



RAPID RISK ASSESSMENT

Increase in *Salmonella* Stourbridge infections in Germany during 2016

Update, 26 January 2017

Main conclusions and risk assessment for the EU/EEA

Germany is the only EU/EEA Member State where there has been a statistically significant increase in the number of cases of *S. Stourbridge* during 2016. The multi-country whole genome sequencing (WGS) analysis suggests that there was a localised outbreak in Lower Saxony in July and August 2016. Sequences were available for only 50% of the German cases, so it is possible that more cases are part of the Lower Saxony outbreaks, that some cases from other federal states are also part of this microbiological cluster, or that there are other undetected clusters. All cases reported in Lower Saxony occurred in July and August 2016 and therefore, the increase in number of cases in the other federal states in Germany in September and October cannot be accounted for by this outbreak. As no new cases have been reported in Germany since October 2016, it is likely that the vehicle of infection is no longer circulating in the food chain.

Whole genome sequence analysis showed that the 14 sequences collected from Germany (7), France (2), Ireland (1) and Luxembourg (4) over a twelve year period are very closely related (limited variability by Core Genome Multilocus Sequence Typing (cgMLST) and Single Nucleotide Polymorphism (SNP) analysis). This may suggest the possibility of a single or very small number of persistent primary sources resulting in intermittent human infection.

The finding of a food isolate positive for *S. Stourbridge* in a burger sample from a restaurant in Germany in late November 2016 is an important element to the investigation. Whole genome sequencing of this isolate will support hypothesis generation and exposure assessment evidence on whether the meat in the burger was the vehicle of German cases.

The high proportion of hospitalised cases and the two deaths highlight the severity of this event.

The striking difference in the age distribution between the cases reported in 2016 in Germany and France compared with other countries may be due to a difference in exposure.

Based on the microbiological evidence, ECDC does not consider this a multi-country ongoing event so the investigation of the event is being closed at the EU/EEA level and routine monitoring of *S. Stourbridge* strains occurrence in humans will continue.

Source and date of request

ECDC internal decision, 19 January 2017.

Public health issue

Potential multi-country outbreak of *Salmonella* Stourbridge in 2016.

Rationale for update

Results of the microbiological investigations conducted by the Robert Koch Institute, Germany.

Consulted experts

ECDC experts: Céline Gossner, Daniel Palm, Saara Kotila, Johanna Takkinen, Denis Coulombier

External experts who contributed to this risk assessment:

- Austria: Christian Kornschober (Austrian Agency for Health and Food Safety)
- France: Nathalie Jourdan-Da Silva (Santé Publique France, the French national public health agency); Simon le Hello (Institut Pasteur, Paris)
- Germany: Lena Boes (Robert Koch Institute), Sandra Simon (National Reference Laboratory for Salmonella, Robert Koch Institute)
- Ireland: Patricia Garvey (Health Protection Surveillance Centre, Dublin), Niall DeLappe and Martin Cormican (National *Salmonella*, *Shigella* and *Listeria* Reference Laboratory, Galway)
- Italy: Ida Luzzi (Istituto Superiore di Sanità, ISS)
- Luxembourg: Joël Mossong (Laboratoire National de Santé)
- The Netherlands: Lapo Mughini Gras (National Institute for Public Health and the Environment, RIVM)
- United Kingdom: Lesley Larkin (Public Health England).

Disease background information

Salmonella Stourbridge (*S. Stourbridge*) is a rare serotype in EU/EEA Member States [1]. Seven Member States reported 92 cases with this serotype between 2010 and 2015 ranging from eleven to 22 cases yearly with an annual median of 15 cases. France and Germany have accounted for 61% and 21% of the reported cases, respectively. Cases have been more common among adults aged 45 to 64 years (30%) and those over 65 years old (25%). There were more male (54%) than female cases reported. Most of the cases (93%) with known travel history were domestic (n=29). No deaths were reported due to *S. Stourbridge* infection between 2010 and 2015 [1].

