Collaboration Agreement

on the management and sharing of molecular typing data of isolates from human, food, feed, animal, and the related environment for public health purposes

Contents

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ABBREVIATIONS

API	Application Programming Interface
BIOHAZ	Biological Hazards
CCB	Coordinating Competent Body
cgMLST	Core genome Multilocus Sequence Typing
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
EDPR	European Data Protection Regulation
EFSA	European Food Safety Authority
EpiPulse	European surveillance portal for infectious diseases
EU	European Union
EURL	European Union Reference Laboratory
EWRS	Early Warning and Response System
FWD	Food- and Waterborne Diseases
FWD-Net	European Food- and Waterborne Diseases and Zoonoses network
GDPR	General Data Protection Regulation
MLST	Multilocus Sequence Typing
MTS	Molecular Typing System
NRL	National Reference Laboratory
PAFF	Standing Committee on Plants, Animals, Food and Feed
RASFF	Rapid Alert System for Food and Feed
ROA	Rapid Outbreak Assessment
STEC	Shigatoxin-producing *Escherichia coli*
TESSy	The European Surveillance System
WGS	Whole Genome Sequencing

This agreement is concluded between

The European Food Safety Authority, hereinafter referred to as "EFSA", represented for the purpose of the signature of this agreement by its Executive Director, Bernhard Url,

and

The European Centre for Disease Prevention and Control, hereinafter referred to as "ECDC", represented for the purposes of the signature of this agreement by its Director, Andrea Ammon

hereinafter collectively referred to as the "Parties".

The Parties have agreed to collaborate on the management and sharing of molecular typing data from selected isolates of food-borne pathogens of human, food, feed, animal, and environmental origin for the detection and investigation of cross-border public health clusters and outbreaks.

Whereas

1. EFSA was established as a decentralised agency of the European Union by 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[1], as amended by Regulation (EU) 2019/1381[2];
2. ECDC was established as a decentralised agency of the European Union by 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[3];
3. EFSA and ECDC have signed a revised Memorandum of Understanding[4], which entered into force on 3 May 2021, aiming at enhancing the co-operation between both agencies on matters of mutual interest in particular through efforts of information exchange, and increased co-operation;
4. ECDC, EFSA and European Union Reference Laboratories (EURL) of *Listeria monocytogenes*, *Salmonella* and Shigatoxin-producing *Escherichia coli* (STEC)[5] have signed a Collaboration Agreement on the management of data on molecular testing of food, feed, animal, and environmental isolates of selected food-borne pathogens and their use with molecular typing data on isolates from human infections for public health purposes, dated 12 April 2016. The latter Collaboration Agreement was terminated on 1 June 2022.

[1] 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, 01/02/2002, p. 1-24, as last amended.

[2] Regulation (EU) 2019/1381 of the European Parliament and of the Council of 20 June 2019 on the transparency and sustainability of the EU risk assessment in the food chain and amending Regulations (EC) No 178/2002, (EC) No 1829/2003, (EC) No 1831/2003, (EC) No 2065/2003, (EC) No 1935/2004, (EC) No 1331/2008, (EC) No 1107/2009, (EU) 2015/2283 and Directive 2001/18/EC, OJ L 231, 6.9.2019, p. 1–28.

[3] 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, 30/04/2004, p. 1–11, as last amended.

[4] Available at: https://www.efsa.europa.eu/sites/default/files/2021-05/efsa-ecdc-mou-signed.pdf.

[5] Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment), Agence Nationale de Securité Sanitaire de l'alimentation de l'environnement et du travail (French Agency for Food, Environmental and Occupational Health and Safety), and Instituto Superiore di Sanità (ISS).

5. Molecular typing provides essential tools for different surveillance purposes, such as monitoring spread of clones and strains, including antimicrobial resistance, early detection of dispersed outbreaks, source attribution and prediction of epidemic potential. Molecular typing data from food-borne pathogens originating from humans, food, feed, animals and the related environment could substantially contribute to preparedness for the epidemiological investigations on food-borne clusters and outbreaks, and to the identification of emerging health threats, including antimicrobial resistance. The EFSA Panel on Biological Hazards (BIOHAZ) has published opinions on the evaluation of molecular typing methods for major food-borne microbiological hazards[6,7]. ECDC has published a strategic framework for the integration of molecular and genomic typing into European surveillance and multi-country outbreak investigations[8];

6. Whole Genome Sequencing (WGS) is an efficient molecular typing methodology enhancing the surveillance and monitoring of emerging health threats and epidemiological investigations of clusters and outbreaks caused by food-borne pathogens. The EFSA BIOHAZ Panel has published an opinion on WGS and metagenomics for outbreak investigation, source attribution and risk assessment of food-borne microorganisms[9]. ECDC has published an expert opinion on WGS for public health surveillance[10];

7. Molecular testing of food-borne pathogens from food, feed, animal and the related environmental samples is mainly carried out by official laboratories designated in accordance with Article 37 of Regulation (EU) 2017/625[11]. This Regulation lays down in Article 100 the designation of National Reference Laboratories (NRLs), who should coordinate the activities of the official laboratories, and the designation of European Reference Laboratories (EURLs) which is done in accordance with Article 93. EURLs coordinate the application of the analytical methods by NRLs.

[6] EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), 2013. Scientific Opinion on the evaluation of molecular typing for major food-borne microbiological hazards and their use for attribution modelling, outbreak investigation and scanning surveillance: Part 1 (evaluation of methods and applications). EFSA Journal 2013;11(12):3502, 84 pp. doi:10.2903/j.efsa.2013.3502.

[7] EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), 2014. Scientific Opinion on the evaluation of molecular typing methods for major food-borne microbiological hazards and their use for attribution modelling, outbreak investigation and scanning surveillance: Part 2 (surveillance and data management activities). EFSA Journal 2014;12(7):3784, 46 pp. doi:10.2903/j.efsa.2014.3784.

[8] European Centre for Disease Prevention and Control. ECDC strategic framework for the integration of molecular and genomic typing into European surveillance and multi country outbreak investigations 2019 2021 . Stockholm: ECDC; 2019.

[9] EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), Koutsoumanis K, Allende A, Alvarez-Ordo~nez A, Bolton D, Bover-Cid S, Chemaly M, Davies R, De Cesare A, Hilbert F, Lindqvist R, Nauta M, Peixe L, Ru G, Simmons M, Skandamis P, Suffredini E, Jenkins C, Malorny B, Ribeiro Duarte AS, Torpdahl M, da Silva Felicio MT, Guerra B, Rossi M and Herman L, 2019. Scientific Opinion on the whole genome sequencing and metagenomics for outbreak investigation, source attribution and risk assessment of food-borne microorganisms. EFSA Journal 2019;17(12):5898, 78 pp. https://doi.org/10.2903/j.efsa.2019.5898.

[10] European Centre for Disease Prevention and Control. Expert opinion on whole genome sequencing for public health surveillance. Stockholm: ECDC; 2016.

[11] Regulation (EU) 2017/625 of the European Parliament and of the Council of 15 March 2017 on official controls and other official activities performed to ensure the application of food and feed law, rules on animal health and welfare, plant health and plant protection products, amending Regulations (EC) No 999/2001, (EC) No 396/2005, (EC) No 1069/2009, (EC) No 1107/2009, (EU) No 1151/2012, (EU) No 652/2014, (EU) 2016/429 and (EU) 2016/2031 of the European Parliament and of the Council, Council Regulations (EC) No 1/2005 and (EC) No 1099/2009 and Council Directives 98/58/EC, 1999/74/EC, 2007/43/EC, 2008/119/EC and 2008/120/EC, and repealing Regulations (EC) No 854/2004 and (EC) No 882/2004 of the European Parliament and of the Council, Council Directives 89/608/EEC, 89/662/EEC, 90/425/EEC, 91/496/EEC, 96/23/EC, 96/93/EC and 97/78/EC and Council Decision 92/438/EEC (Official Controls Regulation), OJ L 95, 7.4.2017, p. 1–142.

