

QUALITY AGREEMENT

1. CONTRACT GIVER, CONTRACT ACCEPTOR

This Quality Agreement (this “Quality Agreement”) is entered by and between:

1.1 The Contract Giver

The University of Oxford
Churchill Hospital
Headington, Oxford, United Kingdom
OX3 7LJ
United Kingdom

(hereafter referred to as “Company”)

1.2 The Contract Acceptor

Fisher Clinical Services U.K. Limited
(and on behalf of itself, its subsidiaries and its affiliates listed on Appendix I
attached hereto)
Langhurstwood Road, Horsham, West Sussex, RH12 4QD, United Kingdom

(hereafter referred to collectively as “Fisher Clinical”)

Company and Fisher Clinical are sometimes hereinafter referred to individually as a “Party”
and collectively as the “Parties.”

2. DEFINITIONS

For the purposes of this Quality Agreement, the following capitalized terms shall have the meanings defined below. Any capitalized terms defined elsewhere in this Quality Agreement shall be given equal weight and importance as though they were set forth in this section.

Note: For clarification throughout the document, the symbol “+” before and after a sentence or section denotes that that section or wording is a commitment to a European regulatory authority and may not be altered.

- “Batch Record” means a compilation of records containing the production history for each batch of Drug Product produced.
- “Blinding” means a procedure in which one or more parties to the clinical trial are kept unaware of the treatment assignment(s).
- “Certificate of Compliance” or “CoC” means written statement certifying compliance in accordance with applicable approved Specifications, SOPs and GxPs.
- “Change Control” means a control system for documenting, evaluating, approving, and implementing changes that describes the actions taken to execute a change that may affect Drug Product and/or Material quality or reproducibility of a qualified or validated process. The change control ensures that sufficient supporting data is generated to demonstrate that the change results in a Drug Product and/or Material or controlled process of the desired quality, consistent with the approved Specifications and regulatory requirements. Change Control levels are defined as follows:
 - “Minor (Level 1) Change” means a change with minor (low risk) or no impact to Drug Product and/or Material quality attributes or protocol and no risk to patient safety.
 - “Major (Level 2) Change” means a change with potential major (medium) impact to Drug Product and/or Material quality attributes or protocol without risk to patient safety.
 - “Critical (Level 3) Change” means a change with critical (high) impact on Drug Product and/or Material quality attributes or protocol and potentially affecting patient safety.
- “Change Order” means authorization approving a change to the most current version of an approved Production Order after operations commenced executing such approved Production Order.
- “Clinical Trial Application” or “CTA” means the application submitted to a Regulatory Authority for approval to initiate a clinical trial in humans.
- “Company” has the meaning set forth in Section 1.1 of this Quality Agreement.
- “Company Representative” has the meaning set forth in Section 5.1.1.

- “Complaint” means a formal expression (oral or written) of GxP related dissatisfaction from Company or a Third Party concerning any Services or a distributed Drug Product and/or Material.
- “Contacts List” has the meaning set forth in Section 4.6.
- “Data” means information derived or obtained from raw data (e.g., a reported analytical result). Data can be static (i.e., paper or PDF) or dynamic (e.g., an electronic record which the user and reviewer can interact with).
- “Data Integrity” means the extent to which all Data is complete, consistent, and accurate throughout the Data lifecycle.
- “Depot Management” means the Fisher Clinical management oversight and compliance monitoring of GxP-related activities, including but not limited to, storage, secondary packaging, labeling / relabeling, and distribution of Drug Product that is performed at its contracted depot facilities.
- “Deviation” means any unexpected or unplanned event occurring during a GxP related activity or any deviation from approved process, procedure, specification, protocols, or regulatory approval. Deviation is hereby further defined as:
 - “Level 0 Deviation” means a deviation that is not attributable to Fisher Clinical. There is no impact to Product Quality Attributes, study protocol or patient safety.
 - “Level 1 Deviation” means a deviation with no impact to Product Quality Attributes, or protocol, and no risk to patient safety.
 - “Level 2 Deviation” means a deviation considered to have a potential major impact on Product Quality Attributes, or protocol, without risk to patient safety.
 - “Level 3 Deviation” means a deviation considered to have a critical impact on Product Quality Attributes, or protocol and potentially affecting patient safety.
- “Drug Product” means the drug product supplied to or sourced by Fisher Clinical on behalf of Company in order to allow Fisher Clinical to perform the services described in a Statement of Work (SOW) and also means the packaged or assembled drug product produced by Fisher Clinical having performed those services on that supplied or sourced drug product. Drug Product may include Drug Substance, investigational drug product, placebos or commercially available products (e.g. comparator, Non-Investigational Medicinal Product).
- “Drug Substance” means any substance or mixture of substances intended to be used in the manufacture of a medicinal product and that, when used in its production, becomes an active ingredient (“active pharmaceutical ingredient” or “API”) of that product intended to exert a pharmacological, immunological or metabolic action with a view to restoring, correcting or modifying physiological functions or to make a medical diagnosis.
- “Effective Date” has the meaning set forth in Section 4.9.