ECDC has collected PFGE data for *Salmonella* in the European Surveillance System since 2012. PFGE data are available for 12 *S. Stourbridge* isolates from four Member States, with the dates used for statistics ranging from 13 July 2005 to 24 October 2016. These isolates comprise four unique PFGE profiles that differ from each other by two bands.

A European-wide outbreak of *S. Stourbridge* associated with unpasteurised goat's cheese was described in 2005, where 77 cases were reported by six EU Member States and Switzerland [2].

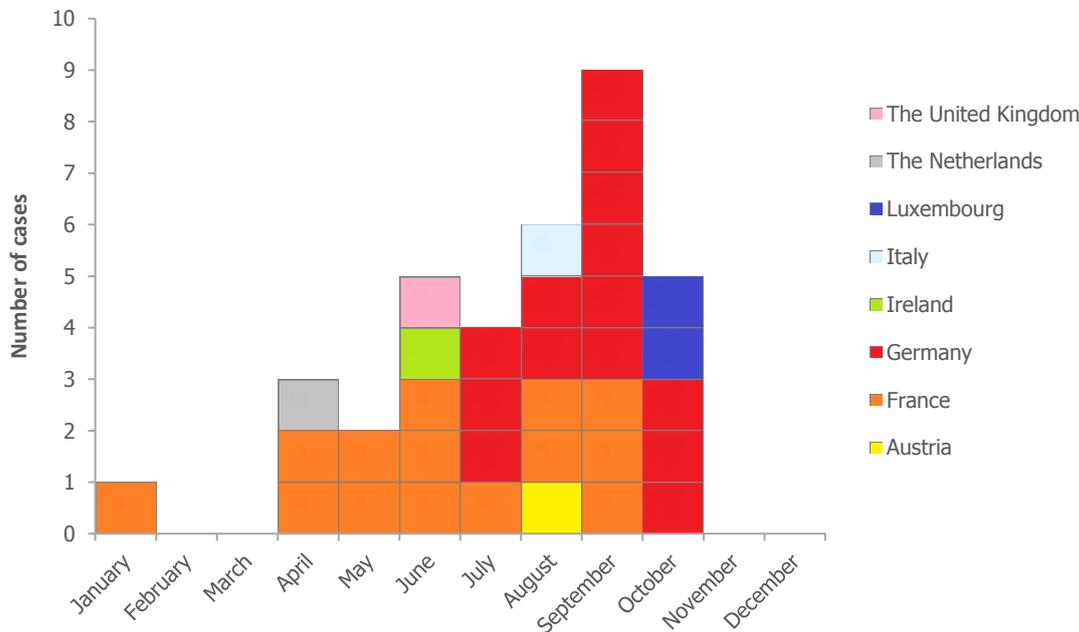
Event background information

On 22 November 2016, Germany reported an increase in the number of *S. Stourbridge* (6,8:b:1,6) infections during the second half of 2016 through the Epidemic Intelligence Information System for Food- and waterborne Diseases and Zoonoses (EPIS-FWD) [3]. Fourteen cases were notified in Germany in 2016, compared with one to five cases per year (median three cases) between 2011 and 2015 (Poisson distribution test $p < 0.0001$). The first case in 2016 was observed in July and the most recent case had disease onset in late October 2016. Cases were notified in different federal states. The median age was 58 years (range: 13 to 84), 36% of cases were male and 64% female. Nine of 13 documented cases (69%) have been hospitalised. Two male cases were fatal. No cases had documented travel outside of Germany before becoming ill.

As of 16 December 2016, 35 cases were reported in the EU/EEA through EPIS-FWD and The European Surveillance System: Austria (1), France (14), Germany (14), Ireland (1), Italy (1), Luxembourg (2), the Netherlands (1) and the UK (1). In comparison, 11 cases were reported in 2014 and 22 cases in 2015. The majority of the cases in 2016 occurred between April and October (Figure 1). The latest dates of onset were reported in October by Luxembourg in two siblings, aged one and two years, who had visited Germany before falling ill.