8. ECDC is managing a network of nominated epidemiologists and microbiologists with special expertise in food-borne diseases through the European Food- and Waterborne Diseases and Zoonoses network (FWD-Net). These experts contribute to the development of EU level surveillance including submission of human data to the European surveillance portal for infectious diseases (EpiPulse), which includes a system for collection, validation, analysis and dissemination of human communicable disease data, covering also molecular typing data (also known as the European Surveillance System, TESSy). There is currently an ongoing revision of the EU decision on cross-border threats to health[12] and the ECDC Founding Regulation[13];

9. The public health laboratories involved in monitoring/surveillance activities coordinated by ECDC have been gradually increasing their ability to perform molecular typing by WGS for food-borne pathogens. ECDC collects this information in a standard format and on a continuous basis from participating laboratories through its EpiPulse system for the use at the EU-level for surveillance as well as early cluster and outbreak detection and investigation;

10. To support the rapid and secure online exchange of information on detected food-borne threats in humans, and hazards in food or feed, three platforms exist:

    - EpiPulse, the European surveillance portal for infectious diseases, contains a specific domain for Food and Waterborne Diseases (FWD). The platform allows nominated national experts in food- and waterborne diseases to report routine surveillance data as well as voluntarily exchange information, validate and assess any unusual increase, outbreak or clustering of cases detected at the national level. Access to specific items can be granted to EFSA, EURLs, and food safety/veterinary users of the involved EU Member States and EEA countries based on pre-defined criteria and nomination process.

    - the Early Warning and Response System (EWRS) requires a mandatory notification of serious cross-border threats to health according to the criteria laid down in EU decision on cross-border threats to health[14][15];

    - the Rapid Alert System for Food and Feed (RASFF) disseminates official information on hazards found in food and feed and trade of (potentially) contaminated batches between Member States[16]. It is an important tool in the tracing back and forward of these batches.

11. On 12 December 2012, the Vision paper of the European Commission (hereinafter referred to as "the EC") on the development of databases on isolates from human, food, feed, animals and the related environment was endorsed by the Standing Committee on Plants, Animals, Food and Feed[17]. The Vision paper describes the context of the request for technical support and the proposed approach, including issues with regards to data ownership, availability, access, use, publication, procedures and confidentiality.

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[12] Proposal for a Regulation of the European Parliament and of the Council on serious cross-border threats to health and repealing Decision No 1082/2013/EU. COM(2020) 727 final 2020/0322(COD), Brussels 11.11.2020, available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52020PC0727.

[13] Proposal for a Regulation of the European Parliament and of the Council amending Regularion (EC) No 851/2004 establishing a European Centre for disease prevention and control. COM(2020) 726 final 2020/0320(COD), Brussels 11.11.2020, available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52020PC0726&qid=1641311042310

[14] Established by Article 8 of Decision No 1082/2013/EU of the European Parliament and of the Council of 22 October 2013 on serious cross-border threats to health and repealing Decision No 2119/98/EC. OJ L 293, 05.11.2013, p. 1-15.

[15] Commission Implementing Decision (EU) 2017/253 of 13 February 2017 laying down procedures for the notification of alerts as part of the early warning and response system established in relation to serious cross-border threats to health and for the information exchange, consultation and coordination of responses to such threats pursuant to Decision No 1082/2013/EU of the European Parliament and of the Council.

[16] Established by Articles 50-52 of 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, 01/02/2002, p. 1-24, as last amended.

[17] Annex to the Mandate from the European Commission dated 18 January 2013 (M-2013-0082): https://ec.europa.eu/food/sites/food/files/safety/docs/biosafety_food-borne-disease_vision-paper.pdf

12. In 2013, the EC requested EFSA to provide scientific assistance in the area of food-borne outbreak investigation, in accordance with Article 31 of Regulation (EC) No 178/2002,[18]. In particular, EFSA was requested to contribute to the ECDC Rapid Outbreak Assessments (ROA) by providing information from the monitoring of zoonoses, zoonotic agents and food-borne outbreaks, in-depth analyses of the food data including the robustness of the link to the suspected food source, and technical assistance to EC in its conduct of tracing-back and forward analyses of the incrimitated batches.

13. In 2013, the EC has requested EFSA, in accordance with Articles 31 of Regulation (EC) No 178/2002, and ECDC, in accordance with Article 9 of Regulation (EC) No 851/2004, to provide technical support on the collection of data on molecular testing in human and non-human isolates of *Salmonella*, *Listeria monocytogenes* and STEC by developing and mantaining two databases and performing joint analysis[19]. EFSA was responsible for managing the database on isolates from food, feed, animals and the related environment. ECDC was responsible for managing the database on human isolates.

14. Following the EC request in 2017 to provide technical support for the implementation and management of a database on relevant WGS data from food-borne pathogens isolated from human and non-human samples[20], a technical report on possible solutions for the WGS data collection and analysis[21], and a 'WGS Roadmap' [22] were produced.

15. Based on the 'WGS Roadmap', the EC requested EFSA and ECDC in December 2019, in accordance with Article 31 of Regulation (EC) No 178/2002 and Article 3 of Regulation (EC) No 851/2004, respectively, to implement and manage a system for the collection and joint analysis of WGS data of food-borne isolates from human and food, feed, animal and the related environmental samples[23]. The mandate highlights that the European Union needs a robust and sensitive tool for rapid detection and management of multi-country food-borne clusters and outbreaks with the ultimate purpose of serving public health interests and protecting European consumers. Emphasis is placed on full interoperability of the molecular typing systems between the food and public health pillars in order to ensure the protection of consumers within the EU single market in the context of a 'One Health' system approach.

16. In accordance with Article 19 of Commission Implementing Decision (EU) 2019/300[24], EFSA and, where relevant, ECDC are required to collaborate with EC for the rapid characterisation and quick identification of sources of outbreaks through the maintenance and use of databases on molecular typing (including WGS) of pathogenic agents detected in humans, animals, food and feed.

17. ECDC and EFSA commit to process personal data of users of the Molecular Typing Systems (MTSs) in accordance with applicable data protection rules. In the field of data protection, ECDC and EFSA are subject to Regulation (EU) 2018/1725 on the protection of natural persons with regard to the processing of personal data by the EU institutions, bodies, offices and agencies ('the EDPR'). The EDPR is aligned with the rules and principles of the General Data Protection Regulation (EU) 2016/679 ('the GDPR'), applicable within the EU. Molecular

[18] Mandate from the European Commission to EFSA dated 09/07/2013 M-2013-0119.
[19] Mandate from the European Commission to ECDC dated 18 January 2013; Mandate from the European Commission to EFSA dated 18 January 2013 M-2013-0082, EFSA-Q-2013-00250, complemented by the letter dated 21 March 2014; Letter from the European Commission to EFSA dated 14 April 2014.
[20] Mandate from the European Commission to EFSA and ECDC dated 10 April 2017, M-2017-0082, EFSA-Q-2017-00397
[21] EFSA and ECDC technical report on the collection and analysis of whole genome sequencing data from food-borne pathogens and other relevant microorganisms isolated from human, animal, food, feed and food/feed environmental samples in the joint ECDC-EFSA molecular typing database. EFSA supporting publication 2019: EN-1337. 92 pp. doi:10.2903/sp.efsa.2019.EN-1337. https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/sp.efsa.2019.EN-1337
[22] Roadmap for the implementation of the EFSA and ECDC systems for joint analysis of WGS. Attachment to the mandate M-2020-0015 (include reference from OPEN EFSA).
[23] Mandate from the European Commission to EFSA and ECDC dated 20 December 2019, M-2020-0015, EFSA-Q-2020-00101.
[24] Commission Implementing Decision (EU) 2019/300 of 19 February 2019 establishing a general plan for crisis management in the field of the safety of food and feed.

typing data or sequencing data from human origin and epidemiological data from humans as defined in Article 4(1) of the GDPR and Article 3(1) of the EDPR can be qualified as personal data.