- “EMA” means European Medicines Agency.
- “EU” means the European Union.
- “FDA” means the U.S. Food and Drug Administration.
- “Fisher Clinical” has the meaning set forth in Section 1 of this Quality Agreement.
- “Fisher SOPs” means Fisher Clinical standard operating procedures.
- “For-Cause Audit” means an audit conducted in response to a critical quality related incident or a significant quality trend.
- “Good Manufacturing Practices” or “GMPs” means the current Good Manufacturing Practices for Packaging/Labeling finished Drug Product as set forth in the U.S. Food, Drug, and Cosmetic Act and any another other applicable equivalent laws, rules, or regulations or GMPs specified by a Regulatory Authority, including, without limitation, any Regulatory Authority in the European Union. For the avoidance of doubt, GMPs shall include, without limitation, United States and European Union’s Guidelines for Good Manufacturing Practices and The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), as applicable.
- “GxP” means all current good practice quality guidelines and regulations, including Good Manufacturing Practices, Good Distribution Practices and Good Clinical Practices.
- “IMPD” means Investigational Medicinal Product Dossier.
- “Manufacturing Batch Records” means records that document that each significant step in the manufacture, processing, packing, or holding of the batch was accomplished. The completed manufacturing batch records become the verification that all critical steps were performed as prescribed and, when combined with laboratory results, the manufacturing firm has adequate documentation for batch disposition.
- “Material” means any material aside from Drug Product, including, but not limited to, primary and secondary packaging materials, excipients, shipping outer packaging, labeling materials, and related medical devices, used in the services performed by Fisher Clinical for Company pursuant to the MSA.
- “MSA” has the meaning set forth in Section 4.1.
- “MSDS” means Material Safety Data Sheets, also known as “SDS” or, “Safety Data Sheets”.
- “Non-Investigational Medicinal Product” or “NIMP” means a Drug Product other than the test product under investigation, placebo or comparator that is to be used as support or escape/rescue medication in a clinical trial.
- “Product Quality Attributes” means the molecular or product characteristics that define the quality of a product (e.g. physical or chemical, traceability, etc.). For the purposes of this Quality Agreement, “product” shall mean Drug Product or Material.

- “Product Specification File” means a reference file containing, or referring to files containing, all the information necessary to draft the detailed written instructions on processing, packaging, quality control testing, batch approval and shipping of an investigational medicinal product (i.e.: Drug Product).
- “Production Order” means the original document (paper or electronic) used to describe in a step-by-step manner the processing or assembling of a batch of Drug Product.
- “Reference Sample” means a sample of Drug Product and/or Material collected for the purpose of being analyzed, should the need arise, to support significant investigations.
- “Regulatory Authority” means any national, supra-national, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity that has jurisdiction over any Material, Drug Product, the conduct of clinical trials or any of the Services performed under this Quality Agreement.
- “Reprocess” or “Reprocessing” means repeating steps that are part of the established production process as a result of a deviation.
- “Retention Sample” means a sample for identification purposes. The Retention Sample is stored under controlled conditions for a defined time period following completion of processing; it may also be known as “retain sample”.
- “Rework” or “Reworking” means subjecting a process material or Product that does not conform to Specifications to one or more process steps that are different from the established process to obtain a material or Product of acceptable quality, i.e., activities to be performed as part of a new packaging run to maintain control, comply with cGMP and to maintain the safety, quality, identity, potency and purity of the Products produced.
- “Qualified Person” or “QP” means a person defined within the EU as defined by Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001. The equivalent role in Switzerland is known as the “Responsible Person”, as defined by the (Swiss) Ordinance on Establishment Licences.
- “Quality Agreement” has the meaning set forth in Section 1. This Quality Agreement may also be known as a Technical Agreement.
- “Services” has the meaning set forth in Section 3.
- “Specification(s)” means any and all technical details, instructions and similar requirements for the Services, and in particular, requirements for the assembly, packaging, processing, and handling of Drug Product and/or Materials that are the subject of a project/SOW.
- “SOW” means a written statement of work, proposal, or quote specifying the basic parameters of a specific project between Fisher Clinical and Company, including, but not limited to, the costs and all Specifications for the assembly, packaging, processing, and handling of Drug Product and/or Material for the particular project and the time period for completing the project.

- “Third Party” means any person or entity other than Fisher Clinical, Company or any of their respective affiliates.
- “TSE/BSE” means transmissible spongiform encephalopathy and bovine spongiform encephalopathy, respectively.

3. SCOPE

3.1 The scope of this Quality Agreement includes but is not limited to the following services: (i) certain manufacturing (for example: over encapsulation, placebo blending and dispensing), (ii) primary packaging, (iii) secondary packaging, (iv) label generation and labeling, (v) storage of Drug Product and/or Material (vi) distribution, (vii) Depot Management, (viii) purchasing of commercially available products (e.g. comparator product or NIMP, etc.), (ix) QP certification, and (x) returns, accountability and destruction of Drug Product and Material for Company’s clinical trials (collectively “Services”).

4. GENERAL ARRANGEMENTS

4.1 Company and Fisher Clinical are parties to or will be entering into an agreement which sets forth the commercial terms pursuant to which Fisher Clinical may perform Services for Company (the “MSA”). The MSA provides that the Parties, from time to time, will enter into SOWs setting forth the responsibilities of each Party for a particular project. This Quality Agreement sets forth the technical and quality terms pursuant to which Fisher Clinical will perform Services for Company under the MSA and applicable SOW. To the extent that there is a conflict between the terms of this Quality Agreement and the MSA and/or a SOW, the terms of this Quality Agreement shall control with respect to GMP and quality issues and the terms of the MSA shall control for all other issues.

