International Association for Food Protection® WEBINAR

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# Listeriosis in South Africa – Lessons Learned

Sponsored by Ecolab and Hosted by GMA Science and Education Foundation and the GMA Science and Regulatory Affairs Division

June 7, 2018 10:00 a.m. CDT

# WEBINAR HOUSEKEEPING

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Questions should be submitted to the presenters during the presentation via the **Q & A section** at the right of the screen.

# WEBINAR HOUSEKEEPING

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Peter K. Ben Embarek is currently working with the World Health Organization (WHO) at its Headquarters in managing the International Food Safety Authorities Network (INFOSAN). Previously from WHO's China Office, he was providing policy and technical advice to the government of China on food safety and nutrition issues. He joined WHO at its HQ in Geneva, Switzerland in 2001. Dr. Ben Embarek served with the Food and Agriculture Organization of the United Nations (FAO) beginning in 1995. Dr. Ben Embarek received his MSc. Degree in Food Science and Technology and a Ph.D. in Food Safety from the Royal Agricultural and Veterinary University of Copenhagen, Denmark.


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Henk C. den Bakker currently works as an assistant Professor in Bioinformatics at the Center for Food Safety of the University of Georgia. He received a PhD in Mycology at Leiden University in the Netherlands in 2005. From 2005 to 2014 Hendrik worked as a Research associate at Cornell University. Dr. den Bakker held a position as assistant professor in population modelling and statistics at the department of animal and food sciences at Texas Tech University. He (co-)authored 50 PubMed indexed publications on genomics and population genetics of foodborne pathogens and spoilage organisms. Dr. Den Bakker's current research focuses on the novel field of food safety informatics.

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# Listeriosis outbreak in South Africa: Lesson learned

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# The burden of foodborne diseases is substantial

## Every year foodborne diseases cause:

almost **1 in 10** people to fall ill

**33 million** healthy life years lost

## Foodborne diseases can be deadly, especially in children <5

**420 000** deaths

Children account for **1/3** of deaths from foodborne diseases

**FOODBORNE DISEASES ARE PREVENTABLE.**
**EVERYONE HAS A ROLE TO PLAY.**

WHO ESTIMATES OF THE GLOBAL BURDEN OF FOODBORNE DISEASES

# Foodborne diseases in the WHO African Region

## Every year

**>91 million** people fall **ill**

**137 000** people **die**

representing **1/3** of the global **death** toll for foodborne diseases

**Diarrhoeal diseases** are **responsible for 70%** of the burden of foodborne diseases

- Non-typhoidal *Salmonella*
- Foodborne cholera
- *E. coli*

**Chemical hazards** (cyanide and aflatoxin) **cause ¼ of deaths**

**Paralysis (Konzo)** caused by cyanide in cassava, is unique to the African Region, resulting in death in **1 in 5** people affected

**FOODBORNE DISEASES ARE PREVENTABLE.**
**EVERYONE HAS A ROLE TO PLAY.**

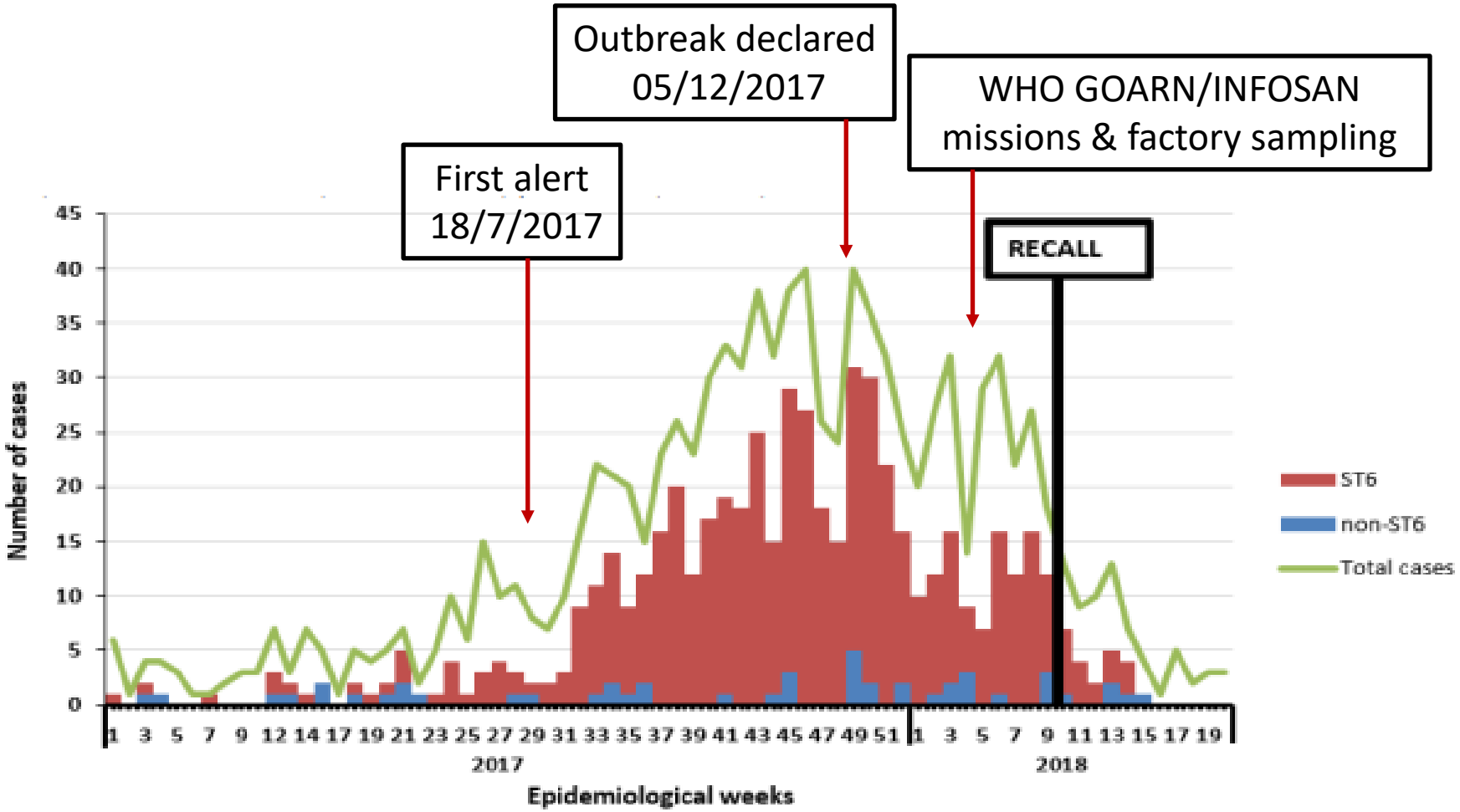
# Estimate of the global burden of listeriosis