The Parties have agreed as follows:

Article 1. Objectives of the collaboration agreement

1. The purpose of this agreement is to specify the terms of collaboration for the management and sharing of 'Data', as defined in Article 3 of the present Agreement, of food-borne pathogen isolates in human, food, feed, animals, the related environment, collected by ECDC, in accordance with Article 11 of Regulation (EC) No 851/2004 and by EFSA, in accordance with Art 33 of Regulation (EC) No 178/2002.
2. The purpose of sharing these Data is to enhance routine surveillance, and outbreak detection and investigation by enabling identification of microbiological links between isolates of human and non-human origin, and subsequently to support EU level actions for prevention and control of cross-border food-borne clusters and outbreaks.
3. This agreement furthermore specifies the data ownership, availability, transformation, access, use and publication during and after their collection with the aim of ensuring a common understanding and approach across multi-sectoral stakeholders and Data Providers from EU/EEA Member States, ECDC, EFSA and EC.

Article 2. Scope of application

This agreement applies to the collection, transformation and sharing of 'Data' on isolates of food-borne pathogens, as defined in Article 3, from human, food, feed, animals, and the related environment for public health purposes as requested to ECDC and EFSA by the EC.

Article 3. Definitions

For the purpose of this agreement:

'Data' means the complete set of information officially provided by the appointed 'Data Provider' to ECDC and EFSA. It comprises 'Microbiological Data' (including 'Molecular Typing Data') and 'Epidemiological Data'.

'Data Dictionary' means a document describing in detail the model used to collect a certain set of data. It provides information on the elements collected, element names, data type, controlled terminology references and other information useful for reporting data while respecting the established data model and the business data requirements.

'Data Provider' means the entity submitting the 'Data' in the context of the present agreement officially appointed by the compentent authorities of the relevant EU Member States or reporting country with agreement with both agencies.

'Data Owner' means the legal or natural person having intellectual property rights in relation to 'Data'. This may be the 'Data Provider', unless the data is owned by a different legal entity based on, for example, a separate agreement or contractual arrangement.

'ECDC's Food- and Waterborne Diseases and Zoonoses Network' (FWD-Net) is a network of Member State contact persons that, among others, provide data on food- and waterborne diseases and zoonoses to ECDC.

'ECDC Molecular Typing System' (ECDC MTS) is the system maintained at ECDC for the collection and analysis of 'Data' on isolates from humans.

'EFSA's Zoonoses Monitoring Data Network' is a pan-European network of national representatives and international organisations which assist EFSA by gathering and sharing information on zoonoses in their respective countries[25].

'EFSA Molecular Typing system' (EFSA MTS) is the system maintained at EFSA for the collection of and analysis of 'Data' on isolates from food, feed, animals and the related environment.

'Epidemiological Data' means the data and information on the food-borne pathogen isolates originating from human, food, feed, animal and related environmental samples. This includes, for example, temporal and geographical information and other descriptions of the source of the isolate such as age and gender (for human origin isolates) or the type of food the sample was taken from (for non-human origin isolates).

'EpiPulse' is the European surveillance portal for infectious diseases that ECDC and nominated users from Member States or additional participating non-EU countries use to discuss and share information on potential and actual threats.

'EpiPulse Cases' is an EpiPulse functionality for collection, validation, analysis and dissemination of data (also known as TESSy) to which all EU Member States (27) and European Economic Area (EEA) countries (3) report their available data on communicable diseases and conditions as described in Decision No 1082/2013/EC and subsequent implementing decisions.

'Microbiological Data' means the data generated by the application of all methods for characterising microbial isolates, and includes 'Molecular Typing Data'.

'Molecular Typing Data' means the data generated by the application of specific molecular biology-based typing methods to characterise microbial isolates including Whole Genome Sequencing data.

'Nominated Authorised Users' refers to specific persons nominated by the Member States' competent authorities for food/feed NRLs and other official control laboratories, and Member States' public health authorities according to ECDC's Coordinating Competent Body (CCB) policy. The nomination includes the assignment of specific access rights, per pathogen, to the ECDC and EFSA MTSs.

'Procedure' means a list of instructions to perform an experiment aimed to produce or interpret 'Molecular Typing Data' within the context of the present agreement.

'Whole Genome sequencing (WGS)' means the determination of the entire genome sequence of an organism, generally through the application of Next Generation Sequencing technology.

Article 4. Advisory Board

1. The interactions between the Parties to the present agreement are supported by the 'Advisory Board on the collection and management of Molecular Typing Data from human, animal, food, feed and the related environmental isolates' (hereinafter referred as 'Advisory Board').
2. The Advisory Board is composed of representatives (a member and an alternate) from the Parties to the present agreement and representatives of official EU reference laboratories

[25] https://www.efsa.europa.eu/sites/default/files/science/Support/Data/Data_ToR_Zoonoses_Network.pdf

from both sectors. Until EURLs for public health[26] are formally established for the respective pathogens covered by this agreement, interim representatives from public health institutions may be invited at the discretion of the Parties, to join the Advisory Board. The Advisory Board may invite *ad hoc* individual participants to provide information to the Advisory Board in the field of their expertise. Moreover, the EC representatives may participate as observers. The Advisory Board may decide to invite additional observers to meetings.

3. The Advisory Board aims to provide technical and scientific advice to the Parties in the area of molecular typing of food-borne pathogens. The Parties to the present agreement decide whether or not to take into consideration the advice provided by the Advisory Board.

Article 5. Cooperation activities

In accordance with the respective provisions of their respective Founding Regulations, the Parties agree to cooperate in order to implement this agreement and to facilitate the proper use and management of the Data in the ECDC and EFSA MTSs. Tasks to be performed jointly or separately by the respective Parties are listed below and are performed according to Annex I ("Joint ECDC and EFSA procedure for the analysis of molecular typing data in the ECDC and EFSA Molecular Typing Systems for the purpose of cluster and outbreak detection and investigation"). Annex I is jointly prepared by the Parties to implement the present agreement and may be subject to further periodical reviews and updates especially as concerns the technological specifications.

1. The Parties agree to perform the following tasks together:
   - to use agreed analytical pipelines for generation and quality assurance of Molecular Typing Data of food-borne pathogens from human, food, feed, animals, and the related environmental isolates as provided in the context of the present agreement;
   - to use an harmonised procedure for the communication of the results of the analyses of the Molecular Typing Data on food-borne pathogens isolated from human, food, feed, animals, and the related environmental isolates hosted in the EFSA and ECDC MTSs;
   - in accordance with their respective Founding Regulations, EFSA shall have the leading role in the analysis and interpretation of Data from food, feed, animal and the related environmental isolates, and ECDC shall have the leading role on the analysis and interpretation of human Data; the tasks related to microbiological cluster or outbreak detection and assessment of the association of the food vehicle to the cluster or outbreak, shall be performed according to Annex I;
   - to update, when appropriate, the scientific parameters used for Molecular Typing Data analysis and interpretation, described in Annex I and included in the ECDC and EFSA MTSs; these include for example thresholds for searching for clusters and matches between isolates, maintaining data dictionary with harmonised parameters for the data fields, using controlled terminologies for data reporting and defining rules for validation of the data provided.