4.2 Company is considered to be the sponsor of a clinical trial and assumes all responsibilities of the sponsor unless Fisher Clinical is informed and agrees to accept such responsibilities in writing, and such sponsor responsibilities of Company to be performed by Fisher Clinical are expressly stated in this Quality Agreement.

4.3 Both Parties will undertake to comply with the applicable regulatory requirements of the EU, FDA, national regulatory and other statutory requirements relating to all applicable GxPs.

4.4 Any proprietary and/or confidential information (whether or not patentable or copyrightable, and whether or not currently patented or copyrighted) which is owned or controlled by either Party or obtained in the course of the performance of the MSA will be treated as confidential information. The protection and use of such confidential information shall be governed by the MSA.

4.5 Company will provide Fisher Clinical with the information necessary to carry out work such that operations can be performed in accordance with the authorized Company requirements.

4.6 Communication between Fisher Clinical and Company, or vice versa, will generally be through designated contacts and the responsible person of each Party as set forth on Appendix II (the "Contacts List") attached hereto.

4.7 Fisher Clinical and Company confirm to hold a valid authorization/license issued by the respective Regulatory Authority where applicable. Company is responsible to ensure that Drug Product is distributed only to parties holding appropriate authorization/license and who are entitled to receive such Drug Product.

4.8 During the term of this Quality Agreement, Fisher Clinical packages and/or handles the Drug Product and conducts the operations in compliance with: (i) applicable GxPs; (ii) the agreed upon Specifications provide in writing by Company; and (iii) the packaging, shipping, distribution and quality procedures described in the relevant Fisher SOPs.

4.9 This Quality Agreement is effective from the date of last signatory (the "Effective Date"), and shall remain in full force and effect until the expiration or termination of the MSA, to which the terms are set forth in the MSA. Any changes or amendments to this Quality Agreement must be mutually agreed in writing. Expiration or termination of this Quality Agreement for any reason will not relieve either Party of any obligation accruing prior to such expiration or termination or of any rights and obligations of the Parties that by their terms survive termination or expiration of this Quality Agreement.

4.10 Quality related disagreements between Company and Fisher Clinical that are not resolved in the normal course of business shall be brought to the attention of the appropriate contact person for notices at the Company and Fisher Clinical, as listed on the Contacts List. The contact people shall work jointly to develop a strategy for resolution and document such resolution in writing.

5. QUALITY RESPONSIBILITIES

	RESPONSIBILITIES		
5.1	AUDIT MANAGEMENT	Fisher Clinical	Company
5.1.1	Company or Company's authorized representative that is reasonably acceptable to Fisher Clinical ("Company Representative"), upon reasonable notice and during Fisher Clinical regular business hours, shall be permitted to audit no more than once per calendar year for compliance purposes Fisher Clinical facilities, equipment and procedures that are directly used by Fisher Clinical to provide Services to Company. Company will limit their representation to two (2) auditors for two (2) days.		X
5.1.2	Company or Company Representative, as applicable, will comply with Fisher SOPs, provided at the time of the audit, for facility access and safety and shall be accompanied by Fisher Clinical personnel at all times.		X
5.1.3	Company will identify and discuss all potential audit observations with Fisher Clinical prior to the completion of		X

	the audit exit meeting. Company will allow Fisher Clinical to discuss and clarify any /all potential audit observations.		
5.1.4	Provide a written confidential audit report to Fisher Clinical within thirty (30) calendar days from the last day of the audit.		X
5.1.5	Provide confidential written responses to audit observations addressed in the audit report to Company within thirty (30) calendar days from the date of receipt of the audit report.	X	
5.1.6	Notwithstanding the above, Company retains the right to conduct a reasonable For-Cause Audit, as warranted, during Fisher Clinical normal business hours. Specific audit objective, proposed dates and names of the auditors will be agreed upon mutually and in writing prior to any such audit.		X
5.2	REGULATORY INSPECTION	Fisher Clinical	Company
5.2.1	Notify Company within two (2) business days of any Regulatory Authority requests to inspect the facilities of Fisher Clinical where the regulatory inspection is directly related to Drug Product.	X	
5.2.2	Notify Fisher Clinical within two (2) business days of any Regulatory Authority requests to inspect the facilities of the Company where the regulatory inspection is directly related to Drug Product or Services performed by Fisher Clinical.		X
5.2.3	Notify Company within one (1) business day of any Regulatory Authority requests (for example during an inspection) to review batch documentation or process directly related to Drug Product.	X	
5.2.4	Company and Fisher Clinical will provide to the other copies of the inspection report, deficiency letter or written regulatory compliance observations directly related to Drug Product and/or Material hereunder. Any such report, letter or observations may be redacted to exclude Company and Fisher Clinical proprietary information. Copies will be provided by facsimile or electronically within two (2) business days of receipt.	X	X
5.3	SUPPLIER AND CONTRACTOR MANAGEMENT	Fisher Clinical	Company
5.3.1	Fisher Clinical shall have written procedure(s) governing supplier/contractor quality management, including the selection, qualification, approval and monitoring for compliance of its' suppliers and contractors in accordance with applicable GxPs.	X	
5.3.2	Where Fisher Clinical is requested to source Material pursuant to the applicable SOW, Fisher Clinical will source Material from approved suppliers in accordance with Fisher SOPs and applicable GxPs.	X	
5.3.3	Where Company is providing Material to Fisher Clinical to be used in manufacturing or packaging operations, Company will source Material from approved suppliers in accordance with applicable GxPs.		X