Germany did not identify new cases in November and December 2016. The case reported by the United Kingdom visited France before falling ill. Twelve cases were hospitalised: nine in Germany, one in Austria, one in Luxembourg and one in the United Kingdom. There is a striking difference in the age distribution between the cases in Germany (median 58 years, ranging from 18 to 34) and France (median 53 years, ranging from 0 to 80) compared with other countries (median one year, ranging from 0 to 10 years of age).

Figure 1. Distribution of *Salmonella* Stourbridge infections by month used for statistics and reporting country, EU/EEA, 2016 (n=35)



Six of seven isolates tested have the PFGE profile *XbaI*.1546, according to The European Surveillance System nomenclature, and the seventh isolate has a very similar profile (*XbaI*.2532) with only a two-band difference, suggesting that the two types may be closely related. Germany performed WGS on seven isolates, four from Lower Saxony and three from other federal states.

In order to assess the potential multi-country dimension of this outbreak, the Robert Koch Institute in Germany performed a comparison of German whole genome sequences and the sequences provided by France, Ireland and Luxembourg.

The following 14 strains were included:

Germany

- Four human isolates from 2016 cases in Lower Saxony. All these cases are from July and August 2016.
- Three human isolates from 2016 cases from the Federal States of Brandenburg, Saxony and Thuringia.

Luxembourg

- Three human isolates from cases from 2005, 2008 and 2016.
- One isolate from bovine faeces sampled in 2007.