2. EFSA agrees:
   - to coordinate the collection of the Data on food-borne pathogens isolated from food, feed, animals and the related environment from the Data Providers;
   - to store the Data in the EFSA MTS and guarantee their integrity, security, safety and confidentiality in accordance with Article 9 of the present Agreement, without prejudice to Article 38 of Regulation (EC) No 178/2002;
   - to make the EFSA MTS accessible for queries by ECDC and to make the sharable data available to ECDC within the agreed timeframe, as defined in Annex I. When possible,

[26]Proposal for a Regulation of the European Parliament and of the Council on serious cross-border threats to health and repealing Decision No 1082/2013/EU. COM(2020) 727 final 2020/0322(COD), Brussels 11.11.2020, available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:52020PC0727

the access should be given through Application Programming Interface (API). Valid data shall only refer, on a per isolate basis, to Data that has successfully passed EFSA's automated validation rules applied upon submission to EFSA. Any Data that did not pass this validation will not be made accessible to ECDC;

3. ECDC agrees:
   - to coordinate the collection of the Data on food-borne pathogens isolated from humans from the Data Providers;
   - to store the Data in the ECDC MTS and guarantee their integrity, security, safety and confidentiality in accordance with Article 9 of the present Agreement, without prejudice to Article 20 of Regulation (EC) 851/2004;
   - to make the ECDC MTS accessable for queries by EFSA and to make the sharable data available to EFSA within the agreed timeframe, as defined in Annex I. When possible the access should be given through API. Valid data shall only refer, on a per isolate basis, to Data that has successfully passed ECDC's automated validation rules applied upon submission to ECDC. Any Data that did not pass this validation will not be made accessible to EFSA.

Article 6. Data ownership and intellectual property

1. The inclusion of Data in the ECDC and EFSA MTSs does not affect the ownership and existing intellectual property rights and copyrights. The Parties will have the right to use these Data for carrying out analyses and for managing and maintaining the ECDC and EFSA MTSs under the terms of the present agreement.

2. For what concerns Data on isolates from food, feed, animals and the related environment submitted under the present agreement:

   a. The EC is the owner of the Data resulting from testing performed under the budget of the EURLs or projects (co-) financed by the EC, without prejudice to data ownership provisions laid down in other agreements;

   b. The Member States or EEA countries own the Data resulting from testing performed by NRLs or other official laboratories under national budgets.

3. For human data submitted to EpiPulse Cases (also known as TESSy), the Data providers remain as data owners, whereas ECDC acts as the Data controller.

4. Neither Party or user can claim any intellectual property rights on discoveries, detections or inventions stemming from the use of the Data or information shared by Member States competent bodies and laboratories for the purpose of this agreement.

Article 7. Data sharing and access

1. The Parties shall share Data received from their Data Providers and provide access to EFSA and ECDC MTS users as specified in Annex I. Annex I outlines the modality of data exchange between the Parties and the visualisation of results to EFSA and ECDC MTS users including also technical details related to sharing and access of Data (e.g. API calls specifications, System logging and Audit trails).

2. Without prejudice to rules on public access to documents, in particular stemming from Regulation (EC) No 1049/2001[27] and Regulation 1367/2006[28], the Parties may not disclose data from human and food, feed, animal and the related environmental isolates to any third party, other than the users as defined in the present agreement, after prior agreement of the Data Providers in accordance with Article 8 of the present agreement.

3. In case ECDC receives a request under Regulation (EC) No 1049/2001, to disclose data of non-human origin stored in the ECDC MTS according to Annex I, it will forward the request to EFSA who will handle it in accordance with this Regulation.

4. In case EFSA receives a request under Regulation (EC) No 1049/2001, to disclose data of human origin stored in the EFSA MTS according to Annex I, it will forward the request to ECDC who will handle it in accordance with this Regulation.

Article 8. Data use and publication

1. The Parties will use the Data, in the context of the present agreement, to make intersectoral analyses (i.e. joint microbiological cluster and outbreak detection and investigation), when possible, on hazards related to zoonotic agents deriving from human, food, feed, animals, and the related environmental isolates for performing joint ECDC-EFSA food-borne outbreak assessments (i.e. food-borne public health risk assessments) and/or supporting the investigation during cross-border food-borne clusters, outbreaks and-crisis events.
2. The Parties must obtain the consent of the Data Providers who are in charge of seeking clearance of the Data Owners before any publication and/or communication of the Data (other than food-borne public health risk assessments) or any work reproducing or using the Data, unless the use and publication is specifically authorised in:
    a. Separate contractual agreements laying down mutual consent of contracting parties, including the Data Owners and/or Data Providers.
    b. Applicable legal acts.

    Consent shall be considered obtained when no reply is given by a Data Provider within 14 calendar days.
3. Without prejudice to Paragraphs 1 and 2, any use or publication of human data combined with non-human data must be agreed upon by the Parties. The Parties shall define and agree on a case-by-case basis how these data will be used, what the content of any applicable publication will be and what the roles and responsibilities of each Party are in this process, in accordance with their respective mandates and applicable law.
4. In case of publication of national data from several or all Member States on isolates from food, feed, animals and the related environment, the Standing Committee on Plants, Animals, Food and Feed (PAFF Committee) will be consulted.
5. In addition to the above, Parties shall restrict the use of Data compiled at the national level according to their respective remit, by means of aggregated overview reports and aggregated summaries as part of the tasks, responsibilities and public mandates under their respective Founding Regulations. For EFSA, this only concerns the Data of non-human origin and for ECDC only the Data of human origin.

[27] Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents, OJ L 145, 31.5.2001, p. 43-48.
[28] Regulation (EC) No 1367/2006 of the European Parliament and of the Council of 6 September 2006 on the application of the provisions of the Aarhus Convention on Access to Information, Public Participation in Decision-making and Access to Justice in Environmental Matters to Community institutions and bodies, OJ L 264, 25.9.2006, p. 13–19.

Article 9. Handling of the Data by the Parties

1. Without prejudice to Articles 7 and 8 of the present agreement, the Data used for the purpose of the present agreement, collected and stored in the ECDC and EFSA MTSs shall be considered sensitive non-classified information in accordance with rules on information security applicable to Union institutions, bodies, offices and agencies, and may not be shared with third parties except as laid out in this agreement or following a legal obligation to disclosure according to Article 8 of this Agreement. Annex I describes which Data are stored in the ECDC MTS and the EFSA MTS and how authorised users have access. The Data shall be handled by persons who are bound to at least one of the Parties by obligations of confidentiality.

2. The Parties shall ensure that the use of the Data complies with the Data Protection Regulation (EU) 2018/1725 ('the EDPR')[29]. Molecular Typing Data or WGS data from human origin and Epidemiological Data from humans qualify as personal data in accordance with Article 4(1) of the GDPR and Article 3(1) of the EDPR. Such data from human origin is duly pseudonymised by ECDC prior to any access and use by other Parties for the purpose of the present agreement. The identification keys related to the pseudonymised data are managed by ECDC and remain exclusively available to them, in a way that other Parties are by no means able to make any personal identification based on the data.

Article 10. Information security and management

The Parties shall guarantee the security of respectively the ECDC and EFSA MTSs. Appropriate technical and organisational measures shall be implemented to ensure a level of security appropriate to the risks represented by the nature of the Data contained in the MTSs, in accordance with the information rules applicable within the Parties, including user access rights and data maintenance.

Article 11. Settlement of disputes and applicable law

1. The law applicable to the present agreement is EU law.

2. In case of dispute on the application of this agreement, the Parties shall try to seek an amicable solution. In case of impossibility to find an amicable solution, the Court of Justice of the EU shall have the sole jurisdiction to decide on any dispute.

Article 12. Working language

For the purpose of the present Agreement, the working language will be English.

Article 13 Responsible units or sections

1. The units or sections identified in Appendix I are intended to be responsible for communications under this Agreement.

2. Each Party will notify the other Party of any changes to their respective Appendix I entries.

3. The updating of such administrative aspects does not constitute an amendment to the provisions of this Agreement.

[29] Regulation (EU) 2018/1725 of the European Parliament and of the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC, OJ 21.11.2018, L 295/39.

