Public Health England

Protecting and improving the nation's health

# Investigation of a case of listeriosis in Yorkshire and the Humber linked to the consumption of hospital sandwiches

July 2017

Incident investigation report

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# Executive summary

In July 2017, *Listeria monocytogenes* was isolated from the blood of a 53-year-old male inpatient in a hospital in Yorkshire and Humberside. The patient had an ongoing underlying health condition for which he was receiving treatment. The *L. monocytogenes* isolate was shown by whole genome sequencing single nucleotide polymorphisms (SNP) analysis to be genetically indistinguishable (<5 SNPs) to isolates from sandwiches and salads produced by Company X who supplied to NHS hospitals, other institutions and to retailers nationwide.

The case had a history of consuming sandwiches produced by Company X in hospital on at least 12 occasions in the 3 weeks prior to onset of illness. An incident management team was established and met on 3 occasions with further investigation occurring outside of the meetings. No further human cases were detected during the investigation. *L. monocytogenes* of this type was not detected in any foods other than those produced by Company X between 2016 and 2017.

*L. monocytogenes* was detected in products from Company X between December 2016 and August 2017, both at the manufacturer's premises and from 2 hospitals' in-house sampling and the same strain as that recovered from the clinical case was recovered from all sites. Company X had been working with the local authority to control this bacterium at their food manufacturing site since December 2016. Control measures were implemented both at the local hospital trust where the case had been a patient and at Company X with follow up inspection and sampling. Over the course of the investigation, the recovery of *L. monocytogenes* from Company X or the hospitals was reduced, and the investigation was closed on the 2 November 2017.

A quantitative risk assessment was undertaken which predicted that under sub optimal storage conditions, a clinical case of listeriosis will occur once every 3 years. This was reduced to one case every twenty years if products were under optimal storage conditions. Thus, control measures to reduce or eliminate *L. monocytogenes* from factory environments together with maintenance of the cold chain at hospitals are important to reduce the occurrence of listeriosis from this source.

Further sampling and testing continued, and the incident *L. monocytogenes* strain continued to colonise the manufacturer's premises as well as to contaminate products up to July 2019.

# Introduction

Listeriosis is a rare but severe infection caused by the bacterium *L. monocytogenes*. The infection is usually acquired through the consumption of contaminated food and has an incubation period between consumption of contaminated food and clinical recognition of infection between 24 hours and 70 days. Groups at increased risk of invasive disease include: those aged over 60; individuals with pre-existing medical conditions who are immunosuppressed; and pregnant women and/or their unborn and newly delivered infants. Invasive listeriosis occurs as sepsis, encephalitis, meningitis, miscarriage or still birth which may or may not be preceded by febrile gastroenteritis. The mortality rate of invasive disease is 20-30%. Listeriosis also occurs, albeit much less commonly, in individuals who are otherwise healthy and can be asymptomatic, or present with symptoms ranging from mild self-limiting diarrhoeal illness with fever to severe invasive infection. The annual rate of reported listeriosis in the UK is about 3 cases per million of the total population [1].

*L. monocytogenes* is widely distributed in the environment, can enter the food chain, and persist in food processing environments for years to decades. The bacterium can grow in a wide range of foods around neutral pH, in high concentrations of salt and sodium nitrite and over a wide range of temperatures, including that used for refrigeration. The organism survives particularly well in moist areas with organic material such as drains and floor surfaces and will persist in equipment that is difficult to disassemble and clean such as cutting machines and conveyor belts which can contaminate foods during manufacture. *L. monocytogenes* is primarily a food-borne pathogen and poses a problem for the food industry particularly with processed ready-to-eat foods with long refrigerated shelf lives, such as pre-packaged sandwiches.

# Background

Between October 2016 and 30th June 2017, the PHE York FW&E microbiology laboratory had tested samples of sandwiches from 2 hospitals in Yorkshire & Humber as part of a commercial contract and had isolated *Listeria monocytogenes* from 38 out of 297 (13%) samples of salads, sandwiches and other products in October and November 2016 and March, April, May and June 2017. All 38 isolates from the hospital and factory samples were recovered at a level of <20 cfu/g. The 38 *L. monocytogenes* isolates were referred to GBRU for WGS typing and 36 of the samples collected from the 2 hospitals and one isolate from a sandwich sampled by the LA directly from the Company X on 15 December 2016 were within a 5 SNP cluster.

FW&E liaised with the affected hospital infection control teams and advice was given to feed vulnerable patients cooked foods only. In consultation between the hospital and PHE FW&E Microbiology and based on public health concern, communication was made to the company who contacted Bradford LA in December 2016 to make them aware of the *L. monocytogenes* contamination. Although no results were categorised as unacceptable, potentially injurious to health: there was no further communication to the Local Authority of the ongoing low-level contamination before June 2017. A Bradford EHO visited Company X in June 2017 and identified a number of issues requiring remediation. Company X was aware of the ongoing isolation of *L. monocytogenes* from its products following the result in December 2016 where *L. monocytogenes* had been detected from a sandwich collected from the factory. Company X had a long-standing arrangement commissioning their own microbiological testing on swabs and food samples collected from the factory using a commercial laboratory. *L. monocytogenes* had not been detected in any of the samples the company had submitted to the commercial microbiology laboratory. Following the investigation of the case of listeriosis, the company entered into a commercial arrangement with the PHE FW&E microbiology laboratory at York for testing in 2017.

Company X are an STS approved NHS supplier and recent audits indicated that the company operated to a high standard. An unannounced visit was undertaken in Dec 2016 following a request from an NHS supplier as a result of the detection of *Listeria* in a sandwich and only one minor non-conformance was identified.

On 10 August 2017, *Listeria monocytogenes* which had been isolated from the blood of a 53-year-old male in July was shown by whole genome sequencing single nucleotide polymorphisms (SNP) analysis to be genetically indistinguishable (<5 SNPs) to isolates recovered from sandwiches and salads produced by Company X since October 2016 and who supplied products to NHS hospitals and retail nationwide.

The case who was an inpatient in a hospital in Yorkshire and Humberside had severe ulcerative colitis for which he was receiving treatment that made him at risk for listeriosis. The patient was first hospitalised at Hospital A in mid-June 2017 and discharged in early July 2017. The patient was readmitted to Hospital B, within the same NHS Trust, in mid-July 2017 with symptoms of confusion, diarrhoea and vomiting. *L. monocytogenes* was isolated from a blood culture taken on 18 July 2017. The food history of the patient indicated that for most of the 30 days prior to onset of illness he consumed food supplied by Hospital A including prepared sandwiches. Further investigation revealed that the patient had been served sandwiches produced by Company X on 12 occasions whilst an inpatient at Hospital A. Due to the risk to vulnerable patients in hospitals receiving sandwiches from Company X, an incident was declared.

# Incident coordination

On 16 August 2017 an Incident Management Team (IMT) was established with the aim of investigating the source of contamination and developing an evidence base to formulate public health interventions. The main objective of the IMT was to prevent further human cases of listeriosis and to provide public health advice to the NHS.

Members of the IMT included staff from:

- PHE Gastrointestinal Infections Department
- PHE Gastrointestinal Bacteria Reference Unit
- PHE Food Water and Environment Microbiology Services
- Food Standards Agency
- PHE Field Services
- PHE Yorkshire & The Humber Health Protection Team
- Environmental Health Team, Bradford Local Authority

All incident related documents including meeting minutes and reports were stored in a dedicated folder in the PHE Colindale electronic system.

# Methods

## Epidemiological investigations

Reporting of laboratory confirmed cases is mandatory, and cases are notified to PHE Health Protection Teams for public health follow-up. This includes collecting clinical, food history (30 days prior to onset of symptoms) and other epidemiological data using standardised surveillance questionnaires.

For the investigation, case finding was undertaken using this confirmed case definition: “A microbiologically confirmed case was a patient with clinical symptoms compatible with Listeriosis and where an isolate of *Listeria monocytogenes* was recovered from a clinical specimen taken from a normally sterile site and recognised as serotype 1/2a, CC121 with a SNP profile of 1.1.17.55.443.450.%.”

## Food and environmental testing

Microbiological testing of food and environmental samples was performed by the PHE Food Water & Environmental (FW&E) microbiology laboratory at York. This laboratory is an official control laboratory (as designated by the FSA) and 25g samples were tested for both presence/absence as well as enumeration of *L. monocytogenes* (as well as other *Listeria* species) using the ISO11290-1 and 2:1998 method.