5.3.4	Where Company requires Material to be sourced by Fisher Clinical from a supplier specified by the Company and to a certain Specification provided by the Company, then Company is responsible for the qualification and compliance monitoring of the supplier and for the approval of such Specification.		X
5.3.5	Fisher Clinical will not subcontract work to a Third Party without Company's written consent, such consent not to be unreasonably withheld. Require that any subcontracted work is carried out in accordance with applicable GxPs.	X	
5.4	COMMERCIAL DRUG PRODUCT USED FOR CLINICAL TRIALS	Fisher Clinical	Company
5.4.1	At Company's written request, Fisher Clinical will source Drug Product from approved suppliers in accordance with Fisher SOPs and applicable GxPs.	X	
5.4.2	Where Company is providing the Drug Product to Fisher Clinical, Company will source from approved suppliers in accordance with internal SOPs and applicable GxPs.		X
5.4.3	Ensure Drug Product is sourced only from approved suppliers who hold the relevant regulatory authorization and in accordance with applicable GxPs.	X	X
5.4.4	Store Drug Product in accordance to Drug Product Specification and applicable SOPs	X	
5.4.5	Define and document the supply chain of the Drug Product sourced in accordance with applicable law.	X	
5.4.6	In the event of a recall, notify Company as per Section 5.16.8.	X	
5.5	RECEIPT AND INVENTORY MANAGEMENT	Fisher Clinical	Company
5.5.1	Ensure the manufacturer(s) / supplier(s) for any Drug Product and/or Material supplied by Company are compliant with current GxPs.		X
5.5.2	Where Drug Product and/or Material is supplied by Company, ensure each lot is compliant with current GxPs, and Specifications. Provide statements of compliance or certification to Fisher Clinical.		X
5.5.3	Provide certification that all Drug Product and Material supplied by Company to Fisher Clinical are in compliance with FDA regulations, EU Directives, EMA Public Statements or relevant regulatory guidelines regarding TSE/BSE contamination (including, but not limited to EMA 410/01 Current Version).		X
5.5.4	+Provide Fisher Clinical with TSE/BSE certificates not older than 3 years and provide updated TSE/BSE certificates for expired certificates or equivalent assurance that TSE/BSE certificate is still valid.+		X
5.5.5	+Notify Fisher Clinical within five (5) business days in case a TSE/BSE certificate is invalidated for any reason.+		X
5.5.6	Provide sampling plan for Reference, Retention or Test		X

	Samples of Drug Product to be taken for any analytical, quality control, stability testing in accordance with the applicable SOW.		
5.5.7	Where Fisher Clinical is responsible for the storage and maintenance of Reference Sample(s) and/or Retention Sample(s), such samples will be stored at appropriate environmental conditions in accordance to Company's written instructions and applicable SOW.	X	
5.5.8	Upon request by Company, Fisher Clinical will perform sampling of incoming Drug Product and/or Material in accordance with Fisher SOPs and applicable GxPs. Prior to the sampling, Fisher Clinical and Company will agree on the sample size, considering the nature of the proposed tests. At a minimum, the sample size must be sufficient to perform the required tests as per local regulation requirements where the Drug Product and/or Material will be tested.	X	X
5.5.9	Where agreed in writing between the Parties, forward the specified number of samples to Company (or a Third Party named by Company) for testing, further processing, sample management or storage.	X	
5.5.10	The minimum labeling requirements for the outer shipping container holding Drug Product and/or Material to be delivered to Fisher Clinical shall include: • description, including strength (if relevant); • batch or lot number; • Company name, and address; • Clinical trial number when available; • expiry date/re-test date (as applicable as per local regulations); • quantity and/or weight (gross/net/tare); • container number (e.g. x of y); and • storage conditions.		X
5.5.11	Inspect incoming Drug Product and Material on receipt and book into the inventory system. On receipt of Drug Product and Material and associated certification check all containers for the following: • external condition; • intact and authentic seals (if appropriate); • temperature control in transit has been maintained within the guidelines provided by Company (if applicable); • compliance of the type and number of containers and labeling with the delivery documentation; and • quantity received.	X	
5.5.12	Document any issues identified upon receipt of the incoming Drug Product and Material and notify the Company within two (2) business days of any such issues.	X	