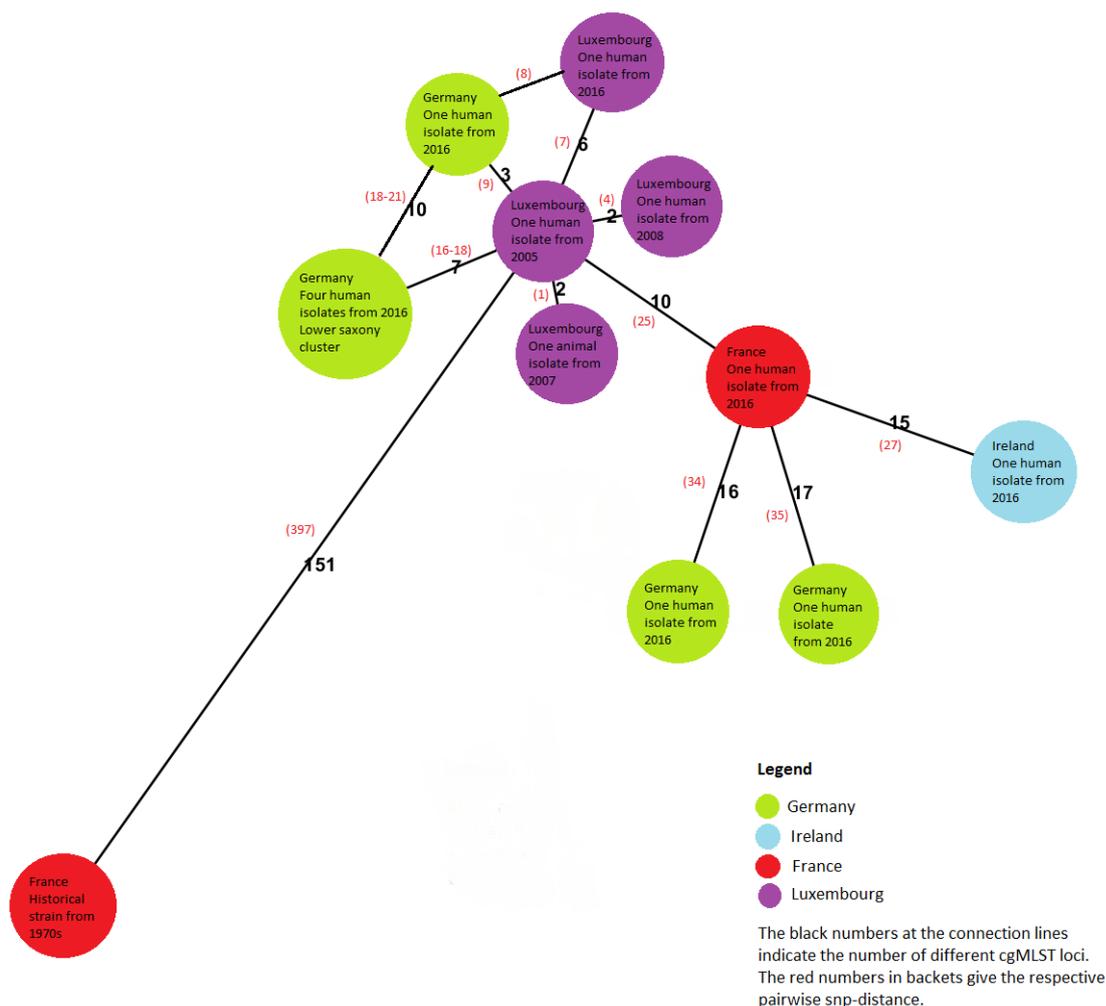
France

- One human isolate from a case in 2016.
- One historical isolate from the 1970s.

Ireland

- One human isolate from a case in 2016.

Figure 2. Results of the whole genome sequencing analysis, 14 *Salmonella* Stourbridge isolates, France, Germany, Ireland and Luxembourg, 2005–2016.



Note: mapping reference: *S. Montevideo* str. NZ_CP007540.1 (identified as the best reference genome by our RefFinder tool)
 Source: Robert Koch Institute (the texts within circles have been added by ECDC).

For core genome Multilocus Sequence Typing (cgMLST) the Robert Koch Institute used an ad hoc scheme for *Salmonella enterica* created with the Ridom SeqSphere+ software. The scheme is based on 2143 target loci, 2112 of which were considered for the calculation of the MST (targets with missing values were excluded). The Single Nucleotide Polymorphisms (SNP) analysis was performed with a Linux-based in-house pipeline, e.g. using bwa-sw for reference mapping and VarScan for SNP-calling.

This analysis is based on 14 sequences from four countries over a period of twelve years. Therefore, this limited set of sequences does not provide a full understanding of *S. Stourbridge* diversity. The genetic distance observed between all 14 isolates is relatively small, with the exception of the historical isolate from the 1970s, suggesting a clonal nature of this serotype.

The isolates from Luxembourg from 2005 and 2008 show a high level of similarity with an isolate from a faecal bovine sample from 2007. This may suggest a continuous bovine source causing sporadic human cases in Luxembourg.

The WGS analysis concluded that only the four isolates from Lower Saxony form a distinct sequenced-based cluster suggesting that cases have had a common exposure (single vehicle/source of infection). The 2016 isolate from Luxembourg (children visiting Germany) is distinguishable from the Lower Saxony cluster. As this isolate is no more closely related to the Lower Saxony cluster than other Luxembourg isolates, this isolate is therefore not regarded as part of this discrete cluster.

The Federal Institute for Risk Assessment in Germany received one food isolate positive for *S. Stourbridge*. This food isolate originated from a burger in a restaurant of the federal state of Hesse. The sampling date was the last week of November 2016. The strain will be sent to the National Reference Centre for WGS. It should be noted that no human cases were reported in the federal state of Hesse.

References

1. European Centre for Disease Prevention and Control. The European Surveillance System Retrieved 13 December 2016, from <http://ecdc.europa.eu/en/activities/surveillance/TESSy/Pages/TESSy.aspx>
2. Espié E, Vaillant V. International outbreak of Salmonella Stourbridge infection, April–July 2005: results of epidemiological, food and veterinary investigations in France. *Euro Surveill.* 2005;10(32). Available at: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=2772>
3. European Centre for Disease Prevention and Control. Increase in Salmonella Stourbridge infections in Germany during 2016 – 16 December 2016. Stockholm: ECDC; 2016.