Sandwiches and salads were tested that had been produced by Company X (either as part of official controls and collected by the local authority or as part of a commercial contract with the company) as well as from Hospital C and Hospital D (both of which are in the Yorkshire and Humber Region) under contract. The FW&E York laboratory also undertook testing of environmental swab samples collected from Company X and taken by Bradford EHOs.

## Reference microbiology

Isolates of *L. monocytogenes* from clinical cases of listeriosis, food samples, or the environment, were voluntarily referred to the PHE Gastrointestinal Bacteria Reference Unit (GBRU) for typing using Whole Genome Sequencing (WGS). Serotype and clonal complex were assigned in accordance with the Institut Pasteur international MLST database for *L. monocytogenes* designation http://bigsdb.pasteur.fr/listeria/listeria.html). Hierarchical single linkage clustering was performed on the pairwise SNP difference between all strains at various distance thresholds (250, 100, 50, 25, 10, 5, 0). The result of the clustering is a SNP profile, or SNP address using single linkage clustering of pairwise SNP differences (≤ 5 SNP differences) [2].

# Results

## Epidemiological findings

No additional cases were identified as associated with this incident or the CC121 incident strain up to the time of reviewing this document in November 2019.

## Investigations at Company X

The LA reported that Company X was an approved food premises mainly producing sandwiches, salads, cooked meat, eggs and egg products. They operated with a fully documented HACCP procedure which was regularly reviewed by a food consultant. They operated during the day and night and produced approximately 40,000 sandwiches a day of which 30% were produced for the NHS. The factory produced 88 different types of sandwiches but also produce salad and other food items with a 2-day shelf life. They supplied 213 NHS outlets across the country (including Hospital A, Hospital B, Hospital C and Hospital D) and supplied to 1,250 other establishments including universities, service stations and railways.

Company X had been conducting its own microbiological swabbing and sampling, whereby they normally conducted their own testing in accordance with the STS (NHS Supply) standards using a commercial UKAS accredited laboratory on a weekly basis (not with the PHE FW&E microbiology laboratory). *L. monocytogenes* had not been detected in any of the samples from the company sent to the commercial laboratory. The company were aware of the sandwich sample taken by the LA in December 2016 where *L. monocytogenes* had been detected but because their own testing was subsequently negative were unaware of further issues until they were informed of the results of the samples taken directly from hospitals in June 2017.

The EHO reported that the procedures at the premises were generally of a good standard but that some changes to their layout to expand their production area had been recently implemented and had identified issues of concern such as the sanitisation systems for washing machines. Wheeled trolleys were not disinfected before moving from low risk to high risk areas. The outdoor to indoor shoe changing area bench was also an issue. One of the floors was draining from a low to high risk area. Sampling taken at the inspection on 11 and 19 July 2017 identified *L. monocytogenes* of the same WGS type as the case in basket wash water, drains and 2 food samples. Additional sampling was undertaken on 15 August and yielded more *L. monocytogenes* isolates of the same type including from a clean butter depositor. On this visit, duplicate samples were taken and sent to the company's private laboratory as well as to the PHE FW&E

laboratory, however the private laboratory did not detect *L. monocytogenes* in those samples.

Following these results a deep clean was conducted by a chemical consultant using a chemical cleaning company. Company X also contacted the manufacturer of the equipment of the tray wash to have it retrofitted but it was suspended from use until that time. The salad washing machine was replaced. The drains were cleaned daily and deep cleaned on the weekend. The LA found that debris built up in floor drains during the week and advised for deep cleaning to take place daily, which was implemented at the factory. The butter depositor, which was positive for *L. monocytogenes* was in the high-risk area. It was partially dismantled and washed before reassembly, but the *L. monocytogenes* was found in the butter depositor after cleaning and before its use for butter distribution: the LA recommended cleaning the butter depositor immediately prior to use.

## Food and environmental testing

Samples collected from Company X's premises: At the time of the first IMT on 16 August 2017, 31 samples had been tested since December 2016 by the York FW&E laboratory which had been sampled directly from Company X. *L. monocytogenes* was detected in 7 (23%) of these 31 samples.

**Table 1. Results for isolation of *L. monocytogenes* from samples collected from Company X**

| | | Environmental | | Food and food components | |
|---|---|---|---|---|---|
| **Year** | **Month** | **Total tested** | ***L. monocytogenes* isolated** | **Total tested** | ***L. monocytogenes* isolated[1]** |
| 2016 | December | 0 | 0 | 5 | 1 |
| 2017 | January | 0 | 0 | 0 | 0 |
| | February | 0 | 0 | 0 | 0 |
| | March | 0 | 0 | 6 | 0 |
| | April | 0 | 0 | 0 | 0 |
| | May | 0 | 0 | 0 | 0 |
| | June | 0 | 0 | 0 | 0 |
| | July | 7 | 3 | 13 | 3 |
| | August | 13 | 4 | 0 | 0 |
| | September | 22 | 1 | 16 | 0 |
| | October | 8 | 0 | 35 | 2 |
| | November | 8 | 0 | 23 | 2 |
| | December | 0 | 0 | 0 | 0 |

[1] all isolates detected at less than 20 cfu/g

On 11 July 2017, 16 samples were taken from the factory by Company X, including 9 samples of ingredients, 2 finished products and 5 environmental swabs in the factory. *L. monocytogenes* was isolated from 5 samples; one sandwich, ready-to-eat sweetcorn, lettuce and 2 environmental swabs (a drain exit and entry swabs). All 5 isolates were within 5 SNPs of the isolates from the clinical case and the sandwiches from the Hospitals. Subsequent sampling at the factory was undertaken at regular intervals throughout August to November 2017 (Table 1).

*L. monocytogenes* was recovered from a further 5 environmental samples in July, August and September which included floor drains, basket wash water sample and a butter depositor, with 3 of these isolates matching the incident strain (Table 2). Two isolates, one from the butter depositor and one from a floor drain were of a different *L. monocytogenes* type (CC9, 2.8.8.10.302.312.%: no infections due to this type were detected). *L. monocytogenes* was not recovered from repeat swabbing of the dismantled butter depositor machine after cleaning and reassembly in September 2017. *L. monocytogenes* was not recovered from any further environmental sampling at Company X in October and November 2017 (Table 1). *L. monocytogenes* was recovered at <20 cfu from 4 foods (2 salads and 2 sandwiches) in October and November 2017 (Table 1).

**Table 2. Results of WGS typing of *L. monocytogenes* isolated from samples collected from Company X.**

| Sample Date | Description | WGS typing (clonal complex, SNP address) |
|---|---|---|
| 15/12/2016 | Egg mayo sandwich | CC121, 1.1.17.55.443.450.472 |
| 11/07/2017 | Egg mayo sandwich | CC121, 1.1.17.55.443.450.472 |
| 11/07/2017 | Env swab prep drain entry | CC121, 1.1.17.55.443.450.472 |
| 11/07/2017 | Env swab prep drain exit | CC121, 1.1.17.55.443.450.580 |
| 11/07/2017 | Rte sweetcorn | CC121, 1.1.17.55.443.450.472 |
| 11/07/2017 | Washed lettuce | CC121, 1.1.17.55.443.450.472 |
| 19/07/2017 | Basket wash tank water sample | CC121, 1.1.17.55.443.450.472 |
| 15/08/2017 | Floor drain prep room (entry to production) dirty | CC121, 1.1.17.55.443.450.561 |
| 15/08/2017 | Floor drain prep room (exit) dirty | CC9, 2.8.8.10.302.312.349 |
| 15/08/2017 | Floor drain prep room (entry from changing) dirty | CC121, 1.1.17.55.443.450.561 |
| 15/08/2017 | Butter depositor (clean) listeria | CC9, 2.8.8.10.302.312.350 |
| 04/09/2017 | Clean drain production entry | CC121, 1.1.17.55.443.450.588 |
| 10/10/2017 | Pork salad bowl[2] | CC121, 1.1.17.55.443.450.595 |
| 28/11/2017 | Tuna mayo sandwich | CC121, 1.1.17.55.443.450.587 |
| 28/11/2017 | Tuna mayo sandwich | CC121, 1.1.17.55.443.450.587 |

[2] *L. monocytogenes* was recovered from one additional pork salad bowl sample which was not submitted to the reference laboratory for characterisation

## Finished food samples collected from the hospitals:

At the time of the first IMT on 16 August 2017, *L. monocytogenes* was recovered from 69 (14%) of 480 samples of finished foods manufactured by Company X and collected from the hospitals. The monthly totals of the 861 foods tested during 2016-17 is shown in Table 3, and of these, *L. monocytogenes* was recovered from 84 (8%) samples. All 84 samples were contaminated at <20cfu/g except for 2 quiche Lorraine salads sampled in March and June 2017 where the bacterium was detected at 20 cfu/g. The highest monthly rates of contamination were in January 2017 (32%), April 2017 (31%), October 2016 (28%) June 2017 (23%), Match (20%) and July 2017 (19%), which is the period leading up to the exposure in the patient. All *L. monocytogenes* isolates from the Company X's foods sampled at the hospitals were the incident strain (CC121) except for one pasta salad collected on 8 February 2017 contaminated with CC2 (SNP profile 1.1.277.285.300.313.%) and one tuna mayonnaise sandwich taken on 27 October 2017, which was type CC1 (SNP profile 1.1.12.21.21.22.%): no infections due to these 2 *L. monocytogenes* types were detected.