5.5.13	Quality personnel shall inspect and review the receipt documentation and inventory system records of the Drug Product and Material and ensure all the appropriate documentation is in place. As a result of such inspection, appropriately determine the disposition of the Drug Product and Material.	X	
5.5.14	Material supplied by Fisher Clinical and printed labels provided by Fisher Clinical will be sampled for testing and/or inspection according to Fisher SOPs and applicable GxPs, unless testing to Company Specifications has been specified in writing.	X	
5.5.15	Sampling and identity testing of incoming Company supplied Drug Product or Material will not be undertaken by Fisher Clinical unless specifically requested by Company, as agreed under Section 5.5.4 above. The testing methodology to be used will be described in or appended to the SOW.		X
5.5.16	All documentation accompanying the distributed Drug Product and/or Material for a clinical trial that is subject to Blinding will be prepared consistent with Section 5.14.1. Where Company does not have knowledge of the Blinding for the applicable clinical trial, a masked version of the pre-executed and fully executed Batch Record will be forwarded to the Company for review, approval and release.	X	X
5.5.17	Where required, package Drug Product and/or Material under quarantine using "conditionally approved" status in accordance with Fisher SOPs; provided, that Company is responsible for such approval.	X	
5.5.18	Company is responsible for maintaining an appropriate number of Reference Samples for Company supplied Drug Product(s) and/or Material(s) in accordance with applicable GxPs.		X
5.5.19	Retain an appropriate number of Reference and Retention Samples of Drug Product and/or Material which are sourced by Fisher Clinical on behalf of Company, in accordance with applicable GxPs and as per the SOW. Reference and/or retention samples will be made available to the certifying QP and/or competent authority upon request.	X	
5.6	DOCUMENTATION / RECORDS MANAGEMENT	Fisher Clinical	Company
5.6.1	Fisher Clinical has a controlled system to initiate, review, revise, approve, retire and archive all GxP-related documentation, records and/or electronic media.	X	
5.6.2	Provide a MSDS or a data sheet with equivalent information for all Drug Product and/or Material supplied by Company.		X
5.6.3	Company will approve Specifications for sampling Material intermediates, bulk and packaged Drug Product as agreed upon in advance in writing.		X
5.6.4	Fisher Clinical will approve sampling Specifications for incoming Material.	X	

5.6.5	Fisher Clinical and Company will review and approve Production Order(s).	X	X
5.6.6	Fisher Clinical and Company will review and approve Batch Record post-production.	X	X
5.6.7	Fisher Clinical and Company will review and approve Change Orders for changes that have a direct impact on Drug Product quality.	X	X
5.6.8	Company shall provide expiry date/re-test date for Drug Product.		X
5.6.9	Retain Batch Record in accordance with Fisher SOPs and applicable GxPs for a retention period of fifteen (15) years. All project documentation will be securely and systematically filed for ease of retrieval. Upon the expiration of the retention period, Fisher Clinical will notify Company in writing of such expiration and Company shall respond in writing within sixty (60) calendar days from the date of receipt providing instruction to Fisher Clinical whether such records should be either (i) retained for a longer period of time, (ii) delivered to the Company, (iii) or destroyed. If the Company does not respond within the sixty (60) calendar days, Fisher Clinical has a right to destroy or dispose of such documentation. If notified in writing by Company to deliver or destroy the documentation sooner than the expiration of that retention period, then Fisher Clinical will comply with Company's request.	X	
5.6.10	Have procedures in place to ensure Data is authentic, complete and accurate; that it can be traced to its source and that it is readily available during regulatory inspections.	X	
5.6.11	Notify the Company of any breach to Data Integrity that may impact the quality or the safety of any of the Company's Drug Products, as soon as reasonably practicable, after becoming aware of the event.	X	
5.7	MANUFACTURING AND PACKAGING (PRIMARY/SECONDARY) SERVICES	Fisher Clinical	Company
5.7.1	Ensure that Services with regard to the manufacturing and packaging of Drug Product and Material are performed in accordance with approved instructions and applicable GxPs, and, where the Fisher Clinical QP is responsible for release, in accordance with the IMPD.	X	
5.7.2	Undertake in-process testing according to Fisher SOPs unless described differently within the SOW. If requested, issues such as defect lists, acceptable quality levels, fill limits, closure torques, seal or vacuum test requirements will be described therein.	X	
5.7.3	Provide all relevant information concerning Health-Based Exposure Limits (HBEL) that may be useful during risk analysis to determine if existing cleaning methods are sufficient or dedicated equipment is required. This may include but is not limited to the following: Permitted Daily Exposure (PDE), Acceptable Daily Intake/Exposure		X

	(ADI/ADE), Occupational Exposure Limit (OEL), or any other data relevant to the medical and pharmacological potency and/or toxicity of products (i.e., sex hormone, cytotoxic, highly potent, highly hazardous, etc.).		
5.7.4	Validate and document methods and procedures for cleaning product contacting surfaces of equipment with acceptance criteria for residues defined and justified by applying matrix approach and worst case scenario, alternatively dedicated equipment can be used.	X	
5.7.5	Inform Fisher Clinical where the Drug Product or compound specific characteristics would be expected to increase the cleaning difficulty so that Fisher Clinical can determine the appropriate cleaning methods. Inform Fisher Clinical anytime changes are made which alter the critical characteristics of a Drug Product or compound. Changes requiring notification include but are not limited to the following: formulation (concentration of API), solubility, minimum batch size, pharmaceutical form, maximum daily dosage (in units), and any changes to health-based characteristics relevant to the Drug Product.		X
5.7.6	Where requested by Company in writing, Fisher Clinical will retain an adequate number of Reference Sample(s) of Drug Product and Material and Retention Sample(s) for each batch of the fully packaged Drug Product, as agreed with Company and in compliance with local regulations.	X	
5.8	REPROCESS AND REWORK (IF APPLICABLE)	Fisher Clinical	Company
5.8.1	Where Reprocessing of Drug Product is required and permitted to the extent allowed by applicable law and Company, review and approve all reprocessing steps. Fisher Clinical will perform Reprocessing in accordance with Fisher SOPs and Company written instructions.	X	X
5.8.2	Where Reworking is required and permitted to the extent allowed by applicable law and Company, have a protocol or procedure that has been approved by both Company and Fisher Clinical prior to implementation. Fisher Clinical will perform Reworking of Drug Product in accordance with Fisher SOPs and Company written instructions.	X	X
5.9	LABEL GENERATION AND LABELING	Fisher Clinical	Company
5.9.1	Where agreed in writing between the Parties that Fisher Clinical will provide the Drug Product label:	X	X
5.9.1.1	Provide final approved label text to Fisher Clinical and ensure that the supplied text complies with all applicable regulatory requirements.		X
5.9.1.2	Where the Parties agree that Company will provide translations for label text and label artwork to Fisher Clinical, Company will ensure that the supplied text and artwork complies with all applicable regulatory		X