Article 14. Amendments

1. This agreement may be amended at any time by mutual written consent of the Parties.

2. The Annex I and Appendixes to the present agreement may be periodically reviewed by the Parties. The Parties agree that such regular reviews of the Annex I and Appendixes shall not require a formal amendment of the agreement.

Article 15. Termination of the Collaboration Agreement

1. This agreement may be terminated by each Party by notifying the other Party in writing of its intention to terminate this Agreement, six months in advance.

2. In case of termination of this agreement, the provisions regarding intellectual property, confidentiality and publications of Data shall remain applicable after the termination of this agreement.

Article 16. Entry into force of the Collaboration Agreement

The present agreement will take effect on the date of its last signature by the representatives of the two Parties, and will remain in effect for a period of five years. It is automatically renewed for another five years if there are not objections from the Parties.

SIGNATURE

Done in two originals in English.

ECDC Executive Director	**EFSA executive Director**
Andrea Ammon	Bernhard Url
Date:	**Date:**
Signature: Digitally signed by: ANDREA AMMON (EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL) Date: 2022-06-28 16:11:27 UTC	**Signature:** Digitally signed by: Bernhard Url Date: 2022.06.20 09:04:56 +01'00'

APPENDIX I: RESPONSIBLE UNITS OR SECTIONS

Responsibile units or sections for the implementation of the Collaboration Agreement on the management and sharing of molecular typing data of isolates from human and food, feed, animal and environment for public health purposes

ECDC and EFSA agree to designate a responsible unit or section for the management and handling of the agreement, including updates in Appendix I and Annex I.

For EFSA:
Unit BIOHAW
Via Carlo Magno 1/a, Parma (ITALY)
Tel: +39 0521 036111/ Email: biohaw@efsa.europa.eu

For ECDC:
Unit PUBLIC HEALTH FUNCTIONS
Gustav den III:s Boulevard 40, Solna (SWEDEN)
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APPENDIX II: LIST OF ANNEXES

Annex I. Joint ECDC and EFSA procedure for the analysis of molecular typing data in the EFSA and ECDC Molecular Typing Systems for the purpose of outbreak detection and investigation.

Joint ECDC and EFSA procedure for the analysis of molecular typing data in the EFSA and ECDC Molecular Typing Systems for the purpose of outbreak detection and investigation

Annex I of Collaboration Agreement on the management and sharing of molecular typing data of isolates from human, food, feed, animal, and the related environment for public health purposes

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European Food Safety Authority
Via Carlo Magno 1A – 43126 Parma, Italy
www.efsa.europa.eu
European Centre for Disease Prevention and Control
Gustav III:s Boulevard 40 - 169 73 Solna, Sweden
www.ecdc.europa.eu

1. Objective of the Procedure

The objective of the Procedure is to describe the process of analysis of the molecular typing data in the European Food Safety Authority (EFSA) and European Centre for Disease Prevention and Control (ECDC) Molecular Typing Systems (MTSs) for the purpose of multi-country outbreak detection and investigation. This includes the definition of criteria for the detection of a **joint microbiological cluster** and subsequent triggered actions and actors involved in the process. The procedure includes also technical specifications related to the interaction between the EFSA and ECDC MTSs. The overall aim of the analysis of molecular typing data is to allow identification of microbiological clusters of public health relevance and support further epidemiological and microbiological investigations.

Groups of similar human and non-human isolates but which do not meet the joint microbiological cluster definition for multi-country outbreak detection may still be relevant for a cross-sectoral study involving actors from both the public health and food and veterinary sectors. One example of such a study would be an investigation of one or more prevalent strains that are consistently found in both the food chain and in humans but that rarely cause an outbreak.

2. Scope of the Procedure

The scope of this procedure covers the use and exchange of typing data, including Whole Genome Sequencing (WGS)-based data, and epidemiological data submitted by data providers to the EFSA and ECDC MTSs (hereafter defined as "Data"). So far, the systems include the data on *Salmonella enterica*, *Listeria monocytogenes* and Shiga toxin-producing *Escherichia coli* (STEC) isolates.

This Procedure is accompanied by a flowchart. It covers the steps of the process of data analysis, i.e. microbiological cluster detection and evaluation, and the actors involved in each phase and the technical specifications related to the interaction between the EFSA and ECDC MTSs.

This Procedure does not include or replace procedures or processes related to crisis or urgent requests in place at European Commission (EC) level. Moreover, this procedure does not replace internal procedures in ECDC and EFSA on the user of Data.

3. Actors involved in the process

The actors involved in the process are the Data Providers from EU/EEA countries, ECDC and EFSA.

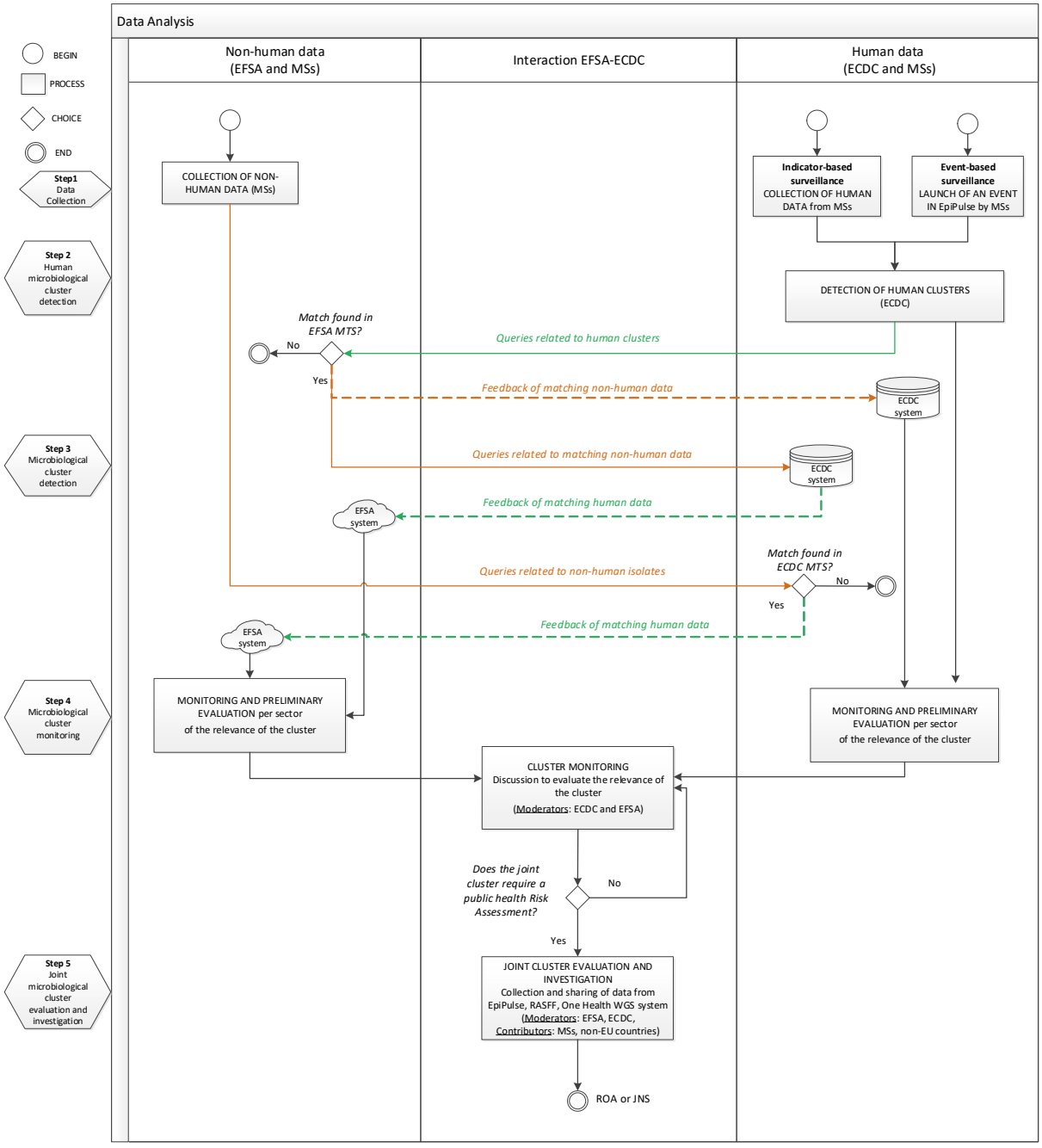
4. Data collection and analysis process

The diagram summarising the process is available below. It shows the steps sequentially numbered. The microbiological clusters may be detected through two surveillance systems in ECDC:

- indicator-based surveillance
- event-based surveillance.