**Table 3. Results for isolation and typing of *L. monocytogenes* from finished food samples collected from hospitals which were manufactured by Company X.**

| | | Completed foods tested for *L. monocytogenes* | | WGS typing of *L. monocytogenes* |
|---|---|---|---|---|
| **Year** | **Month** | **Total** | ***L. monocytogenes* isolated[3]** | **Number indistinguishable from incident strain/total** |
| 2016 | October | 18 | 5 (28%) | 3/5 |
| | November | 46 | 2 (4%) | 2/2 |
| | December | 25 | 0 | - |
| 2017 | January | 19 | 6 (32%) | 6/6 |
| | February | 33 | 8 (24%) | 7/8 |
| | March | 49 | 10 (20%) | 10/10 |
| | April | 32 | 10 (31%) | 10/10 |
| | May | 48 | 7 (15%) | 6/6 |
| | June | 87 | 20 (23%)* | 19/20 |
| | July | 80 | 15 (19%) | 15/15 |
| | August | 100 | 8 (8%) | 8/8 |
| | September | 119 | 0 | - |
| | October | 76 | 1 (1%) | 1/1 |
| | November | 90 | 7 (8%) | 6/7 |
| | December | 39 | 1 (3%) | 1/1 |

[3] all isolates detected at less than 20cfu/g, with the exception of 2 samples detected at 20 cfu/g (*March & June)

## Investigations at the hospitals

Investigations were undertaken at the 2 hospitals, Hospital A and Hospital B, where the infected case had been an inpatient during his exposure period and at Hospital C and Hospital D, where positive food samples contaminated with the incident strain had been identified. No communication was sent to any other hospitals or other recipients of Company X's products.

At Hospital A, the kitchen had last been inspected on 16 November 2015, including food service at wards. They received a Food Hygiene Rating of 5 and the only issue identified was a damaged floor around the dishwasher (which had since been fixed). The LA visited on 23 August 2017 and reported on the sandwich supply and cold chain. Deliveries were received from Company X in a refrigerated vehicle. There were daily deliveries to ensure sandwiches were used quickly and not stored longer than 48 hours. The probe thermometer used to check deliveries was in working order and calibration records available. The sandwiches were stored in a walk-in chiller at 3° C, at the time of the visit the chiller was 3°C and the probe temperature was 3.8°C. Patients pre–ordered all meals/sandwiches. The sandwiches were taken onto each ward by the catering staff in chilled trolleys and the catering staff served the patients. No sandwiches were left for the patients to eat later or were out of temperature control.

The LA for Hospital B carried out a routine food hygiene inspection at Hospital B on 24 August 2017 prompted by the investigation and again primarily focused on the provision of sandwiches to patients. The EHO was made aware that the sandwich provider for them was a different supplier and not Company X. There had been no breakdowns or issues of concern with any refrigeration units. Sandwiches were assembled in a temperature-controlled environment and then placed into refrigerated trolleys prior to being taken to the wards. The delivery temperatures of the sandwiches, the refrigeration units and the temperature of the food items in refrigeration trolleys immediately prior to service were recorded. The time taken between service and retrieval of plates/waste food was usually within 30-40 minutes. On inspection of some of the chilled temperature records, many of the refrigeration trolley temperatures were above 5°C and the ones that the LA checked were 6°C or above and in one case 7.9°C. These temperatures were legally compliant but not in line with guidance.

At Hospital A and Hospital B, a separate investigation was conducted by infection control staff on the pathway of sandwiches to patients. Some parts of the hospitals were found not to have adequate control measures in place for the storage of sandwiches on the wards, such as the use of drug fridge charts being used on food fridge charts and vice versa: drugs were stored at 2-8°C, food at 0-5°C, so there was scope for confusion on what was the "correct" temperature for that fridge.

The kitchen at Hospital C had last been inspected on 24 May 2017 including food service at wards. The storage and service of sandwiches and salads was found to be satisfactory. Deliveries were received daily from Company X in a refrigerated vehicle. This daily delivery meant that sandwiches were used quickly and not stored for more than 48 hours. The hospital had probe thermometers which automatically sent temperature information to their information system. The products were stored in a sandwich walk-in chiller at or below 3°C within 10 minutes of delivery. At the time of inspection, the chiller was operating at 1.5°C and a sandwich probed was less than 3°C. All refrigeration equipment was connected to the automatic recording system. This system raised an alarm if there was an issue and a manager would carry out corrective action. Patients pre-ordered food and these were made up in the sandwich chiller. Sandwiches and salads were placed into polystyrene cool boxes with ice packs. These were taken to the wards just prior to service and stayed in the cool box until service. Any sandwiches returned were discarded. On return to the kitchen the sandwiches had a temperature of below 5°C. Nursing staff were not allowed to save sandwiches on the ward for later consumption if a patient was sleeping or receiving treatment. The nurse must order sandwiches from the kitchen, then catering staff took sandwiches to wards in a cool box. Labels were placed on the sandwiches instructing staff to discard unused sandwiches.

At Hospital D, sandwiches were delivered chilled (temperature checked on delivery and recorded) and then stored for 24-hours in a monitored chiller unit until ready for packing. They were packed in a temperature-controlled packing hall into thermal wheeled boxes with eutectic plates to ensure they arrived chilled at the various hospitals. A representative sample of the thermal boxes regularly underwent a thermal tag trace to check they were maintaining temperature. Once delivered they were put directly into ward fridges (temperature checked 3 times daily and recorded). However, *L. monocytogenes* had been detected at <20 cfu/g in 6 of 7 sampled sandwiches supplied by Company X in November 2016. These sandwiches, where *L. monocytogenes* was detected, contained salad and the hospital immediately decided to no longer purchase sandwiches containing salad from Company X and continued to carry out further monitoring. The EHO carried out an inspection and an informal sampling visit on 15 December 2016 and *L. monocytogenes* was detected in an egg mayonnaise sandwich sample that was taken during this visit. The Trust then removed egg mayonnaise sandwiches from the menu. Further sampling indicated that *L. monocytogenes* was also detected in tuna mayo sandwiches. The Trust continued to work with Company X but then only purchased cheese, ham or turkey sandwiches. All salads, egg mayonnaise and tuna mayonnaise sandwiches were subsequently made in-house at the hospital. They applied *E. coli* guidance for the preparation of ready-to-eat food and used bought-in sandwich fillings which were also regularly sampled. The NHS supply chain were made aware of the above and the Trust had discussions with colleagues at PHE Colindale to determine a practical way forward on sandwich and salad provision. At Hospital D, all food was ordered at ward level for each meal service. However, some

wards offered a variety of sandwiches that were not pre-ordered for example chemotherapy unit or dialysis unit where patients did not necessarily order a meal or sandwich. If a patient was not available at meal service, they were offered a sandwich. Sandwiches offered as part of lunchtime service that were not consumed were discarded.

Relevant staff at the 4 hospitals were asked about their familiarity with the FSA guidance on reducing the risk of vulnerable groups contracting listeriosis. All apart from staff at Hospital B were aware of the guidance, although the manager onsite at Hospital B had attended in-house training on *Listeria.*

# Control measures

## Company X

The LA requested that Company X seek advice from their food hygiene consultant to assess the cleaning frequency and methodology and it was recommended to carry out daily deep cleaning. The LA also assessed the cleaning frequency of a butter depositor where *L. monocytogenes* of same WGS type as isolated from the case had been detected and provided advice to clean the butter depositor prior to use rather than the night before. Other issues identified are detailed below.