	requirements.		
5.9.1.3	Where the Parties agree that Fisher Clinical will provide label transcription and translation services and label artwork to Company, Company will ensure that the text, as translated, and artwork complies with all applicable regulatory requirements.	X	X
5.9.1.4	Generate and supply Company with label proof(s) for Company's review and approval.	X	
5.9.1.5	Provide written approval by appropriate Company personnel to Fisher Clinical confirming the review and approval of the Fisher Clinical supplied label proof(s), including approval of Fisher Clinical label translations and artwork, as applicable.		X
5.9.1.6	Generate a report which outlines the information that will be printed on the labels, including the barcode, material ranges, and lot number. This report is part of the electronic production order/executed batch record.	X	
5.9.1.7	Provide written approval by appropriate Company personnel to Fisher Clinical confirming the review and approval of such report prior to label printing.		X
5.9.1.8	Where the Parties agree that Fisher Clinical shall generate the randomization code, Fisher shall generate such randomization code and provide it to Company for review and approval.	X	
5.9.1.9	Where the Parties agree that Company shall generate the randomization code, Company will provide such randomization code to Fisher Clinical in electronic form.		X
5.9.1.9.1	Fisher Clinical will manage randomization codes in its inventory system. Where requested by Company in writing, Fisher Clinical will provide Company with a hard copy of such randomization code.	X	X
5.9.1.9.2	Verify that the hard copy randomization code provided by Fisher Clinical and the Company supplied electronic randomization code are in agreement as applicable in 5.9.1.9.1.		X
5.9.1.10	Provide written approval by appropriate Company personnel to Fisher Clinical confirming the review and approval of the randomization code, if applicable as in 5.9.1.9.1.		X
5.9.1.11	Print Drug Product labels in accordance with Company approved label proof and Company approved randomization code.	X	
5.10	CHANGE CONTROL MANAGEMENT	Fisher Clinical	Company
5.10.1	Have a Change Control management system with documented procedures for tracking and controlling changes impacting the Drug Product and Material related to the Services.	X	
5.10.2	All Change Control will be documented, evaluated,	X	

	reviewed and approved by Fisher Clinical Quality Assurance in accordance with applicable Fisher SOPs.		
5.10.3	Provide written notification to Company within a reasonable time of the intent to make any Critical (Level 3) Changes that directly impact the Drug Product and/or Material.	X	
5.10.4	Company will provide written review and approval for a Critical (Level 3) Change as determined to directly impact Drug Product or Services; such review and approval not to be unreasonably delayed.		X
5.10.5	Company shall notify Fisher Clinical in writing of any change impacting Fisher Clinical, Drug Product or Services, and Fisher Clinical and Company shall agree how to implement such changes.		X
5.11	DEVIATION MANAGEMENT	Fisher Clinical	Company
5.11.1	Investigate, evaluate, and document Deviations in accordance with Fisher SOPs and applicable GxPs.	X	
5.11.2	Review and approve Level 1 Deviations that are determined to be associated with the manufacturing and/or packaging of Drug Product in accordance with Fisher SOPs will be included with the post-production Batch Record.	X	
5.11.3	Inform Company of any Level 2 Deviation or Level 3 Deviation within two (2) business days.	X	
5.11.4	Investigate, evaluate and document deviations in collaboration with Company, as appropriate.	X	X
5.11.5	Review and approve deviation report and provide to Company.	X	
5.11.6	Review and approve supplied deviation report where requested by Fisher Clinical and return to Fisher Clinical.		X
5.12	DRUG PRODUCT DISPOSITION	Fisher Clinical	Company
5.12.1	Ensure Regulatory Authority approval is in place in each of the countries where the clinical trial taking place before the clinical trial starts.		X
5.12.2	Fisher Clinical Quality Assurance or Fisher Clinical QP within the EU will perform the review and approval of the post-production Batch Record, assuring compliance with all applicable Specifications, Fisher SOPs and GxPs, and if satisfactory, provide a Certificate of Compliance for the packaged Drug Product to Company.	X	
5.12.3	For clinical trials taking place within the US or non-EU countries or for Drug Product manufactured, packaged and released within the US or non-EU countries, Company is responsible for the final release of all Drug Product to be shipped to depots and clinical trial sites.		X
5.12.4	For clinical trials taking place within the EU or for Drug Product manufactured, packaged and released within the EU:		