- In 2010, it was estimated that globally, listeriosis resulted in
  - **23 150 illnesses** (95% credible interval 6061–91 247),
  - **5463 deaths** (1401–21 497), and
  - **172 823 DALY*s** (44 079–676 465). The proportion of perinatal cases was 20·7% (SD 1·7).

Urgent efforts are needed to fill the missing data in developing and emerging economies. The authors were unable to identify incidence data for Africa, the Middle East and South Asia.

*DALY : disability-adjusted life year

# Epidemiological investigations



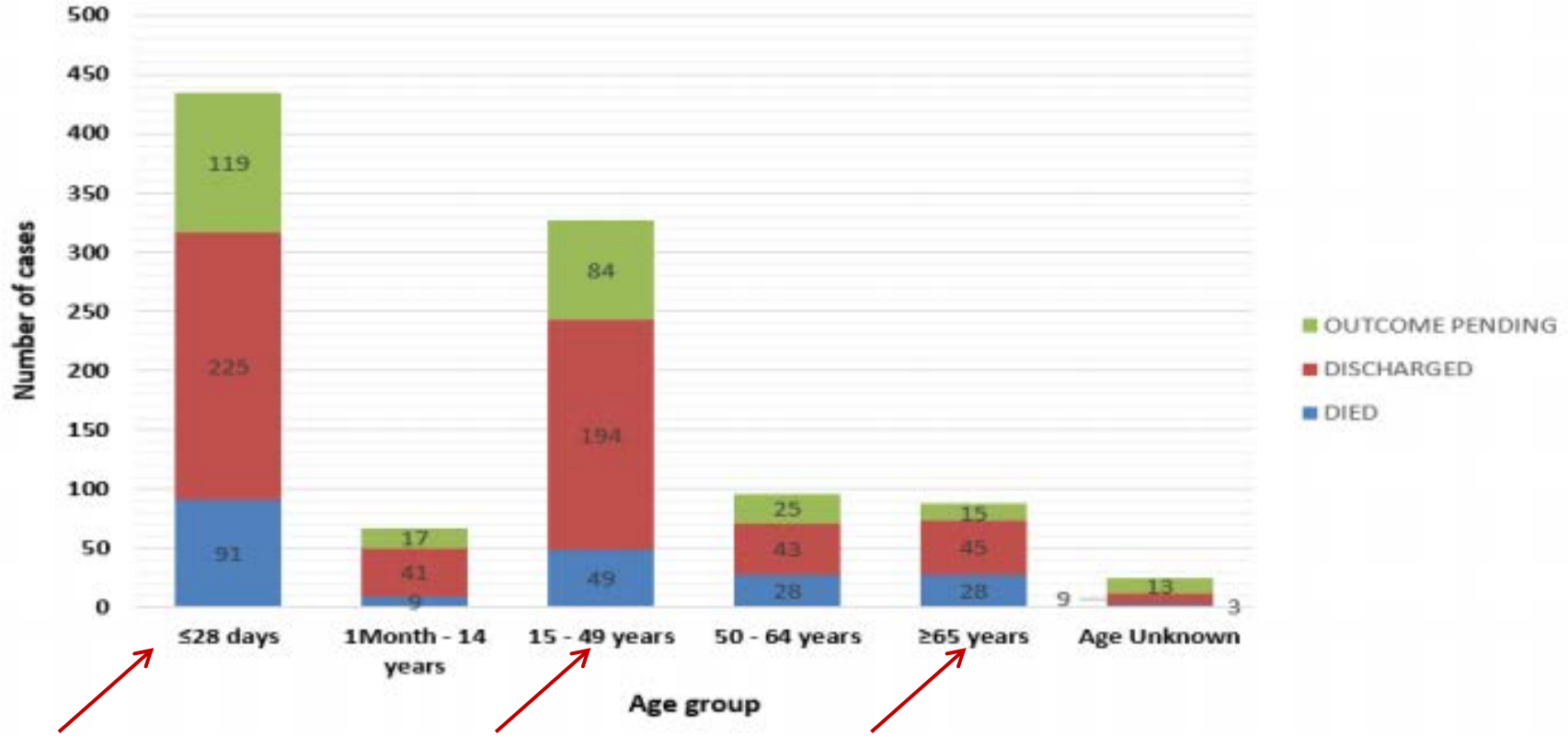

**Epidemic curve of laboratory-confirmed listeriosis cases listed according to date of sample collection (n=1 038) and sequence type (ST) (n=564), South Africa, 01 January 2017 to 22 May 2018**

As of 22 May, 1038 Cases, including 208 deaths

http://www.nicd.ac.za

SITUATION UPDATE ON LISTERIOSIS OUTBREAK, SOUTH AFRICA

# Listeriosis: high risk groups




Age distribution and outcome of laboratory-confirmed listeriosis cases, South Africa, 01 January 2017 to 22 May 2018 (n=1 038)

http://www.nicd.ac.za

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

SITUATION UPDATE ON LISTERIOSIS OUTBREAK, SOUTH AFRICA

Date of issue: 13 April 2018. Issued by: Centre for Enteric Diseases and Division of Public Health Surveillance and Response

# Food most often associated with listeriosis include:

- Foods with a long shelf-life under refrigeration
- Ready-to-eat foods consumed without further cooking
- In past outbreaks, foods involved included ready-to-eat frankfurters, meat spread (paté), smoked salmon, fermented sausages, dairy products (including soft cheeses, unpasteurized milk and ice cream) and prepared salads as well as fresh vegetables and fruits








# The outbreak investigation

- **Surveillance & Epidemiological investigation :**
  - Strengthened surveillance and reporting; Listeriosis made to a notifiable disease; Sharing of data from provincial and local level & private and public laboratories and health facilities
- **Case investigation :**
