RAPID RISK ASSESSMENT

Multi-country outbreak of *Salmonella* Enteritidis PT8 infection, MLVA type 2-10-8-5-2, associated with handling of feeder mice

1 December 2016

Conclusions and options for response

A persistent common-source, multi-country outbreak of *Salmonella* Enteritidis phage type (PT) 8 infection, characterised by MLVA type 2-10-8-5-2, has been ongoing in the United Kingdom (since at least 2011) and Denmark (since at least 2014). Cases are further defined through whole-genome-sequencing (WGS) analysis and are associated with exposure to pet reptiles, in particular corn snakes, and feeder mice. The British outbreak investigation team identified the feeder mice as being imported into the United Kingdom from a rodent farm in Lithuania. Additional EU/EEA countries where the implicated feeder mice were also distributed are likely to be affected by this outbreak.

In order to describe the full extent of this outbreak, to propose tailored response options, and to inform countries not performing routine WGS for *Salmonella* surveillance, ECDC will support WGS services for selected isolates with MLVA type 2-10-8-5-2 and from patients with reported exposure to reptiles or feeder mice.

New cases and critical developments should be reported to EPIS-FWD (Epidemic Intelligence Information System for Food- and Waterborne Diseases and Zoonoses), whereas information on control measures should be reported on EWRS (Early Warning and Response System).

In order to reduce the risk of developing a *Salmonella* infection when handling a reptile, Public Health England advises reptile owners to do the following [1]:

- Always wash your hands thoroughly with soap and water immediately after handling your reptile, their cage or any other equipment such as soaking pools.
- Defrost frozen feeds on newspaper or kitchen towels preferably overnight, and away from food and food preparation surfaces and equipment and avoid defrosting in warm water or microwave as this can lead to a risk of cross contamination.
- Always wash your hands thoroughly with soap and water immediately after feeding your reptile, in particular after handling raw (frozen or defrosted) mice, rats or chicks.
- Ensure that all surfaces that have come into contact with the defrosting feed are cleaned thoroughly afterwards.
- Do not eat or drink while handling your reptile or its feed and associated equipment.
- Always supervise children to ensure that they do not put your reptile, or objects that the reptile has been in contact with, near their mouths, and wash their hands thoroughly with soap and water immediately after handling your reptile or such objects.
- Keep your reptile out of rooms where food is prepared and eaten.
- Limit the parts of the house where your reptile is allowed to roam freely.

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- Do not use kitchen sinks to bathe your reptile, wash their cage or equipment or defrost feed, and if you use a bathroom sink or bathtub, it must be cleaned thoroughly with disinfectant afterwards.
- Dispose of waste water, droppings and urine from your reptile down the toilet instead of a sink or bathtub.

EU public health practitioners should consider addressing the public on the risk associated with handling reptiles or feeder mice by providing information through pet stores, veterinarians and physicians, as it is currently done in several EU countries [2].

Source and date of request

ECDC internal decision, 24 November 2016.

Public health issue

This document assesses the risk of *Salmonella* infection associated with exposure to feeder mice in the context of a multi-country outbreak of *S.* Enteritidis PT 8 infection, characterised by MLVA type 2-10-8-5-2, and confirmed and delineated by WGS methods.

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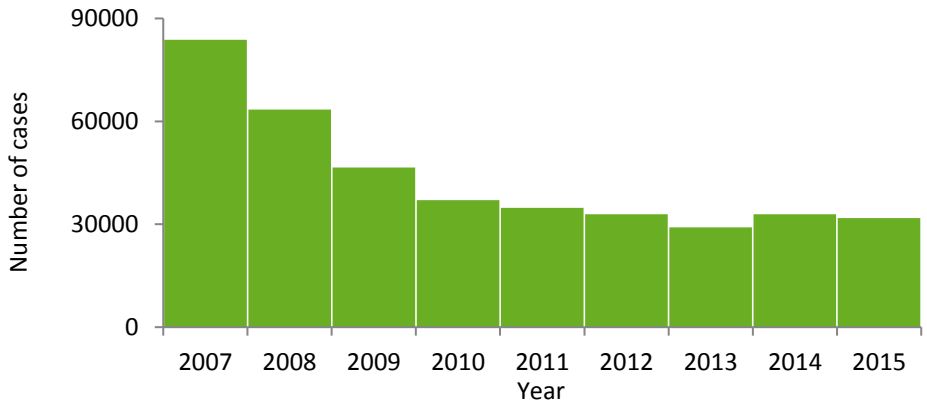
Disease background information