### Actions were taken

Company X replaced the washer. The contamination problem was suspected to be related to one particular dishwasher and this was replaced. Three new washers were installed; one for utensils, another for food baskets and one for non-food baskets.

Company X improved the basket washing which went through a deep clean. Grey baskets for washing, where the implicated *L. monocytogenes* strain was detected, were replaced.

The new lettuce washer dryer and the hollow aeration pipe were sent to the PHE FW&E laboratory for further testing and *L. monocytogenes* was not detected.

Work was done to improve the drainage system.

Improvements to the floor covering was agreed to be implemented over the longer term.

Dry floor cleaners were used to minimise the water on the factory floor.

Company X's processes and procedures were re-assessed, taking into account the new equipment that was installed.

A new management tool was agreed to be set up for the training of all their employees in-house with non-conformance notices issued to any staff not following procedures.

An assessment was performed on the interventions at the factory to establish control of the likely harbourage sites at the factory. This included repeat sampling at various sites where the bacterium was recovered, and food samples tested at the PHE FW&E laboratory at York.

## Hospitals

Processes within the hospital kitchen were satisfactory but there were a number of issues related to the storage of sandwiches on the wards. These issues were addressed by:

- ensuring that refrigerators used for storing patient/staff food are temperature monitored daily, the results of which were recorded, and the record sheets available for inspection
- using the correct temperature record chart (the hospital consultant microbiologist found drug fridge charts being used on food fridge charts and vice versa – drugs are stored at 2-8°C, food at 0-5°C, so there was scope for confusion on what was the 'correct' temperature for that fridge)
- following a clear escalation procedure if temperatures were out of range (that is if the second reading taken 1 hour after initial 'out-of-range' reading is >5°C then take refrigerator out of use and escalate to Estates immediately)
- including food refrigerator temperature monitoring in infection control and environmental audits
- banning the storage of patient sandwiches in refrigerators in the hospitals if they were not going to be consumed immediately
- making Level 1 Food Hygiene training mandatory within the Trust for all staff members handling patient's food
- making the hospital infection control leads aware of the risks and empowering them to make decisions regarding patient safety
- the hospitals (Hospital D specifically) undertaking steps to identify the vulnerability of the patients and making sandwiches in house for vulnerable patients and giving sandwiches from Company X to lower-risk patients

# Risk assessment

All sandwiches were prepacked at the factory and the detection of *L. monocytogenes* of the same type from the patient's blood, unopened packs of salad and sandwiches collected from the hospitals and from products and environmental sites at the manufacturer's premises indicated a common source of contamination. The patient was identified as having consumed sandwiches from the manufacturer on multiple occasions. Whilst the measures undertaken at Company X reduced the prevalence of *L. monocytogenes* within the factory and in finished products (Tables 1 and 3), products from Company X were contaminated with the incident strain of *L. monocytogenes* during 2017 (and remained identified as contaminated by this strain up to May 2019), albeit all were within legal standards.

By October 2017 the number of samples testing positive from the Company and from Hospital C had reduced to levels which were similar to products from other producers and the investigation was closed on 2 November 2017, with ongoing monitoring of Company X and its products agreed going forward. The IMT agreed that the ongoing contamination of sandwiches known to be supplied to hospitals represented a risk to hospitalised patients and a quantitative risk assessment investigating the likelihood of further cases was conducted by PHE statisticians (Appendix).

The results obtained from the quantitative risk assessment estimated the probabilities of the occurrence of cases of invasive listeriosis from the supplied contaminated sandwiches. The model predicted a single case approximately once every 3 years under sub-optimal storage conditions. Under ideal storage conditions the simulations indicate a single case of invasive listeriosis occurring once every twenty years.

The company continued to supply hospitals and therefore there was an ongoing risk of exposure to *L. monocytogenes* to vulnerable individuals in hospitals and control measures should be implemented and reinforced to reduce the risk.

Following the incident, recommendations were provided to the NHS on the provision of hospital food. It was recommended that hospitals implement advice outlined in the FSA guidance document "Reducing the risks of vulnerable groups contracting listeriosis: guidance for healthcare and social care organisations"[5]. This guidance includes opportunities for improvements in temperature control of food in hospitals.

# Discussion

An incident was declared in August 2017. The incident was initiated when an isolate of *L. monocytogenes* from the blood of a clinical case of listeriosis who was hospitalised during their incubation period was recognised using WGS typing to be within 5 SNPs of isolates from sandwiches and salads supplied to hospitals. The implicated strain was detected in food, food components and environmental sites sampled at Company X from December 2016. The patient had consumed sandwiches supplied to the hospital by Company X on 12 occasions prior to onset of symptoms. These data indicate a common route of contamination, the most plausible being that the cause of the infection in the clinical case was from consuming contaminated sandwiches whilst a hospital inpatient.

There are 3 strategies to control foodborne listeriosis. Firstly, to reduce or eliminate contamination by *L. monocytogenes* throughout the food chain. Secondly, to eliminate the *L. monocytogenes* in food, such as by cooking, or minimise growth of the bacterium in food by controlling temperature and shelf life (as well as modifying the composition of foods). Thirdly by restricting the exposure by modifying the diet, particularly for vulnerable individuals.

Firstly, to reduce or eliminate contamination by *L. monocytogenes* throughout the food chain. Commission Regulation (EC) no. 2073/2005 established microbiological criteria for specific food categories [3]. All food samples tested in this incident when placed on the market and during their shelf life (that is those sampled from hospitals) had levels of *L. monocytogenes* contamination that were below the legal limit (100 cfu/g): there are no legal limits in this regulation for these types of ready-to-eat foods before they have left the immediate control of the food business operator.

Investigations at Company X identified contamination of environmental sites. Control measures were recommended and implemented at the factory including to improve the floor drainage at the premises, replace specific washing machines and washing baskets. The ongoing microbiological surveillance of environmental swabs and foods at Company X indicated that until the end of October 2017, these measures had reduced although not eliminated, the presence of the incident strain in food produced by the company. FW&E continued testing Company X's products and the incident strain of *L. monocytogenes* was isolated after this incident investigation had finished in January, February, May, August, October, November and December 2018 as well as January, May and July 2019. Company X ceased supplying the NHS in September 2019 for other commercial reasons.

There were discrepancies in the results of microbiology testing between a private laboratory and PHE FW&E laboratory: when duplicate samples collected at Company X

were submitted to both laboratories, *L. monocytogenes* was only detected by PHE. Following the incident, Company X changed to having all testing performed by the PHE FW&E laboratory. However, this highlights the possibility of varying sensitivity and/or specificity of detection methods used by accredited laboratories. The result of this discrepancy might have changed the response by Company X and prevented the infection: the company was under the false impression that their food safety management systems were controlling the bacterium since all samples tested by the commercial laboratory were satisfactory and were reported as not containing *L. monocytogenes.* This is also an issue for enforcing authorities and purchaser audits in their ability to interpret results of manufacturers' in-house testing which is usually conducted by commercial laboratories. Performance of analytical methods can be variable, and some are more sensitive than others. It is the experience of PHE that decisions on testing laboratories and testing regimes are not well understood by food manufacturers and are often made on the basis of cost and not on the performance of the testing method, despite the accreditation status.

For food manufacturers to detect this bacterium and apply appropriate controls to their manufacturing environment, analytical test methods must be used to detect *L. monocytogenes* in 25g samples and not just above the 100 cfu/g limit. The FSA Guidance (FSA, 2016) states "Methods other than the analytical reference methods can be used provided alternative methods deliver equivalent results and the methods are validated appropriately". There is a need for better communication to all those involved with controlling *L. monocytogenes* in the food chain to ensure that results are robust and meaningful which will allow the application of interventions to eliminate or reduce, as much as possible, the bacterium in food production environments.

*L. monocytogenes* is widespread in the environment, therefore raw food components such as salad products will inevitably be contaminated by this bacterium, albeit occasionally. Manufacturers of ready to eat foods must be aware of this and take all reasonable steps to control contamination of raw materials by controlling the quality of raw materials, by cleaning and by the use of sanitisers. *L. monocytogenes* persists in harbourage sites in factories which can lead to contamination of foods. This colonisation can remain for years up to decades and be difficult to eliminate. The factory site of Company X was contaminated by the incident strain for almost 3 years (October 2016 to July 2019).