  - Case or relatives interviewed using detailed questionnaires

- **Whole genome sequencing of listeria isolates:**
  - By mid-May, more than 1200 strains from clinical samples and food/environmental samples had been sequenced. 92% of clinical isolates belong to the sequence type 6 (ST6).
  - During the on-going investigation and follow up activities, all clinical, food and environmental isolates are undergoing whole genome sequencing.
  - NICD* has deposited 10 representative ST6 sequences in the global public GenBank - NCBI database (https://www.ncbi.nlm.nih.gov/Traces/study/?acc=SRP142281).

*NICD: National Institute for Communicable Diseases, South Africa - http://www.nicd.ac.za

# The outbreak investigation


- **Identification of the food source :**
  - Vast majority of patients yielded the same WGS ST6 type pointing towards one common source.
  - Patients interview indicated ready-to-eat meat product most likely to be the source. Especially polony sausages.
  - Breakthrough came from investigation of a cluster of children in a creche which led to a particular processing factory producing polony sausages and other ready-to-eat meat products.
  - ST6 Listeria monocytogenes was found in several places in the processing factory and on final products


- **Announcement of the food source and recall :**
  - The source was announced publicly on 4th March 2018 and a nation wide recall was initiated.
  - Subsequently, additional processing RTE factories were found positive for Listeria monocytogenes (other ST types) and additional recalls initiated.

# The follow up

- **Managing the outbreak response and strengthen systems :**
  - Incident Management Team put in place with participation from multiple sectors and international
  - Objectives are to control and end the outbreak and strengthen systems to prevent future outbreaks
  - Work on-going to revise regulations and standards; strengthen food inspections ad enforcement of regulations; evidence based food monitoring and surveillance program; assess closed factories; increase consumer education.

