

Vision paper on the development of data bases for molecular testing of foodborne pathogens in view of outbreak preparedness.

1. Background

1.1. *Molecular testing*

Molecular typing or microbial DNA fingerprinting has developed rapidly in recent years. Many typing methods, like PCR techniques and sequencing, have become part of routine strain characterization in many laboratories. Molecular typing provides essential tools for different surveillance purposes, such as monitoring spread of clones and strains, early detection of dispersed (international) outbreaks, and prediction of epidemic potential.

Data on the molecular testing of food-borne pathogens such as *Salmonella*, *Listeria*, *Escherichia coli* (*E. coli*) and *Campylobacter* could substantially contribute to the epidemiological investigations of food-borne outbreaks and to the identification of emerging health threats. This has been illustrated on many occasions but perhaps most prominently during the 2011 Shiga-toxin producing *E. coli* O104:H4 outbreak, causing over 4 000 cases and over 50 deaths. Molecular testing demonstrated that the stain from the German and French cluster were the same, and resulted in the identification of fenugreek sprouts as the common source of infection.

1.2. *Outbreak investigations and emerging risks*

Member States must ensure that epidemiological investigations of food-borne outbreaks are carried out in accordance with the provisions in Directive 2003/99/EC¹. The reports on these investigations must be sent to the European Commission (EC), which must forward them to the Biological Monitoring Unit of the European Food Safety Authority (EFSA) who must examine and publish the information. This information is also used by EFSA's Panel on Biological Hazards to provide scientific advice and scientific and technical support to EU legislation and policies in accordance with its mission laid down in Regulation (EC) No 178/2002². EFSA typically uses the information to carry out risk assessments and source attribution studies. EFSA's Emerging Risks Unit is responsible for establishing procedures to

¹ Directive 2003/99/EC of the European Parliament and of the Council of 17 November 2003 on the monitoring of zoonoses and zoonotic agents, amending Council Decision 90/424/EC and repealing Council Directive 92/117/EC (OJ L 325, 12.12.2003, p. 31)

² Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety (OJ L 31, 1.12.2002, p. 1)

monitor, collect and analyse information and data in order to identify emerging risks in the field of food safety, in accordance with the provisions in Regulation (EC) No. 178/2002³.

The European Centre for Disease Prevention and Control (ECDC) must, in cooperation with the Member States, establish procedures for systematically searching for, collecting, collating and analysing information and data with a view to the identification of emerging health threats which could affect the EU, in accordance with the provisions in Regulation (EC) No 851/2004⁴. For food- and waterborne diseases, ECDC moderates a technical platform, the Epidemic Intelligence Information System for Food and Waterborne Diseases (EPIS-FWD), which allows national experts in food- and waterborne diseases to exchange information, validate and assess unusual increase, outbreak or clustering of cases detected at national level. It also allows national experts and ECDC to coordinate epidemiological investigations in the human health sector. The sharing of molecular subtyping data is the most commonly used method to link cases from one country to another and thus attempt to identify a potentially common source of a multinational foodborne outbreak. ECDC has a mandate to coordinate human data collection, validation, analysis and dissemination of data at Community level for multinational foodborne outbreak investigations and to provide expert assistance and mobilise and coordinate investigation teams based on a request by a Member State. It will cooperate with EU food safety bodies (EFSA, EC) in carrying out this task.

In addition, the restricted EPIS-FWD communication platform allows national risk assessment bodies from the 27 Member States, EEA and some non-EU countries to exchange technical information regarding food- and waterborne threats with a potential impact in the EU. The system enables validation of signal of emerging strains in the EU and provides the scientific evidence based information to national public health authorities to notify through the Early Warning and Response System (EWRS) the events matching the criteria for reporting under the current EU legislation on communicable diseases. In addition the EPIS-FWD platform allows during EU investigation, case finding, hypothesis building and linkage of cases across countries through a wide pool of experts, and thus facilitates detection and confirmation of cross border multinational foodborne outbreaks.

³ Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety (OJ L 31, 1.2.2002, p. 1)

⁴ Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European centre for disease prevention and control (OJ L 142, 30.4.2004, p. 1)

1.3. Networks relevant for molecular testing and information exchange on food-borne pathogens

1.3.1. European Union and national Reference laboratory (EURL, NRL) networks

Molecular testing of foodborne pathogens from food, feed and animal samples is mainly carried out by official laboratories designated in accordance with the provisions in Regulation (EC) No 882/2004⁵. The Regulation also lays down the designation of national reference laboratories (NRL), who should coordinate the activities of the official laboratories, and the designation of EU reference laboratories (EURL), coordinating the application of analytical methods by national reference laboratories. These networks provide a good opportunity to exchange information on the analytical methods used. Eleven EURL-NRL networks exist in the area of biological food safety, and most of them are already carrying out molecular testing to a variable degree.

