



Department
for Environment
Food & Rural Affairs

www.gov.uk/defra

R&D Contract: Use of FMDV sequence data to trace outbreaks and monitor disease incursion risks to the UK.



Contract Ref. Project: 26298

June 2019

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procurement@defra.gsi.gov.uk

SECTION 1

FORM OF CONTRACT

This agreement is made on 19 June 2019 PARTIES:

- (1) **THE SECRETARY OF STATE FOR ENVIRONMENT, FOOD AND RURAL AFFAIRS**
of Nobel House, 17 Smith Square, London, SW1P 3JR (the “**Authority**”);

AND

- (2) **THE PIRBRIGHT INSTITUTE** (the “**Institute**”) [REDACTED]
[REDACTED]

(each a “**Party**” and together the “**Parties**”)

NOW IT IS HEREBY AGREED:

1. The Contractor and the Authority agree to observe and comply with the Defra Terms and Conditions for Research and Development Projects which are incorporated into this agreement.
2. Annex A shall list the Project awarded non-competitively. The Agreement shall not include grants made under the Government’s LINK scheme, or projects that are joint funded or where the Contractor is acting jointly with another contractor.
3. The Contractor will carry out the Project in accordance with the objectives, approaches and research plan, and milestones contained in the appropriate Application. Annex A will give the Project Code, the agreed price, and the Start Date and Completion Date of the Project.
4. The Authority will pay to the Contractor the Costs properly incurred in carrying out the Project.
5. This agreement supersedes and replaces any and all previous contracts, agreements and statements relating to the Project, and consists of:
 - this Form of Contract;
 - Defra Terms and Conditions for Research and Development Projects;
 - the Schedules (Intellectual Property Schedule A; Contacts Schedule);
 - the objectives, approaches and research plans, and milestones contained in the Application(s);
 - Annex A Pricing Schedule & Scope of Works.

(together referred to as “**the Agreement**”).

6. In the Defra Terms and Conditions for Research and Development Projects, conditions 7.1.3, 13 (to the extent that it relates to the warranty in 7.1.3), 16, 23.1 and 34.2, shall not apply as between the Authority and a Contractor who is part of the Crown or a Research Council. Further, where the Contractor enters into a contract with a subcontractor who is

part of the Crown or a Research Council, the Contractor will not require the sub-contractor to comply with provisions comparable to the said Conditions.

7. To the extent that a Party is part of the Crown this Agreement is not intended to, and does not create any legally binding relationship between the Authority and that Party.
8. For the purposes of condition 17 of the Defra Terms and Conditions for Research and Development Projects (conflict or inconsistency), the documents shall take precedence in the order in which they appear in clause 5 of this Form of Contract.
9. Execution of the Agreement is carried out in accordance with the 1999 EU Directive 99/93 (Community framework for electronic signatures) and the UK Electronic Communications Act 2000. The Agreement is formed on the date on which both the Authority and the Contractor have communicated acceptance of its terms on the Authority's electronic contract management system ('Bravo').
10. The Contract duration is 1/04/2019 to 31/03/2022.

SECTION 2

DEFRA TERMS AND CONDITIONS FOR RESEARCH AND DEVELOPMENT PROJECTS

1. DEFINITIONS

1.1 In these terms and conditions the following words and expressions shall have the meanings given to them below, unless the context otherwise requires:

“Agreement”	The agreement between the Authority and the Contractor incorporating the Form of Contract and documents referred to therein.
“Application”	The application submitted by the Contractor containing his proposal for a Project, which is subsequently agreed for funding by the Authority, amended if necessary.
“Authority”	THE SECRETARY OF STATE FOR ENVIRONMENT, FOOD AND RURAL AFFAIRS and any persons authorised to act on the Secretary of State’s behalf.
“Authority’s Property”	Anything issued or otherwise provided in connection with the Agreement by or on behalf of the Authority or any person authorised to act on its behalf.
“Authority’s Representative”	The person named in paragraph 1 of the Contacts Schedule, subject to the provisions of condition 5.
“Contractor”	The organisation named on the Form of Contract as the Contractor.
“Contractor’s Representative”	The person named in paragraph 2 of the Contacts Schedule, subject to the provisions of condition 5.
“Completion Date”	The date set out in Annex A unless the Authority has not received a final report as set out in paragraph 3 of the Reports Schedule, in which case the Completion Date shall be the date on which the Authority receives such a report.
“Costs”	Costs incurred by the Contractor for the purposes of the carrying out of the Project, limited to those costs identified in the ‘Financial Guidelines for Project Cost Estimates’ section of the Application.
“Equipment”	All equipment, materials, consumables and plant, other than the Authority’s Property, to be used by the Contractor in carrying out the Project.

“Form of Contract”	The contract document signed by the parties.
“GDPR”	means the General Data Protection Regulation (Regulation (EU) 2016/679).
“Income”	Any revenues received by the Contractor (including without limitation the sale or disposal of products or services, royalties, payments for licences or options and stage payments) irrespective of whether such payment is in money or other consideration,
“Intellectual Property”	Any patent, copyright, design right, registered design, trademark or service mark, trade name, Know-how, patentable invention for the purposes of the Patents Act 1977, database right for the purposes of the Copyright and Rights in Databases Regulations 1997, domain name, technical information or know how and any application for any of the foregoing and any similar rights in any jurisdiction.
“Key Personnel”	Any member of the Contractor’s personnel identified by name or job title as key personnel in the Contacts Schedule.
“Know-how”	All information not in the public domain held in any form (including, without limitation, that comprised in or derived from oral and written instructions, diagrams, drawings, data formulae, patterns, specifications, notes, samples, chemical compounds, biological materials, computer software, component lists, instructions, manuals, brochures, catalogues and process descriptions and scientific approaches and methods) used in connection with or arising as a result of the Project.
“Parties”	The Authority and the Contractor.
“Period for the Project”	The period for the carrying out of the Project, being the period between the Start Date and the Completion Date.
“Project”	A research project particulars of which are set out in the Application and Annex A.
“Project Manager”	A person authorised by the Authority to manage a Project.
“Project Year”	Each period of 12 months during the Period of the Project calculated from the Start Date.

“Results”	Any Intellectual Property created by agents, employees, students or sub-contractors of the Contractor as a result of the Project.
“Schedule”	Any of the schedules annexed to the Agreement.
“Start Date”	The date set out in Annex A.
“Terms and Conditions”	The Defra Terms and Conditions for Research and Development Projects.

1.2 Unless the context otherwise requires, references in these Terms and Conditions

1.2.1 to the Contractor or to the Authority shall, where appropriate, be references to any lawful successor, assignee or transferee;

1.2.2 to the Contractor shall, where appropriate, be references to each individual person constituting the Contractor;

1.2.3 to conditions are references to the conditions of these Terms and Conditions

1.2.4 to "person" or "third party" include any individual, company, corporation, firm, partnership, joint venture, association, organisation, institution, trust or agency, whether or not having a separate legal personality;

1.2.5 to one gender include all genders, and references to the singular include the plural and vice versa;

1.2.6 to any statute, statutory provision or regulation, are references to that statute, statutory provision or regulation, as from time to time amended, extended or re-enacted.

1.3 The headings in this document are for convenience only, and shall be ignored in construing these Terms and Conditions.

2. DURATION

2.1 The Contractor shall commence work on the Project no later than the Start Date.

2.2 The Contractor shall complete the Project sufficiently in advance of the Completion Date to enable it to submit a final report as set out in paragraph 3 of the Reports Schedule.

2.3 Subject to the Authority’s right of termination, the Agreement shall remain in force for the Project from the Start Date until the Completion Date, unless the Parties agree to extend the duration of the Project.

3. FINANCIAL ARRANGEMENTS

3.1 The Contractor shall calculate Project costs in accordance with the “Financial Guidelines for Project Cost Estimates” contained in the Application.

3.2 The Authority shall pay all sums due to the Contractor within 30 days of Receipt of a Valid Invoice. Valid Invoices should be submitted for payment to the following address: ssd.apdefra@defra.gsi.gov.uk (the Authority’s preferred option); or SSCL AP, Defra, PO Box 790, Newport Gwent, NP10 8FZ. The Authority agrees to pay the Contractor the price for the Project quoted in Annex A and, subject to any variation of the Agreement, these shall individually remain fixed for the period of the Project.

- 3.3 In the event that the Agreement is varied, the prices shown in Annex A shall be adjusted by such reasonable sum as may be agreed, in writing, between the Authority and the Contractor.
- 3.4 Subject to the Contractor performing its obligations in accordance with the Agreement, the Authority shall pay the values set out in Annex A to the Contractor monthly.
- 3.5 Where the Contractor is not VAT exempt, and is required to charge VAT to the Authority at the current rate, the Contractor shall submit a VAT invoice at the beginning of each financial year (April- March) covering all payments to be made during that year. No payment will be made by the Authority to such Contractor unless and until this invoice is received by the Authority. The Contractor must exercise care not to charge VAT on expenses which are not chargeable to VAT.
- 3.6 Any overpayment to the Contractor made by the Authority, whether of Project price or VAT, shall be a sum of money recoverable by the Authority from the Contractor.
- 3.7 Failure to comply with the requirements of paragraphs 3.1 or 3.5 may result in payments being withheld or the Agreement being terminated in accordance with the provisions of condition 23.

4. PAYMENT OF SUB-CONTRACTORS

- 4.1 Where the Contractor enters into a sub-contract for the provision of services as part of a Project, the Contractor shall ensure that a term is included in the sub-contract which requires the Contractor to pay all sums due to the sub-contractor within a specified period not exceeding 30 days after the Contractor has verified the relevant invoice.
- 4.2 The Contractor shall use all reasonable endeavours to verify the invoices promptly.
- 4.3 Where the Contractor becomes liable to pay interest payments to a sub contractor under the provisions of the Late Payments of Commercial Debts (Interest) Act 1998, the Authority will not reimburse those costs unless they are incurred due to the negligence or default of the Authority.

5. NOMINATED OFFICERS

- 5.1 The Authority's Representative shall be the person named in paragraph 1.1 of the Contacts Schedule, or such other person that the Authority may nominate having given 14 days' notice to the Contractor.

5.2 The Contractor's Representative shall be the person named in paragraph 2.1 of The Contacts Schedule, or such other person that the Contractor may nominate having given 14 days' notice to the Authority.

6. CONTRACTOR'S STATUS

6.1 In carrying out the Projects, the Contractor shall be acting as principal and not as agent or employee of the Authority. Accordingly:

6.2 The Contractor shall not (and shall ensure that any other person engaged in relation to the Agreement shall not) say or do anything that might lead any other person to believe that the Contractor is acting as the agent or employee of the Authority, and

6.3 Nothing in the Agreement shall impose any liability of the Authority in respect of any liability incurred by the Contractor to any other person but this shall not be taken to exclude or limit any liability of the Authority to the Contractor that may arise by virtue of either a breach of the Agreement or any negligence on the part of the Authority its staff or agents.

7. WARRANTIES

7.1 The Contractor warrants to the Authority that:

7.1.1 the Contractor shall carry out and shall ensure that his employees, agents and sub-contractors also carry out the Projects with all reasonable skill, care and due diligence, in accordance with best professional, technical and scientific knowledge and practice, and any legislative requirements;

7.1.2 any materials or processes used in connection with the carrying out of the Projects shall be in accordance with standards set out in the Agreement;

7.1.3 the proper use by the Authority or any Crown body of any documentation, materials or results delivered by the Contractor pursuant to the Agreement, shall not to the best of the Contractor's knowledge and belief, constitute an infringement of the Intellectual Property rights of any third party. The Contractor warrants to the Authority to undertake appropriate patent, registered design right, trade mark, and/or literature searches to identify any actual or potential third party Intellectual Property rights;

7.1.4 the Contractor has understood the nature and extent of the Projects to be carried out and satisfied himself in relation to all matters connected with the Projects including the supply of and conditions affecting labour, the suitability of the premises where the projects are to be carried out and any Equipment necessary for the carrying out of the Projects subject to all such matters being reasonably discoverable by the Contractor.

7.2 Nothing in this Agreement shall be taken as limiting or excluding the Authority's rights or the Contractor's obligations pursuant to any statute, statutory instrument or the common law.

