

Technical Agreement between IPS Pharma and Nuffield Department of Primary Care Health Sciences for the provision of Favipiravir tablets as an Investigational Medicinal Product (IMP)

A Technical Agreement between

**Vertical Pharma Resources Ltd t/a IPS Pharma
41 Central Avenue
West Molesey
KT8 2QZ**

Hereinafter referred to as IPS Pharma (Contract Acceptor)

and

**The Chancellor, Masters and Scholars of the University of Oxford, whose
administrative offices are at Wellington Square, Oxford, OX1 2JD
Hereinafter referred to as Oxford University (Contract Giver)**

Approved on behalf of the Client:

Approved by (Oxford University)	Approved by (IPS Pharma)
Name: Denis Murphy	Name:
Position: Research Contracts Manager	Position:
Signature: <i>Denis Murphy</i>	Signature:
Date: 01 March 2021	Date:

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Approved on behalf of the Client:

Approved by (Oxford University)	Approved by (IPS Pharma)
Name:	Name: AMANDA PETER
Position:	Position: DIRECTOR OF QA AND REGULATORY
Signature:	Signature: PP [Signature]
Date:	Date: 26 Feb 2021

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1 Purpose of contract

IPS and The Secretary of State for Health and Social Care (the “Authority”) have entered into a separate agreement dated 3rd Feb 2021 (the “Business Agreement”) under which the Authority has procured certain goods and services from IPS, and a copy of which is attached at Annex 1 of this Technical Agreement. The parties acknowledge and agree that the goods and services referred to in the Business Agreement are provided for the purpose of Oxford’s clinical trial entitled “Platform Randomised trial of INterventions against COVID-19 In older peoPLE” (the “Trial”). This Technical Agreement relates to the quality and operational responsibilities for the provision of Goods between the Contract Acceptor, and the Contract Giver.

This Technical Agreement does not replace or override any existing quality agreement in place between IPS and Oxford University, but serves to augment and clarify aspects relating to quality and operations.

This Technical Agreement is effective as of the date of the last party to sign and, unless terminated earlier in accordance with the terms of this Technical Agreement, shall continue until the end of the Term. In the event the Business Agreement is terminated, this Technical Agreement will also terminate.

Words beginning with a capital letter shall have the meaning defined either herein or in the Business Agreement including its Schedules.

2 Compliance requirements

All Goods and services (as more particularly described in Schedule 5 of the Business Agreement) delivered to Oxford University under the Business Agreement will be at all times processed and controlled in compliance with the terms of the Business Agreement, and the appropriate regulations, where applicable, such as:

- EU Directive 2003/94/EC “Principles and Guidelines of GMP in respect of medicinal products for human use”.
- Rules Governing Medicinal Products in the EU Volume 4 Good Manufacturing Practice.
- EU Directive 2001/20/EC “Clinical Trials Directive”.
- EU Directive 2001/83/EC – Requirements for Qualified Persons (QP)
- The Medicines For Human Use Regulations 2004 SI 1031, as amended to current law
- Human Medicines Regulations. SI 2012/1916

All work done by IPS shall be done in accordance with IPS standard operating procedures, unless otherwise agreed in writing.

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3 Provision of requirements

3a. Responsibilities of the Contract Giver

The Contract Giver will be responsible for providing IPS with the following.

- All written information's necessary for IPS to provide services described in Section 3B.

Including (but not limited to)

- A copy of the CTA Amendment and evidence of MHRA approval
- Copy of Approved Annex 13 Compliant CTA Label

3b. GMP responsibilities of IPS

- Source on behalf of the Authority and Oxford University, the Goods. IPS shall procure that the Goods have been manufactured in accordance with all applicable laws, including GMP. Convert the Goods into IMP for the Trial.
- If required, break down the quantity in the original procured and re-assemble/label according to quantity required by Oxford University
- Compilation of Batch Manufacturing/assembly records.
- Assembly and Labelling of subject specific IMPs
- Production of the CTA Label
- Final QP Certification of the IMPs reassembled and labeled by IPS
- In relation to the Goods, IPS shall be responsible for providing the Investigator Brochure and for ensuring the Investigator Brochure is validated and provided to Oxford University at least once a year. IPS will procure that the Investigator Brochure, and any update, presents the information it contains in a concise, simple, objective, balanced and non-promotional form that enables a clinician or potential investigator to understand it and make an unbiased risk-benefit assessment of the appropriateness of the Trial, and it will provide the Investigator Brochure to Oxford University in a timely manner sufficient to meet Oxford University's obligations under applicable law

4 Change control

IPS will notify Oxford University of any planned changes that may impact the IMPs in advance of the planned change. IPS will notify Oxford University within 24 hours or by the next working day of an unplanned change that may impact the IMPs.