The British Sandwich Association states [6] "when they do persist it is generally because they survive in a harbourage point and are protected from the actions of cleaning and disinfection. This may be due to poor hygienic design of processing equipment or damaged areas of the fabrication of the buildings, reducing the ability to effectively clean and disinfect". Manufacturers should take stringent actions to control colonisation of food production environments and reduce as much as possible contamination of foods from these sites. It may be of note that Company X's finished

products when tested in the hospitals during the exposure period to the patient (June to July 2017) showed a higher proportion of contamination than both immediately before and after this period (Table 3), suggesting food safety management systems at the factory were not under sufficient control. Although in this incident this resulted in the identification of a single case, much larger incidents have occurred elsewhere. For example, in Canada in 2008 an outbreak of 57 cases (24 deaths) occurred when persistent contamination occurred in a cooked meat slicing plant [4]. The cooked meat products in this outbreak were consumed by patients (including in sandwiches), 72% of which were residents of long-term care facilities or hospital inpatients during their exposure period.

There is a need to clarify communication routes of microbiological test results between the various partners (the food business operator, the hospitals, STS, local authorities and the wider NHS). In this instance, microbiological testing was done as commercial contracts by PHE with either the hospital or the food business operator and in the first half of 2017, there was no or limited communication of this on-going contamination problem to the Local Authority (as well as to STS, to other hospitals or other recipients of Company X's products). Although the slowness of reporting was compounded by discrepancies between the commercial and PHE laboratories, there was communication from the hospital to the food business operator who raised a non-conformance. There should be drivers to report contamination by the food business operator to the various partners as well as greater encouragement for verification sampling aligned to the local authority inspection regimes.

The second strategy for control of listeriosis is to eliminate the *L. monocytogenes* in food, such as by cooking, or minimise growth of the bacterium in food by controlling temperature and shelf life (as well as modifying the composition of foods). The sandwiches (as well as salad products) supplied by Company X are a ready-to-eat food and therefore it is not possible to eliminate the bacterium by cooking. There are also limited options to reformulate the composition of these products to prevent multiplication of *L. monocytogenes*. Control of *L. monocytogenes* in these products at the hospital is therefore to prevent further contamination and to reduce as much as possible growth by shelf life and temperature controls. The quantitative risk assessment indicated that under sub-optimal temperature storage conditions, one case of listeriosis could be expected every 3 years caused by consumption of these sandwiches, which was reduced to one in twenty years under optimal storage conditions. Varying measures were implemented at the 4 hospitals under consideration in this incident investigation and these highlight the need to implement advice outlined in the FSA guidance [5]. This guidance was issued in 2016 but was preceded by hospital workshops run in 2015 to explain the introduction of the guidance; it is therefore concerning that hospitals were not fully implementing the guidance. Problems detected in similar incidents indicate there are opportunities for improvements in temperature control at hospitals, although this may be difficult in hospital environments. Further consideration needs to be given

on how to achieve this as it is clearly one of the important controls in preventing listeriosis in hospitals.

The final method of controlling listeriosis is by restricting the exposure through modification of the diet, particularly for vulnerable individuals. In this incident, all 4 hospitals served sandwiches to vulnerable patients although one hospital varied this to exclude specific products.

The NHS website states that “Listeriosis is usually caught from eating food containing *Listeria* bacteria. You can get it from lots of types of food, but it's mainly a problem with:

- unpasteurised milk
- dairy products made from unpasteurised milk
- soft cheeses, like camembert and brie
- chilled ready-to-eat foods, like prepacked sandwiches, pâté and deli meats”[7]

For the pregnant woman, the NHS website advises that “If you're pregnant, you should avoid eating foods that have the highest risk of causing listeriosis. These include:

- some uncooked soft cheeses – including brie and camembert
- all types of pâté – including vegetable pâté
- unpasteurised milk or dairy products
- any undercooked food”[7]

There is no advice specifically for the immunocompromised, but the NHS website advises the elderly that “There are several simple ways to avoid a *Listeria* infection. The FSA advises the following:

- Don’t eat foods that are past their use-by date, even if they smell fine. Use-by dates indicate how long a food will remain safe (if food is frozen or cooked before the use-by date, it can be kept for longer).
- Follow the storage instructions on food packaging, such as 'freeze on day of purchase', 'cook from frozen' or 'defrost thoroughly before use and use within 24 hours'.
- Make sure your fridge is at the right temperature, ideally between 0°C and 5°C.”[8].

The FSA guidance, states “with appropriate food safety controls and monitoring in place there should be no need to limit or restrict menu choice for vulnerable individuals”[5].

PHE is aware of 10 similar incidents in England and Wales of listeriosis infections resulting from consumption of pre-prepared sandwiches served in hospitals. Further incidents have occurred in Northern Ireland and Scotland. There may be a need to recommend better and consistent advice to provide safe food for the NHS.

Hospitals should implement the advice outlined in the FSA guidance [5]. This advice reminds those in healthcare and social care organisations serving food that they are legally required to manage food safety using a documented Food Safety Management System (FSMS) based on HACCP principles. In addition to establishing controls, critical limits, monitoring procedures and corrective actions in relation to *L. monocytogenes*, the FSMS should include key procedures for the control of *L. monocytogenes* including:

- procurement/purchase
- training, instruction and supervision
- management of on-site retailers and caterers, where applicable
- food brought in by patients and/or visitors
- microbiological testing, where applicable

However, the most effective control to reduce or eliminate contamination by *L. monocytogenes* is at the point of production, as this would reduce the importance of the second and third intervention strategies.

# References


1. European Food Safety Authority (EFSA) & European Centre for Disease Prevention and Control (ECDC), The European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2017. EFSA Journal, 2018. 16(12): p. e05500.
2. Dallman, T., et al., SnapperDB: a database solution for routine sequencing analysis of bacterial isolates. Bioinformatics, 2018. 34(17): p. 3028-3029.
3. Commission Regulation (EC) No 2073/2005 of 15 November 2005 on microbiological criteria for foodstuffs. [Online]. [Accessed March 2019]. Available from https://eur-lex.europa.eu.
4. Currie, A., et al., Multi-Province Listeriosis Outbreak Linked to Contaminated Deli Meat Consumed Primarily in Institutional Settings, Canada, 2008. Foodborne Pathog Dis, 2015. 12(8): p. 645-52.
5. Reducing the risks of vulnerable groups contracting listeriosis: guidance for healthcare and social care organisations. [Online]. [Accessed March 2019]. Available from www.food.gov.uk/sites/default/files/media/document/listeria-guidance-june2016-rev_0.pdf/
6. The British Sandwich Association, Controlling Listeria in the Supply Chain. Issue 3
7. Listeriosis. [Online]. [Accessed March 2019]. Available from www.nhs.uk/conditions/listeriosis/
8. Elderly take Listeria 'gamble'. [Online]. [Accessed March 2019]. Available from www.nhs.uk/news/older-people/elderly-take-listeria-gamble/

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# Abbreviations

| | |
|---|---|
| **CC** | Clonal complex |
| **cfu/g** | Colony forming units per gram |
| **EHO** | Environmental Health Officer |
| **FS** | Field Service |
| **FW&E** | Food Water and Environmental |
| **FSA** | Food Standards Agency |
| **GBRU** | Gastrointestinal Bacteria Reference Unit |
| **GID** | Gastrointestinal Infections Department |
| **HACCP** | Hazard analysis critical control point |
| **IMT** | Incident management team |
| **ISO** | International Standards Organisation |
| **LA** | Local Authority |
| **NHS** | National Health Service |
| **PHE** | Public Health England |
| **SNP** | Single nucleotide polymorphism |
| **STS** | Support Training and Services Ltd (NHS Supply Chain) |
| **UKAS** | United Kingdom Accreditation Services |
| **WGS** | Whole genome sequencing |
| **Y&H HPT** | Yorkshire and The Humber Health Protection Team |

# Appendix

## Quantitative Microbiological Risk Assessment

### Risk assessment of invasive listeriosis from *L. monocytogenes* in pre-packed sandwiches served in the National Health Service

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05/10/2018

## Introduction

A single case of invasive listeriosis was identified as having occurred within an English hospital, in which whole genome sequencing identified that the type of *L. monocytogenes* causing the patients illness was identical (CC121 t5.450) to that found in sandwiches and salads on several occasions on samples tested since the end of 2016.

The patient who had invasive listeriosis was immunocompromised and consumed sandwiches served by the hospital on 11 occasions whilst an in-patient, between 13 June and 1 July 2017. To date this was the only patient identified as infected by this specific strain of *L. monocytogenes.*

The sandwich manufacturer produces approximately 40,000 sandwiches per day, of which around 30% (12,000 sandwiches per day) are sent to hospitals in England.