8. MEETINGS

The Contractor shall, subject to reasonable notice, attend all meetings specified in the Agreement or otherwise arranged by the Authority, for the discussion of matters concerned with the Projects.

9. LIMITATION OF LIABILITY

9.1 In the event that either party breaches this Agreement, subject to Condition 9.3, neither party shall be liable to the other for the following:

9.1.1 loss of profit, business, revenue, goodwill or anticipated savings;

9.1.2 indirect or consequential loss or damage.

9.2 Subject to Condition 9.3 in respect of any Project, the aggregate liability of either party to the other arising out of any breach or breaches of this Agreement shall be limited to the sum identified against it in Annex A.

9.3 Nothing in this Agreement limits or excludes either party's liability for:

9.3.1 personal injury or death arising from its negligence;

9.3.2 fraud; or

9.3.3 any other liability that cannot be excluded by law.

10. INDEMNITY AND INSURANCE

10.1 The Contractor shall ensure that any sub contractor shall indemnify the Authority, the Crown, its employees, agents and contractors, on demand from and against all liability for:

10.1.1 death or personal injury;

10.1.2 loss of or damage to property (including property belonging to the Crown or the Authority, or for which it is responsible "Authority Property");

10.1.3 breach of statutory duty; and

10.1.4 actions, claims, demands, costs, charges and expenses (including legal expenses on an indemnity basis)

which arises out of or in connection with the sub contractor's provision of a Project.

10.2 The indemnity contained in Condition 10.1 shall not apply to the extent that:

10.2.1 any loss, damage injury, cost and expense is caused by the negligent or willful act or omission of the Authority, its employees, agents or contractors, or by the breach by the Authority, of its obligations under the Agreement; or

10.2.2 the sub contractor is able to demonstrate that the loss, damage or injury arose as a direct result of the sub contractor acting on the instructions of the Authority.

10.3 The Contractor shall require any sub contractor to take out and maintain insurance with a reputable insurance company, including (but not limited) to employer's liability, public liability and professional indemnity insurance, covering at least all matters which are the subject of indemnities or compensation obligations under these Conditions in such sum as may be specified by the Authority in writing, [REDACTED].

10.4 The policy or policies of insurance referred to in paragraph 10.3 shall be shown to the Authority's Representative whenever he requests, together with satisfactory evidence of payment of premiums.

- 10.5 The Contractor shall ensure that no sub-contractor shall take any action or fail to take any reasonable action, or (to the extent that it is reasonably within its power) permit anything to occur in relation to it, which would entitle any insurer to refuse to pay any claim under any insurance policy in which that sub-contractor is an insured, a co-insured or additional insured person.
- 10.6 The provisions of these conditions do not apply where the sub-contractor is part of the Crown or a Research Council.

11. MONITORING OF PROGRESS AND ACCESS TO DOCUMENTS

- 11.1 In order to monitor the Contractor's performance of the Projects, the Authority or its representative (which for these purposes may include the Controller and Auditor General and any of his representatives) or his servants or agents, may enter into and inspect at all reasonable times and, save where the Authority has good reason not to give any notice, on reasonable notice, all facilities (whether at the Contractor's premises or elsewhere) used by the Contractor in its performance of its obligations under the Agreement.
- 11.2 The Contractor agrees that the Authority shall be entitled to audit the Contractor's performance of the Projects and inspect at all reasonable times and, save where the Authority have good reason not to give any notice, on reasonable notice, any and all records of the Contractor connected with its activities under the Agreement.
- 11.3 The Contractor agrees to make available to the Authority, free of charge, whenever requested, copies of audit reports obtained by the Contractor in relation to the Projects.
- 11.4 The Contractor shall retain or ensure that it has access to all records which relate to the Projects. On completion of the Projects, or in the event that the Agreement is terminated pursuant to condition 23 or otherwise, the Contractor shall at the direction of the Authority either retain or transfer to the Authority those records required by the Authority, or, where such records are in the possession of any third party, procure that the same is done. If the Authority requires the Contractor to transfer the records to it or to any third party, the Contractor shall be entitled to retain a copy of them.
- 11.5 For a period not less than 3 years after the completion of the Project or, where relevant, its termination, the Contractor shall retain in its possession all records and documentation relating to the Project unless they have been transferred to the Authority or a third party in accordance with condition 11.4 above.
- 11.6 The Contractor shall permit duly authorised agents of the Authority and/or the National Audit Office or European Court of Auditors to examine the Contractor's records and documents relating to the Agreement and to provide such copies and oral or written explanations as may reasonably be required.
- 11.7 This condition does not constitute a requirement or agreement for the examination, certification or inspection of the accounts of the Contractor under section 6(3) and 6(5) of the National Audit Act 1983.

12. CONTRACTOR'S PERFORMANCE AND PERSONNEL

- 12.1 The Contract will be monitored throughout the year, specifically at bi-monthly and annual contract review meetings. The Contractor shall properly manage and monitor the Projects and immediately inform the Authority if any aspect of the Agreement is not being or is unable to be performed.

Any performance issues highlighted at the bi-monthly contract review meetings will be

addressed by the Contractor, who will be required to provide an improvement plan to address all issues highlighted within a week of the meeting. Performance management and KPI performance will be a key feature of the Contract Review meetings.

- 12.2 The Contractor shall provide all the necessary facilities and Equipment necessary to complete the Projects.
- 12.3 The Contractor shall deploy sufficient personnel of appropriate qualifications, competence and experience to complete the Projects to time and shall ensure that those personnel are properly managed and supervised.
- 12.4 The Contractor shall give the Authority, if so requested, such particulars as the Authority may reasonably require of all persons who are or may be at any time employed on the Projects.
- 12.5 If, after due consultation with the Contractor, the Authority gives the Contractor notice that any person or Equipment is to be removed from involvement in a Project, the Contractor shall take immediate steps to comply with such notice and such decision of the Authority shall be final and conclusive.
- 12.6 The Contractor shall take all reasonable steps to avoid any changes of Key Personnel, but where the Contractor considers it necessary to do so, he will give the Authority not less than one month's notice of any intention to change any Key Personnel and the reasons for such change.

13. UNSATISFACTORY PERFORMANCE

13.1 Where in the reasonable opinion of the Authority the Contractor has failed to:

13.1.1 comply with any of the warranties in Condition 7;

13.1.2 fulfil his obligations under the Reports and Intellectual Property Schedules; or

13.1.3 progress the Project in accordance with the objectives, approaches and research plan, and milestones agreed for the Project.

the Authority may give the Contractor a notice specifying the way in which his performance falls short of the requirements of the Contract, or is otherwise unsatisfactory.

13.2 Where the Contractor has been notified of a failure in accordance with Condition 13.1 the Authority may:

13.2.1 direct the Contractor, to remedy the failure at his own expense within such time as may be specified by the Authority; and/or

13.2.2 withhold or reduce payments to the Contractor, in such amount as the

Authority reasonably deems appropriate in each particular case.

13.3 If, having been notified of any failure, the Contractor fails to remedy it in accordance with Condition 13.2, the Authority may treat the continuing failure as a material breach of the Agreement.

14. UNLAWFUL DISCRIMINATION

14.1 The Contractor shall perform its obligations under this Agreement in accordance with:

- 14.1.1 all applicable equality law (whether in relation to race, sex, gender reassignment, age, disability, sexual orientation, religion or belief, pregnancy maternity or otherwise), including but not limited to the obligations under the Equality Act 2010;
- 14.1.2 the Authority's equality and diversity policy as given to the Contractor from time to time;
- 14.1.3 any other requirements and instructions which the Authority reasonably imposes in connection with any equality obligations imposed on the Authority at any time under applicable equality law; and
- 14.1.4 the taking of all necessary steps and to inform the Authority of the steps taken to prevent unlawful discrimination designated as such by any court or tribunal, or the Equality and Human Rights Commission (or any successor organisation).

15. HEALTH AND SAFETY

In carrying out the Projects, the Contractor shall comply with best practice and all relevant provisions, whether statutory or otherwise, relating to health and safety at work and shall ensure that any person engaged in relation to the Agreement also so complies, and shall produce evidence of such compliance, if asked by the Authority to do so.

16. PREVENTION OF FRAUD AND BRIBERY

- 16.1 The Contractor shall comply with all applicable laws, statutes and regulations relating to anti-bribery and anti-corruption including but not limited to the Bribery Act 2010 (the "**Relevant Requirements**").
- 16.2 The Contractor shall have and maintain in place throughout the term of this agreement its own policies and procedures, including adequate procedures under the Bribery Act 2010, to ensure compliance with the Relevant Requirements and will enforce them where appropriate. The meaning of adequate procedures shall be determined in accordance with section 7(2) of the Bribery Act 2010 (and any guidance issued under section 9 of that Act).
- 16.3 The Contractor will promptly report to the Authority any request or demand for any undue financial or other advantage of any kind received by the Contractor in connection with the performance of this Agreement.

17. CONFLICT OF INTEREST

- 17.1 The Contractor shall ensure that there is no conflict of interest as to be likely to prejudice his impartiality and objectivity in performing the Projects and undertakes that upon becoming aware of any such conflict of interest during the performance of the Projects (whether the conflict existed before the award of the Agreement or arises during the performance of the Projects) he shall immediately notify the Authority in writing of the same, giving particulars of its nature and the circumstances in which it exists or arises and shall furnish such further information as the Authority may reasonably require.
- 17.2 Where the Authority is of the opinion that the conflict of interest notified to it under Condition 17.1 is capable of being avoided or removed, the Authority may require the Contractor to take such steps as are necessary to avoid or remove the conflict at the Contractor's expense.
- 17.3 If the Contractor fails to avoid or remove the conflict the Authority may terminate the Agreement and recover from the Contractor the amount of any loss resulting from such termination.
- 17.4 Where the Authority is of the opinion that the conflict of interest which existed at the time of

the award of the Agreement could have been discovered with the application by the Contractor of due diligence and ought to have been disclosed, the Authority may terminate the Agreement immediately for breach of a fundamental condition and, without prejudice to any other rights, recover from the Contractor the amount of any loss resulting from such termination.

18. PUBLICATION AND DISCLOSURE

- 18.1 Subject to the provisions of conditions 18.3, 18.4 and 18.6, the Contractor shall endeavour to make information about, and results from the Projects generally available, and may do so provided he acknowledges in any public statement the financial support of the Authority.
- 18.2 Subject to the requirements of the Reports Schedule, the Authority shall have the right to disclose, copy or otherwise distribute to the public or use in any way any information arising out of the Projects or comprised in any work relating to the Projects, as it sees fit.
- 18.3 Where any Project, or any matter related to it, has been identified as being sensitive by:
- 18.3.1 the Contractor, or
- 18.3.2 the Authority, as notified in writing to the Contractor,
- the Contractor shall give written notice to be received by the Authority at least 10 working days before any planned public statement or other disclosure relating to the Project, providing details of the information proposed to be disclosed, the reason, and the medium of disclosure.
- 18.4 The Contractor shall notify the Authority immediately if approached by the media about any Project. The Contractor shall notify the Authority immediately if approached by anyone about a matter related to any Project which is considered sensitive by the Contractor, or by the Authority as notified to the Contractor in accordance with condition 18.3.2.
- 18.5 For the avoidance of doubt, the notifications required by conditions 18.3 and 18.4 are for the purposes of informing the Authority or the Contractor (as the case may be) and are not designed to interfere with the issue of any public statement.
- 18.6 Where the carrying out of any Project results in, or materially contributes to, the creation of Intellectual Property which the Contractor or the Authority considers may be suitable for commercial exploitation no disclosure of information may be made by the Contractor which would jeopardise such exploitation.
- 18.7 The Parties acknowledge that, in order to be compliant with the Freedom of Information Act 2000, the Environmental Information Regulations 2004, or any other applicable legislation governing access to information (the "FOI Legislation"), the Parties may be obliged to provide information, on request, to third parties that relates to this Agreement.
- 18.8 In the event that either Party receives a request for information relating to the Agreement falling within the scope of the FOI Legislation, the Party shall be entitled to disclose such information as necessary in order to ensure its compliance with the FOI Legislation. Where the Party reasonably considers that information is exempt from disclosure, it shall use reasonable endeavours to consult with the other Party.
- 18.9 In the event that either Party requires the other Party's assistance in supplying any information falling within the scope of the FOI legislation that is held or controlled by the other Party or any other person engaged in relation to the Agreement, the disclosing Party will provide such assistance, at its own cost within ten (10) days of receiving the request.
- 18.10 A Party shall not be liable for any loss, damage, harm or other detriment suffered by the

other Party arising from the disclosure of any information falling within the scope of the FOI Legislation.