Several EURL already consolidated typing capacity of the NRL network by regularly organizing typing training sessions and PT trials.

The national reference level laboratories in the ECDC FWD network have largely the ability to perform molecular typing for foodborne pathogens. ECDC has recently agreed to support a pilot project for a more structured collection of molecular typing data for use in EU-level surveillance and epidemic preparedness. The pilot is limited to four pathogens (Salmonella, Listeria monocytogenes, STEC/VTEC and multidrug resistant Mycobacterium tuberculosis) and will be carried out from July 2012 to December 2013. Participation of Member States in the pilot project is voluntary.

1.3.2. EFSA Task Force for Zoonoses data collection

Routine annual monitoring and reporting of food-borne pathogens, zoonoses and foodborne outbreaks applies under Directive 2003/99/EC. The Commission has mandated EFSA to directly collect information on food and animals as well as foodborne outbreaks on an annual basis from the Member States. For this purpose, EFSA has created a Task Force on Zoonoses Data Collection with participants from all Member States, EEA countries, Switzerland, DG SANCO, ECDC and WHO. Each year, an EU Summary Report is issued in collaboration with ECDC based on the analyses of the data. For this data collection, EFSA runs a web-based reporting application as well as a more automated Data Collection Framework (DFC).

1.3.3. ECDC Food- and Waterborne Diseases and Zoonoses (FWD) network

⁵ Regulation (EC) No 882/2004 of the European Parliament and of the Council of 29 April 2004 on official control performed to ensure the verification of compliance with food and feed law, animal health and animal welfare rules (OJ L 165, 30.4.2004, p. 1)

ECDC is managing a network of nominated epidemiologists and microbiologists with special expertise in six priority foodborne diseases: salmonellosis, campylobacteriosis, STEC/VTEC infection, listeriosis, shigellosis and yersiniosis. These experts contribute to the development of EU level surveillance and submit data to The European Surveillance System (TESSy), which is a highly flexible metadata-driven system for collection, validation, cleaning, analysis and dissemination of human communicable disease data. One of the key aims of surveillance is to provide information for public health action. All EU Member States and three EEA countries report their available data on communicable diseases in humans to TESSy as described in the Decision No 2119/98/EC⁶ and Regulation 851/2004⁷.

1.3.4. Early warning systems

Two emergency networks exist for a quick and secure online exchange of information on detected threats in humans, and hazards in food or feed:

- The Early Warning and Response System application (EWRS) allows the notification of events of cross border relevance due to communicable diseases and the sharing of information on public health measures planned or undertaken in order to coordinate the response at EU level.
- The Rapid Alert System for Food and Feed (RASFF) disseminates information on hazards found in food and feed and trade of (potentially) contaminated batches between Member States. It is an important tool in the tracing back and forward of these batches.

2. Purpose

The purpose of this initiative is to encourage the collation of data on molecular testing so that the linkage of molecular typing data from humans to similar type of data from food and animals is possible. This will enable rapid detection of clusters and outbreaks, and suggest links with potential sources. Such linking will allow the speeding-up of epidemiological investigations, a better evaluation of the importance of certain foods and animal populations as sources of food-borne infections and outbreaks through case-by-case source attribution studies, and a better understanding of the ecology of food-borne infections. Agreement on the data availability must be clearly established between the involved parties (see section 5.1).

Maximum use should be made from the existing networks (e.g. EURLs, ECDC FWD network, EFSA Task Force, Networks of laboratories co-funded under the Public Health Programme) and data collection systems so that any duplication is avoided, and both management and handling of information is under the responsibility of the national authorities and institutes as appropriate. This is part of the EU follow-up / lessons learnt of the *E. coli* O104:H4 outbreak.

⁶ Decision No 2119/98/EC of the European Parliament and of the Council of 24 September 1998 setting up a network for the epidemiological surveillance and control of communicable diseases in the Community (OJ L 268, 3.10.1998, p.1)

⁷ Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European centre for disease prevention and control (OJ L 142, 30.4.2004, p.1)

3. Proposed approach

Two databases will be developed:

- EFSA will be responsible for managing the database on isolates from food and animals. The relevant EURL should be consulted concerning the parameters for the data fields and terminology (Data dictionary) and the quality of data on molecular testing. More precisely, the relevant EURL would be involved in (i) curation of the incoming molecular testing data, (ii) regular verification of database consistency and (iii) updating scientific parameters (experiment settings, terminology, new experiments). EFSA will be responsible for verifying the additional information on the isolates from food and animals.
- ECDC will be responsible for verifying the information on human isolates and manage the database on human isolates.

