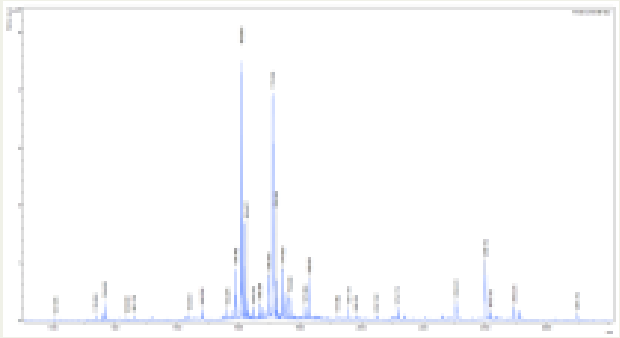
Whole Genome Sequencing for food safety

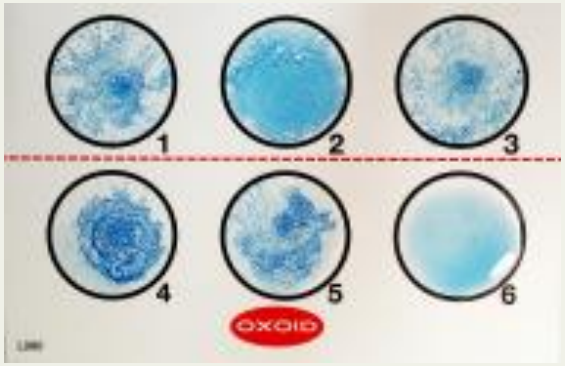
Subtyping bacteria

- By identifying bacterial species, and distinguishing subtypes within a species, we can link cases together and start to understand pathogen spread

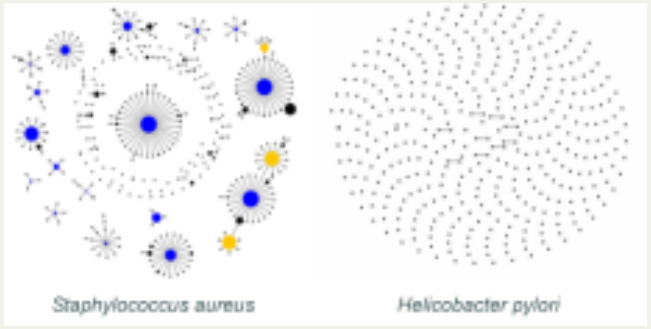
Ways to ID bacteria

- MALDI-TOF – rapid method for identifying species

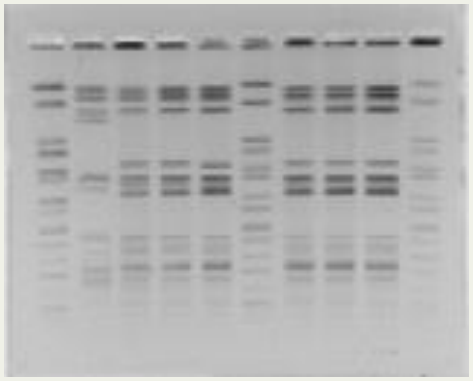




- Serotyping – identifies subtypes based on surface antigens



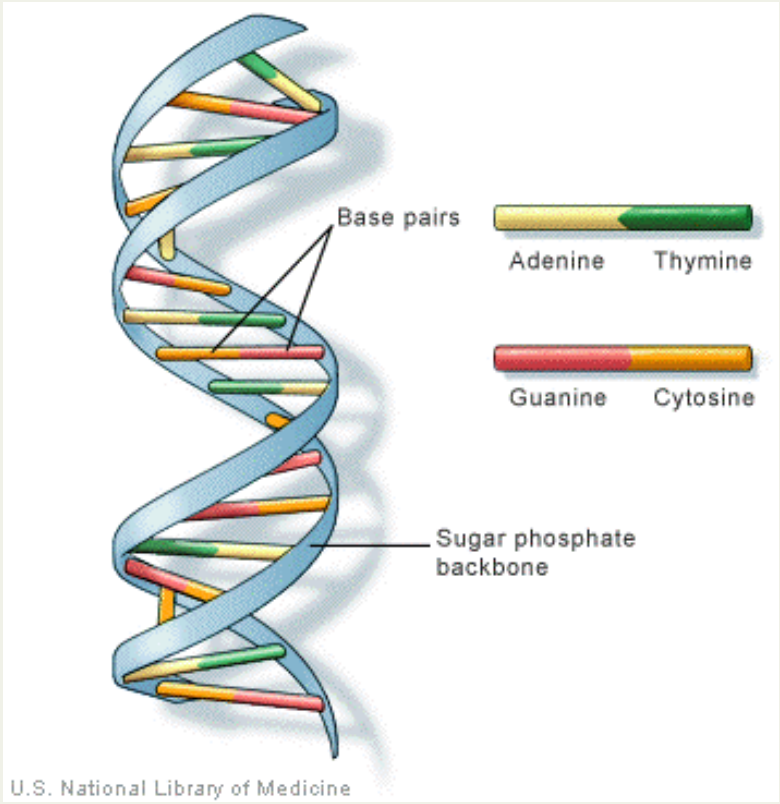
- MLST (Multi Locus Sequence Typing) – more discriminatory