# The international dimension : WHO Response

## International Food Safety Authorities Network

Voluntary network of national authorities involved in food safety from around the world (600+ participants from 188 Member States) managed jointly by FAO and WHO

# International Food Safety Authorities Network

## INFOSAN Aims:


**Promote the rapid exchange of information during food safety related events**


**Share information on important food safety related issues of global interest**


**Promote partnerships and collaboration between countries, and between networks**


**Help countries strengthen their capacity to manage food safety emergencies**

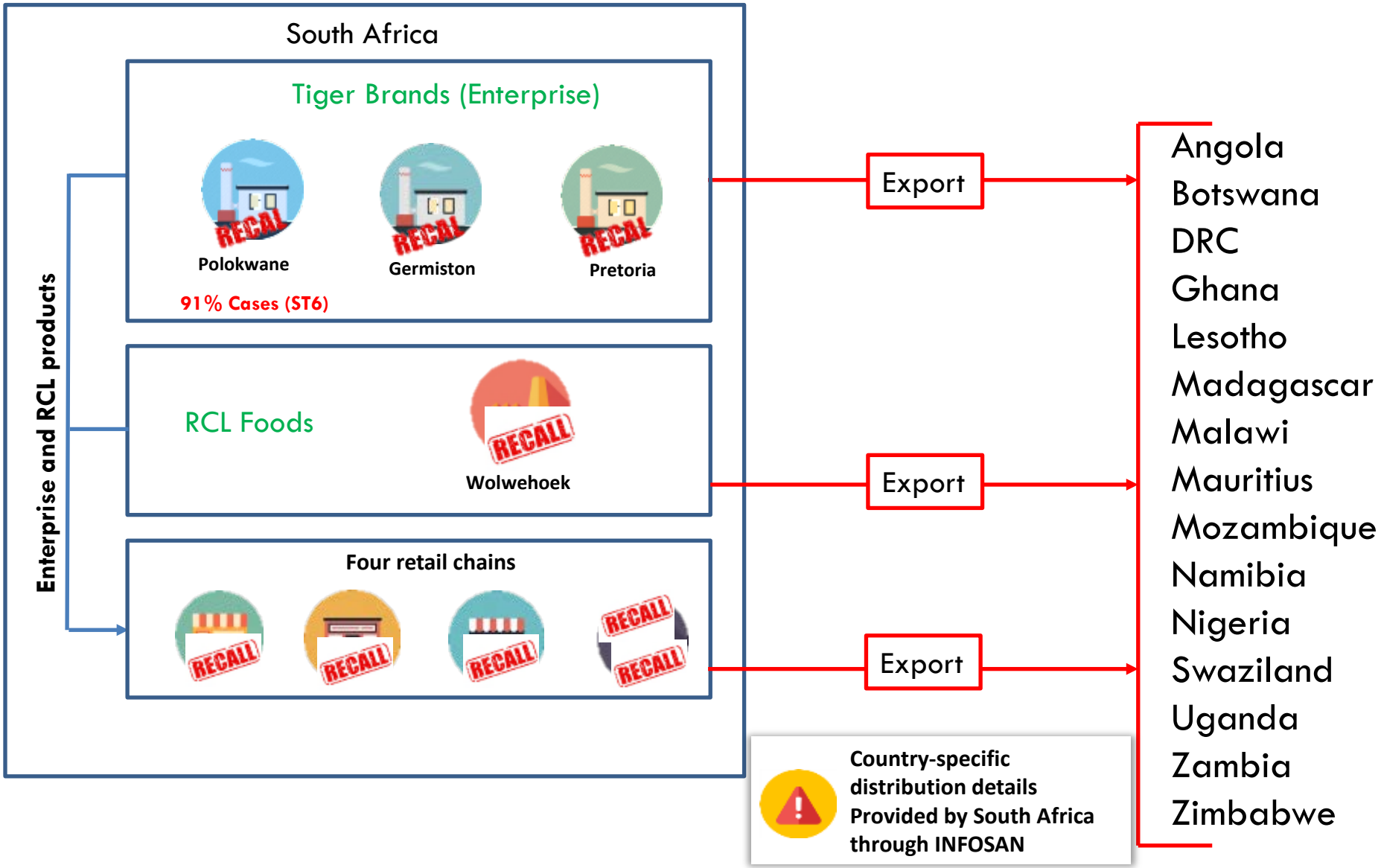
# More than just a website

- The INFOSAN Community Website (ICW) now supports nearly 600 users from around the world
- The ICW is more than just a website --- it is a knowledge exchange portal meant to assist in knowledge management for evidence-informed decision making on issues related to food safety
- Can also be thought of as a house with many rooms – totally adaptable to meet users needs
- To improve these kinds of functionalities, we are also working towards an upgrade

# Role of INFOSAN in Current Event

- INFOSAN Alert to entire network in December 2017
- Multiple information requests to INFOSAN Emergency Contact Point in South Africa before and after potential source(s) identified
- Provision of updates on the INFOSAN Community Website for all INFOSAN members
- Communication directly to INFOSAN Emergency Contact Points in 15 countries with export details provided by South Africa
- Provision of support and guidance to countries with respect to response and risk management

# Internationally distributed ready-to-eat meat products



# Thank You


## Dr Peter K. Ben Embarek

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Slides: C. Savelli, PK. Ben Embarek