5.12.4.1	Provide copies of each country clinical trial approval from the relevant Regulatory Authority, with the English translation where requested, before final certification and release by the Fisher Clinical QP. Where a Regulatory Authority does not provide approval in writing, then provide confirmation that any period required to have elapsed for consent to be deemed granted has elapsed.		X
5.12.4.2	Where Company requires Fisher Clinical Qualified Person to perform final certification of the packaged Drug Product this shall be requested in the applicable SOW.	X	X
5.12.5	If final batch certification is to be performed by the Fisher Clinical QP, as requested in the applicable SOW, Fisher Clinical will perform certification on the basis of the following documentation being made available in English (or bilingual, with English as one of the languages), based upon the Drug Product, the supply chain and the specific study protocol on a case by case basis, which includes but is not limited to: • Certificates of release for the packaged Drug Product and Drug Substance confirming GMP and IMPD compliance; • A protocol specific supply chain list (preferably in the form of a diagram) detailing the supply chain including starting materials, packaging materials, Drug Substance manufacturers, Drug Product manufacturers and intermediary steps, release and stability testing. • Product Specification File • Label requirements or specifications for the IMP • Certificates of analysis for the bulk Drug Product formulation; • Certificates of analysis of the Drug Substance; • GMP certification of the facilities, manufacturing, packaging, testing or storing the Drug Substance and Drug Product; • Other relevant documentation such as shipping documentation and storage temperature; • Audit reports (or equivalent assessment) of any GMP facility processing the Drug Product, Drug Substance and packaging and starting materials, they must be supplied by Company or authorized Third Party, and be acceptable to the QP. • An assessment detailing that appropriate level of supplier assessment/audit frequency and continued supply of audit reports in real time for the supply chain. • GMP compliance certificates for Drug Substance; bulk Drug Product, pre-packaged Drug Product and any intermediate stages of the Drug Product manufacturing process; This will include at least a statement that the lot	X	

	was manufactured to GMP and compliance with the clinical trial authorization / IMPD. • Any Deviations, Change Controls or other issues which have been identified during manufacture or testing which may impact GMP or IMPD / Clinical trial authorization compliance. • Certificate of Conformance for the starting materials and packaging materials; • Copies of clinical trial authorization country approvals with English translations as required; • Manufacturing Batch Records; • Stability reports; • Importation documentation to support import into EU (if not imported by Fisher Clinical) • The IMPD and Clinical Trial Application; including any updates or amendments to the dossier whilst clinical trials are in progress; • Product Specification File; • +TSE/BSE statements and certificates within their validity period+; • Any other factors relevant to assessment of the quality systems of the manufacturing process as deemed necessary by the certifying QP.		
5.12.6	Where the Fisher Clinical QP is responsible for certification, forward immediately any updates or amendments to the documents required for such certification or associated regulatory information. Any information transferred electronically must be positively acknowledged between both Parties. Where electronic transfer is not possible, any documents physically transferred must be addressed to the relevant personnel via recorded delivery.		X
5.12.7	Where there is an established written agreement by and between respective Qualified Persons which outlines the process and responsibilities of each QP with respect to QP arrangements as required under EU GMP Annex 16 (the "QP Agreement"), Company QP will submit a written statement to the Fisher Clinical QP verifying that all relevant documentation has been reviewed and approved and all applicable audits were completed as required for acceptance and final certification ("the "Certification of Review"). This Certification of Review can be used by the Fisher Clinical QP in lieu of the respective documentation listed in section 5.12.5 above.		X
5.12.8	Any/all Reference Sample(s) and Retention Sample(s) must be readily accessible by the certifying QP, upon written request.		X

5.12.9	Where the Fisher Clinical QP is responsible for certification, Company will allow Fisher Clinical to audit the sites involved in the manufacturing, packaging, storage, analytical testing of the Drug Product, on a case by case basis.		X
5.12.10	Fisher Clinical will not ship Drug Product to depots and clinical trial sites without the prior written approval provided by Company who retains the final release authority for Drug Product shipment.	X	
5.12.11	Where the Fisher Clinical QP is responsible for certification and Drug Product is transferred between clinical trial sites, the Fisher Clinical QP must be informed and involved in the decision to transfer. The Drug Product should be returned to Fisher Clinical for re-labeling and certification where required.		X
5.12.12	Where further packaging or labeling activities take place outside of the EU such as expiry date/re-test date updating or secondary packaging, the Parties will follow the provisions within this Quality Agreement.	X	X
5.13	STORAGE AND DISTRIBUTION MANAGEMENT	Fisher Clinical	Company
5.13.1	Provide secure storage at all Fisher Clinical managed locations appropriate for the Drug Product and Material, including systems for controlling quarantined, rejected or recalled materials, and in accordance with applicable GxPs.	X	
5.13.2	Qualify and monitor storage areas for compliance with GMP climate control standards.	X	
5.13.3	Ensure that all Drug Product and Material are status controlled and properly segregated (either physically or electronically).	X	
5.13.4	Store Material and/or Drug Product at the specified conditions.	X	
5.13.5	Notify Fisher Clinical of any special handling and/or storage conditions for any incoming Material and/or Drug Product. This notification shall be in writing and at least seven (7) business days in advance of any shipment of the Material and/or Drug Product to Fisher Clinical.		X
5.13.6	Ship Drug Product and Material on receipt of written or electronic authorization by Company.	X	
5.13.7	Provide information concerning special requirements for packaging and monitoring Drug Product and/or Material during shipment.		X
5.13.8	Manage the following activities relating to distribution and Depot Management: • Receiving; • Storage; • Shipment of Drug Product and Material and delivery notification; • Support recalls initiated by Company;	X	