This quantitative risk assessment was undertaken to estimate what could be the range of possible numbers of cases of invasive listeriosis in one year in NHS hospital patients that eat sandwiches from a particular manufacturer contaminated with low levels of a specific strain of *L. monocytogenes*, for scenarios of “ideal” and “sub-optimal” storage, and prevailing or reduced microbial load.

## Method

The number of sandwiches supplied by this manufacturer that are consumed by NHS hospital patients in England in a day

Given the information on the number of sandwiches supplied to hospitals it has been assumed in this risk assessment that there are, on average 12,000 sandwiches supplied to NHS

hospitals in England each day, including weekends from this particular manufacturer. The number supplied on a particular day ($N_t$) is assumed to have a Poisson distribution with a mean of 12,000. It has been assumed that there is no wastage, and that all sandwiches are consumed by NHS patients, rather than staff and visitors.

The probability of a sandwich from this particular supplier being contaminated on a particular day

The "detection test" is based on testing a homogenised solution containing a 25g sample taken from each sandwich and testing the entirety of this solution.

From November 2016 to August 2017 a total of 376 sandwich samples from the supplier was tested. *L. monocytogenes* was detected in 13 samples (3.5%). It has been assumed that the probability of sandwiches contaminated with *L. monocytogenes* can vary from day to day, around an average probability. No information is provided as to whether *L. monocytogenes* contamination is dependent upon the sandwich filling or type of bread used. Therefore, it has been assumed that contamination is independent of sandwich type. The probability of a sandwich from this particular supplier being contaminated on a particular day was assumed to follow a Normal distribution with mean ($m$) equal to 13/376, and with standard deviation ($se$) equal to $\sqrt{\frac{m(1-m)}{376}}$.

The level of contamination in a contaminated sandwich from this manufacturer

The "enumeration test" is based on testing a small fraction of the solution used for the "detection test". From this it is attempted to grow colonies, and these are then counted to be 0, 1, 2, etc….

All 13 samples that were found to be contaminated in this study of sandwiches from this supplier were found to be contaminated with <20 cfu/g (that is between 1 and 19 cfu/g).

A published LACORS study[1] conducted between April 2005 and March 2006, tested 3249 sandwiches in hospitals and care homes. This study found 88 (2.7%) to be contaminated with *L. monocytogenes*. Eighty-seven of these were found to be contaminated with <10 cfu/g (that is between 1 and 9 cfu/g). This value follows from there being no colonies forming in a dish. One sample was found to be contaminated with 20 cfu/g. This follows from 2 colonies forming in the dish.

Due to its "heavy upper tail" a lognormal distribution has been assumed to characterise the distribution of the level of contamination in a contaminated sandwich from this manufacturer.

While the samples tested in the LACORS study are not necessarily from the supplier, it was decided to pool the values from the 88 contaminated samples in the LACORS study, and the 13 contaminated samples from testing sandwiches from this manufacturer. Interval censored values (that is values only known to be within some interval) and the one uncensored value of 20cfu/g were fitted to an interval censored regression model with no explanatory variables. And before fitting this model the values were converted to their log base 10 equivalent. Using the 100 interval censored values and the 1 value of exactly 20cfu/g, the regression model failed to converge to a solution. Thus, one of the 87 <10 cfu/g values was altered to be a value of 9 cfu/g (which is consistent but not equal to the measured value). This provided estimates of the mean and standard deviation equal to 0.5733089, and 0.21304657 (calculated as $(\sqrt{\frac{\hat{\sigma}^2}{n} + \hat{\sigma}^2}$ )
where *n* is the sample size and $\hat{\sigma}^2$=estimated residual variance).

The equivalence of sampling from this Normal distribution for the log transformed values to sampling from a lognormal distribution for the untransformed values, means that any draw of $x$ from a Normal distribution with this mean and standard deviation is a random draw of $10^x$ from the best fitting lognormal distribution for the level of contamination in cfu/g.

It has been assumed that the sample tested is representative of the whole sandwich, that is there is negligible variation within a sandwich, that is if there are $d$ cfu/g and a sandwich weighs $G$grams, then the total number of cfu in that sandwich is $dG$.

Information on the weight of an egg sandwich and a plain beef sandwich was provided. For each half egg sandwich there was: 40g of filling and 104g of bread/butter; and for each beef sandwich there was: 36g of filling and 107g of bread/butter. Thus, it has been assumed that the approximate weight ($G$) of a pre-packed sandwich with 2 rounds is 280g.

Reduction in microbial load

Simulations were also performed for the scenario of a reduction in the microbial load from that described above. The chosen scenario was that the manufacturer was able to reduce the initial load to one tenth of that describes in the above section.

Time of microbiological testing and pathogen growth

No information has been provided on when the microbiological testing was performed in relation to the time of production. For this risk assessment a worse case situation would occur if the microbiological testing was assumed to have been performed early into the shelf-life of the product. It was decided to assume this worst-case situation, and

therefore it has been assumed that the bacterial load of *L. monocytogenes* was obtained from samples taken 12 hours post production. Thus, if the time period between production and consumption is 12 hours, and the sandwich is contaminated, we take the level of contamination as a valued sampled at random from the lognormal distribution (described above). But if the time period between production and consumption is 18 hours or more and the sandwich is contaminated we assume exponential growth of the pathogen from the level of contamination we sample from the lognormal distribution at 12 hours. This exponential growth is assumed to continue for *t* hours where *t* is the sampled time period between production and consumption.

Shelf life and the time period between production and consumption

While both of these parameters may be obtained from information held within the Food, Water and Environment laboratories, they were not provided apart from an assumed shelf-life of 3 days (72 hrs). The British Sandwich Association recommends that the use-by date should be the day of production plus 2 days. Thereby ensuring that the time between production and the end of the use-by period is a maximum of 3 days.

With no data on the timing of consumption some reasonable distribution needs to be used to represent this within a hospital setting. It has been assumed that at least the first 12 hours post production is required for distribution and that at 72 hours post production there are no sandwiches remaining to be consumed. It has been assumed that the time period between production and consumption follows a discrete triangular distribution with parameters a (the shortest possible time period in hours)=12, b (the longest possible time period in hours)=72 and c (the most likely time period in hours)=12. Sandwiches are assumed to be consumed at meal times which occur every 6 hours in hospitals. Thus, the probability density function for $c$ (which is related to the time period in hours) is assumed to be;

$$P(X = c) = \frac{11 - c}{55}, where\ c = 1,2, \dots ,11$$

and where $c$ =1 corresponds to a time period between production and consumption of 12 hours, $c$ =2 corresponds to a time period between production and consumption of 18 hours and $c$ =11 corresponds to a time period between production and consumption of 72 hours.

**Table 1: Probability density function for the time period between production and consumption**

| Time period between production and consumption (hours) | $c$ | P(X=c) |
|---|---|---|
| 12 | 1 | 0.1818182 |
| 18 | 2 | 0.1636364 |
| 24 | 3 | 0.1454545 |
| 30 | 4 | 0.1272727 |
| 36 | 5 | 0.1090909 |
| 42 | 6 | 0.0909091 |
| 48 | 7 | 0.0727273 |
| 54 | 8 | 0.0545455 |
| 60 | 9 | 0.0363636 |
| 66 | 10 | 0.0181818 |
| 72 | 11 | 0 |

Exponential growth in *L. monocytogenes* load

Simulations have been done for 2 different assumptions about how bacteria grow in number. One assumption is that there is a doubling of the number of bacteria every 18.1 hours (this is assumed to be the growth in an ideal storage temperature of 5 °C). The other assumption is that there is a doubling of the number of bacteria every 6.86 hours (this is assumed to be the growth in a "sub-optimal" storage temperature of 10 ˚C).

An exponential growth model of the form

$$d_t = d_0\left(1 + \frac{p}{100}\right)^t$$

is used, where $p$ is the percentage increase every hour; $t$ is the number of hours from some initial time point; $d_0$ is the number of bacteria at that initial time point; and $d_t$ is the number of bacteria $t$ hours after that initial time point.