- PFGE (Pulsed Field Gel Electrophoresis) – highly discriminatory, but labour intensive

DNA sequencing

- Genetic material in organisms encoded in a chemical polymer
- DNA sequencing reveals the order of base pairs along the DNA strand



Why does the sequence matter?

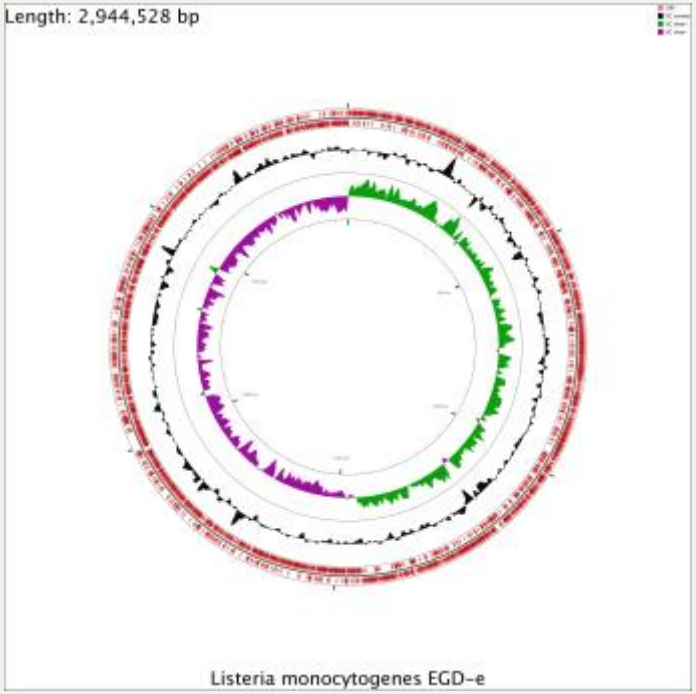
- Genes encode proteins, the building blocks of cells
- Relatedness between organisms can be inferred from sequence similarity

Whole Genome Sequencing (WGS)

- Conceptually straightforward
- Extract total DNA from bacterial culture, sequence this in a massively parallel manner, interpret bioinformatically
- Bacterial genome sizes vary:
  - *Campylobacter jejuni* = 1,600,000 base pairs (1.6 Mb)
  - *Listeria monocytogenes* = 2.9 Mb
  - *Salmonella* Enteritidis = 4.7 Mb

- Coverage – to sequence

  L. monocytogenes at 20x coverage (to correct for sequencing errors) would require generation of 58,000,000 bases of DNA sequence.



Analysis

- Different analysis techniques fall into two main camps

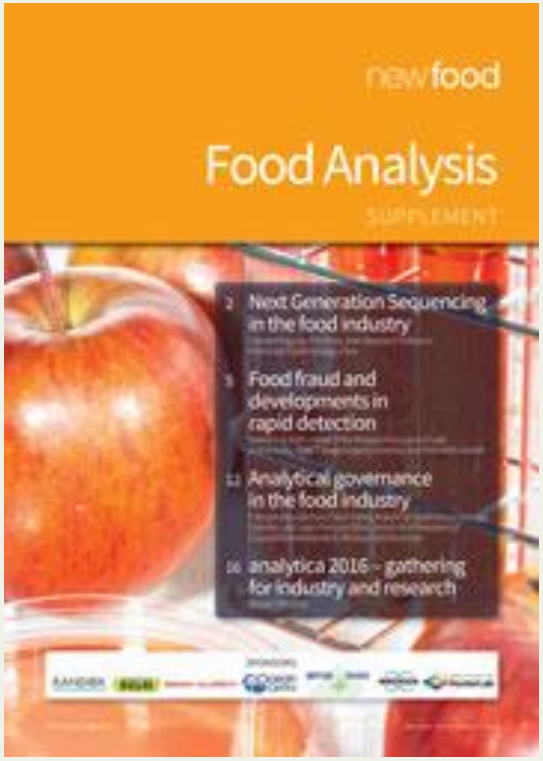
- Single Nucleotide Polymorphism (SNP) calling
  - Good for fine level differences between closely-related strains
  - Some issues with nomenclature (though PHE has developed ‘SNP address’