IPS must notify an authorised Oxford University representative of any deviation from IPS standard operating procedures (SOPs) applicable to the Oxford University's IMP. Oxford University must inform IPS within 24 h of any changes to documents/information supplied to IPS in writing.

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5 Quality investigations

IPS will promptly inform Oxford University of any quality issues with regard to EU GMP that require a QA investigation and that may impact the Oxford University's IMP.

IPS will promptly report to Oxford University all safety information (meaning all filings, submissions and reports concerning the safety of the Goods) relating to other clinical trials that test or use the Goods, for which Oxford University is not the sponsor.

IPS has in place an environmental monitoring system that continually records the temperature/humidity of all the ambient IMP storage and processing areas, and the internal temperatures of all the cold chambers.

IPS will notify Oxford University, if the IMP storage temperatures fall outside the required range for a potentially significant length of time, defined as more than 3 hours.

6 Audit and inspection of facilities and data

Oxford University reserves the right to be present during any processing steps and to examine processing records pertaining to the IMPs assembled and labelled.

Oxford University will have access to IPS premises for the purpose of performing GMP audits, after written notification with at least 7 days' notice.

IPS shall, at the request of a Licensing Authority permit or procure permission for representatives of such Regulatory Authority to inspect all facilities associated with the IMP and/or services. IPS will inform Oxford University in the event of a Regulatory Agency inspection in which the Oxford University's IMPs or studies will be concerned.

7 Subcontracting

IPS will not subcontract any of the work entrusted to it by Oxford University to any third party or any of its present or future Affiliates without notifying and obtaining the prior consent of Oxford University.

8 Complaint handling

Oxford University shall evaluate IMP complaints and IPS shall evaluate complaints that Oxford University makes known to IPS related to the processes or services IPS has undertaken, for those IMPs. IPS will notify the Client of the results of its investigation/evaluation within 30 days after notification from Oxford University of a complaint.

9 Equipment qualification, calibration and maintenance

IPS will qualify, maintain, and calibrate as necessary all equipment used in the manufacture and/or assembly of Oxford University's IMPs in accordance with IPS SOPs and appropriate regulations.

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10 Documentation

IPS is responsible for ensuring that all relevant data generated by IPS is recorded according to the requirements of EU GMP and IPS SOPs (if applicable). IPS will make all data or materials pertaining to Oxford University available for review by Oxford University on request.

11 Recalls

IPS will notify Oxford University of any recalls which may impact the quality of any IMPs supplied, within 24 hours or the next working day if out of hours.

It is the responsibility of IPS to carry out the recall procedure for all IMPs already supplied to and on the premises of IPS, in accordance with IPS SOPs.

In the event of a recall, where the fault is with IPS; IPS will notify the MHRA within 24 hours or the next working day.

12 Retention of samples and documents

IPS is responsible for retaining all relevant data and/or documents in a secure manner for a minimum of 15 years after the end of the study or as otherwise determined by Oxford University's SOPs if longer. Thereafter, IPS will either destroy the data and/or documents or return them to Oxford University, as directed in writing by the Oxford University.

13 Liability and Indemnity

13.1 IPS shall be liable to Oxford University for, and shall indemnify and keep Oxford University indemnified against any loss, damages, costs, expenses (including without limitation legal costs and expenses), claims or proceedings in respect of:

13.1.1 any injury or allegation of injury to any person, including injury resulting in death; and/or

13.1.2 any loss of or damage to property (whether real or personal);

that arise or result from the IPS' negligent acts or omissions or breach of contract in connection with the performance of this Technical Agreement including the supply of the Goods and its failure to comply with GMP and/or applicable law, except to the extent that such loss, damages, costs expenses (including without limitation legal costs and expenses), claims or proceedings have been caused by any act or omission by, or on behalf of, or in accordance with the instructions of, Oxford University.