Indicator-based surveillance includes isolate-based reporting of WGS data to ECDC. The event-based surveillance includes events reported by countries in European surveillance portal for infectious diseases (EpiPulse).

Figure 1: Diagram of the process for data analysis and exchange triggered by indicator- and event-based surveillance



4.1. Data collection (Step 1 in the flowchart)

4.1.1. Human data

As part of indicator-based surveillance Member States (MSs) submit microbiological data, including molecular typing data, and associated epidemiological data to the ECDC MTS on a voluntary basis according to the ECDC molecular surveillance working documents. ECDC MTS collects WGS data[1] in the form of reads or assemblies and generates WGS-derived data such as core genome Multilocus Sequence Typing (cgMLST) allelic profiles from the submitted reads or assemblies as well as other pathogen-specific *in silico* data.

As part of event-based surveillance, MSs and other ECDC partner countries can share sequence data (in the form of raw reads or assemblies) through EpiPulse.

4.1.2. Food, feed, animals and the related environment data (non-human data)

Food and veterinary data providers submit microbiological data, including molecular typing data, and associated epidemiological data to EFSA MTS according to the data model described in "Guidelines for reporting Whole Genome Sequencing-based typing data through the EFSA One Health WGS System"[2]. EFSA MTS collects cgMLST allelic profiles and other pathogen-specific *in silico* data which are either generated by the EFSA MTS upon uploading reads to the system, or directly generated and submitted by the data provider.

4.2. Human microbiological cluster detection (Step 2 in the flowchart)

Microbiological clusters based solely on cgMLST data from human isolates are defined in accordance with ECDC's molecular surveillance working documents. The analysis for human microbiological clusters is performed within the ECDC MTS (indicator-based surveillance) from the WGS data routinely submitted by the MSs.

ECDC may also detect a likely multi-country cluster based on an event reported by a country in EpiPulse and identified based on analyses performed by national pipelines. This event alert may be an indication of an ongoing cross-border cluster or outbreak at the EU/EEA level, which requires immediate attention and further investigation, including centralised WGS analysis.

The ECDC molecular surveillance working documents, including the microbiological cluster definitions, may be updated by ECDC at any time.

4.3. Microbiological cluster detection (Step 3 in the flowchart)

A **joint microbiological cluster** is defined as a microbiological cluster that includes human isolates and at least one non-human isolate. The cluster is calculated in the ECDC MTS after the identification of the matches between human and non-human isolates as the result of the ECDC query to the EFSA MTS.

[1] For WGS-based data, a further distinction needs to be made between (i) raw sequence reads data (i.e. reads), (ii) whole genome assembly data (i.e. assemblies), (iii) core genome MLST (cgMLST) locus and allele identifiers designated by the hash of the corresponding sequence (i.e. allelic profiles) and (iv) cgMLST strain nomenclature.

[2] EFSA (European Food Safety Authority), Costa G, Di Piazza G, Koevoets P, Iacono G, Liebana E, Pasinato L, Rizzi V, Rossi M, 2022. Guidelines for reporting Whole Genome Sequencing-based typing data through the EFSA One Health WGS System. EFSA supporting publication 2022:EN-7413. 29 pp. doi:10.2903/sp.efsa.2022.EN-7413

4.3.1. Querying process between ECDC and EFSA

The interaction between ECDC and EFSA MTSs is performed through a machine-to-machine protocol, enabling the systems to perform queries and retrieve data based on cgMLST allelic profiles, as specified in the Technical Specifications (Section 5). A match is identified when the pairwise difference between the reference(s) cgMLST allelic profile(s) provided in the query and those present in the queried database (DB) is within a range of thresholds agreed between ECDC and EFSA. The pathogen-specific thresholds are subject to revision if supported by gained evidence. Data is retrieved upon finding a match between a query and the queried DB.

On a weekly basis, the ECDC MTS sends automatically to the EFSA MTS queries related to all human microbiological clusters identified in the ECDC MTS with fixed thresholds for allelic distance (indicator-based surveillance). In addition to the weekly automatic requests, ECDC MTS can perform *ad hoc* queries with user-defined allelic thresholds at any time (event-based surveillance). If the EFSA MTS identifies matching entries, the EFSA MTS sends automatically to the ECDC MTS a query for retrieving human isolate(s) of matching cgMLST profile(s) applying the same threshold used by the ECDC query.

When there is the need to compare one or multiple non-human isolates with human isolates for possible matches, users of the EFSA MTS can perform queries with user-defined allelic thresholds on demands.

4.3.2. Data exchange between ECDC and EFSA MTSs

The exchange of WGS data between ECDC and EFSA MTSs is limited to cgMLST allelic profiles. No reads or assemblies are exchanged automatically as response to the query. In addition to the cgMLST allelic profiles, also metadata are exchanged. The full list of metadata exchanged between ECDC and EFSA MTSs is presented in Table 1.

Table 1: List of metadata exchanged between ECDC and EFSA MTSs

Type of metadata	Description
Date	In EFSA MTS, it refers always to sampling date In ECDC MTS, it might refer to sampling date, received at the laboratory date, or notification date
Country[1]	In EFSA MTS, it might refer to the country where the sample has been taken or the country reporting the information to the system. In ECDC MTS, it refers always to country reporting the information to the system (i.e. reporting country).
Sample category	Description of the type of matrix of the sample taken. In EFSA MTS, the categories are: feed, non-food matrices (including samples from animals and environment) and food categories at second level of the hierarchy in FoodEx2 which includes for example the following: "Grains and grain-based products", "Garden vegetables and primary derivates thereof", "Legume seeds and primary derivates thereof", Fruit and primary derivates thereof", "Nuts and primary derivates thereof", "Oilseeds and oilfruits", "Starchy roots and tubers and primary derivates thereof", "Sugar plants", "Herbs, spices and similar", "Fruit/vegetables/plant drinks, spreads and related products", "Mammals and birds meat and products thereof", "Fish meat and products thereof", "Seafood and products thereof", "Terrestrial animals other than mammals and birds", "Milk and milk products (dairy)", "Eggs and egg products", "Meat and dairy imitates", "Water, water-based beverages and related ingredients", "Ingredients for hot drinks and infusions", "Hot drinks and similar (coffee, cocoa, tea and herbal infusions)", "Alcoholic beverages", "Confectionery

Type of metadata	Description
	including chocolate", "Food products for young population", "Food for particular diets", "Composite dishes", "Seasoning, sauces and condiments", "Isolated purified ingredients (including mineral or synthetic)". In ECDC MTS, the category is human
Cluster ID	This information is only relevant in ECDC MTS representing the single linkage cluster identifier based on weekly cluster ID or the EpiPulse ID

1. Data with restricted access

4.3.2.1. Access to exchanged data by users at EU level

The access to data exchanged between EFSA MTS and ECDC MTS does not have restrictions among users in the EFSA MTS and ECDC MTS belonging to EFSA, ECDC and EU laboratories organisations (including European Union Reference Laboratory - EURL - users in the EFSA MTS).