Salmonella Enteritidis phagetype 8 isolations in humans

S. Enteritidis is the most commonly detected serovar in human non-typhoidal salmonellosis in Europe. It has declined substantially in recent years (Figure 1), most likely as a result of successful control measures in poultry populations, implemented under Regulation (EC) No. 2160/2003*.

Figure 1. Distribution of confirmed cases of *Salmonella* Enteritidis by year, EU/EEA, 2007–2015



Source: ECDC [3]

* Regulation (EC) No 2160/2003 of the European Parliament and of the Council of 17 November 2003 on the control of salmonella and other specified food-borne zoonotic agents. Official Journal L 325, 12/12/2003 p. 0001–0015. Available from: http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32003R2160&from=EN

From 2007 to 2014, 364 450 cases of *S.* Enteritidis were reported to The European Surveillance System (TESSy) (mean number of cases per year 45 056, range 29 090 to 83 760) by 27 countries, with Germany and the Czech Republic reporting 51% of all cases. In 2014, the Czech Republic observed an increase in the number of foodborne outbreaks of *Salmonella,* contributing to a slight increase in the number of cases reported for the year at EU level. The median age for all cases with information available was 19 years (interquartile range IQR=5-49); 52% (n=184 906) were female and 89% (n=268 865) were acquired within the reporting country. Symptom onset was distributed over the year, with a peak from July to September. To date, 31 829 *S.* Enteritidis cases have been reported to TESSy for 2015 (data not yet published), and 18 countries reported 3 536 cases in the first two quarters of 2016 [4].

During the period 2011–2014, 12 EU/EEA countries (Austria, Belgium, Denmark, Estonia, Hungary, Ireland, the Netherlands, Romania, Slovakia, Spain, Sweden and the United Kingdom) reported between 1 025 and 1 705 confirmed cases of *S.* Enteritidis PT8 to TESSy annually. The majority of PT8 cases were reported by the United Kingdom (40%) which, together with Austria and Hungary, accounted for 84% of reported cases. Seventy-seven percent of the cases for which this type of information was known were domestic. Cases occurred among all age groups, and the median age was 24 years (IQR=6–51). No gender difference could be observed. Eight countries reported 1 034 *S.* Enteritidis PT8 cases to TESSY in 2015, and five countries reported 98 cases in the first two quarters of 2016.