- Whole Genome MLST (wgMLST)
  - Standard nomenclature
  - Reference-independent
  - May not be as discriminatory as SNP calling

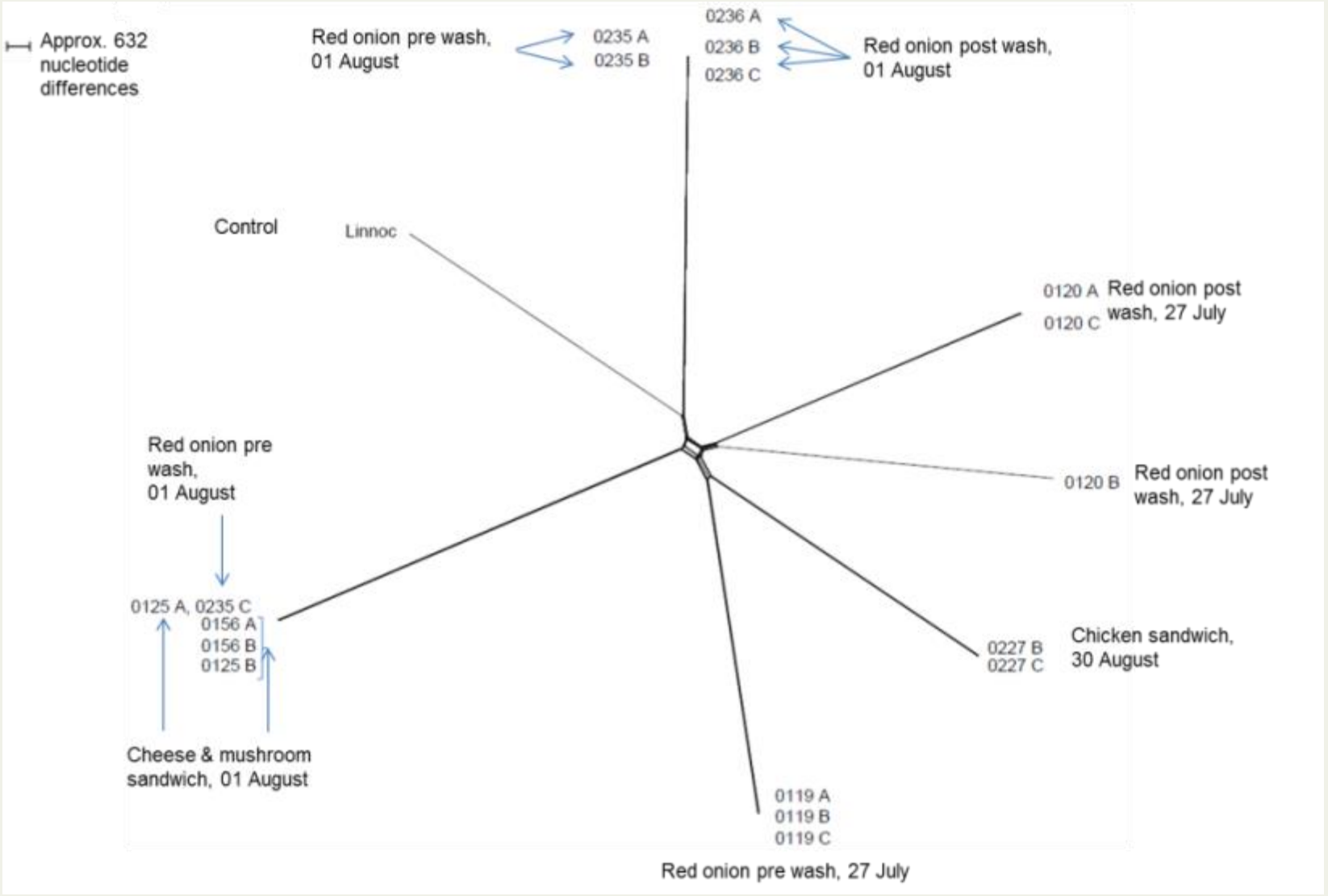
Benefits to industry

- Identify multiple types vs continuous contamination with a resident strain
- Monitor trends over time
- Potential to implicate processes or equipment
- Reduce risk of recalls/demonstrate due diligence
- Suggest external sources of contamination – could require sharing anonymised data

- For broader applications of high throughput sequencing, see “Next Generation Sequencing in the Food Industry”, Food Analysis Supplement 2016, New Food.