4.3.2.2. Access to exchanged data by users at country level

The access to data exchanged between EFSA MTS and ECDC MTS other than "Country" does not have restrictions among any users at country level in the EFSA MTS and ECDC MTS. The access to "Country" by EFSA and ECDC Data Providers follows the rules below:

- In the EFSA MTS, the "Country" of human data as a result of a query performed against the ECDC MTS is visible to the EFSA Data Provider only if the human data are from the same country of the EFSA Data Provider.

- In the ECDC MTS, the visibility of the "Country" of non-human data as a result of a query performed against the EFSA MTS is visible to ECDC Data Provider if his/her country is part of a microbiological cluster. However, the EFSA Data Provider user has the possibility to decide not to share the information "Country" with ECDC as a result of a query performed by ECDC MTS against the EFSA MTS.

4.4. Microbiological cluster monitoring and evaluation (Step 4 in the flowchart)

A preliminary evaluation of the microbial clusters is performed independently by ECDC and EFSA in their respective MTS. A joint evaluation is then performed during the weekly TC meeting. ECDC decides, based on available public health information, which human-only clusters are brought under joint evaluation.

The microbiological cluster monitoring and evaluation consists of an assessment of the joint microbiological cluster identified during Step 3 to determine if they should be further investigated. Moreover, this step includes the evaluation of those microbiological clusters for which a cross-sectorial match has not been found and where an active data collection from MSs would be necessary.

The microbiological clusters should be actively monitored using for example the following criteria:

- Microbiological cluster size, severity, population at risk, and growth rate
- Temporal and spatial distribution of microbiological cluster isolates
- Background data on prevalence of the type of the pathogen in non-human samples and disease occurrence in humans
- Human descriptive/epidemiological data
- Non-human (food, feed, animals and the related environment) descriptive/epidemiological data.

On case-by-case basis, for each joint microbiological cluster, ECDC and EFSA may decide to share between them additional descriptive or epidemiological data for their respective isolates. In case of

needs, ECDC and EFSA may decide to exchange the raw reads of the genomes of the relevant isolates for performing analyses not included in the ECDC and EFSA MTS, such as *ad hoc* SNP analysis. This exchange occurs after approval from MSs and using available tools.

Potential outcomes of the microbiological cluster monitoring and evaluation include:

- Escalation to joint microbiological cluster investigation and public health risk assessment
- Continue active monitoring and evaluation of the joint microbiological cluster in weekly TCs.

4.5. Joint microbiological cluster evaluation and investigation (Step 5 in the flowchart)

In case of escalation to an investigation of the joint cluster or event, ECDC and EFSA may agree on raising attention on the joint cluster or event to the ECDC Round Table meeting and to Directorate-General for Health and Food Safety (SANTE), that can evaluate the need for the production of a public health risk assessment.

In case of a production of a public health risk assessment, if needed, EFSA and ECDC can initiate a data call to their respective data providers. Moreover, data from EpiPulse and Rapid Alert System for Food and Feed (RASFF) are extracted and used in the weekly discussion.

Depending on the nature of the cross-border event as well as availability of information from both sectors at that time, two different types of joint outputs can be requested by ECDC Round Table or SANTE: Joint Notification Summary (JNS) or Rapid Outbreak Assessment (ROA).

A JNS is a working document with restricted distribution that includes the description of the event from the public health view and a summary of the information related to the contaminated food, a description of its traceability (where it was produced and distributed) and of the control measures implemented. The JNS is produced according to the principles and process agreed between EFSA and ECDC and the aims are:

- To notify in a timely manner risk managers in the EU and EU/EEA countries when a cross-border foodborne event has been verified by ECDC with a suspicion of food item(s) as vehicles of infections and/or common source(s) of infection but there is no information about matching isolates in non-human samples;
- To stimulate interaction at EU and national level, particularly between national food safety and public health authorities;
- To support the national competent authorities (NCA) in the Member States (MS) and EC in the investigation of the event.

A ROA is a public document that includes the epidemiological and microbiological description of the event/outbreak and an in-depth analysis of the information available in the RASFF, the identification of the food-vehicle, its origin, and the point of contamination along the food production line. The ROA is produced according to the principles and process agreed in the relevant joint ECDC-EFSA SOP and the aims are:

- To support risk managers in the EU and EU/EEA countries in identifying and implementing further or additional control measures needed to mitigate the risk of occurrence of new cases of infections
- To inform consumers on the multi-country event

5. Technical specifications

5.1. Core genome MLST schemas and allele calling procedure

The cgMLST analysis is performed in both ECDC and EFSA MTS with chewbbaca (version > 2.8.5; https://github.com/B-UMMI/chewBBACA) and with the schemas available at https://chewbbaca.online:

- *Salmonella enterica*: subset of the 3255 loci as described in 10.5281/zenodo.6655441 from the schema https://chewbbaca.online/species/8/schemas/1
- *Escherichia coli*: subset of the 2360 loci as described in 10.5281/zenodo.6655441 from the schema https://chewbbaca.online/species/5/schemas/1
- *Listeria monocytogenes*: schema https://chewbbaca.online/species/6/schemas/1

The shared profiles are composed by alleles expressed as CRC32 unsigned integer of the discovered allele nucleotide sequence.

5.2. API call content

The Application Programming Interface (API) call (query and response) is a JSON file including field described in Boxes 1 to 3. In both MTS APIs there will be one URL pointing to a relevant pathogen DB.

5.2.1. Query

The query includes, as mandatory fields, the query identification (query ID), the threshold of allelic distance for searching possible matches and the reference allelic profile/s (as object within the JSON file). Optionally, the query might contain a range of sampling dates for restricting the search. Regardless if the query includes a time range of sampling for limiting the search or not, EFSA MTS will always include in the response also isolates for which sampling time was not provided. ECDC will always include in the query an ID of the cluster as defined in The European Surveillance System (TESSy) and/or EpiPulse.

5.2.2. Response

Response can be either synchronous or asynchronous. In case the response is asynchronous, upon queries are received, the MTS immediately returns the query ID and provides endpoint where response will be available. The querying MTS is responsible for pulling the response from the provided endpoint.

The response contains as mandatory fields the timestamp and query ID, and of the response, allelic profile/s (as object within the JSON file) and their identification in the queried MTS. As optional fields, the response includes sampling date, sampling matrix category, sampling country, reporting country and cluster type.

Box 1, Box 2 and Box 3 show an example of the payload of the query, response with match and response without match.

The content of the response to ECDC from EFSA related to epidemiological data might differ depending on the availability of epidemiological data in the EFSA MTS and on the decision from EFSA Data Provider to share or not to share the "Country" information (Table 2).

Table 2: Examples of the expected content of a response to ECDC related to an entry submitted by an EFSA MTS German data provider based on the availability of epidemiological data and the decision by the data provider to share the information on "Country"

Data element	**Example of payload based on different options**			
Available Epidemiological data in the EFSA MTS	*Yes*	*Yes*	*No*	*No*
Decision of the EFSA Data Provider regarding sharing "Country information"	*Yes*	*No*	*Yes*	*No*
SubmittingOrganizationCountry	Germany	*null*	Germany	*null*
SamplingYear	2018	2018	*null*	*null*
SamplingCountry	Germany	*null*	*null*	*null*
SamplingMatrixType	Food	Food	*null*	*null*
SamplingMatrixCategory	Milk and milk products (dairy)	Milk and milk products (dairy)	*null*	*null*