13.2 Nothing in this Technical Agreement shall exclude or restrict the liability of either party:

13.2.1 for death or personal injury resulting from its negligence;

13.2.2 for fraud or fraudulent misrepresentation; or

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13.2.3 in any other circumstances where liability may not be limited or excluded under applicable law.

- 13.3 IPS shall put in place and/or maintain in force at its own cost with a reputable commercial insurer, insurance arrangements in respect of employer's liability, public liability and product liability in accordance with Good Industry Practice with the minimum cover per claim of the greater of five million pounds (£5,000,000) or any sum as required by Law unless otherwise agreed with Oxford University in writing. Upon expiry or termination of this Technical Agreement, IPS shall ensure that any ongoing liability it has or may have arising out of this Technical Agreement shall continue to be the subject of appropriate indemnity arrangements for the period of (21) years from termination or expiry of this Technical Agreement or until such earlier date as that liability may reasonably be considered to have ceased to exist.
- 13.4 Subject to Clauses 13.1 and 13.2 of this Technical Agreement, the total liability of each Party to the other under or in connection with this Technical Agreement whether arising in contract, tort, negligence, breach of statutory duty or otherwise shall be limited in aggregate to five million GBP (£5,000,000).

14 Confidentiality

- 14.1 In this Technical Agreement "Confidential Materials" shall, subject to Clause 14.2, mean any and all data, plans, business information, technical information and other information and materials, whether oral, in writing or in any other form, disclosed before, on or after the date of this Technical Agreement by one party (the "Disclosing Party") to the other party (the "Receiving Party") either directly or indirectly.
- 14.2 In this Technical Agreement "Confidential Materials" shall not include any information which the Receiving Party can prove:
- 14.2.1 is or becomes public knowledge through no improper conduct on the part of the Receiving Party or its personnel;
 - 14.2.2 is obtained subsequently by the Receiving Party from a third party without any obligations of confidentiality and such third party is in lawful possession of such information and not in violation of any contractual or legal obligation to maintain the confidentiality of such information; and/or
 - 14.2.3 is already lawfully possessed by the Receiving Party prior to first receiving it from the Disclosing Party;

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- 14.3 The Receiving Party shall not use, copy or disclose to any third party any Confidential Material received from the Disclosing Party (whether before, on or after the date of this Agreement) except as set out in Clause 14.4 and 14.5 below.
- 14.4 The Receiving Party may:
- 14.4.1 only use Confidential Material received from the Disclosing Party to the extent that such use is necessary for the purpose of carrying out its obligations under this Agreement or, in the case of Oxford University, as necessary or desirable to use the Goods;
 - 14.4.2 disclose Confidential Material received from the Disclosing Party to its Personnel but only, (i) in the case of IPS, to the extent necessary to enable IPS to carry out its obligations under this Technical Agreement and provided that IPS shall remain responsible for procuring that its personnel do not further disclose the Confidential Material or use it for any purpose other than that set out in Clause 14.4.1; and (ii) in the case of Oxford University, to the extent necessary to enable Oxford University to carry out its activities under this Technical Agreement and/or make use of the Goods; and/or
 - 14.4.3 disclose any part of the Confidential Material received from the Disclosing Party solely to the extent that it is legally required to do so pursuant to an order of a court of competent jurisdiction or governmental authority provided that the Receiving Party will use its best endeavours to limit such disclosure and to provide the Disclosing Party with an opportunity to make representations to the relevant court or governmental authority;
- 14.5 Oxford University shall be permitted to disclose Confidential Material received from IPS to regulatory authorities to the extent necessary to obtain regulatory approvals.
- 14.6 If either party at any time requests the return of the Confidential Material that it provided to the other, or on termination or expiry of this Agreement, the other party shall promptly return to the requesting Party all documents, records, notes, copies, computer files containing the Confidential Material of the requesting party provided that it shall be allowed to retain one copy of the Confidential Material solely for: (i) archive purposes; and/ (ii) in the case of Oxford University, the purposes of making submissions to the regulatory authorities.
- 14.7 The provisions of this Clause 14 shall commence on the Effective Date and shall survive termination or expiry of this Technical Agreement for a period of (10) years.