19. DATA PROTECTION

- 19.1 The Parties acknowledge that for the purposes of the Data Protection Legislation, the Authority is the Controller and the Contractor is the Process or unless otherwise specified in Schedule D. The only processing that the Contractor is authorised to do is listed in Schedule D by the Authority and may not be determined by the Contractor.
- 19.2 The Contractor shall notify the Authority immediately if it considers that any of the Authority's instructions infringe the Data Protection Legislation.
- 19.3 The Contractor shall provide all reasonable assistance to the Authority in the preparation of any Data Protection Impact Assessment prior to commencing any processing. Such assistance may, at the discretion of the Authority, include:
- (a) a systematic description of the envisaged processing operations and the purpose of the processing;
 - (b) an assessment of the necessity and proportionality of the processing operations in relation to the Services;
 - (c) an assessment of the risks to the rights and freedoms of Data Subjects; and
 - (d) the measures envisaged to address the risks, including safeguards, security measures and mechanisms to ensure the protection of Personal Data.
- 19.4 The Contractor shall, in relation to any Personal Data processed in connection with its obligations under this Contract:
- (a) process that Personal Data only in accordance with Schedule D unless the Contractor is required to do otherwise by Law. If it is so required the Contractor shall promptly notify the Authority before processing the Personal Data unless prohibited by Law;
 - (b) ensure that it has in place Protective Measures which are appropriate to protect against a Data Loss Event, which the Authority may reasonably reject (but failure to reject shall not amount to approval by the Authority of the adequacy of the Protective Measures), having taken account of the:
 - nature of the data to be protected;
 - harm that might result from a Data Loss Event;
 - state of technological development; and
 - cost of implementing any measures;
 - (c) ensure that :
 - the Staff do not process Personal Data except in accordance with this Contract (and in particular Schedule D);
 - it takes all reasonable steps to ensure the reliability and integrity of any Staff who have access to the Personal Data and ensure that they:
 - are aware of and comply with the Contractor's duties under this clause;

are subject to appropriate confidentiality undertakings with the Contractor or any Sub-processor;

are informed of the confidential nature of the Personal Data and do not publish, disclose or divulge any of the Personal Data to any third party unless directed in writing to do so by the Authority or as otherwise permitted by this Contract; and

have undergone adequate training in the use, care, protection and handling of Personal Data; and

not transfer Personal Data outside of the European Union unless the prior written consent of the Authority has been obtained and the following conditions are fulfilled:

the Authority or the Contractor has provided appropriate safeguards in relation to the transfer (whether in accordance with the GDPR Article 46 or LED Article 37) as determined by the Authority;

the Data Subject has enforceable rights and effective legal remedies;

the Contractor complies with its obligations under the Data Protection Legislation by providing an adequate level of protection to any Personal Data that is transferred (or, if it is not so bound, uses its best endeavours to assist the Authority in meeting its obligations); and

the Contractor complies with any reasonable instructions notified to it in advance by the Authority with respect to the processing of the Personal Data;

at the written direction of the Authority, delete or return Personal Data (and any copies of it) to the Authority on termination of the Contract unless the Contractor is required by Law to retain the Personal Data.

19.5 Subject to clause 19.6 the Contractor shall notify the Authority immediately if, in relation to any Personal Data processed in connection with its obligations under this Contract, it:

- (a) receives a Data Subject Request (or purported Data Subject Request);
- (b) receives a request to rectify, block or erase any Personal Data;
- (c) receives any other request, complaint or communication relating to either Party's obligations under the Data Protection Legislation;
- (d) receives any communication from the Information Commissioner or any other regulatory authority;
- (e) receives a request from any third party for disclosure of Personal Data where compliance with such request is required or purported to be required by Law; or
- (f) becomes aware of a Data Loss Event.

19.6 The Contractor's obligation to notify under clause 19.5 shall include the provision of further information to the Authority in phases, as details become available.

19.7 Taking into account the nature of the processing, the Contractor shall provide the Authority with full assistance in relation to either Party's obligations under Data Protection Legislation in relation to any Personal Data processed in connection with its obligations under this

Contract and any complaint, communication or request made under Clause 19.5 (and insofar as possible within the timescales reasonably required by the Authority) including by promptly providing:

- (g) the Authority with full details and copies of the complaint, communication or request;
- (h) such assistance as is reasonably requested by the Authority to enable the Authority to comply with a Data Subject Request within the relevant timescales set out in the Data Protection Legislation;
- (i) the Authority, at its request, with any Personal Data it holds in relation to a Data Subject;
- (j) assistance as requested by the Authority following any Data Loss Event;
- (k) assistance as requested by the Authority with respect to any request from the Information Commissioner's Office, or any consultation by the Authority with the Information Commissioner's Office.

19.8 The Contractor shall maintain complete and accurate records and information to demonstrate its compliance with this clause. This requirement does not apply where the Contractor employs fewer than 250 staff, unless:

- (l) the Authority determines that the processing is not occasional;
- (m) the Authority determines the processing includes special categories of data as referred to in Article 9(1) of the GDPR or Personal Data relating to criminal convictions and offences referred to in Article 10 of the GDPR; or
- (n) the Authority determines that the processing is likely to result in a risk to the rights and freedoms of Data Subjects.

19.9 The Contractor shall allow for audits of its Personal Data processing activity by the Authority or the Authority's designated auditor.

19.10 Each Party shall designate its own Data Protection Officer if required by the Data Protection Legislation.

19.11 Before allowing any Sub-processor to process any Personal Data related to this Contract, the Contractor must:

- (o) notify the Authority in writing of the intended Sub-processor and processing;
- (p) obtain the written consent of the Authority;
- (q) enter into a written agreement with the Sub-processor which give effect to the terms set out in this clause 19 such that they apply to the Sub-processor; and

- (r) provide the Authority with such information regarding the Sub-processor as the Authority may reasonably require.

- 19.12 The Contractor shall remain fully liable for all acts or omissions of any of its Sub-processors.
- 19.13 The Authority may, at any time on not less than 30 Working Days' notice, revise this clause by replacing it with any applicable controller to processor standard clauses or similar terms forming part of an applicable certification scheme (which shall apply when incorporated by attachment to this Contract).
- 19.14 The Parties agree to take account of any non-mandatory guidance issued by the Information Commissioner's Office. The Authority may on not less than 30 Working Days' notice to the Contractor amend this Contract to ensure that it complies with any guidance issued by the Information Commissioner's Officer.
- 19.15 This clause 19 shall apply during the Contract Period and indefinitely after its expiry.

20. AUTHORITY'S PROPERTY

- 20.1 The Authority's Property shall include any property owned by the Authority including any item of equipment costing in excess of £2,000 which will yield continuous service for at least one year, for which the Authority has reimbursed the Contractor.
- 20.2 The Authority's Property shall remain the property of the Authority and shall be used in the performance of the Agreement and for no other purpose without prior approval of the Authority.
- 20.3 The Contractor shall ensure that the title in the Authority's Property is brought to the attention of any third party dealing with the Authority's Property.
- 20.4 On receipt of the Authority's Property, the Contractor shall subject it to a visual inspection and such additional inspection and testing as may be necessary to check that it is not defective. If the Contractor discovers any defect, he shall notify the Authority within 14 days of receipt of the Property, or such other period as may be agreed with the Authority. The Authority shall, within 14 days of receiving such notification, inform the Contractor of the action to be taken
- 20.5 The Authority shall be responsible for the repair or replacement of its Property unless the need for repair or replacement is caused by the Contractor's failure to comply with Condition 20.4, or by the negligence or default of the Contractor.
- 20.6 The Contractor shall maintain all items of the Authority's Property in good and serviceable condition (fair wear and tear excepted), and in accordance with the manufacturer's recommendations.
- 20.7 The Contractor shall be liable for any loss of or damage to any of the Authority's Property unless the Contractor is able to demonstrate that such loss or damage was caused or contributed to by the negligence or default of the Authority.
- 20.8 The Authority shall have the right to require the Contractor either to pass the Authority's Property into the Authority's possession or to dispose of it. In the latter event, the Contractor shall pass to the Authority any monies realised by the disposal.

21. EQUIPMENT

- 21.1 All Equipment purchased by the Contractor for use on the Projects shall, where reasonably practicable, be acquired by competitive tender.

- 21.2 Unless otherwise agreed in writing with the Authority, the Contractor shall provide the Equipment necessary for the provision of the Projects.
- 21.3 The Contractor shall maintain all items of Equipment in good and serviceable condition.
- 21.4 All Equipment shall be at the risk of the Contractor and the Authority shall have no liability for any loss of or damage to any Equipment except to the extent that the Contractor is able to demonstrate that such loss or damage was caused or contributed to by the negligence or default of the Authority.

22. INTELLECTUAL PROPERTY

- 22.1 Each Party shall comply with Intellectual Property Schedule A.
- 22.2 Each Party shall inform the other Party promptly if it becomes aware of any infringement or potential infringement of any of the Intellectual Property rights, and the Parties shall consult with each other to decide the best way to respond to such infringement.
- 22.3 If any warning letter or other notice of infringement is received by a party, or legal suit or other action is brought against a party, alleging infringement of third party rights in the manufacture, use or sale of any licensed product or use of any patents or Intellectual Property rights, that party shall promptly provide full details to the other party, and the parties shall discuss the best way to respond.
- 22.4 The Contractor shall indemnify the Authority and keep the Authority fully and effectively indemnified against all claims, damages or losses arising from or incurred by reason of any infringement or alleged infringement (including but not limited to the defence of such alleged infringement in the United Kingdom) of any Intellectual Property rights in connection with the use, exercise or commercial exploitation of the Results (other than where any such claim arises as a result of the Authority's negligence or willful default).

23. TERMINATION

- 23.1 The Contractor shall notify the Authority in writing immediately upon the occurrence of any of the following events:
- 23.1.1 being an individual:-
- a) is the subject of a bankruptcy order; or
 - b) has made a composition or arrangement with his creditors;
- 23.1.2 being a company :-
- a) goes into compulsory winding up; or
 - b) passes a resolution for voluntary winding up; or
 - c) suffers an administrator, administrative receiver or receiver and manager to be appointed or to take possession over the whole or any part of its assets
 - d) has entered into a voluntary arrangement with its creditors under Part I of the Insolvency Act 1986, or has proposed or entered into any scheme of arrangement or composition with its; or
 - e) has been dissolved;
- 23.1.3 being a partnership or unregistered company :-
- a) goes into compulsory winding up; or
 - b) is dissolved; or (in the case of a partnership only)

- c) suffers an administrator or receiver and manager to be appointed over the whole or any part of its assets ; or
- d) has entered into a composition or voluntary arrangement with its creditors; or
- e) any individual member of the partnership falls within Condition 23.1.1 above;

23.1.4 Or is in any case affected by any similar occurrence to any of the above in any jurisdiction.

On the occurrence of any of the events described in this condition 23.1 or, if the Contractor shall have committed a material breach of the Agreement and (if such breach is capable of remedy) shall have failed to remedy such breach within thirty days of being required by the Authority in writing to do so, the Authority shall be entitled to terminate this Agreement by notice to the Contractor with immediate effect and without compensation to the Contractor.

23.2 The Authority may terminate the Contract at any time by giving 30 days' notice to the Contractor.

23.3 Without prejudice to the provisions of this condition, the Contractor may submit a request to the Authority to withdraw from the Agreement. The Agreement may be terminated by written agreement between the Contractor and the Authority at any time.

23.4 Without prejudice to the provisions of this condition, either Party may submit a request to the other Party to withdraw from the Agreement. The Agreement may be terminated by written agreement between the Contractor and the Authority at any time.