# Analysis of the WGS data of the outbreak associated isolates

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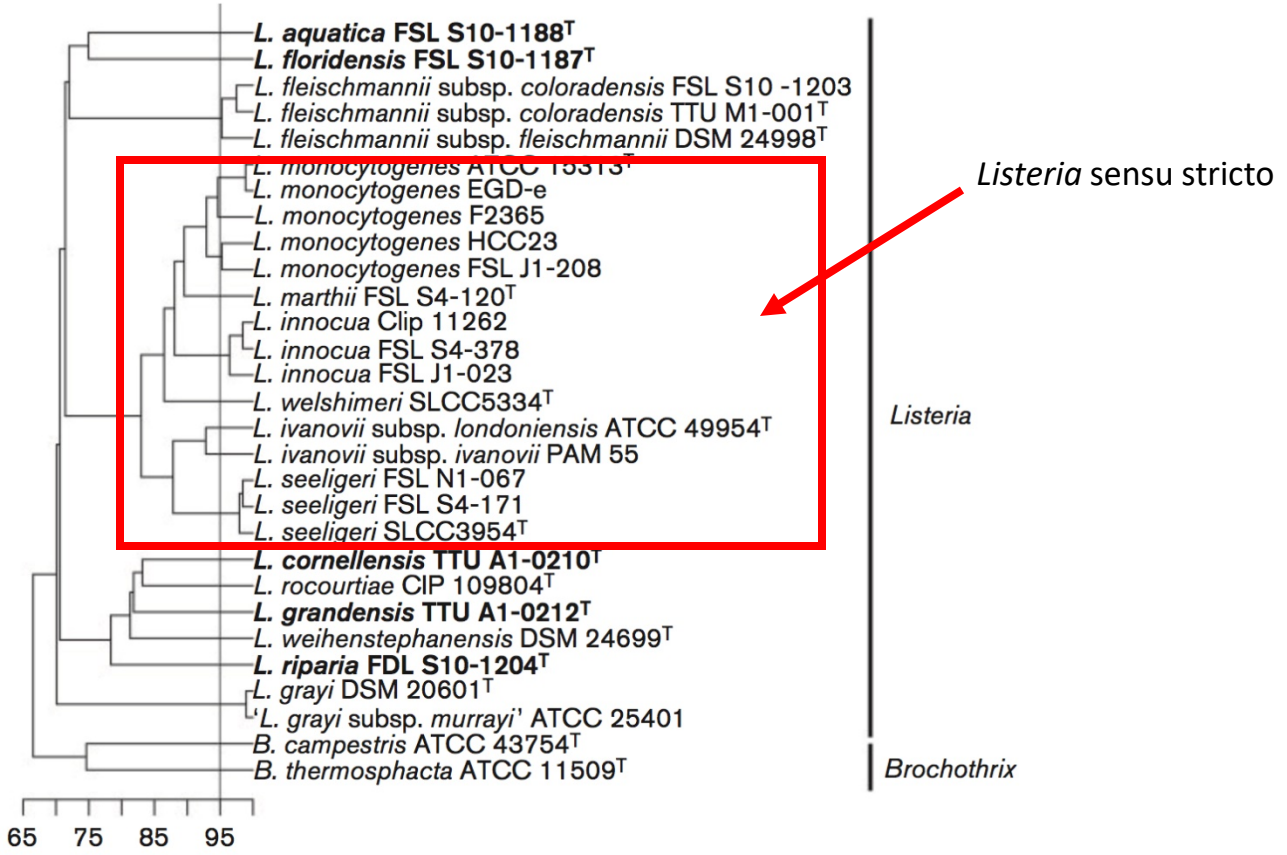
# *Listeria* taxonomy

- 18 species (as of 02-2018)
- Only two species are pathogens:
  - *L. monocytogenes*
  - *L. ivanovii*
- *L. ivanovii* rarely infects humans, mainly a pathogen of ruminants




Den Bakker, H. C. et al. (2014). *IJSEM*, *64*(Pt 6), 1882–1889.

# Characteristics of *L. monocytogenes* with importance for food safety

- *L. monocytogenes* is a facultative pathogen, and a ubiquitous pathogen in most (temperate) environments
- *L. monocytogenes* can grow at temperatures between 0 and 45 ℃, even below 0 ℃…
- This means that *L. monocytogenes* can grow to critical levels at refrigeration temperatures
- *L. monocytogenes* is able to grow in the presence of 10 to 12% NaCl and can grow to high populations at moderate salt concentrations (6.5%). The bacterium survives for long periods at high salt concentrations, with survival in such environments significantly increased at lower temperatures.