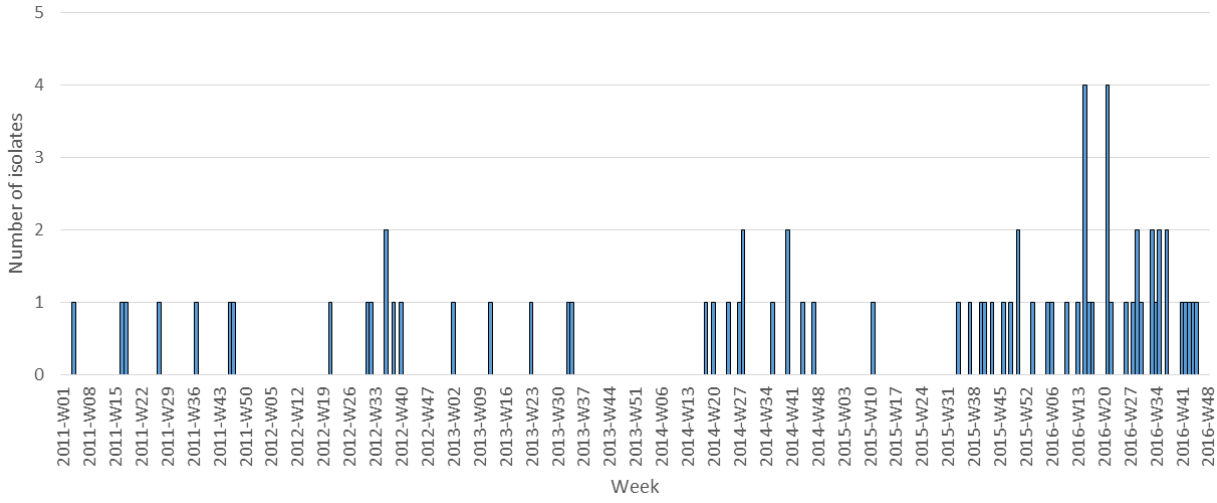
S. Enteritidis is the predominant serovar associated with *Salmonella* outbreaks in Europe. *S.* Enteritidis accounted for 142 outbreaks in 2014, representing 46.1% of *Salmonella* outbreaks. Phage type PT8 was the most frequently reported phage type among documented *S.* Enteritidis outbreaks, with 18 outbreaks identified [5].

Exposure to reptiles is a known risk factor for salmonellosis in humans. Studies from the Netherlands, Sweden and the United Kingdom estimated that 2%, 6% and 0.9%, respectively, of all reported human salmonellosis from 1985 to 2014 in the Netherlands, from 1998 to 2000 in Sweden, and from 2004 and 2007 in the United Kingdom were associated with this kind of exposure [6-8]. In the three countries, a range of *Salmonella* serotypes, including *S.* Enteritidis, were associated with exposure to reptiles. Outbreaks of salmonellosis associated with reptile exposures have been reported in the United Kingdom and in the USA, with a large proportion of these being associated with snakes or feeder mice used to feed pet reptiles [9-12].

Salmonella Enteritidis MLVA type 2-10-8-5-2 in TESSy

EU/EEA-wide data collection for *S.* Enteritidis MLVA data in TESSy began in June 2016. As of 24 November 2016, seven countries have submitted MLVA data for *S.* Enteritidis, including 73 isolates with the MLVA type 2-10-8-5-2, with dates used for statistics ranging from 30 January 2011 to 11 August 2016 (Figure 2). Of these, 40 isolates are part of a multi-country MLVA cluster, i.e. two or more countries reporting identical MLVA profile within 56 days, involving Denmark, Luxembourg, the Netherlands, Norway and the United Kingdom, with the first date used for statistics on 18 August 2015.

Figure 2. Distribution of *Salmonella* Enteritidis isolates with MLVA type 2-10-8-5-2 by week, 2011–2016 (N=73)



Source: The European Surveillance System (TESSy)

Event background information

In September 2015, the United Kingdom reported an urgent inquiry in the Epidemic Intelligence Information System for Food- and Waterborne Diseases and Zoonoses (EPIS FWD) on an outbreak of *Salmonella* Enteritidis PT8 infections. The outbreak had been detected in May 2015 by WGS, using the Public Health England (PHE) in-house pipeline and nomenclature for WGS analysis [11]. Inclusion criteria for the sequence-based cluster definition was set to a threshold of ≤5 single nucleotide polymorphisms (SNP) difference to at least one other case in the outbreak (t5 level) [13]. Following the PHE nomenclature, the outbreak strain was given the t5 cluster designation 1.5.159.280.280.280.%.

Retrospective analysis of WGS data in PHE identified 147 additional cases fulfilling the microbiological inclusion criteria since at least 2011. These cases could only be linked to this outbreak when, in 2015, PHE implemented routine WGS-based *Salmonella* surveillance.