23.5 Except as expressly provided in this Agreement, termination of the Agreement shall not affect:

23.5.1 any obligation or liability of any Party which has accrued at the date of termination;

23.5.2 any of the provisions of this Agreement which are intended to continue to have effect after the Agreement has been terminated including without limitation the obligations contained in the Intellectual Property Schedule.

23.6 The initial Contract period will be for three (3) years and there is a break clause included at every 6 months of the contract. This break clause may be implemented by the Authority only.

24. PAYMENT ON TERMINATION

24.1 Without prejudice to any other rights or remedies of the Authority, in the event of the Agreement being terminated:

24.1.1 by the Authority in accordance with condition 23 by reason of the default of the Contractor; or

24.1.2 otherwise by reason of the Contractor's breach of the Agreement;

the Authority shall be under no obligation to make any payment to the Contractor for such period as is reasonable for the Authority to assess the loss and/or damage suffered as a result of the termination.

24.2 After such period, the Authority may set off against any sums otherwise due to the Contractor, or recover as a debt, the amount of loss and/or damage the Authority has reasonably assessed as resulting from the termination of the Agreement.

24.3 Any overpayment by the Authority to the Contractor, whether of the agreed price or Value

Added Tax, shall be a sum of money recoverable by the Authority from the Contractor.

25. MERGER, TAKEOVER OR CHANGE OF CONTROL

The Contractor shall forthwith inform the Authority in writing of any proposal or negotiations which will or may result in a merger, take-over, change of control, change of name or status, including, where the Contractor is a company as defined in the Companies Act 2006, any change in "control" as defined in Section 1124 of the Corporation Taxes Act 2010.

26. TRANSFER OF RIGHTS AND OBLIGATIONS

26.1 The Contractor shall not sub-contract, transfer, assign, charge, or otherwise dispose of the Agreement or any part of it without the prior written consent of the Authority.

26.2 The Contractor shall ensure, if so requested by the Authority, that an assignee enters into a novation agreement with the Authority to perform the Agreement as if the assignee were a party to the Agreement in lieu of the Contractor.

26.3 The Contractor shall ensure that any sub-contractor complies with the terms and Conditions of the Agreement, so far as they are applicable and shall provide to the Authority, at its request copies of any sub-contracts. Any sub-contract shall not relieve the Contractor of his obligations under the Agreement.

26.3 The Authority may at any time, on written notice to the Contractor, transfer or assign all or any rights and/or obligations under the Agreement.

27. RIGHTS OF THIRD PARTIES

For the purposes of the Contracts (Rights of Third Parties) Act 1999, this Agreement is not intended to, and does not give any person who is not a party to it any right to enforce any of its provisions.

28. WAIVER AND VARIATION

28.1 The failure of the Authority or the Contractor to exercise any right or remedy shall not constitute a waiver of that right or remedy.

28.2 A waiver of any right or remedy arising from a breach of the Agreement shall not constitute a waiver of any right or remedy arising from any other breach of the Agreement.

28.3 No waiver shall be effective unless it is communicated to either the Authority or the Contractor in writing.

28.4 Any variation of any provision of this Agreement must be effected in writing and issued by the Authority. No purported variation by any other means shall bind the Authority.

29. SEVERANCE

If any condition, clause or provision of the Agreement which is not of a fundamental nature is held to be invalid, illegal or unenforceable for any reason by any court of competent jurisdiction in any proceedings relating to the Agreement, such provision shall be severed and the validity or enforceability of the remainder of the Agreement shall not be affected thereby.

30. NOTICES

- 30.1 Any notice required to be given under, or any communication between the parties with the respect to any of the provisions of the Agreement shall be in writing in English and shall be deemed duly given if signed by or on behalf of a duly authorised officer of the party giving the notice and if left at, or sent by pre-paid registered or recorded delivery post, or by facsimile transmission or other means of electronic telecommunication in permanent written form to the address of the receiving party as specified in the Agreement (as or amended from time to time by due notice in writing to other party).
- 30.2 Any such notice or other communication shall be deemed to have been given and received by the addressee:-
- 30.2.1 at the same time as it is left at the address of or handed to a representative of the party to be served;
- 30.2.2 by post on the day (not being a Sunday or public holiday two days following the date of posting);
- 30.2.3 in the case of a facsimile or email or other type of electronic telecommunication on the day following dispatch.
- 30.3 In proving the giving of a notice it shall be sufficient to prove that the notice was left, or that the envelope containing the notice was correctly addressed and was posted, or that the facsimile or e-mail or other form of electronic communication was correctly addressed and was dispatched and dispatch of the transmission was confirmed and (in the case of a facsimile) confirmed as having been sent to the number above with all pages successfully transmitted.

31. SPECIAL PROVISIONS

Subject to paragraph 8 of the Form of Contract, in the case of any conflict or inconsistency between these Terms and Conditions and any conditions contained within the Form of Contract or the Schedules, the latter conditions shall prevail.

32. ENTIRE AGREEMENT

The Agreement and any variation made in accordance with condition 28 sets out the entire agreement between the Parties and supersedes any prior agreement whether formal or informal and whether legally within the Agreement.

33. LEGAL RELATIONSHIP

Nothing in this Agreement shall be construed so as to create a partnership or joint venture between the Parties or have the effect of making any employee of any one party a servant of the other party. Neither party shall act or describe itself as the agent of the other nor shall it make or represent that it has authority to make any commitments on the other's behalf.

34. DISPUTE RESOLUTION

- 34.1 The Parties shall in good faith attempt to negotiate a settlement to any dispute between them arising out of or in connection with the Agreement.
- 34.2 If any such dispute cannot be resolved in accordance with condition 34.1, the relevant Parties shall consider referring the matter to mediation in accordance with condition 34.3.
- 34.3 The procedure for mediation shall be as follows:

- 34.3.1 a neutral person ("the Mediator") shall be chosen by agreement between the relevant Parties, alternatively, any Party may within 14 days from the date of the proposal to appoint a mediator, or within 14 days of notice to any Party that the chosen mediator is unable or unwilling to act, apply to the Centre for Dispute Resolution ("CEDR") to appoint a mediator;
- 34.3.2 the relevant Parties shall within 14 days of the appointment of the Mediator meet with him or her to agree a timetable for the exchange of all relevant and necessary information and the procedure to be adopted for the mediation. If appropriate, the relevant Parties may at any stage seek from CEDR guidance on a suitable procedure;
- 34.3.3 unless otherwise agreed, all negotiations and proceedings in the mediation connected with the dispute shall be conducted in strict confidence and shall be without prejudice to the rights of the relevant Parties in any future proceedings;
- 34.3.4 if the relevant Parties reach agreement on the resolution of the dispute, that agreement shall be put in writing and shall be binding upon the relevant Parties;
- 34.3.5 failing agreement, any relevant Party may invite the Mediator to provide a non-binding but informative opinion in writing. Such opinion shall be provided on a without prejudice basis and shall not be used in evidence in any proceedings relating to the dispute without the prior written consent of the relevant Parties.
- 34.4 For a period of sixty days from the date of the appointment of the Mediator, or such other period as the relevant Parties may agree, none of the Parties to the dispute may commence any proceedings in relation to the matters referred to the Mediator.

35. OFFICIAL SECRETS ACT

The Contractor shall take all reasonable steps to ensure that any persons employed by him or by any sub-contractor in connection with the Projects are aware of the Official Secrets Acts 1911 to 1989, and that these Acts apply to them during and after performance of any services under or in connection with the Agreement.

36. RE-TENDERING AND HANDOVER

- 36.1 Within 21 days of being so requested by the Authority's Representative, the Contractor shall provide, and thereafter keep updated, in a fully indexed and catalogued format, all the information necessary to enable the Authority to issue tender documents for the future provision of any Project.
- 36.2 Where, in the opinion of the Authority, the Transfer of Undertakings (Protection of Employment) Regulations 2006 are likely to apply on the termination or expiration of any Project or Projects, the information to be provided by the Contractor under Condition 36.1 shall include, as applicable, accurate information relating to the staff who would be transferred under the same terms of employment under those Regulations, including in particular:
- 36.2.1 the number of staff who would be transferred, but with no obligation on the Contractor to specify their names;
- 36.2.2 in respect of each of those members of staff their age, sex, salary, length of service, hours of work, overtime hours and rates, any other factors affecting redundancy entitlement and any outstanding claims arising from their employment;
- 36.2.3 the general terms and conditions applicable to those members of staff, including probationary periods, retirement age, periods of notice, current pay agreements, working hours, entitlement to annual leave, sick leave, maternity and special leave,

terms of mobility, any loan or leasing schemes, any relevant collective agreements, facility time arrangements and additional employment benefits.

- 36.3 The Authority shall take all necessary precautions to ensure that the information referred to in Conditions 36.2 is given only to service providers who have qualified to tender for the future provision of any Project.
- 36.4 The Authority shall require that all potential providers treat the information in confidence; that they do not communicate it except to such persons within their organisation and to such extent as may be necessary for the purpose of preparing a response to an invitation to tender issued by the Authority; and that they shall not use it for any other purpose.
- 36.5 The Contractor shall indemnify the Authority against any claim made against the Authority at any time by any person in respect of any liability incurred by the Authority arising from any deficiency or inaccuracy in information which the Contractor is required to provide under Condition 36.2
- 36.6 The Contractor shall not –
- 36.6.1 at any time during the Agreement, including any extension, move any staff into the undertaking or relevant part of the undertaking which provides the Projects, who do not meet the standards of skill and experience, or who are in excess of the number, required for the purposes of the Agreement; or
- 36.6.2 make any substantial change in the terms and conditions of employment of any staff engaged in providing the Projects, which is inconsistent with the Contractor's established employment and remuneration policies.
- 36.7 Where, in the opinion of the Authority, any change or proposed change in the staff employed in the undertaking or relevant part of the undertaking, or any change in the terms and conditions of employment of such staff, would be in breach of Condition 36.6 the Authority shall have the right:
- 36.7.1 to make representations to the Contractor against the change or proposed change;
- 36.7.2 to give notice to the Contractor requiring him to remedy the breach within 30 days; and
- 36.7.2 if the Contractor has not remedied the breach to the satisfaction of the Authority by the end of the period of 30 days, to terminate the Agreement by reason of the default of the Contractor, in accordance with Condition 23.2.
- 36.8 The Contractor shall allow access to his premises, in the presence of the Authority's Representative, to any person representing any potential provider whom the Authority has selected to tender for the future provision of the Project or Projects.
- 36.9 For the purpose of access to the premises in accordance with Condition 36.8, the Authority shall give the Contractor 7 days' notice of a proposed visit together with a list showing the names of all persons who will be attending those premises. Their attendance shall be subject to compliance with the Contractor's security procedures, subject to such compliance not being in conflict with the objectives of the visit.
- 36.10 The Contractor shall co-operate fully with the Authority during the handover arising from the completion or earlier termination of any Project. This co-operation, during the setting up operations period of the new Contractor, shall extend to allowing full access to, and providing copies of, all documents, reports, summaries and any other information necessary in order to achieve an effective transition without disruption to routine operational requirements.

- 36.11 Within 10 working days of being so requested by the Authority's representative, the Contractor shall transfer to the Authority, or any person designated by the Authority, free of charge, all computerised filing, recording, documentation, planning and drawing held on software and utilised in the provision of the Project or Projects. The transfer shall be made in a fully indexed and catalogued disk format, to operate on a proprietary software package identical to that used by the Authority.

37. OCCUPATION OF GOVERNMENT PREMISES

Any land or premises (including temporary buildings) made available to the Contractor by the Authority in connection with the Agreement shall be made available to the Contractor free of charge and shall be used by the Contractor solely for the purposes of performing the Agreement. The Contractor shall have the use of such land or premises as licensee and shall vacate the same upon completion or determination of the Agreement. Any utilities required by the Contractor shall be subject to such charges as are set out elsewhere in the Agreement.