# *L. monocytogenes* population structure

- *L. monocytogenes* can be subdivided into four subpopulations (Lineages):
  - Lineage I: associated with most early outbreaks, most prominent serotypes 1/2b, 4b
  - Lineage II: increasingly associated with outbreaks, most prominent serotypes 1/2a, 1/2c
  - Lineage III: predominantly associated with animal cases, serotypes 4a, 4b and 4c
  - Lineage IV: very rare, predominantly associated with animal cases
- Most strains (irrespective of lineages) can cause disease in humans

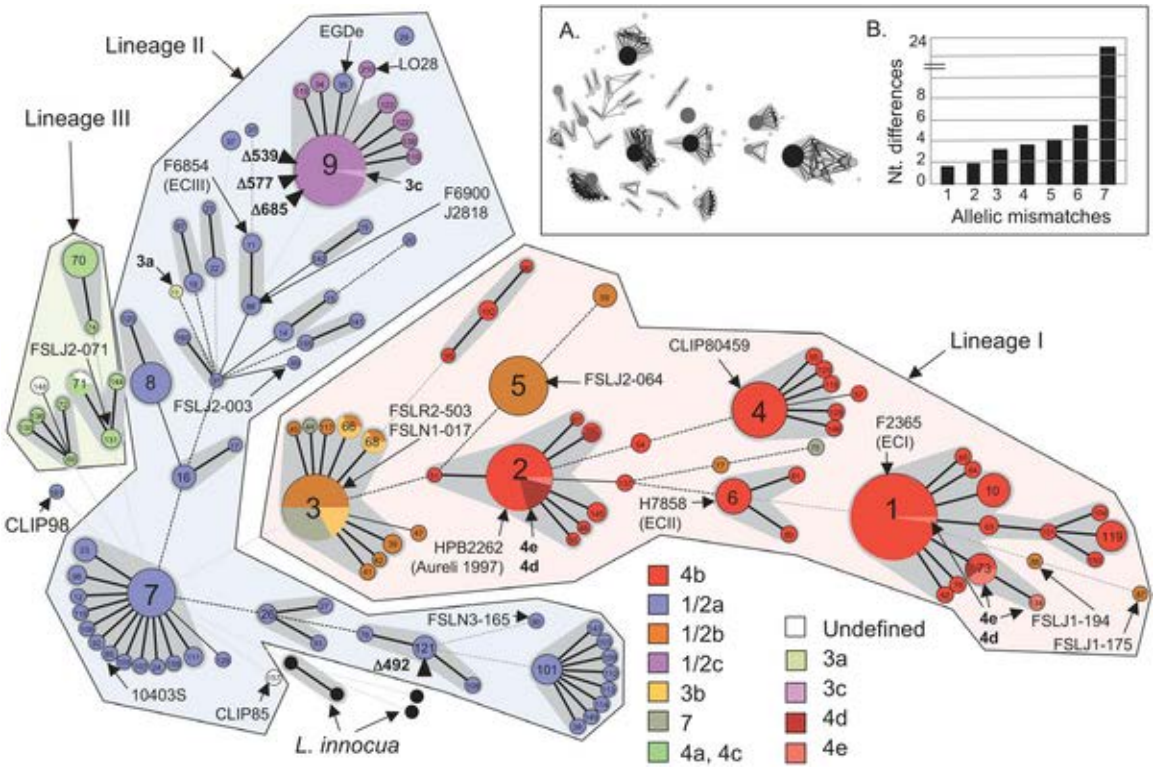
# Multi Locus Sequence Typing (MLST)

- Nucleotide Sequence based subtyping method
- Sequence 7 gene fragments of ~400 bp
- Give each allele of each gene a numerical designation
- Each unique set of allele designations if referred to as a sequence type

| ST | abcZ | bglA | cat | dapE | dat | ldh | lhkA | CC | Lineage |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 3 | 1 | 1 | 1 | 3 | 1 | 3 | CC1 | I |
| 2 | 1 | 1 | 11 | 11 | 2 | 1 | 5 | CC2 | I |
| 3 | 4 | 4 | 4 | 3 | 2 | 1 | 5 | CC3 | I |
| 4 | 1 | 2 | 12 | 3 | 2 | 5 | 3 | CC4 | I |
| 5 | 2 | 1 | 11 | 3 | 3 | 1 | 7 | CC5 | I |
| 6 | 3 | 9 | 9 | 3 | 3 | 1 | 5 | CC6 | I |

# Sequence Types and Clonal Complexes in *L. monocytogenes*

**Minimum spanning tree analysis of 360 *L. monocytogenes* and four *L. innocua* strains based on MLST data.**




Ragon M, Wirth T, Hollandt F, Lavenir R, Lecuit M, et al. (2008) A New Perspective on Listeria monocytogenes Evolution. PLOS Pathogens 4(9): e1000146. https://doi.org/10.1371/journal.ppat.1000146
http://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1000146

PLOS | PATHOGENS

# What do we know about ST6 and CC6?

- CC6 is one of the more prevalent CCs in France[1] and the US
- In France[1] CC6 was strongly associated with clinical cases, and was more prevalent among patients with ..'few or no immunosuppressive comorbidities…'
- In a humanized mouse model (compared to lab strains EGDe and 10403S):
  - CC1, CC4 and CC6 induced significantly more weight loss
  - CC1 and CC6 were more efficient in invading liver
  - CC1, CC4 and CC6 were more efficient in invading brain

[1]Maury, Mylène M, Yu-Huan Tsai, Caroline Charlier, Marie Touchon, Viviane Chenal-Francisque, Alexandre Leclercq, Alexis Criscuolo, et al. 2016. *Nature Genetics* 48 (3): 308–13. doi:10.1038/ng.3501.