**Figure 1: Growth under 'ideal' conditions (5°C)**

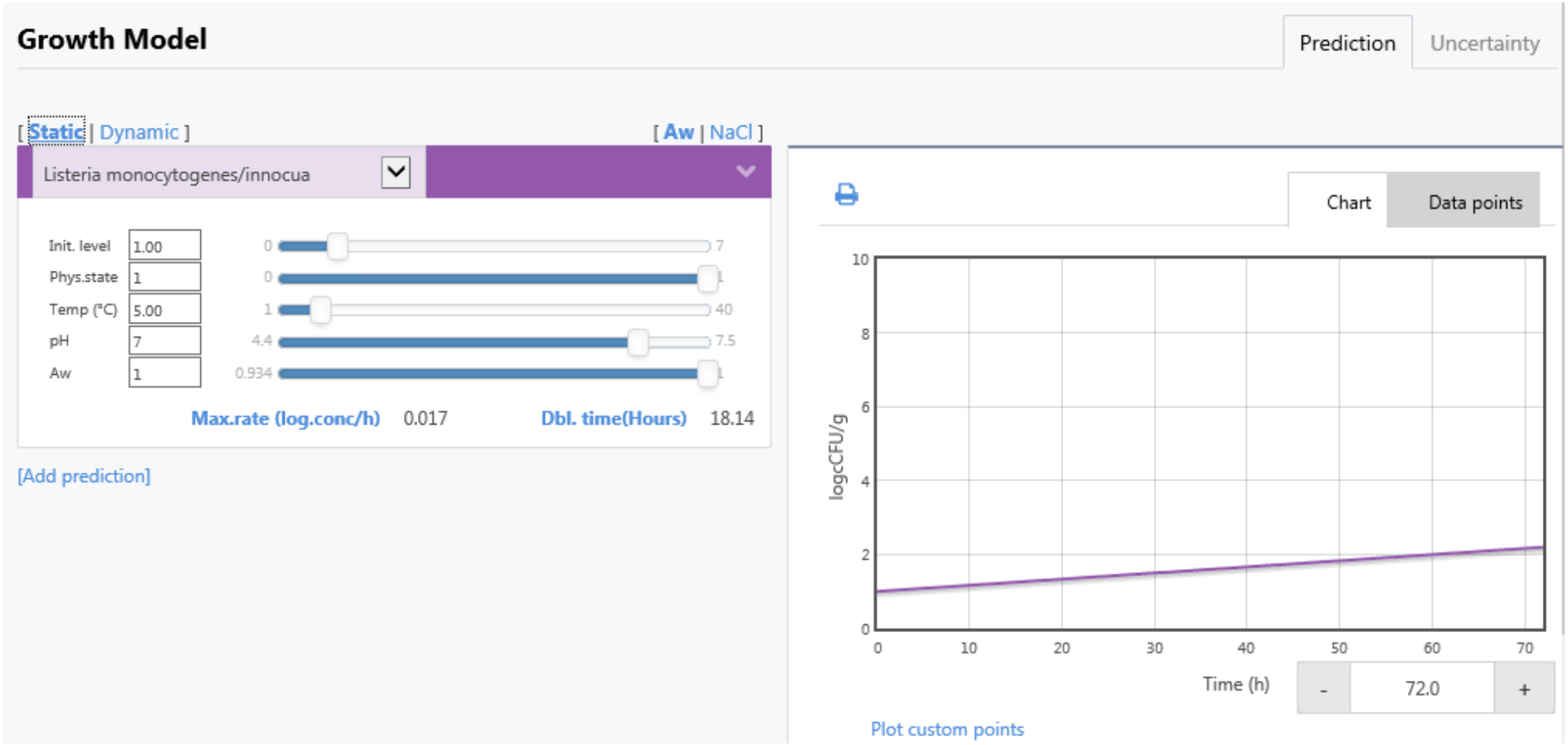


**Figure 2: Growth under 'sub-optimal' conditions (10˚C)**

If there is a doubling in *t* hours, this means:

$$\left(1+\frac{p}{100}\right)^{t}=2$$

$$t\left\{log_{10}\left(1+\frac{p}{100}\right)\right\}=log_{10}(2)$$

$$log_{10}\left(1+\frac{p}{100}\right)=\frac{log_{10}(2)}{t}$$

$$1+\frac{p}{100}=10^{\left(\frac{log_{10}(2)}{t}\right)}$$

From this we calculate that if $t$=18.1 (based on "ideal" storage conditions of 5 ˚C in Figure 1) then $p$ is 3.9 (that is there will be a 3.9% increase in bacteria every hour). And if $t$=6.86 (based on "sub-optimal" storage conditions of 10 ˚C in Figure 2) then $p$ is 10.6 (that is there will be a 10.6% increase in bacteria every hour).

Dose-response

There has been much written about the estimation of dose-response relationships for *L. monocytogenes*. A dose-response relationship estimates the probability of an adverse outcome for a given dose of *L. monocytogenes*. Most are models for invasive listeriosis. Most are based on a single strain of *L. monocytogenes*. Different dose-response relationships have been estimated for those of different susceptibility.

**Table 2: The estimated probability of invasive illness for an individual aged 65 or older for a range of ingested dose.**

| $\log_{10}$(dose) | Estimated marginal probability of invasive illness for an individual aged 65 or older ($p$) |
|---|---|
| 0.0 | 1.50e-10 |
| 0.5 | 4.80e-10 |
| 1.0 | 1.50e-09 |
| 1.5 | 4.80e-09 |
| 2.0 | 1.50e-08 |
| 2.5 | 4.70e-08 |
| 3.0 | 1.50e-07 |
| 3.5 | 4.60e-07 |
| 4.0 | 1.40e-06 |
| 4.5 | 4.30e-06 |
| 5.0 | 0.000013 |
| 5.5 | 0.000038 |
| 6.0 | 0.00011 |
| 6.5 | 0.00029 |
| 7.0 | 0.00075 |
| 7.5 | 0.0018 |
| 8.0 | 0.0043 |
| 8.5 | 0.0093 |
| 9.0 | 0.019 |
| 9.5 | 0.037 |
| 10.0 | 0.066 |
| 10.5 | 0.11 |
| 11.0 | 0.18 |

Table III of Pouillot et al [2] shows the estimated probability of invasive listeriosis for a $\log_{10}$ dose of between 0 and 11 (equivalent to a dose of between 0 and $10^{11}$ cfu), for a number of sub-populations of different susceptibility. The estimated probabilities for the sub-population of those aged 65 or older are reproduced in Table 2.

In order to use this dose-response relationship in a quantitative risk assessment, it is desirable to obtain an explicit functional form for the relationship. Pouillot et al provide the parameter estimates of the lognormal-Poisson model they used. However, a simple cubic model fits the published estimated probabilities in the above table well and provides a simple algebraic form of the relationship.

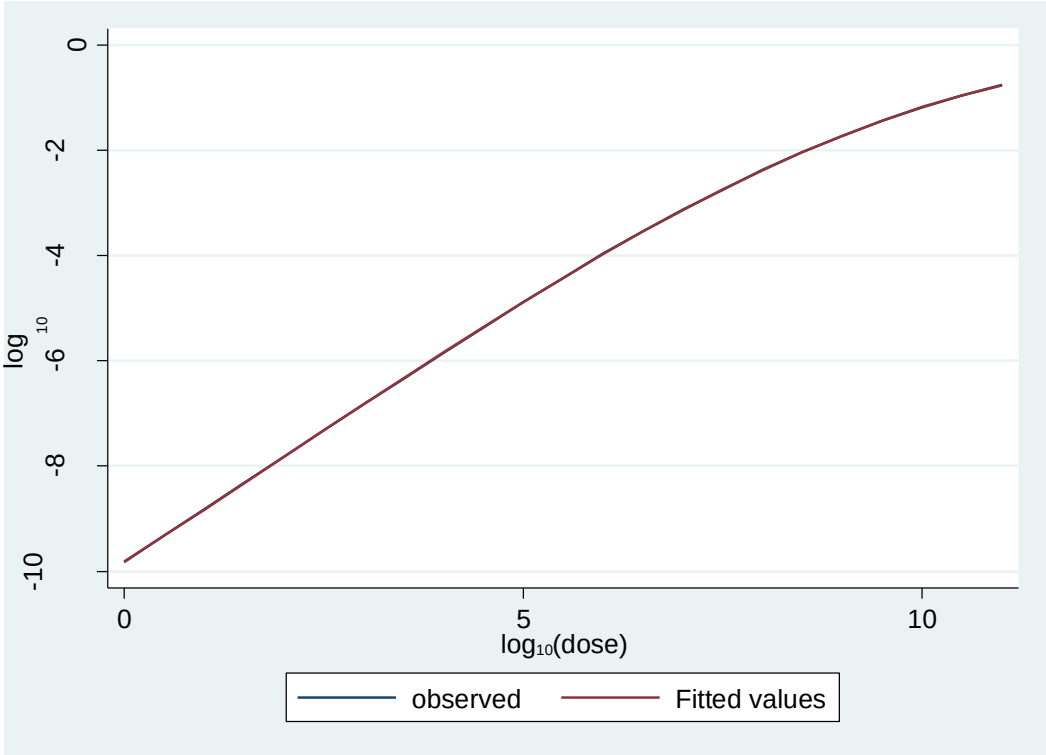
The following provided the best fit model to the probabilities in the above table:

$\log_{10}(p) \approx -4.4214+9.0775*d-2.8593*(d^2)-2.8055*(d^3)$

where $d = log_{10}(dose) - 5.5$

A random draw for the $\log_{10}$ of the dose of *L. monocytogenes* (after allowing for exponential growth if the random draw for the time period from production to consumption is greater than 12 hours) can be input into this equation to obtain the value for the $\log_{10}$ of $p$. Anti-logging this then obtains the probability of invasive illness for a patient if receiving a given dose of *L. monocytogenes*.