38. ENVIRONMENTAL REQUIREMENTS

- 38.1 The Contractor shall perform the Agreement in accordance with the Department's environmental policy, which is to conserve energy, water, wood, paper and other resources, reduce waste and phase out the use of ozone depleting substances and minimise the release of greenhouse gases, volatile organic compounds and other substances damaging to health and the environment.
- 38.2 The Contractor shall pay due regard to the use of recycled products, so long as they are not detrimental to the provision of the Projects or the Environment, to include the use of all packaging, which should be capable of recovery for re-use or recycling.
- 38.3 The Contractor shall take all possible precautions to ensure that any equipment and materials use in the provision of the Projects do not contain chlorofluorocarbons, halons or any other damaging substances, unless unavoidable, in which case the Authority shall be notified in advance of their use.
- 38.4 All written work in connection with the Agreement shall (unless otherwise agreed with the Authority) be produced on recycled paper containing at least 80% post consumer waste and used on both sides where appropriate.

39. GOVERNING LAW

The Agreement shall be governed by and interpreted in accordance with English law and shall be subject to the jurisdiction of the Courts of England and Wales. The submission to such jurisdiction shall not (and shall not be construed so as to) limit the right of the Authority take proceedings against the Contractor in any other court of competent jurisdiction, nor shall the taking of proceedings in any other court of competent jurisdiction preclude the taking of proceedings in any other jurisdiction whether concurrently or not.

INTELLECTUAL PROPERTY SCHEDULE A - INTELLECTUAL PROPERTY RIGHTS VESTED IN THE CONTRACTOR

Ownership and protection

1. Subject to the Contractor complying with the Agreement, any prior rights and the rights of third parties, all rights in relation to the Results shall be vested in the Contractor. Where the Contractor is a Crown body, any copyright shall vest in the Crown.
2. The Contractor shall:
 - 2.1 ensure that all its staff, students and sub-contractors are and will be engaged in relation to the Agreement and the Projects on terms which vest all rights in Results in the Contractor;
 - 2.2 continue to report to the Authority at regular intervals (and in any case at least once in every Project Year for so long as the Results are capable of or are being exploited) on the progress of commercial exploitation of the Results and on any assignment or licence of the Results; and
 - 2.3 do all things and execute at the Authority's expense any documents reasonably required to give effect to such vesting or assignment/licensing in the Authority as is necessary to give effect to paragraph 12 of Schedule A.

Licence back

3. The Contractor hereby grants to the Authority an irrevocable world-wide non-exclusive licence in perpetuity free of any charge or royalty to use the Results for:
 - 3.1 the purposes of paragraph 4 of the Reports Schedule;
 - 3.2 the purposes of Condition 18.2 of the Defra Terms and Conditions for Research and Development Projects in the Agreement;
 - 3.3 any other Government purposes;and to sub-licence and sub-sub-licence the Authority's rights on the same terms as the licence. The Contractor shall ensure that any such licence shall be binding on any successor, transferee or assignee of the Contractor.
4. Where such use of the Results by the Authority or sub-licensees also requires a licence to use any Intellectual Property rights of the Contractor other than the Results, the Contractor shall grant such a licence, subject to existing third party rights, which shall be royalty-free where such use is for non-commercial purposes, but shall be on reasonable terms to be agreed between the Parties in good faith where such use is for commercial or revenue generating purposes.

Commercial exploitation

5. The Contractor will use its reasonable endeavours to exploit the Results commercially for its benefit and the benefit of the Authority.
6. In order to comply with Government policy:
 - 6.1 the Contractor shall identify and inform the Authority of any Results which he considers suitable for commercial exploitation, and shall use reasonable endeavours to pursue or procure commercial exploitation thereof;

- 6.2 the Contractor shall provide to the Authority such information as the Authority may reasonably require regarding commercial exploitation of the Results, including details of any licences to third parties granted in respect of the Results/Intellectual Property.
7. Subject to paragraph 12, the Contractor shall:
 - 7.1 identify and inform the Authority of any Results which may be suitable for protection and exploitation;
 - 7.2 secure such protection for the Results in all or any part of the world, and shall maintain such protection as is necessary to promote commercial exploitation of the Results at his own expense; and
 - 7.3 inform the Authority of any such Results so protected, and of any subsequent assignment or licence of such Results.
8. Subject to paragraph 9 and without prejudice to paragraph 12, and irrespective of whether the Contractor has assigned the Results, the Income from the commercial exploitation of the Results shall, after deduction of allowable costs as described in paragraph 10, be apportioned between the Parties as follows:
 - 8.1. The Authority, 10%;
 - 8.2 The Contractor, 90%.
9. The income referred to in paragraph 8 shall be payable for the longer of:
 - 9.1 The term of any patent arising from or incorporating any of the Results; or
 - 9.2 The period in which any Know-How arising from the Results and used in any products or services exploited by the Contractor remains secret and substantial.
10. The allowable costs of the Parties, for the purposes of paragraph 8, shall not include any of the sums referred to in Annex A and shall be limited to:
 - 10.1 the registration fees for the registering or maintaining of any rights and any associated filing and prosecution costs in relation to such Results;
 - 10.2 any legal or other professional fees and costs reasonably incurred in relation to legal proceedings in relation to such Results in any appropriate forum and before any appropriate tribunal in any country and any costs ordered by any such tribunal to be paid by the Parties or any of them;
 - 10.3 any other reasonable cost or expenditure which may be agreed from time to time by the Authority and the Contractor;
 - 10.4 subject to the Authority's prior agreement, any reasonable marketing, packaging and/or distribution costs, and any relevant experimental development costs including costs of field trials and/or demonstration projects incurred at the Contractor's expense.
11. The Contractor shall have sole responsibility for making any payments due to his employees, students or contractors under any rewards or incentive schemes, whether contractual, ex gratia, or statutory, in relation to the Results, and any such payments shall not be a cost or expenditure liable to be subtracted from any Income pursuant to paragraph 8 above.

12. If so requested by the Authority, the Contractor will inform the Authority, in writing, whether or not he intends to protect or exploit any part of the Results in any part of the world. If the Contractor does not intend to protect or exploit the Results but the Authority desires such protection to be obtained or to carry out such exploitation then the Authority shall be entitled to obtain such protection at its own cost and to have assigned at no charge any such part of the Results which the Contractor has given notice that he does not intend to pursue or no longer has interest in pursuing. The Contractor will not be entitled to any share of the income generated as the result of the exploitation of Intellectual Property by the Authority.
13. The Contractor shall keep at its normal place of business detailed accurate and up to date records and accounts showing details of its commercial exploitation of the Results including the sale of products or services which incorporate the Results, Income received, allowable costs deducted and the amount of licensing revenues received by it in respect of the Results in a format sufficient to ascertain that revenue sharing pursuant to this Agreement has been properly accounted for and apportioned in accordance with this Agreement. The Contractor shall make such records and accounts available at its premises in the United Kingdom on reasonable notice for inspection during business hours by the Authority or its representatives for the purpose of the verifying the accuracy of any statement or report given by the Contractor to the Authority and to take copies and shall supply the Authority or its representative with such explanation as it may request.
14. Subject to paragraph 12, the Contractor shall indemnify the Authority and sub-licensees and keep them fully indemnified from and against any claims which they may sustain or incur, or which may be brought or established against any of them, by any person, and which in any case arise directly or indirectly out of or in relation to or by reason of:
 - 14.1 any instruction or advice given by the contractor on how to apply the Results;
 - 14.2 the Contractors' or his licensee's or sub licensee's possession, operation, copying or use of the Results; or
 - 14.3 product liability rights arising out of any product developed from the Results or any work resulting in such a product (save to the extent that such liability arises solely as a result of the acts of omissions of or on behalf of the Authority or sub-licensee).

Miscellaneous

15. If the Contractor is unable to carry out his obligations or satisfy any requirements under the Agreement due to any infringement or alleged infringement of any Intellectual Property right which he cannot rectify within a reasonable period such inability shall be deemed a breach by the Contractor and the Authority may without prejudice to any other rights and remedies exercise the powers and remedies available to it under Condition 22.
16. For the avoidance of doubt, and subject to the provisions of paragraph 4, the provisions of this Schedule do not apply to and do not affect any Intellectual Property in existence before the commencement of the Projects.

CONTACTS SCHEDULE B

1. Authority

The Authority's Representative will be:

[REDACTED]

[REDACTED]

[REDACTED]

The Authority's address for correspondence and service in respect of this Agreement will be:

Dept. of the Environment, Food and Rural Affairs (Defra)

[REDACTED]

Nobel House
17 Smith Square
London
SW1P 3JR

2. Contractor

The Contractor's Representative(s) will be:

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

The Contractor's address for correspondence and service in respect of this Agreement will be:

The Pirbright Institute

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

REPORTS SCHEDULE C

1. Unless otherwise authorised in writing by the Authority, the Contractor shall submit an annual report for the Project to the appropriate Project Manager of the Authority. The Contractor shall provide one hard copy of the report, and one copy on either computer readable disk or by e-mail in the format specified by or agreed with the Authority, no later than 4 weeks after the end of the Project Year, or, for work lasting one year or less, no later than 4 weeks after the end of the first six months. This report shall:
 - 1.1 list the scientific objectives as set out in the Agreement, indicating where amendments have been agreed;
 - 1.2 indicate in non-scientific terms the scientific progress achieved since the commencement of the Project or since the last report; how this relates to the policy objectives as set out in the relevant current statement of policy rationale and programme objectives relating to research and development issued by the Authority using the Rationale Objectives Appraisal Monitoring Evaluation. (ROAME) system, plus any findings of particular interest;
 - 1.3 indicate whether the scientific objectives in the Agreement are appropriate for the remainder of the Project, giving reasons for any changes, together with financial, staff and time implications;
 - 1.4 list the milestones for the relevant Project Year as set out in the Agreement, indicating which milestones have been met and whether the remaining milestones appear realistic;
 - 1.5 list any outputs, e.g. published papers or presentations and identify any opportunities for exploiting any Intellectual Property or technology transfer arising out of the Project and any action taken to protect and exploit such Intellectual Property;
 - 1.6 comment briefly on any new scientific opportunities which may arise from the Project.
2. The Contractor shall also submit an Intellectual Property Report for each financial year (April-March) covering all the projects placed under this Agreement. The contractor shall provide one hard copy of the report, and one copy on either computer readable disk or email in the format of Annex B, no later than 31 May of each year.
3. For the Project the Contractor shall submit by the project completion date a final report to the appropriate Project Manager of the Authority consisting of two hard copies, and one electronic copy on either computer readable disk or by e-mail in a format specified by the Authority. The report shall include the following:
 - 3.1 the Project's code and title as set out in Annex A; the name of the Contractor; the total Defra Project costs; and the Project's Start Date and Completion Date.
 - 3.2 an executive summary of not more than two sides of A4 written in a style understandable to the intelligent non-scientist. This should include the main objectives of the Project; the methods and findings of the research; and any other significant events and options for new work.
 - 3.3 a scientific report (which as a guide should be no longer than 20 sides of A4) to include:

- 3.3.1 the scientific objectives as set out in the Agreement;
- 3.3.2 the extent to which the objectives set out in the Agreement have been met;
- 3.3.3 details of methods used and the Results obtained, including statistical analysis where appropriate;
- 3.3.4 a discussion of the Results and their reliability;
- 3.3.5 the main implications of the findings;
- 3.3.6 possible future work;
- 3.3.7 any action resulting from the research (eg protection of Intellectual Property, knowledge transfer).

- 4. Final reports will usually be published on the Authority's website. When submitting the final report to the Authority the Contractor shall indicate any information contained in the report which he considers to be commercially sensitive and the Authority shall not disclose such information without first having consulted the Contractor.
- 5. The Authority reserves the right to return to the Contractor any annual, final, or Intellectual Property report submitted by the Contractor which is not, in the reasonable opinion of the Authority, satisfactory, either in form or content, having regard to the provisions of this Schedule. In the event that such a report is returned to the Contractor, the Contractor shall remedy any deficiencies identified by the Authority and submit a revised report at no additional cost to the Authority.
- 6. The Contractor shall supply any additional reports in respect of the Project, including project, Intellectual Property and financial reports, at such time or times, and in such form, as the Authority may reasonably require.