[2] Based on count of submissions by FDA, USDA, CDC to Genbank's SRA (https://www.ncbi.nlm.nih.gov/sra)

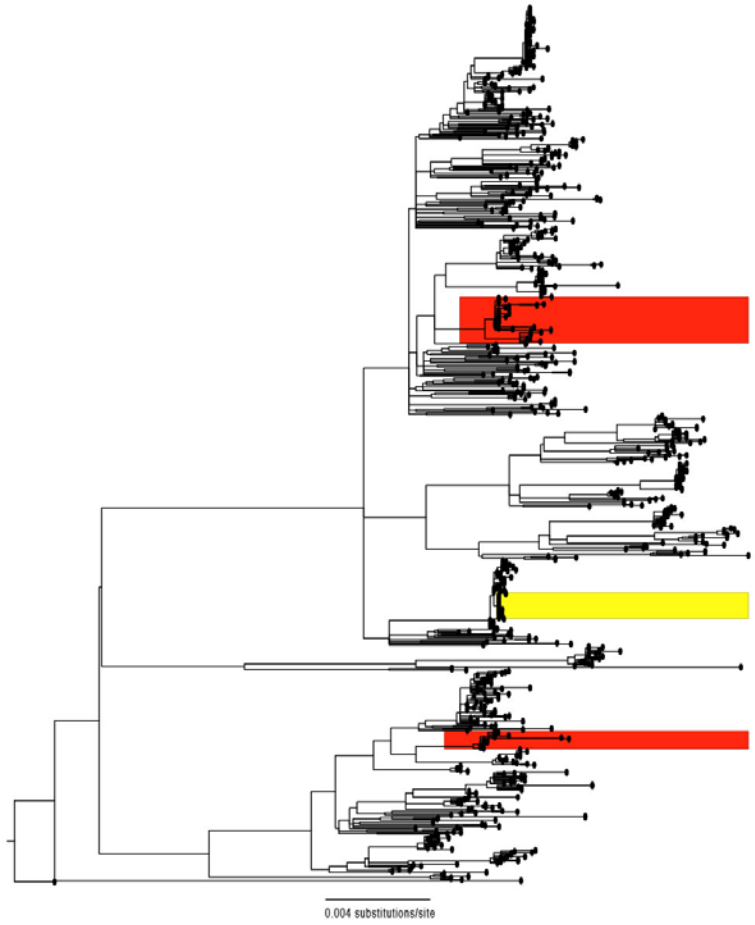
# *Listeria monocytogenes* WGS

- Whole genome sequencing
- In theory makes it possible to interrogate the entire genome (~ 3,000,000 nucleotides for the average L. monocytogenes genome), delivering a high resolution picture of the bacterial population.
- Tool of choice for FDA and CDC for outbreak investigations
- Cluster/phylogenetic analyses based on SNPs
- Much more can be done with WGS data, e.g., predicting resistance, serotypes (*Salmonella*) etc.

# Analysis of CC6

- 839 SRA accessions
- Mostly from USA
- 53 from South Africa:
  - 10 sequenced by Natl. Inst. for Communicable Diseases
  - 43 sequenced by CDC
- SNPs inferred with mcOutbryk (soon to be made publicly available on Github) using J1779 as reference
- Searches for genes unique to the SA outbreak with bigs_id (https://github.com/hcdenbakker/bigs_id)