From January 2012 to 24 November 2016, the British outbreak investigation team identified 275 human cases as part of this outbreak. Cases were distributed across the United Kingdom, and 40% of them were below 10 years of age. Information from routinely collected surveillance data showed that around 30% of cases interviewed in 2015 reported owning or being exposed to reptiles, particularly to corn snakes. A case in Scotland reported being exposed to a bird of prey. A case-control study found that cases were strongly associated with exposure to reptiles and/or feeder mice. The British outbreak investigation team reported also that local authorities sampled feeder mice and rats from three pet shops visited by identified cases. The outbreak strain was identified in the feeder mice from a single chain of pet shops but not from an independent retailer. The outbreak strain was also identified after analysing samples submitted by the UK importer of feeder mice to the veterinary laboratory of the UK Animal and Plant Health Agency (APHA). The feeder mice originated from a rodent farm in Lithuania and were imported frozen to the United Kingdom. *Salmonella* spp. were also detected after sampling the rodent farm in Lithuania although these have not been further characterised. Lithuanian authorities informed that the rodent farm was known to export also to Germany and Poland.

In Denmark, three isolates of *Salmonella* Enteritidis with MLVA type 2-10-8-5-2 were found to fulfil the inclusion criteria for the sequence-based cluster definition. The isolates were sequenced in October 2016 and had been sampled in 2014, 2015 and April 2016. It was not possible to establish whether the Danish cases from which the isolates derived had had any contact to snakes/feeder mice. One isolate with this MLVA type, detected in a human case in Luxembourg in 2015, was found to be 25 SNPs away from the British cluster and therefore not considered as part of this outbreak. WGS of isolates with this MLVA type identified in the Netherlands and Norway in 2015 and 2016 is currently ongoing.

ECDC threat assessment for the EU

Outbreak cases, defined by WGS, have been reported in the United Kingdom and Denmark. The distribution of cases in time indicates a persistent common-source, multi-country outbreak ongoing since 2011. The outbreak was identified through the routine use of WGS introduced in 2015 for *Salmonella* surveillance in England and Wales.

The sampling time of the three Danish isolates included in the outbreak suggests that this outbreak has also been ongoing outside the United Kingdom for at least three years. Additional isolates with the outbreak MLVA type are currently being sequenced to better define the extent of this outbreak in the EU/EEA. The isolate from Luxembourg, also with MLVA type 2-10-8-5-2, was excluded from the outbreak by WGS, which supports that sequencing is necessary for outbreak case identification. Suspected cases identified through MLVA and reported exposure to reptiles should therefore be analysed by WGS.

The British outbreak investigation team indicated that the source of infection is likely to be a rodent farm in Lithuania. The farm already implemented control measures in 2015 and has continued to work with experts to implement further controls. However, the fact that cases continue to occur throughout 2016 suggests that the effectiveness of the control measures is limited or that it is taking longer than expected before results are seen.

In addition to the United Kingdom and Denmark, the Netherlands and Norway also reported isolates with the outbreak MLVA type, and are therefore considered affected by this outbreak. This could also be the case for Germany and Poland, where the Lithuanian rodent farm reportedly distributes frozen feeder mice.

Feeder mice are used to feed different species of pet reptiles and birds of prey. However, feeder mice are not considered as pet food but animal by-products, which are not required to be free from *Salmonella enterica* spp. or other human pathogens. Animal by-products are dealt with under Regulation (EC) 1069/2009 and Regulation (EU) 142/2011.

Information for consumers about the risk of *Salmonella* infection associated with exposure to reptiles or feeder mice have been issued in the United Kingdom and in the Netherlands due to this or previous outbreaks. Information, provided through leaflets in pet shops and veterinary clinics, included advice on how to hygienically handle reptiles, birds of prey and their feed. A press release was issued in the United Kingdom to inform the public of the ongoing outbreak and provide instructions on how to safely handle pet reptiles and their feed [1].

Pet reptiles are common in the EU. It was estimated that between 5.9 and 9.8 million reptiles were legally imported into the Union in 2009 [14]. The challenges of implementing control measures at the farm level are likely to result in additional *Salmonella* Enteritidis cases associated with the handling of reptiles or their feed.

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