15 Intellectual Property

- 15.1 Unless specified otherwise in the Specification, IPS hereby grants to Oxford University, for the life of the use of Goods by Oxford University, an irrevocable, royalty-free, non-exclusive licence of any Intellectual Property Rights required for the purposes of receiving and using, and to the extent necessary to receive and use, the Goods (to include any associated technical or other documentation and information

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supplied or made accessible to Oxford University in any media) in accordance with the Business Agreement.

16 Payment

- 16.1 The parties acknowledge and agree that the Authority pays for the Goods and services provided under this Technical Agreement whereas payment is made under the Business Agreement, and Oxford University shall have no obligation to make any payments to IPS in respect of the Goods. For the avoidance of doubt, Oxford shall not, in any event, be liable to IPS for any breach of Schedule 2, Clause 9 of the Business Agreement by the Authority.

17 Termination

- 17.1 Either party may terminate this Technical Agreement with immediate effect by notice in writing to the other party if the other party commits a material breach of this Agreement provided that, in the case of breaches capable of remedy, the party wishing to terminate shall first have served a written notice on the other party specifying the nature of such breach and the other party shall have failed to remedy such breach within sixty (60) days from the date of service of such notice.
- 17.2 On termination of this Technical Agreement for any reason IPS shall promptly at Oxford University's request deliver to Oxford University or its nominee all Goods existing at the date of such termination.
- 17.3 On termination of the Business Agreement by either IPS or the Authority, IPS agrees to promptly notify Oxford University. IPS and Oxford University shall work together to facilitate an orderly cessation of the services provided under this Technical Agreement, taking into account the rights, safety, well-being and continuity of treatment of the Trial subjects.
- 17.4 On termination or expiry of this Technical Agreement for any reason, the following provisions shall continue in full force and effect: Section 5 (Quality investigations), Section 10 (Documentation) Section 11(Recalls), Section 12 (Retention of samples and documents), Section 13(Liability and indemnity), Section 15(Intellectual Property), Section 17 (Termination) and Section 18 (Miscellaneous).

18 Miscellaneous

This Technical Agreement may be executed in any number of counterparts, each of which, when executed shall be an original, and all the counterparts together shall constitute one and the same instrument.

This Technical Agreement will be interpreted in accordance with English Law and the parties submit irrevocably to the exclusive jurisdiction of the English courts in relation to any dispute arising out of or in connection with this Technical Agreement or the activities carried pursuant to this Technical Agreement.

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19 Primary contacts

Oxford University

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20 Summary of roles and responsibilities

	Item	Oxford	IPS
1	Procurement of various Medicinal Products (Licenced/Unlicenced) required by Oxford University		X
2	Evidence of MHRA approval of the Clinical Trial Authorisation (CTA) Amendment	X	
3	Copy of Approved Annex 13 Compliant CTA Label	X	
4	Summary of the Product Characteristics (SMPC)/Material Safety Data Sheet (MSDS) or equivalent - If applicable	X	
5	Convert the Medicinal Products into IMPs for the Trial		X
6	If required, break down the quantity in the original procured and re-assemble/label according to quantity required by Nuffield		X
7	Compilation of Batch Manufacturing/assembly records		X
8	Assembly and Labelling of subject specific IMPs		X
9	Printing of the various CTA Labels		X
10	Final QP Certification of the IMPs reassembled and labeled by IPS		X
11	Temperature control, if applicable, of IMPs during shipment to Oxford University		X
12	Notification of recall(s) to MHRA (only if recall originated from IPS)		X
13	Notification of recall(s) to Oxford University		X
14	Destruction of excess IMPs remaining at IPS with Oxford University's written confirmation		X
15	IMP Complaint handling	X	X
16	Preparation of randomisation schedule and code breaks (if applicable)	X	
17	Execution of labelling according to a randomization code (if applicable)		X

* Any activity carried out by a third party on behalf of Oxford University will remain the responsibility of Oxford University.

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21 Technical Agreement History/Summary of Changes

Version	Reason for revision	Date
01	Original agreement	

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Health Sciences for the provision of Favipiravir tablets as an Investigational Medicinal
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ANNEX 1
Business Agreement

[copy provided separately]