

**Technical Agreement between IPS Pharma and Nuffield Department of Primary Care
Health Sciences for the provision of colchicine 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)	Approved by (IPS Pharma)
Name: Dr Gavin Brown	Name:
Position: Research Contracts Manager	Position:
Signature: 	Signature:
Date: 23 February 2021	Date:

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1. Purpose of contract

This Technical Agreement relates to the quality and operational responsibilities for the provision of an Investigational Medicinal Products (the “IMP”) and related services between the Contract Acceptor, and the Contract Giver and as further described in Business Agreement.

This Technical Agreement does not replace or override any existing quality agreement in place between IPS and the 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.

Arrangements on prices and other commercial terms between the parties on the subject matter for the IMP (including but not limited to confidentiality, liabilities and guarantees) shall be specified in a separate commercial agreement/purchase order (“Business Agreement”). In the event of a conflict between the provisions of this Technical Agreement and the Business Agreement, the provisions of this Technical Agreement shall control solely for quality-related responsibilities as set forth herein, and the Business Agreement shall control for all other provisions. In the event the Business Agreement is terminated, this Technical Agreement will also terminate.

2. Compliance requirements

The IMP and services to Oxford University will be at all times processed and controlled in compliance with 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.

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)

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- A copy of the CTA Amendment and evidence of MHRA approval
- Copy of Approved Annex 13 Compliant CTA Label
- Summary of the Product Characteristics (SMPC)

3b. GMP responsibilities of IPS

- Procure, if required, on behalf of Oxford University, further supply of colchicine tablets and convert the Medicinal Products into IMP. To the extent IPS is required to procure further supplies of colchicine tablets, IPS will procure that these supplies have been manufactured in accordance with all applicable laws, including GMP.
- 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

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.

5. Quality investigations

IPS will inform the 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 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.

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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 Regulatory Agency 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. 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.

8. 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.

9. 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.

10. 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.

11. Retention of samples and documents

IPS is responsible for retaining all relevant data and/or documents in a secure manner for a minimum of 5 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.

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12. Miscellaneous

This 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 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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13. Primary contacts

Oxford University

Name	Phone /e-mail
Prof. Chris Butler Trial Chief Investigator	Tel: 01865 289670 email: christopher.butler@phc.ox.ac.uk
Emma Ogburn CTU Director of Operations	Tel: 07710676303 email: emma.ogburn@phc.ox.ac.uk

IPS

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Shay Gopalakrishnan QA Team Leader	0208 481 9747 Shager.Gopalakrishnan@ipsspecials.com
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14. Summary of roles and responsibilities

	Item	Oxford	IPS
1	Procurement of colchicine tablets if required by Oxford University		X
2	Copy of the CTA Amendment and approval	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, if required, colchicine tablets into IMP for Oxford University		X
6	If required, break down the quantity in the original procured and re-assemble/label according to quantity required by Oxford University		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
12	Temperature control of IMPs during shipment to Oxford University		X
13	Notification of recall(s) to MHRA (only if recall originated from IPS)		X
14	Notification of recall(s) to Oxford University		X
15	Destruction of excess IMPs remaining at IPS with Oxford University's written confirmation		X
16	IMP Complaint handling	X	X
17	Preparation of randomisation schedule and code breaks (if applicable)	X	
18	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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15. Technical Agreement History/Summary of Changes

Version	Reason for revision	Date
01	Original agreement	