SCHEDULE D - PROCESSING, PERSONAL DATA AND DATA SUBJECTS

1. This Schedule shall be completed by the Authority, who may take account of the view of the Contractor, however the final decision as to the content of this Schedule shall be with the Authority at its absolute discretion.
2. The contact details of the Authority Data Protection Officer are:
 [REDACTED]
3. The contact details of the Contractor Data Protection Officer are:
 [REDACTED]
4. The Contractor shall comply with any further written instructions with respect to processing by the Authority.
5. Any such further instructions shall be incorporated into this Schedule.

Data Processing descriptor	Narrative
Identity of the Controller and Processor	[REDACTED]
Subject matter of the processing	
Duration of the processing	
Nature and purposes of the processing	
Type of Personal Data	
Categories of Data Subject	
Plan for return and destruction of the data once the processing is complete UNLESS requirement under union or member state law to preserve that type of data	

Annex A – Pricing Schedule & Scope of Works

1. The Authority will pay to the Contractor no more than the firm price of:

[REDACTED]

Amount to be paid each Financial Year as follows;

[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]

2. Subject to any variation of the Project, the amount in paragraph 1, above, shall remain firm throughout the duration of the Contract.
3. In the event that the Contract is varied, the amount in paragraph 1 shall be adjusted by such reasonable sum as may be agreed, in writing, between the Authority and the Contractor.
4. The Payment arrangements shall be as follows:

- 4.1 In accordance with the Defra Terms and Conditions for Research and Development Projects, payments shall be made in monthly instalments in accordance with condition 3.5. The instalments to be paid will be as follows:

■	[REDACTED]

Note the Authority retain the right to suspend payments of installments to the contractor in the event of failure to deliver against 2 or more successive milestones in table 2.3 in Annex A - Scope of works.

Note that the final monthly payment will only be made once all work has been completed to the satisfaction of Defra Project Officer as detailed in the Contracts Schedule. All payments quoted are exclusive of VAT.

5. The Contractor shall provide the Authority with an invoice of the eligible costs properly incurred by the Contractor in carrying out the Research Project during the relevant period, indicate the relevant milestone(s), Purchase Order (to be notified separately) and show separately the costs to be met by the Authority.
6. Within 30 days of receiving an invoice satisfactory to the Authority, the Authority shall pay to the Contractor the amount of the eligible costs which the Authority reasonably consider to have been properly incurred by the Contractor in the carrying out of the Research Project during the relevant period.

7. The Authority is liable to the Contractor only for their respective payments in accordance with The Pricing Schedule. Any overpayment to the Contractor made by the Authority, whether of Research Project price or of VAT, shall be a sum of money recoverable by the Authority from the Contractor.

8. Breakdown of costs

	Year 19 / 20	Year 20 / 21	Year 21 / 22	Total
Cost	£	£	£	£
Pay costs	██████	██████	██████	██████
Consumables	██████	██████	██████	██████
Equipment	0	0	0	0
Travel expenses	██████	██████	██████	██████
Overheads Access cost £80,550 pa Indirect costs £179,528 pa Infrastructure technicians £3,286 pa Biosecurity £3,864 pa	██████	██████	██████	██████
Sub contracts ¹	0	0	0	0
Publication costs	██████	██████	██████	██████
Other	n/a	n/a	n/a	0
Total costs* (FINANCIAL year)	██████	██████	██████	██████

SCOPE OF WORKS

Foot-and-mouth disease (FMD) is a highly infectious disease that affects cloven-hooved animals, including farmed livestock (e.g. cattle, pigs, goats and sheep) and wildlife (e.g. deer and wild boar). The United Kingdom (UK) is currently free of FMD. However, when outbreaks occur, as they did in 2001 and 2007, they have a substantial impact on the farming community and on the wider economy. The 2001 epidemic resulted in >2000 infected farms and the slaughter of over 6 million animals and is estimated to have cost the farming industry >£3 billion (the majority of which was borne by Government) and the wider economy >£5 billion, mainly through the impacts on tourism.

FMD is caused by foot-and-mouth disease virus (FMDV; genus Aphthovirus, family Picornaviridae) that exists as seven distinct serotypes (O, A, C, Asia 1, Southern African Territories [SAT] 1, 2, and 3). The virus has an RNA genome that evolves rapidly as a consequence of errors that are introduced and inherited during replication. These characteristics allow nucleotide sequence data to be used to reliably reconstruct the relationship between viruses recovered from different locations, or at different times. The focus of this project is to generate and analyse FMDV genomic sequence data to trace the origins of FMD outbreaks. At the broadest scale, these analyses are used to categorise field strains into discrete variants (or topotypes) which frequently show geographical clustering based on the historical distribution of FMDV. The pattern of serotypes and variants around the world is not static and sequencing of these viruses allows us to precisely characterise new isolates of FMDV and trace their origin and movements across international boundaries. Sequence data can also be used to define the farm-to-farm relationship between closely related samples collected during FMD outbreaks as demonstrated for previous outbreaks in the UK (2007, 2001) and Europe (Bulgaria, 2011). Analysis of these complete genome sequences provides data at high-resolution, playing a central role in the event of a future FMD outbreak in the UK.

Key capabilities that will be provided to Defra by this project:

- Rapid response to characterise FMD viruses submitted to the FMD NRL at Pirbright associated with outbreaks in the UK;
- Analytical tools that can be used in real-time to support a more effective National control and eradication policy (in the event of an FMD incursion into the UK);
- Critical surveillance of FMD virus lineages that are circulating in different parts of the world;
- On-going assessment of FMD virus risks that pose greatest threats of disease incursions into the UK livestock sector.

This project will provide vital information to Defra regarding the emergence and circulation of new FMDV lineages that pose a threat to the livestock industries in the UK, and will also develop and validate bespoke analytical and statistical pipelines that can be used to increase our confidence in local FMDV transmission pathways, particularly focusing on approaches that can be used in real-time during FMD outbreaks in the UK.

Foot-and-mouth disease (FMD) is endemic in many countries in Africa and Asia, including those in North Africa, the Middle East, and Southeast/East Asia. Since 2010, there has been an upsurge in cases of the disease in regions neighbouring Europe (such as North Africa and The Near/Middle East), as well as in countries with strong trade links to the UK (such as China). The greatest concern surrounds the introduction of certain FMD virus lineages into a new geographical region via long-distance spread (key events summarised in Figure 1). The elevated circulation of FMDV in these regions inevitably poses increased risks for onward spread to FMD-free countries.

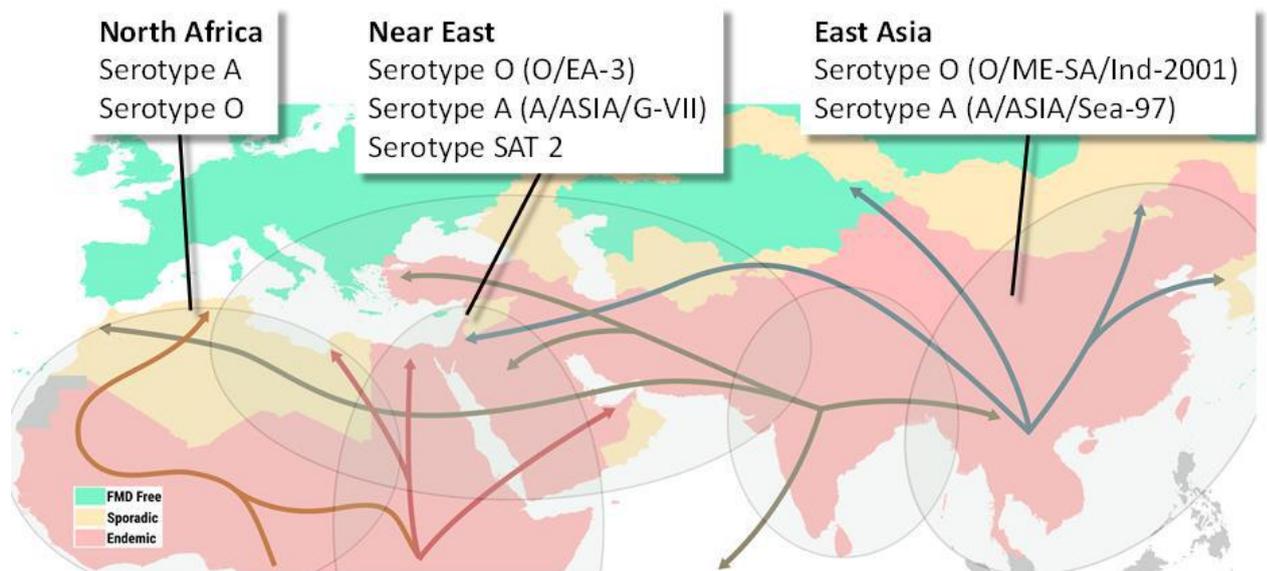


Figure 1. A summary of recent long-distance movements of different FMD virus lineages that threaten FMD-free countries (in green) highlighted by the work of the OIE FMD Reference Laboratory and FAO WRLFMD at Pirbright. A number of different FMD viruses have recently emerged from endemic pools (shown by the ovals in sub-Saharan Africa, South Asia and Southeast Asia) to cause outbreaks in North Africa, the Near East and East Asia.

FMD is caused by a picornavirus (FMD virus: FMDV) that has a single-stranded positive-sense RNA genome which evolves rapidly as a consequence of errors that accrue during replication. These characteristics allow nucleotide sequence data to be used to reliably reconstruct the relationship between viruses collected from different locations, or at different times. Working with international partners within the OIE/FAO FMD Laboratory Network (www.foot-and-mouth.org), the World Reference Laboratory for FMD (WRLFMD) at The Pirbright Institute plays a leading role to generate genetic sequences that can be used to trace the movements of FMD virus lineages across international boundaries. As part of this work, approximately 500 clinical samples (from ~25 different countries) are received to the WRLFMD at Pirbright annually for referral diagnostic and strain characterisation purposes. Sequence data for these samples are routinely included in quarterly reports generated by WRLFMD (sent to Defra and international organisations such as the Food and Agriculture Organisation of the United Nations (FAO)), and provide Defra with critical early warning information to monitor potential risks and emerging threats to the UK livestock industry. This work also monitors the performance of vaccines that can be used to control FMD outbreaks due to virus lineages present in different parts of the world, providing evidence that can be used to quickly select an appropriate vaccine, should vaccination be considered as a control measure in the UK. All reports generated by the WRLFMD can be retrieved from www.wrlfmd.org.

If FMD was to enter the UK, it would be difficult and expensive to control since FMDV is highly contagious and spreads rapidly through susceptible animals. Identifying the transmission networks between infected farms plays an important role in disease control: however, this can be confounded by incomplete epidemiological evidence and the numerous and unpredictable routes by which the virus can spread. Improvements to sequencing protocols and the development of refined phylogenetic models have opened up opportunities to study the evolution of RNA viruses in real-time. These advances open up the potential for using genome sequencing to reconstruct virus transmission trees with extremely high resolution and to reveal and identify the origin of unresolved transmission events within discrete infection clusters quickly. This approach was first used in real-time to support epidemiological investigations during the outbreaks of FMD that occurred in 2007. We have also shown (in previous Defra-funded projects) that whole-genome sequence (WGS) relationships are robust and not overtly influenced by the biases that occur due to sampling of particular animals on an IP. It is anticipated that these methods would be used by the UK NRL for FMD to trace the spread of FMDV between IP in the event of an FMD outbreak in the UK. WGS data can now be readily generated using next-generation sequencing (NGS) methods (with equipment housed within the high-containment laboratory at Pirbright), and during

this project we plan to continue to improve the technical approaches to accommodate robotic processing of samples to increase the reliability and sample throughput of the sequencing pipeline.