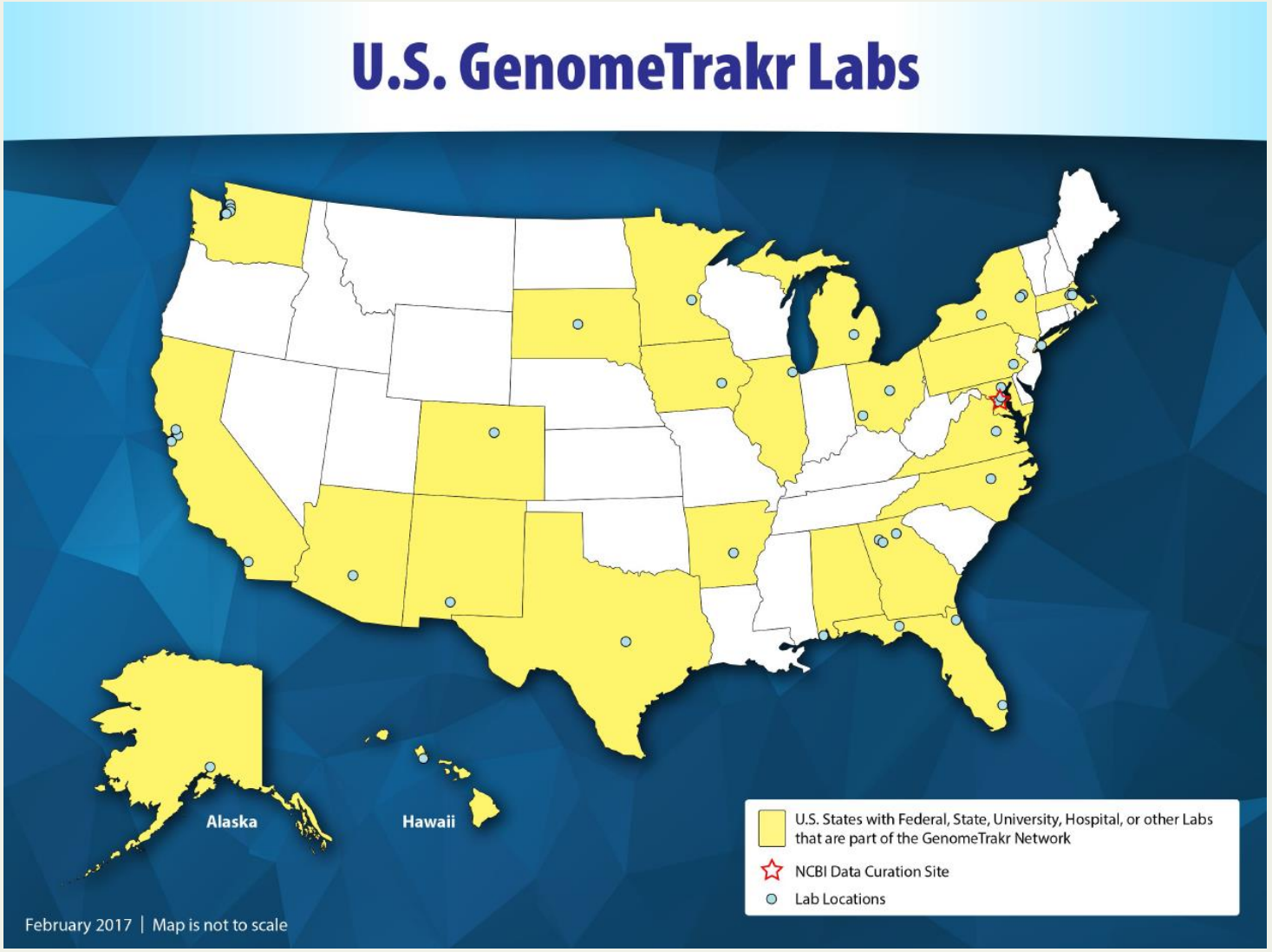


Listeria innocua



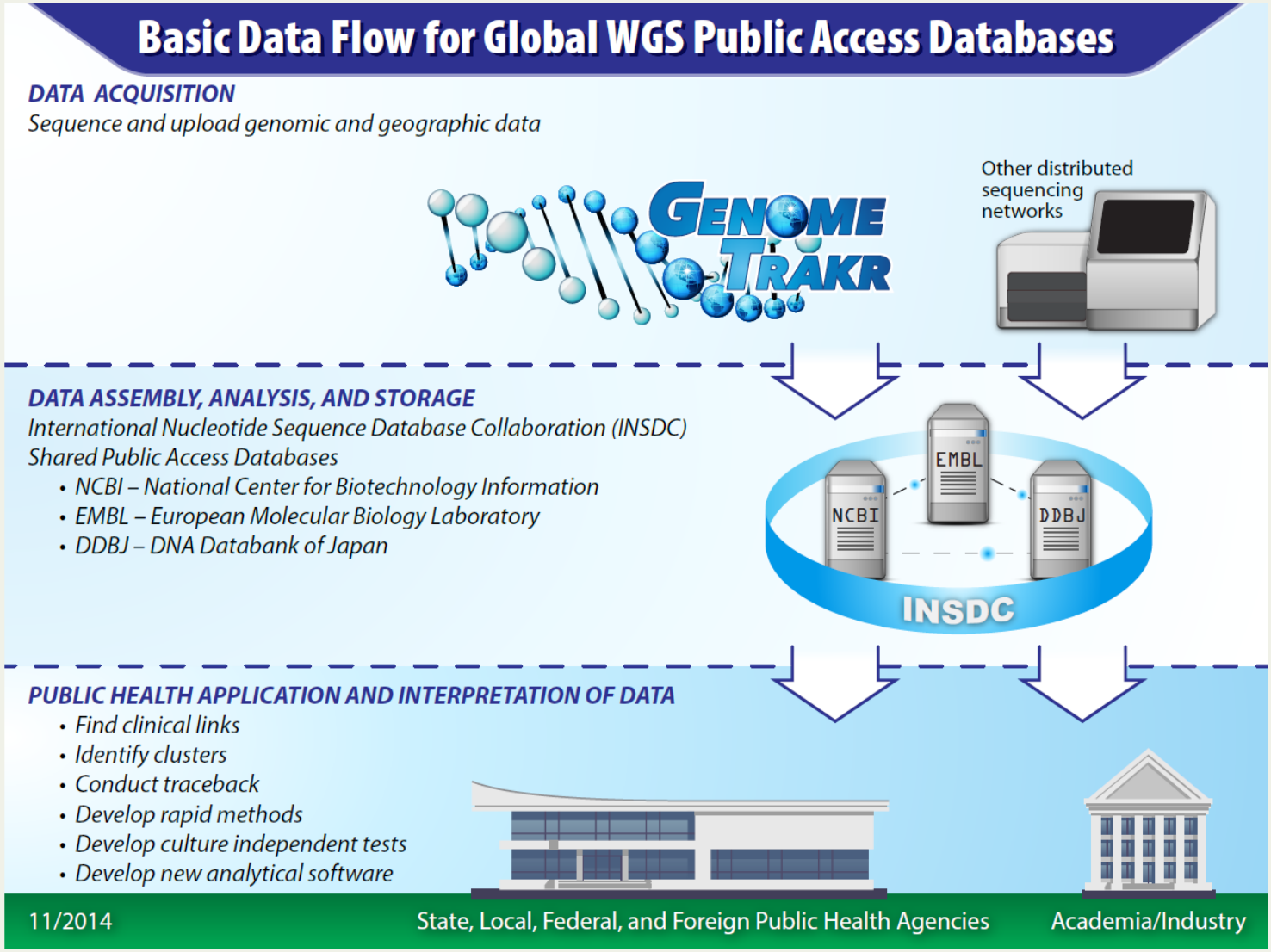
Regulatory Approaches

GenomeTrakr



FDA, 2018

GenomeTrakr



FDA, 2018

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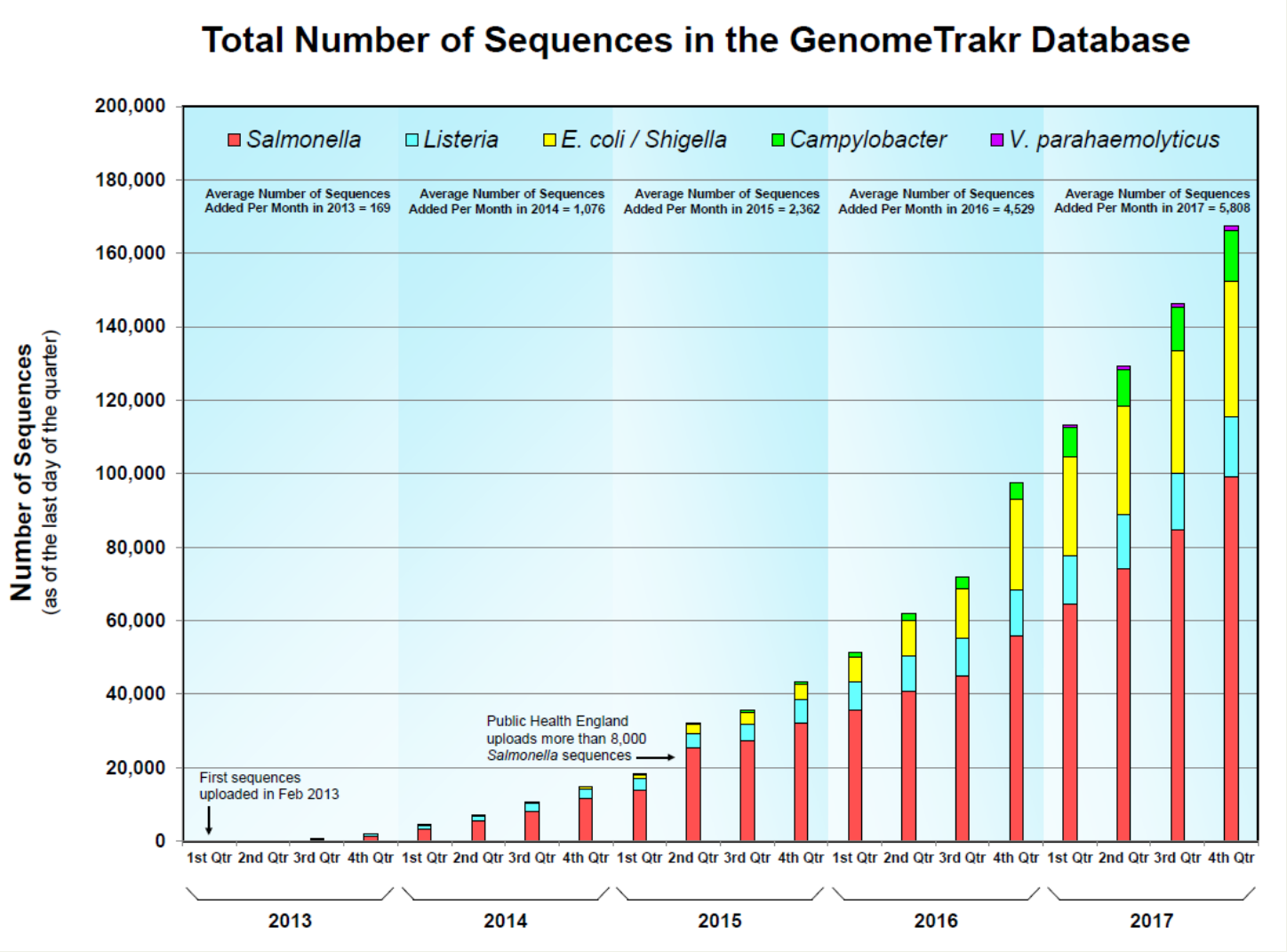

FDA, 2018

UK Situation

- Public Health England is primary organisation undertaking WGS for food safety in the UK

- Latest figures for genomes released by PHE
  - >200 *L. monocytogenes*
  - >6,000 *E. coli* and *Shigella*
  - >17,000 *Salmonella*

- Has been used for large-scale outbreak investigations (e.g. *Salmonella* Enteritidis in eggs)

- FSA funding many projects on WGS

"My last two reports focused on microbiological and chemical risks, and the expert advice we receive from our scientific advisory committees. This report focuses on the exciting developments in whole-genome sequencing, and how this powerful and rapidly developing technology is being increasingly utilised by the FSA."

Professor Guy Poppy,
FSA Chief Scientific Adviser