Box 1: Payload example query from ECDC


```
{
  "query_id": 7235,
  "cluster_id": "3923:3283",
  "sampling_date_from": null,
  "sampling_date_to": null,
  "threshold": 10,
  "isolate_species_code": "RF-00000251-MCG",
  "reference": [
    {
      "id": "71IT_2011_FOOD132_contigs.fa",
      "Pasteur_cgMLST-00023625.fasta": "138852938",
      "Pasteur_cgMLST-00023626.fasta": "782725232",
      "Pasteur_cgMLST-00023627.fasta": "1934109537",
      "Pasteur_cgMLST-00023628.fasta": "2837436334",
       …
      "Pasteur_cgMLST-00025369.fasta": "0",
      "Pasteur_cgMLST-00025370.fasta": "2949521824",
      "Pasteur_cgMLST-00025371.fasta": "869953176",
      "Pasteur_cgMLST-00025372.fasta": "419818200"
    }
  ]
}
```

Box 2: Payload example response to ECDC with match by EFSA


```
{
 "query": {
  "query_id": 7235,
  "query_date": "2022-04-05T08:02:48.422Z"
 },
 "response": {
  "response_id": 7235,
  "response_date": "2022-04-05T08:02:48.454Z",
  "response_match_found": true,
  "response_profile_number": 3
 },
 "matching_profiles": [
  {
   "SubmittingOrganizationCountry": Germany,
   "SamplingYear": null,
   "SamplingCountry": null,
   "SamplingMatrixType": null,
   "SamplingMatrixCategory": null,
   "EntryId": "MIG-2021-000068",
   "EntryPublic": false,
   "Mlstst": 8,
   "Serotype": null,
   "allelic_profile": {
    "Pasteur_cgMLST-00023625.fasta": "138852938",
    "Pasteur_cgMLST-00023626.fasta": "782725232",
    "Pasteur_cgMLST-00023627.fasta": "1934109537",
    "Pasteur_cgMLST-00023628.fasta": "2837436334",
    "Pasteur_cgMLST-00023629.fasta": "198052190",
     …
    "Pasteur_cgMLST-00025369.fasta": "0",
    "Pasteur_cgMLST-00025370.fasta": "2949521824",
    "Pasteur_cgMLST-00025371.fasta": "869953176",
    "Pasteur_cgMLST-00025372.fasta": "419818200"
    }
  }
  {
   "SubmittingOrganizationCountry": null,
   "SamplingYear": 2018,
   "SamplingCountry": null,
   "SamplingMatrixType": ”Food”,
   "SamplingMatrixCategory": ”Milk and milk products (dairy)”,
   "EntryId": "MIG-2021-000112",
   "EntryPublic": false,
   "Mlstst": 8,
   "Serotype": null,
   "allelic_profile": {
    "Pasteur_cgMLST-00023625.fasta": "138852938",
    "Pasteur_cgMLST-00023626.fasta": "782725232",
    "Pasteur_cgMLST-00023627.fasta": "1934109537",
    "Pasteur_cgMLST-00023628.fasta": "2837436334",
    "Pasteur_cgMLST-00023629.fasta": "198052190",
     …
    "Pasteur_cgMLST-00025369.fasta": "0",
    "Pasteur_cgMLST-00025370.fasta": "2949521824",
    "Pasteur_cgMLST-00025371.fasta": "869953176",
    "Pasteur_cgMLST-00025372.fasta": "419818200"
    }
  {
```

```
      "SubmittingOrganizationCountry": Germany,
      "SamplingYear": 2018,
      "SamplingCountry": Germany,
      "SamplingMatrixType": ”FOOD”,
      "SamplingMatrixCategory": ”Milk and milk products (dairy)”,
      "EntryId": "MIG-2021-000112",
      "EntryPublic": false,
      "Mlstst": 8,
      "Serotype": null,
      "allelic_profile": {
        "Pasteur_cgMLST-00023625.fasta": "138852938",
        "Pasteur_cgMLST-00023626.fasta": "782725232",
        "Pasteur_cgMLST-00023627.fasta": "1934109537",
        "Pasteur_cgMLST-00023628.fasta": "2837436334",
        "Pasteur_cgMLST-00023629.fasta": "198052190",
         …
        "Pasteur_cgMLST-00025369.fasta": "0",
        "Pasteur_cgMLST-00025370.fasta": "2949521824",
        "Pasteur_cgMLST-00025371.fasta": "869953176",
        "Pasteur_cgMLST-00025372.fasta": "419818200"
        }
    }
]
}
```


Box 2 Payload example response to ECDC without match


```
{
  "query": {
    "query_id": 7235,
    "query_date": "2022-04-05T08:02:48.422Z"
  },
  "response": {
    "response_id": 7235,
    "response_date": "2022-04-05T08:02:48.454Z",
    "response_match_found": false,
    "response_profile_number": 0
  },
  "matching_profiles": []
}
```


5.3. System Logging

ECDC MTS submits queries to EFSA MTS and retrieve response from dedicated endpoints through the partner API of EFSA using subscription key generated by EFSA.

EFSA is submitting queries and retrieve response from the ECDC MTS accessing directly the API of ECDC. ECDC whitelisted the IP address of EFSA MTS.

5.4. Audit trail

For each query sent to or received from the ECDC MTS, EFSA is storing in the EFSA MTS DB the following information: date when the query was submitted, response time, Internet Protocol (IP) address of the ECDC MTS system, and the returned status code. For each query received by the ECDC MTS, a hashed IP address, the date and time of the query, and the request and response bodies are stored in the ECDC logging system.

5.5. Performance indicators

Both EFSA and ECDC will keep track of the response time from the queried MTS and take note of any downtime or other deviations from normal operations to monitor the performance of the system over time.

6. Legal basis and other reference documents

- EC (European Commission), 2013. Mandate from the European Commission to EFSA dated 9 July 2013, M-2013-0119.
- EC (European Commission), 2019. Mandate from the European Commission to EFSA and ECDC dated 20 December 2019, M-2020-0015.
- Memorandum of understanding between the European Food Safety Authority and the European Centre for Disease Prevention and Control. Available at: https://www.efsa.europa.eu/sites/default/files/2021-05/efsa-ecdc-mou-signed.pdf

7. Glossary

Data provider	the entity who submits the data in the context of the present data collection activities.
ECDC's Molecular Typing System	the system maintained at ECDC for the collection and analysis of data (Molecular Typing data and Epidemiological data) on isolates from humans. In addition, it stores and analyses PFGE and MLVA data from isolates from food, feed, animals and the related environment collected under the previous joint EFSA and ECDC molecular typing database.
EFSA's Molecular Typing system	the system maintained at EFSA for the collection of and analysis of data (Molecular Typing data and Epidemiological data) on isolates from food, feed, animals and the related environment.
European surveillance portal for infectious diseases	the platform for European public health authorities and global partners to collect, analyse, share, and discuss infectious disease data for threat detection, monitoring, risk assessment and outbreak response
Epidemiological data	the data and information on the food-borne pathogen isolates and the related food, feed, animal and the related environment samples or human cases that are not microbiological information. This includes temporal and geographical information and other descriptions of the source of the isolate such as age and gender (for human origin isolates) or the type of food the sample was taken from (for non-human origin isolates).
Isolate	a culture of a biological agent, isolated from a specific 'sample taken'.
Molecular Typing Data	the data generated by the application of specific molecular biology-based typing methods to characterise microbial isolates, including WGS data.

8. Abbreviations

API	Application Programming Interface
cgMLST	core genome Multilocus Sequence Typing
SANTE	Directorate-General for Health and Food Safety
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
ECDC MTS	ECDC Molecular Typing System
EFSA	European Food Safety Authority
EFSA MTS	EFSA's Molecular Typing system
EpiPulse	European surveillance portal for infectious diseases
EURL	European Union Reference Laboratory
JNS	Joint Notification Summary
MLST	Multilocus Sequence Typing
MLVA	Multiple Loci Variable -number tandem repeat Analysis
MTS	Molecular Typing System
PFGE	Pulsed Field Gel Electrophoresis
RASFF	Rapid Alert System for Food and Feed
ROA	Rapid Outbreak Assessment
STEC	Shiga toxin-producing *E. coli*
TESSy	The European Surveillance System
WGS	Whole Genome Sequencing

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