This three-year project identifies and assesses these risks, and provides Defra with:

- (i) critical surveillance information about the circulation of established and emerging viral lineages that threaten the UK livestock sector, and
- (ii) tools that can be used in real-time to support a more effective National control and eradication policy in the event of an FMDV incursion in the UK

Objectives

Objective 1: Development of analytical tools to reconstruct disease transmission networks at the farm-level

Policy Issue: In the event of an incursion of FMD into the UK, the infection can be expected to spread very rapidly between farms with susceptible species. Contact-tracing data (i.e. lesion-ageing, farmer surveys and forward/back tracing) collected through field epidemiological investigations are essential to identify the sources of outbreaks and reconstruct the most likely transmission pathways between farms. However, the extent of the 2001 epidemic and speed with which the virus spread hindered attempts to trace the exact origin of infection for many premises; numerous cases were simply attributed to “local spread”. Our previous work (funded by Defra) has shown that WGSs can be used to reliably reconstruct transmission events at the level of farm-to-farm spread, and during the 2007 FMD outbreak in the UK full genome sequencing was used in real-time to support epidemiological investigations. Analyses of these data revealed the most likely chain of transmission events, and predicted undisclosed infected premises prior to their discovery by serological surveillance. The potential contribution of this work to the control of FMD outbreaks (including interpretation of full-genome sequencing reports) was highlighted in "EXERCISE BLACKTHORN" organised in 2018.

Activity 1.1: Maintenance of capability (including technical; protocols, staff, equipment and lab resources) at The Pirbright Institute to generate FMD virus sequence data as quickly as possible after disease is confirmed in the UK.

Activity 1.2: Optimisation of new bioinformatics approaches that can be used to reconstruct transmission trees and to predict “missing” farms.

Activity 1.3: Integration of high-resolution sequencing methods into National epidemiology expertise at NEEG and EPIC (Scotland).

Activity 1.4: An assessment of the suitability of new sequencing pipelines for FMDV using rapid sequencing methods (such as the Oxford Nanopore minION)

Objective 2: Monitoring and mapping the global distribution of FMDV strains to define risk to the UK

Policy Issue: The circulation of FMD virus in endemic regions poses a continuous threat to the UK, via uncontrolled movement of animal products, contaminated persons or objects (fomites). Staff employed on this project are embedded in the WRLFMD at Pirbright and during the course of the project will sequence FMDV positive samples (clinical samples and FMDV isolates) received for FMD diagnosis and characterisation from regional or national FMD laboratories from all around the world. These activities will feed into the work of the OIE/FAO FMD Laboratory Network which is coordinated by Pirbright.

Activity 2.1: *Molecular Epidemiology* reports for contemporary FMDV positive field samples received to Pirbright from countries in Africa and Asia.

Activity 2.2: Development of new tools to reconstruct the regional spread of FMDV lineage with greatest epizootic potential

Activity 2.3: Evaluation of new approaches to classify FMD viruses based on their mosaic genome structures to characterise their evolutionary signature and potentially predict viral phenotypic properties

Activity 2.4: Development of a new web-based portal to visualise the global genomics of FMDV and facilitate exchange of FMD viral sequence data with other researchers

Activity 2.5: Regular review of FMD viral risks to the UK and assessment of FMDV vaccine priorities (through use of the PRAGMATIST tool for FMDV vaccine selection).

In addition to the milestones associated with these objectives (see Section 2.3e), quarterly reports from the NRL and WRLFMD will provide an update on the circulation of different FMD virus lineages in endemic settings and a review of risks to the UK (including updated advice regarding the suitability of FMDV vaccines).

Approach and methodology

The nine research activities within this proposed project (described below) fall under two top-level objectives:

Objective 1: Development of analytical tools to reconstruct disease transmission networks at the farm-level

Activity 1.1: Maintenance of capability (including technical; protocols, staff, equipment and lab resources) at The Pirbright Institute to generate FMD virus sequence data (VP1 and complete genome) as quickly as possible after disease is confirmed in the UK (Milestones 3, 8, and 9).

In the early phases of an outbreak, sequence data play an important role to (i) provide independent confirmation of serotyping results generated by other laboratory methods (such as antigen-ELISA), (ii) help to identify the most likely country/region source of the FMD virus causing the outbreak and (iii) provide evidence that might be used to predict the phenotype of the FMD virus involved (including likely host range and antigenic properties). For these reasons, the FMD NRL maintains capability to rapidly characterize FMD viruses present in clinical samples. The quickest methods currently used in the NRL utilize RT-PCR and “Sanger” approaches to generate VP1 sequences (~640 nucleotides) that encode an important component protein of the viral capsid. These sequences can be used to define the viral topotype, and characterize the geographical origin of the FMD virus present in the sample by phylogenetic analyses. However, the VP1 coding region only comprises ~8% of the FMDV genome and therefore a large proportion of the genetic information is not accounted for. As an alternative to “Sanger” methods, complete or nearly-complete FMDV genome sequences can now be obtained using next-generation sequencing (NGS) technologies (Logan et al., 2014). Furthermore, use of an NGS approach has the potential to eliminate the requirement to continuously review and update specific RT-PCR primer sets, and will simultaneously allow larger regions of the FMDV genome to be characterized. As the costs continue to decline for NGS approaches, we aim to review whether all routine FMDV sequencing activities should be transitioned to these platforms. As part of work to continuously evaluate these methods, during this new project we will optimise new full-genome sequencing protocols that can be employed for rapid and high throughput characterisation of FMD viruses. Current priorities addressed within this project include the development of technical pipelines for use on a new library preparation robot (Hamilton LabSTAR) and sequencing methods for the new iSeq (Illumina) and NextSeq (Illumina) equipment located within the high-containment (SAPO 4) laboratory at Pirbright. We also aim to improve sequence annotation and assembly pipelines to facilitate real-time analyses of large sequence data sets that might be generated in an FMD outbreak, including: (i) assembling full-length consensus level FMDV genomes; (ii) variant calling; (iii) genome annotation. Linking with the activities 1.3, 2.2 and 2.4, downstream sequences analysis workflow will be further developed in order to readily construct phylogenies and transmission trees from the resulting WGSs.

NB: The technical activities covered by this project contribute to the specific outputs of the UK NRL for FMD (at The Pirbright Institute - outlined in *Annex A* of the annually renewable Defra Surveillance Contract). However, no specific funding is provided from the Reference Laboratory Surveillance Contract to support staff costs, purchase of laboratory consumables, and maintenance of equipment and facilities for FMDV sequencing, and consequently these activities have always been supported via Defra research projects.

Activity 1.2: Optimisation of new bioinformatics approaches that can be used to reconstruct transmission trees and to recognise “missing” farms (Milestone 15).

Complete FMDV genomic sequences provide high-resolution data that can be used to define the farm-to-farm level relationships between closely related samples collected during FMD outbreaks. This approach has been pioneered by previously Defra-funded projects (SE2938, SE2940 and SE2943) for use to successfully support real-time outbreak investigations in the UK (2007) and Bulgaria (2010-11). The goal of this work is to (i) reconstruct pathways by which FMDV has spread between the affected farms and (ii) to identify incongruent connections that may be indicative of missing farms in the transmission network. Our previous work has highlighted some of the challenges of these analyses, particularly when FMD outbreaks are only partially sampled. These partially observed cases mask the true extent of epidemiological trajectories of infected cases, so the network and dynamics of virus transmission need to be reconstructed using inferential statistics. As part of previous projects, we have generated complete FMDV genome sequences from 684 of the 2026 designated IPs that comprise the 2001 epidemic. As expected, sequences from the different farms are not identical, and preliminary analyses show that nucleotide substitutions become fixed and accrue within the dataset at a rate of approx. 1 mutation/week (Figure 2). This data has been used to inform a simulation framework, and during a previous project (SE2943) we have established how the demographic signal of ‘effective number of infected population’ can be recovered from virus sequence data, and how sampling affects the reconstruction of viral population dynamics. Within this new project, together with collaborators at the University of Glasgow, we will continue to use this sequence dataset from 2001 to seek to optimise non-parametric models that enable us to identify the presence of ‘missing farms’ from epidemiological data by estimating the probability of observing a case from genetic data (addressing such questions as: how many sequence mutations typically arise on an IP?, how many mutations arise on a farm after transmission of the virus?, and what proportion of sampled IPs leave descendants that are sampled?). These methods will ultimately inform in ‘real-time’ on the likely extent of a progressing epidemic as sequence data are generated from field cases.

Activity 1.3: Integration of high-resolution sequencing methods into National epidemiology expertise at NEEG and EPIC (Scotland) – (Milestone 4)

Experience from the FMD cases in the UK during 2007 highlighted the role that could be played by high-resolution (full genome) sequence analyses to provide real-time support of epidemiological investigations. Analyses of these data revealed the most likely chain of transmission events, and predicted undisclosed infected premises prior to their discovery by serological surveillance. Known patterns of spread of the virus were reconstructed using statistical parsimony-based methods. However, in some cases, these genetic data supported alternative hypotheses of the transmission history that were different from those suggested by conventional contact tracing studies. Therefore, in future outbreaks it will be vitally important to communicate these findings with colleagues within NEEG and EPIC and agree most parsimonious conclusions from the different strands of molecular and conventional epidemiological evidence. Indeed, the recent contingency exercise (exercise “BLACKTHORN”) held during 2018, reaffirmed the role of sequence analyses in a UK outbreak response, and an expert group was established to review dummy datasets that were provided from Pirbright. During the previous project (SE2943), we organized a half-day meeting at APHA-Weybridge with colleagues from the UK epidemiology teams to explain how molecular data can be used to assist in resolving the origin and farm-to-farm connectivity within FMD outbreaks. During this new project, we propose to hold an additional meeting with NEEG (and EPIC) to review these approaches. We anticipate that these activities could be accomplished within a one-day workshop held at Pirbright or hosted by APHA/Defra (exercise could include opportunities for hands-on analyses/interpretation of real and dummy datasets).

Activity 1.4: An assessment of the suitability of new sequencing pipelines for FMDV using rapid sequencing methods (Milestone 13)

Current sequencing approaches for FMDV employed at Pirbright include dideoxy “Sanger” (ABI) and NGS (Illumina) platforms. These established methods can generate FMDV sequence data with high confidence, but the equipment or sequencing reagents used are expensive (up to several £100Ks for a replacement ABI sequencer, or >£2K for a Illumina reaction kit). An alternative technology, known as nanopore sequencing, has recently emerged which has shown promise in its ability to facilitate a decentralised sequencing approach. In particular, there are numerous examples of the MinION (Oxford Nanopore) being used in resource-poor and field situations. Furthermore, MinION technology has allowed real-time tracing of viral outbreaks, including Ebolavirus in West Africa and Zika virus in Brazil. Our preliminary (unpublished) data collected from a previous project funded by EMIDA (ERA-net: www.episeq.eu) shows that the MinION platform and our in-house bioinformatics workflows can be used to recover FMDV capsid sequence data equivalent to the amplicon length of a pan-capsid RT-PCR (Xu et al., 2013) for FMDV (Figure 3). Importantly, the necessity to perform a RT-PCR reaction remains a limitation of this technology. Therefore, in addition to maintaining a watching brief on developments of this technology, during this project we intend to explore alternative methods of generating amplicons upstream of the sequencing steps. Notably, the sequence-independent, single-primer amplification (SISPA) approach commonly used for metagenomics studies has been successfully combined with the MinION in a Lassa fever study, demonstrating that this technology can be used to amplify and sequence RNA viruses with variable genomes. In addition, we will seek opportunities (such as the EuFMD real-time training courses) to test this new methods for FMDV sequencing in field conditions (funded from separate source).

Objective 2: Monitoring and mapping the global distribution of FMDV strains to define risk to the UK

Activity 2.1: Molecular Epidemiology reports for contemporary FMDV positive field samples received to Pirbright from countries in Africa and Asia (Milestones 1, 6, and 10).