The following approach will be applied:

- A common nomenclature and similar standard operating procedures for molecular typing data validation should be ensured where appropriate for human, food and animal isolates so that any molecular typing data produced is comparable.
- The uploading of data on isolates from food and animals should be made possible for EURLs and respective food/feed national reference laboratories and other official control laboratories.
- The uploading of data on isolates from humans should be made possible for national reference level laboratory users or other public health laboratories nominated by Coordinating Competent bodies
- Historical data should be reported when possible.
- Recommendations on management of molecular typing data should be developed in collaboration with the public health and food/veterinary sectors.
- For the food, feed and animal isolates, only existing results from molecular testing and new results obtained from the monitoring of zoonoses, outbreak investigations and from research projects will be collected. National authorities and NRLs must always have access to their respective national data in the database. EFSA will coordinate the reporting of the molecular typing data on food/feed animal isolates in collaboration with the relevant EURLs, which shall support the technical coordination with the NRLs on the development and management of molecular typing methods on isolates from food and animals. For the human isolates, technical coordination with the relevant laboratories will be managed by ECDC in accordance with agreed procedures and revised as needed after testing in an on-going pilot project to assess the feasibility of the ECDC roadmap for integration of molecular typing data in EU outbreak response preparedness. The development of molecular typing of a specific pathogen for which a substantial number of molecular testing is already available, both from human and from food/animal isolates, should be prioritised although any such decision must also take into account all relevant plans and policies already developed by the EC, ECDC, EFSA . ECDC is currently in the process of developing a roadmap for integrating molecular typing data into

routine EU-level surveillance and epidemic preparedness, and a first draft is expected at the end of 2012.

In an initial phase of developing molecular typing data sharing across food/feed/animal/human sources, isolate-based molecular typing database(s) should be created for *Salmonella*, *Listeria monocytogenes* and STEC/VTEC isolates.

4. Ownership of the data

For all human data submitted to TESSy, Member States are the original data owners and provide data in compliance with the EU regulations including EC decisions (notably Decision No 2119/98/EC). ECDC is the co-owner and controller of the data, which is in its trusteeship, and can assist Member States in data upload and reporting.

For other purposes, the ownership of the data does not change when the data are uploaded:

- The EC in case of testing performed under the budget of the EURLs or (co-)financed research projects;
- The Member States or EEA country in case of testing performed by own NRLs or other official laboratories;

5. Procedures

5.1. *Memorandum of Understanding*

All involved parties shall sign a Memorandum of Understanding before getting access to the database. The Memorandum will include information on the issues described in this vision paper with regards to data ownership, availability, access, use, publication, procedures, confidentiality etc.

5.2. *Data dictionary*

A data dictionary will be coordinated by EFSA and ECDC based on input from:

- The EFSA Zoonoses Task Force, the EURLs and the ECDC FWD network, in coordination with ECDC, with regards to the information on molecular testing of all isolates;
- EFSA with regards to any additional information on isolates from food and animals. EFSA should ensure consistency with the values for the reporting in accordance with Directive 2003/99/EC;
- ECDC with regards to any additional information on human isolates;
- The EURL on antimicrobial resistance (AMR) and/or the ECDC FWD network for additional information on AMR testing.

The data dictionary should also indicate who should submit each parameter and how. Certain parameters may be reported voluntarily.

5.3. Use and publication of data

Owners of data will always be consulted for their authorisation before any publication or oral communication of the data which have not been published before. In case of the publication of national data from several Member States on isolates from food or animals, the SCoFCAH will be consulted for this purpose. In case of human data, the Network Committee under Decision 2119/98/EC will be consulted.

In case of food alert situations, the RASFF and EWRS shall be used, supplemented by bilateral contacts with the Commission and all involved national authorisations.

In case of human alert situations, EPIS-FWD shall be used.

Without prejudice to the above EFSA and ECDC may always use the data compiled at national level in overview reports and opinions.

In case of use of data from outside the EU, the country of origin will be consulted before publication.

6. Confidentiality of data

Apart from the above agreements, the confidentiality obligations and protection of personal data in Directive 95/46/EC⁸ and Regulation (EC) No 45/2001⁹ shall be respected.

⁸ Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data (OJ L 281, 23.11.1995, p. 31)

⁹ Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data(OJ L 8 of 12.1.2001, p. 1)

List of acronyms

AMR	Antimicrobial Resistance
DFC	Data Collection Framework
DG SANCO	(European Commission) Directorate General for Health and Consumers
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EFSA	European Food Safety Authority
EPIS	Epidemic Intelligence Information System
EU	European Union
EURL	European Union Reference Laboratory
EWRS	Early Warning and Response System
FWD	Food- and Waterborne Disease
NRL	National Reference Laboratory
RASFF	Rapid Alert System for Food and Feed
SCoFCAH	Standing Committee on the Food Chain and Animal Health
STEC/VTEC	Shiga toxin/verocytotoxin -producing <i>Escherichia coli</i>
TESSy	The European Surveillance System
WHO	World Health Organisation