# *L. monocytogenes* Clonal Complex 6

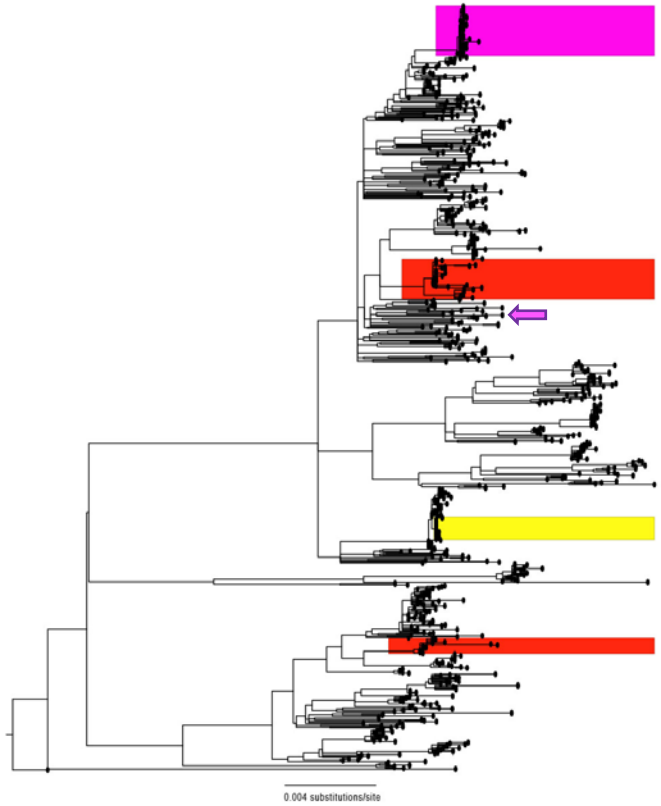



1998 U.S. multistate hot dog outbreak:
108 case patients, 14 deaths, 4 fetal deaths

2013 U.S. multistate French-style cheese outbreak
6 case patients, 1 death, 1 fetal death

2002 U.S. multistate turkey deli meat outbreak:
54 case patients, 8 deaths, 3 fetal deaths

# *L. monocytogenes* Clonal Complex 6




2017/2018 South African Outbreak:
1033 cases, 204 deaths

1998 U.S. multistate hot dog outbreak:
108 case patients, 14 deaths, 4 fetal deaths

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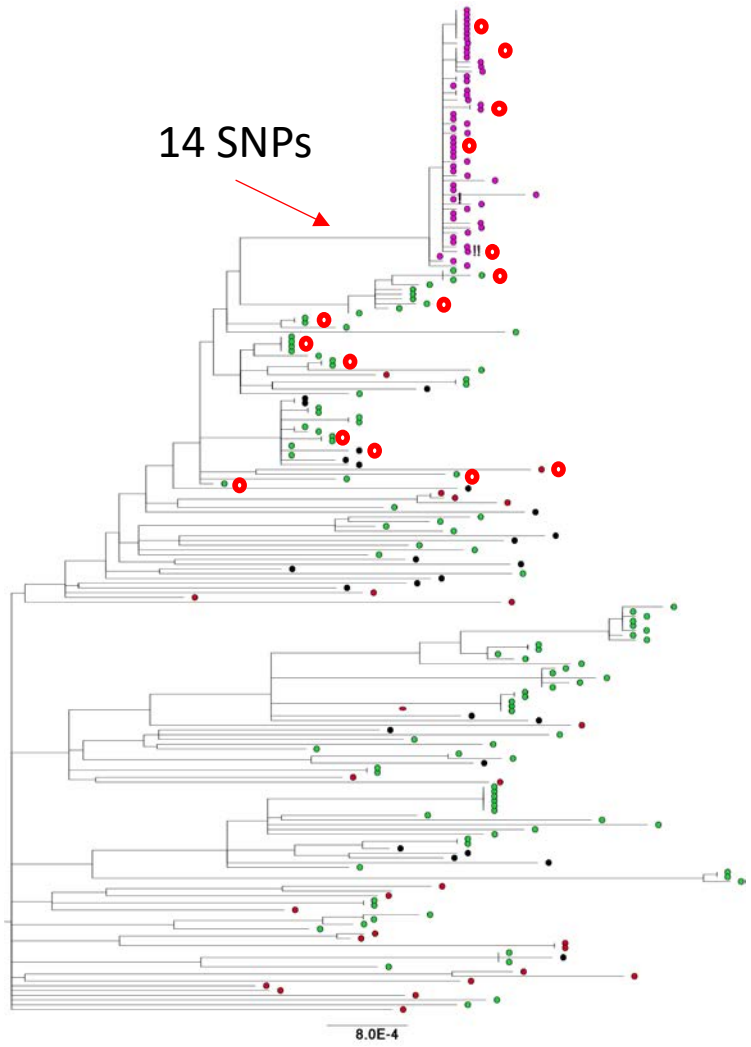


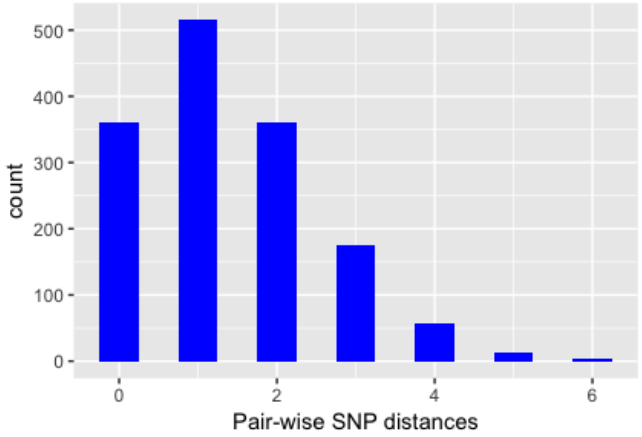


- Outbreak isolates differ by 1 SNP on average
- Outbreak cluster is nested in a predominantly Western European clade, but divergent by 14 SNPs
- This population harbors a small 4.5 kbp ICE/plasmid with a for *L. monocytogenes* rare Quaternary ammonium compound resistance gene (QacC).

# Thank you!

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# Audience Questions & Answers