The work undertaken within this project will be embedded within the NRL for FMD at TPI. We participate in international surveillance activities that are facilitated via links to the FAO as the FAO WRLFMD, and the OIE (World Organisation for Animal Health) as an OIE Reference Laboratory for FMD. As part of these international activities, approximately 500 samples per annum are received at TPI for confirmatory diagnosis and strain characterisation. These specimens derive from suspect cases of FMD in endemic settings as well as viral isolates previously generated by FMD Reference Laboratories in other countries. During this project, we will continue to produce molecular epidemiology reports for contemporary field samples received to the FMD Reference Laboratory at TPI from countries in Africa and Asia (at least 200 samples sequenced/year). While NGS costs remain relatively high, these data will continue to be generated using routine methods at TPI that utilize one-step RT-PCR to amplify the viral genome region encoding VP1 (encompassed in a VP3-2B fragment) using different sets of DNA primers, followed by subsequent sequencing of PCR fragments by Sanger sequencing. During this project new PCR and/or sequencing primers will be developed to cover new viral variants, if, and when they arise. New data will be analysed in the context of the established database of >4000 sequences that has been generated as part of previous projects, or is regularly exchanged with other FMD Reference Laboratories such as those within the OIE and FAO Network (www.foot-and-mouth.org). Phylogenetic trees embedded in the reports provide knowledge that underpins the continuous surveillance of FMD viral lineages throughout the world and serve as an early warning to Defra by highlighting the emergence of new virus strains in endemic countries. The important contribution of this work to FMD surveillance has been highlighted by recent unexpected movements of novel FMD virus lineages into North Africa (Knowles et al., 2016; Pezzoni et al., 2019), the Middle East (Bachanek-Bankowska et al., 2018) and Southeast Asia (Bo et al., IN PRESS). During this project, we will particularly focus on monitoring the circulation of FMDV in countries in the European Neighborhood (such as North Africa and The Middle East), or elsewhere where there have been recent epidemiological events that heighten the threats in the UK. These outputs will be summarised in the Quarterly Reports provided to Defra/APHA from the UK NRL for FMD, and will be published on our website (<http://www.wrlfmd.org/>).

Activity 2.2: Development of new ways to reconstruct the regional spread of FMDV lineages with greatest epizootic potential (Milestones 2, 7, and 11)

An appreciation of FMDV evolutionary dynamics is essential to aid epidemiological understanding of the way FMD virus lineages spread at global level, in order to identify current and future risks posed by established and emerging FMDV lineages (including those emerging locally and acquiring epizootic potential) and to assist in their control. Our previous studies have employed both VP1 and WGS datasets to study the phylogeography of FMDV lineage dispersal within endemic systems (Di Nardo et al., 2014; Bachanek-Bankowska et al., 2018). Results indicate that the dynamics that govern the evolution of FMDV serotypes in endemic systems is defined by a complex process of competition between geographically co-existing lineages that are co-evolving and adapting in different host populations. Dissecting the processes that cause variation in the evolutionary dynamics of FMDV lineage at endemic level represents a key question in FMD epidemiology. Within this activity, we will expand on the FMD genomic epidemiological analysis to a larger collection of both VP1 and WGS, in order to map the evolutionary history of the most epidemiologically active FMDV lineages, defining the geographical structure of their virus populations and their competitive dynamics on an evolutionary scale. Building on the understanding of the spatial dynamics of co-existing FMDV lineages, we will also investigate virus-host interactions and host-specific contributions to the evolutionary mode of FMDV transmission, assessing how meta-population dynamics might drive the relative fitness of FMDV lineages on host species. The growing importance of data integration in phylogeographic inference illustrates how epidemiological data coupled with genetic information provides insights into the factors that drive virus spread. We will further exploit these new computational methods in order to gather a better understanding of how geographic, population, economic and trade factors contribute to the dispersal of FMDV at a regional level and beyond. It is expected that these results will provide additional resources to aid further epidemiological understanding in how FMD diffuse and evolve on a regional and (potentially) global scale.

Activity 2.3: Evaluation of new approaches to classify FMD viruses based on their mosaic genome structures (to enable more precise reconstruction of viral movements and potentially to predict viral phenotypic properties) – (Milestone 12)

Previous studies with FMDV have demonstrated that genomic recombination frequently occurs under experimental conditions in tissue culture. These findings suggest that genomic recombination is an evolutionary mechanism frequently used by FMDV, as well as other picornaviruses. However, elucidation of the overall frequency of recombination and its biological significance as an important mechanism that can rapidly drive the diversification, spread, and emergence of new FMDV variants with enhanced fitness has only become apparent as more WGS are generated and integrated with field knowledge of circulating viral lineages. During SE2943, our analyses revealed unexpected recombination signals estimated from WGS of the O/ME-SA/Ind-2001 lineage (Bachanek-Bankowska et al., 2018a). From a practical perspective phylogenetic analyses that include recombinant sequences lead to misrepresentation of the true relationship between virus isolates (i.e. tree topology), and represent a potential confounding effect for resolving their evolutionary history. Therefore, we have recommended that reconstruction of virus movements across and within complex epidemiological systems should be performed using only structural protein coding sequence data for VP3-VP1 (where recombination signals are likely to be absent, or present at a very low frequency) (Ferretti et al., 2018). Further recent collaborative studies undertaken in East Africa (Lasecka-Dykes et al., 2018) and Southeast Asia (Brito et al., 2018) have also detected inter- and intra-lineage recombination signals in WGS. For the African sequences, analyses revealed that while there was evidence for recombination events between different SAT isolates and different Eurasian isolates, there was relatively less evidence for recombination between SAT and Eurasian isolates. The obvious interpretation of these results is that geographical clustering of viruses limits the opportunities for genomic recombination between most of SAT and Eurasian FMDVs. During this project, we propose to undertake systematic analyses to define key mosaic genome structures present in representative viruses, with the goal to better understand the evolutionary signature of the different segments of FMDV lineages that circulate across Africa and Asia. We will focus these studies on emerging FMDV lineages in North Africa (O/EA-3 and A/AFRICA/G-IV) as well as those that circulate in the Middle East (O/ME-SA/PanAsia-2, A/ASIA/Iran-05 and A/ASIA/G-VII). Elucidation of these evolutionary mechanisms

of FMDV may help understand the relative fitness of co-circulating lineages and predict the likelihood of the emergence of new viral lineages, informing the risk posed by their epizootic potential.

Activity 2.4: Development of a new web-based portal to visualise the global genomics of FMDV and facilitate exchange of FMD viral sequence data with the FMD community (Milestone 14)

Conveying up-to-date information about epidemiologically critical events in near 'real-time' is crucial to inform and assist governments and health organisations to devise and implement effective strategies for improving disease control and intervention. Within this activity, we plan to collaborate with researchers at the Big Data Institute in Oxford, to develop a new web-based platform that can be used to display global genomics of FMDV, assisting in the understanding of the geographical diffusion and evolution of different FMDV lineages. Supporting the theoretical and computational works of activity 2.2 and 2.3, we will implement bioinformatics pipelines and visualisation tools that can efficiently annotate FMDV genetic relationships and analyse patterns of molecular evolution. This framework will further advance the field of FMDV phylodynamics by exploiting the entire repository of VP1 coding sequences (~8000 sequences in the archive held at Pirbright that have been generated as part of previous projects, such as SE2940 and SE2943) and vaccine matching data in order to: (i) characterize the genetic relationships between FMD viruses at improved resolution, to aid our epidemiological understanding of the way that FMDV lineages spread at a global level; and (ii) define the processes that drive the antigenic evolution and suitability of FMDV vaccines. This new online platform will be readily offered as an open-access resource for the benefit of the global community of researchers and public health officials, providing analytics and visualisation tools that can be interactively queried and used by the public for exploring historical evolutionary trends of FMDV lineages in space and time, and learning about emerging risks and vaccines efficacy. This process of open science will further engage and promote new research collaborations within and beyond the FMD scientific community.

Activity 2.5: Regular review of FMD viral risks to the UK and assessment of FMDV vaccine priorities (through use of the PRAGMATIST tool for FMDV vaccine selection) – (Milestone 16 and updates delivered via NRL Quarterly Reports).

The sequencing activities undertaken within this project will contribute to the global surveillance of FMDV, allowing us to monitor the spread of FMD virus lineages in different parts of the world. In some cases, the genomic data together with vaccine-matching work undertaken within the WRLFMD/NRL at Pirbright provides evidence for the emergence of new antigenic variants of FMDV that are not adequately protected by existing FMDV vaccines. Recent examples include the spread of the A/ASIA/G-VII lineage that is not protected by the A/Iran-05 vaccine in countries in the Middle East (Bachanek-Bankowska et al., 2018b), and the detection of a new antigenically distinct serotype O lineage (within the O/ME-SA/PanAsia-2) that does not appear to be well-matched to any commercial FMDV vaccines produced by Boehringer-Ingelheim or MSD (Bachanek-Bankowska et al., 2019). In partnership with the EuFMD (FAO, Rome), we have recently developed a new tool called Prioritisation of Antigen Management with International Surveillance Tool (PRAGMATIST) to assist vaccine bank managers in selecting which strains are most important to maintain in their vaccine bank. This tool provides a transparent, evidence-based framework to evaluate available vaccine antigens that can be adapted according to the region at risk. During the course of this project, we will regularly (at least quarterly) update the data encompassed within the Excel tool using insights from our international surveillance activities and any corresponding changes to vaccine antigen priorities will be immediately communicated to Defra. In addition, we will work towards the refinement of the existing tool to a more robust (visually appealing) and automated framework, and potentially integrated within the web-based portal developed by the activity 2.4.

Project Outputs and Deliverables

In line with the BBSRC data sharing policy, the TPI project team involved in this work is committed to making data generated in the project available to the wider scientific community and as part of our work as an International Reference Laboratory for FMD, TPI will endeavor to place the data generated from this project into the public domain. Where possible, annotated consensus Sanger sequencing data will be made available via GenBank, and raw sequence data from the MiSeq will be deposited to the short read archive (SRA) at EBI.

The results from this project will be presented locally at Pirbright seminars, and at national and international meetings and conferences. In particular, work will be presented at meetings organized by FAO (such as EuFMD Open Session) or OIE to ensure dissemination of these methods to other National Reference Laboratories. We anticipate that at least one manuscript may result from each of the listed objectives and will be submitted for publication in journals such as Emerging Infectious Diseases, or Transboundary and Emerging Diseases. In addition, we will continue to provide presentations and updates outlining this work to the Defra National Emergency Epidemiology Group (NEEG) – see activity 1.3.

This project will utilise clinical samples and other materials collected from third countries. Therefore, the Pirbright Institute is developing a policy to address the Nagoya Protocol that covers access to genetic resources and the fair and equitable sharing of benefits arising from their utilization.

Milestone Table

Target date (dd/mm/yyyy)	Project month	Description of milestone including the deliverable	Suggested payment (£)
31/03/2020	12	Generate VP1 sequence data for at least 200 FMD virus positive samples received from endemic countries (C/SAPO4)	<i>In accordance with the stage payment scheme at Annex A.</i>
31/03/2020	12	Generate at least 50 full genome sequences for samples collected from endemic countries (C/SAPO4)	
31/03/2020	12	Optimise and evaluate a rapid sequencing protocol using the iSeq (Illumina) (C/SAPO4)	
31/03/2020	12	Organise a national meeting to review the use of full genome sequences for outbreak use	
31/09/2020	18	Mid-project review	
31/03/2021	24	Generate VP1 sequence data for at least 200 FMD virus positive samples received from endemic countries (C/SAPO4)	
31/03/2021	24	Generate at least 50 full genome sequences for samples collected from endemic countries (C/SAPO4)	
31/03/2021	24	Implementation (and annotation) of new full genome sequence assembly pipeline	
31/03/2021	24	Optimise and evaluate a high-throughput sequencing protocol using the NextSeq (Illumina) (C/SAPO4)	
31/03/2022	36	Generate VP1 sequence data for at least 200 FMD virus positive samples received from endemic countries (C/SAPO4)	
31/03/2022	36	Generate at least 50 full genome sequences for samples collected from endemic countries (C/SAPO4)	
31/03/2022	36	Using available full-genome sequences, report on the ancestral origins of different parts of the FMDV genome (and the impact of genomic recombination)	
31/03/2022	36	Testing of Oxford NanoPore sequencer for FMDV and report of capabilities (C/SAPO4)	
31/03/2022	36	Implementation of a new web-based portal for the visualisation of FMDV molecular epidemiology and FMD virus sequence exchange (with partners from the OIE/FAO FMD Laboratory Network)	
31/03/2022	36	Report on the development (and testing) of new statistical methods to reconstruct outbreak transmission trees	
31/03/2022	36	Publication of the PRAGMATIST tool used for vaccine antigen selection	
31/03/2022	36	Preparation of a final report for the project	