strain was to be determined in collaboration with the national reference laboratory.
- The 126 samples whose results were available on 28 July 2011 and sent to the Agency, tested negative for virulence factors *stx1*, *stx2* and *eae*.

Moreover, sprout producers in France have indicated that, since the onset of the outbreak that occurred in Germany, they have strengthened their microbiological self-inspections, specifically taking into account the hazard represented by STEC strains in their monitoring plans.

4.3.3. Withdrawals/recalls

In accordance with the European Commission Decision of 6 July 2011 on emergency measures to be taken for fenugreek seeds and certain seeds and beans imported from Egypt, notified under the number C(2011) 5000, the French authorities ordered the withdrawal from all points of sale and distribution, and destruction of all batches of fenugreek seeds, whether sprouted or intended for sprouting, in France, and prohibited the marketing of the other seeds and beans listed by this European Decision (work orders for the decentralised authorities and French Order of 12 July 2011). These measures were implemented (see RASFF Notification no. 2011-0842 updated on 22 July 2011). However, to date, ANSES has not received any further information from the authorities that would allow it to quantify the effectiveness of these withdrawal/recall measures.

4.4. Analysis and recommendations

- Regarding the epidemiological situation:

The outbreak related to *E. coli* O104:H4 that was due to the consumption of sprouts during an open house day that took place on 8 June 2011 in a recreation centre for young children (CLPE) in Bègles was considered to be over as of 19 July 2011 according to the InVS, after a period that was sufficient to cover case declaration time, time for human-to-human transmission and the disease's incubation time. Nevertheless, this epidemic and other epidemics reported in the literature (Mohle-Boetani, Farrar et al. 2001) show that the consumption of contaminated sprouts can cause serious infectious episodes.

It is therefore essential to draw the population's attention to the importance of adopting good hygiene measures when sprouting seeds at home (thorough cleaning/disinfection of seed germinators in particular, and careful hand washing before and after handling seeds and sprouts).

It is important to remind the population of the need to adopt good hygiene measures when preparing meals, as personal and collective hygiene is critical in the prevention of infectious risks and cases of secondary infection.

- **Regarding the management measures taken in response to the outbreak that occurred in France in June 2011 and that was related to the one that occurred in Germany in May-June 2011:**
 - The health authorities implemented measures for the withdrawal/recall and destruction of batches of Egyptian fenugreek seeds. These measures were intended to increase the safety of products on the market. However, the Agency is not able to assess the exhaustiveness of the batch recall and further points out that consumer access to information may be limited (e.g. the episode related to hamburgers contaminated with *Escherichia coli* O157 :H7 in northern France, June 2011). It therefore cannot exclude the possibility that contaminated seeds may have been kept in the homes of consumers and could cause infectious episodes if eaten.
 - The results from the analyses performed in the framework of the extensive investigation (which included official inspections and professional self-inspections) did not detect any contamination in the tested batches. However, the Agency does not yet have all of the results from these analyses. Furthermore, it is important to stress the limits of sampling plans and analyses in this situation characterised by very low-level contamination. A negative result is not sufficient proof that the monitored batch is not contaminated.

In conclusion

- The information available to date indicates that the outbreak that affected southwest France in June 2011, related to the consumption of germinated seeds in a non-professional environment during a festive event, is over.
- The epidemiological and track-back surveys that were conducted following the first outbreak (May-June 2011) in Germany, and following the episode in France in June 2011, led the European authorities to conclude that a batch of fenugreek seeds imported from Egypt and used to produce sprouts was the most likely common factor in these two outbreaks, and that it could not be excluded that other fenugreek batches imported from Egypt between 2009 and 2011 were contaminated.
- No information on the source of contamination of these batches prior to importation has been obtained to date.
- Management measures have been implemented in France:
 - withdrawal-recall-destruction measures: these measures have been implemented for the seed batches listed in the European Commission's Executive Decision. However, to date, ANSES has not received information that would allow it to quantify the effectiveness of these withdrawal/recall measures. Furthermore, it cannot exclude the possibility that there may still be packets of fenugreek from the contaminated batches (purchased from 2009 to 2011) in consumers' homes, which could cause new cases.
 - surveillance measures: these measures have been implemented by the supervisory authorities and professionals since June 2011, in all stages of the food chain. The results of these measures have not revealed contamination in the tested batches of sprouts and seeds for sprouting. However, these results should be put into perspective, in light of difficulties in detecting this bacterium (due to the very low level of contamination) and the intrinsic limits of the sampling plans, which mean that a negative result is not always sufficient proof that the monitored batch has not been contaminated. Moreover, ANSES wishes to stress that the data were collected with the goal of verifying batch conformity, and that the interpretation of these data for risk assessment purposes is therefore limited.

Regarding this situation, and to limit the risk of new cases:

- The Agency wishes to emphasise that it is critical to eliminate the fenugreek batches responsible for the outbreaks (purchased between 2009 and 2011) in Germany and France,

and that all measures must be taken to destroy any batches that may remain in consumers' homes.

- Regarding producers and distributors of sprouts and seeds for sprouting in France, the Agency considers that it is necessary to enforce the withdrawal of these fenugreek batches from the food chain.
- The Agency also emphasises the importance of being able to track back along the entire food chain, which is essential for controlling and mitigating risks, particularly during investigations of outbreaks.

These measures also apply to seed mixes containing fenugreek from the implicated batches.

Once the above conditions have been entirely met,

- an absence of prior declared French epidemics related to the consumption of industrially produced sprouts;
- establishment of a strong epidemiological link with the consumption of seed batches imported from Egypt;
- and the guarantee by French sprout producers of strengthened control measures since the outbreak of the epidemic in Germany and conditional upon compliance with and effectiveness of these measures, and which the Agency is nevertheless not capable of assessing based on the information currently at its disposal;

may be considered as valid arguments in favour of lifting restrictions on the consumption of raw sprouts produced by professionals in the French sector, with the exception of the fenugreek seeds and beans imported from Egypt and mentioned in the European Commission's decision.

Moreover, ANSES wishes to emphasise that the recommendations made in its Opinion of 7 July 2011, concerning the investigation of the French outbreak and its relation to the German episode; the strain responsible for the outbreak; the specific human populations affected by these outbreaks; and germination practices, remain relevant. It especially wishes to draw the population's attention to the importance of adopting good hygiene measures when sprouting seeds at home (thorough cleaning/disinfection of seed germinators in particular, in addition to thorough hand washing before and after handling seeds and sprouts).

It is also important to remind the population of the need to adopt good hygiene measures when preparing meals in general, as personal and collective hygiene is essential to the prevention of primary EHEC infection as well as transmission through secondary infection.

5. THE AGENCY'S CONCLUSION AND RECOMMENDATIONS

These are the points of analysis that the French Agency for Food, Environmental and Occupational Health & Safety is able to provide, in the changing context of the epidemic of haemolytic-uraemic syndrome (HUS) observed in France (Bordeaux region) in June 2011, suspected as being linked to the consumption of sprouts on the basis of exposure estimation data which, it should be emphasised, involve a very high level of uncertainty.

Furthermore, the development of a guide on good hygiene practices and the application of HACCP principles specific to this product could be useful in order to take this industry's specific requirements into account.

The Director General

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KEYWORDS

Pathogenic *Escherichia coli*, Shigatoxins, haemolytic-uraemic syndrome (HUS), seeds for sprouting, sprouts, seeds.

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