**Figure 3: The fitted dose response model from a cubic regression.**




The simulated probability of invasive illness ($p_i$) for a patient eating a contaminated sandwich of the simulated dose was used to categorise the patients as having invasive illness or not. A random number was generated from a uniform(0,1) distribution ($r_i$), and the patient was simulated to develop an invasive illness if $p_i < r_i$ and to not develop an invasive illness if $p_i > r_i$.

The number of simulations performed

For each of the "ideal" and "sub-optimal" storage conditions a total of 1,000 simulations were run. A period of 365 days was considered, and the number of patients in each simulation with an invasive illness (patients simulated to get an invasive illness in a year), was obtained. All simulations were undertaken using random number generators in Stata 13.0, with initial seeds of 29156862 and 15442477 used for "ideal" and "sub-optimal" simulations respectively. For the simulations with a reduced microbial load, initial seeds of 12176437 and 48751010 used for "ideal" and "sub-optimal" simulations respectively.

## Results

Simulated results were obtained for 1,000 simulated years when the sandwiches were stored at an “ideal” 5 °C. In 56 (5.6%) of these simulated years there occurred at least one case of invasive listeriosis. For 52 of these simulated years a single case occurred; for 2 of these simulated years 2 cases occurred; and in 2 of these simulated years 3 cases occurred.

Simulated results were also obtained for 1,000 simulated years when the sandwiches were stored at a “sub-optimal” 10 °C. In 381 (38.1%) of these simulated years there occurred at least one case of invasive listeriosis. For 306 of these simulated years a single case occurred; for 64 of these simulated years 2 cases occurred; and in 11 of these simulated years 3 cases occurred. The results are presented in Table 3.

**Table 3: The frequency and percentage of simulations in which invasive listeriosis was obtained by the 2 storage conditions considered**

| Number of cases occurring | “Ideal” storage conditions | | “Sub-optimal” storage conditions | |
|---|---|---|---|---|
| | Frequency | Percentage | Frequency | Percentage |
| 0 | 944 | 94.4% | 619 | 61.9% |
| 1 | 52 | 5.2% | 306 | 30.6% |
| 2 | 2 | 0.2% | 64 | 6.4% |
| 3 or more | 2 | 0.2% | 11 | 1.1% |
| Total | 1000 | 100.0% | 1000 | 100.0% |

Reducing the simulated microbial load to one tenth of that used in Table 3, simulated data for 1000 years were also obtained. For “ideal” storage conditions simulations, only 8 (0.8%) of the simulated years had a single case of invasive listeriosis, and no years had more than one case of invasive illness. For the “sub-optimal” storage, of the 1000 simulations in 56 (5.6%) of these simulated years a single case occurred; and for 1 of these simulated years 2 cases occurred. The results of the simulations from these scenarios are presented in Table 4.

**Table 4: The frequency and percentage of simulations in which invasive listeriosis was obtained by the 2 storage conditions considered when the microbial load is reduced to one tenth.**

| Number of cases occurring | “Ideal” storage conditions | | “Sub-optimal” storage conditions | |
|---|---|---|---|---|
| | Frequency | Percentage | Frequency | Percentage |
| 0 | 992 | 99.2% | 943 | 94.3% |
| 1 | 8 | 0.8% | 56 | 5.6% |
| 2 | 0 | 0.0% | 1 | 0.1% |
| 3 | 0 | 0.0% | 0 | 0.0% |
| Total | 1000 | 100.0% | 1000 | 100.0% |

## Conclusions

In situations like this where we have some direct evidence of the rate of invasive listeriosis from a specific source (a rate of invasive listeriosis of 1 case per year among NHS hospital patients in England) it is reasonable to expect an adequate simulation model to be consistent with the observed rate. So, we expect the overall rate of illness predicted by our simulation model to be consistent with 1 case per year.

The simulation model assuming ideal storage conditions (5 °C) predicts that we would observe one or more cases a year every 18 years (1000/56). And the simulation model assuming sub-optimal storage conditions (10 °C) predicts that we would expect to observe one or more cases a year every 3 years (1000/381).

From these simulated results it is possible to draw some evidence for the storage conditions being sub-optimal. However, this is not particularly strong as there is just a single time period of data, making any attempt to understand whether the observed data is more likely to have been generated from an ideal or sub-optimal storage scenario. For the ideal storage simulations, we could expect to have observed a single case of invasive listeriosis within a year in 5.2% of simulations, while in the sub-optimal storage 30.6% of simulations generate a single case in a year.

This quantitative risk assessment does indicate a reasonably high probability of the occurrence of a single case of invasive listeriosis from consumption of the supplied contaminated sandwiches.

The simulations performed under the scenario that microbial load is reduced to one tenth of that currently observed in the available microbiological testing data, provide as expected fewer cases of invasive listeriosis. The “sub-optimal” storage and reduced microbial load simulations provide results very similar to those obtained from the “ideal” storage when using the microbial load observed in testing data.

In all scenarios, there are years in which simulated cases of invasive listeriosis occur, indicating that there is a risk of invasive listeriosis, albeit small in absolute terms from the consumption of sandwiches with what is currently considered to be acceptable levels of contamination of 'Not Detected in 25g'.

Limitations

There are a number of assumptions used in this risk assessment. Probably the most important is that it assumes that microbiological testing was carried out 12 hours after production. This assumption would not have had to be made if the time from production to testing was either always some standard or was recorded along with test results at the time of testing. As a result of this assumption we have allowed for the number of bacteria in a contaminated sandwich to grow exponentially from the time of testing up

until the time of consumption (assumed to be between 12 and 72 hours after production). This is a worst-case scenario because we assume that testing and thus the initial dose as enumerated in the contaminated sandwiches that were tested, was when sandwiches might be first consumed rather than when they might be last consumed.

It was also assumed that all the sandwiches supplied were consumed by patients, without wastage. This is very unlikely to be the actual situation, with both staff and visitors consuming a proportion of the supply. There is also likely to be some wastage at the end of shelf-life. A more realistic situation would result in some contaminated sandwiches not being consumed by patients, and again result in in fewer cases of invasive illness.

The estimated dose-response relationship we have assumed is that which has been published by Pouillot et al for the general population aged over 65 years old. A hospital population, whilst largely being composed of those over 65 isn't exclusively so. It is also more likely to have a large proportion of patients that are immunocompromised. Pouillot et al does provide estimated dose-response relationships for other population subgroups, including immunocompromised. If a dose-response relationship more representative of a hospital population were available, then this would result in a greater number of cases of invasive illness.

Overall, it is difficult to assess which of the above assumptions is more serious in the sense of affecting whether the simulated data provides results that could be realised. However, even if information were available to make more realistic simulations whether this would make a substantive change to the conclusions drawn from the relatively unsophisticated risk assessment presented is difficult to gauge.

## References

1. Little CL, Barrett NJ, Grant K, McLauchlin J. Microbiological safety of sandwiches from hospitals and other health care establishments in the United Kingdom with a focus on Listeria monocytogenes and other Listeria species. *J Food Prot*. 2008 Feb;71(2):309-18.
2. Pouillot R, Hoelzer K, Chen Y, Dennis SB. Listeria monocytogenes dose response revisited--incorporating adjustments for variability in strain virulence and host susceptibility. *Risk Anal*. 2015 Jan;35(1):90-108. doi: 10.1111/risa.12235. Epub 2014 Jun 26.