	- Shipping request management; - Re-labeling of packaged Drug Product and Material where appropriate; and - Returns, accountability and destruction of Drug Product and/or Material.		
5.14	INTERACTIVE RESPONSE TECHNOLOGY SYSTEMS	Fisher Clinical	Company
5.14.1	Company will establish required procedures with the interactive response technology systems supplier to ensure critical areas such as Blinding are addressed.		X
5.14.2	For clinical trials taking place in the EU, where the Fisher Clinical QP is responsible for certification and/or release, Company must inform Fisher Clinical of any changes to the expiry date/re-test date. The changes must have the necessary regulatory approval and stability data must be available to justify the new expiry date /re-test date.		X
5.15	COMPLAINT MANAGEMENT	Fisher Clinical	Company
5.15.1	Fisher Clinical will document and investigate all reported Complaints in accordance with Fisher SOPs and applicable GxPs. Company will provide assistance with the Complaint investigation upon Fisher Clinical request.	X	X
5.15.2	Fisher Clinical Quality Assurance will review and approve Complaint investigation report(s) and provide a copy of the final report to Company upon completion.	X	
5.16	RECALL MANAGEMENT	Fisher Clinical	Company
5.16.1	Initiate a recall of Drug Product and promptly notify Fisher Clinical, in accordance with applicable GxPs and established written procedures.		X
5.16.2	Initiate a recall process in accordance with applicable GxPs and established written procedures for Drug Product, if required to do so by any Regulatory Authority and notify Company of such recall within two (2) business days.	X	
5.16.3	Where Fisher Clinical QP certified the Drug Product, Fisher Clinical QP will notify Company of a potential recall of such Drug Product. Company will not unreasonably withhold agreement to initiate a recall.	X	X
5.16.4	Notify Fisher Clinical of a potential recall of Drug Product certified by Fisher Clinical.		X
5.16.5	Notify and communicate with the respective Regulatory Authority(ies) in the event of any Drug Product recall.		X
5.16.6	Provide Fisher Clinical with a written request for pertinent documentation, data and information needed for the recall of the Drug Product.		X
5.16.7	Provide reasonable assistance to Company and cooperate fully with any recall of Drug Product.	X	
5.16.8	Notify Company within two (2) business days when information relating to a recall involving commercial Drug	X	

	Product used in the clinical trial becomes available where such Drug Product is sourced by Fisher Clinical.		
5.16.9	Notify Fisher Clinical within two (2) business days when information relating to a recall involving commercial Drug Product used in the clinical trial becomes available where such Drug Product is sourced by Company.		X
5.16.10	Company acknowledges and agrees that Fisher Clinical cannot protect the Blinding of the packaged Drug Product in the event of a recall whether the recall is voluntary or mandated by a Regulatory Authority.		X
5.17	RETURNS, ACCOUNTABILITY AND DESTRUCTION	Fisher Clinical	Company
5.17.1	Notify Fisher Clinical in writing of the disposition for expired/unusable lots of Drug Product and/or Material. Include details of the level of Drug Product accountability to be performed.		X
5.17.2	Provide written authorization to Fisher Clinical for the disposal or destruction of returned Drug Product and/or Material.		X
5.17.3	Make transport arrangements for return of Drug Product and/or Material, as applicable, from clinical trial site(s) to Fisher Clinical intended for disposal or destruction in accordance with Fisher SOPs and the terms and conditions of the MSA and/or SOW.	X	
5.17.4	Document the receipt, storage, disposal or destruction of returned Drug Product and/or Material in accordance with Fisher SOPs and applicable GxPs.	X	
5.17.5	Use facilities as permitted under applicable environmental law for the disposal or destruction of returned Drug Product and/or Material.	X	
5.17.6	Except as stated in this Section 5.17, return, accountability and destruction Services will be governed by the MSA.	X	X

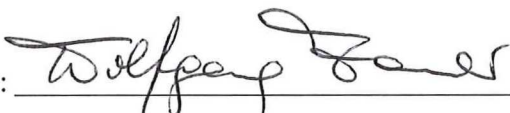
[SIGNATURE PAGE FOLLOWS]

6. COUNTERPARTS

This Quality Agreement may be executed by the Parties in separate counterparts, each of which when so executed and delivered shall be an original, but all such counterparts shall together constitute one and the same instrument. Facsimile or PDF image signatures shall be treated as original signatures.

7. APPROVAL SIGNATURES

IN WITNESS WHEREOF, the Parties have authorized this office or representative to execute this Quality Agreement as of the Effective Date.

Fisher Clinical Services U.K. Limited By:  Name: <u>WOLFGANG ZAUNER</u> Title: <u>SENIOR QP</u> Date: <u>20-APR-2020</u>	The University of Oxford By:  Name: <u>Carly Banner</u> Title: <u>Head of Research Services (Medical Sciences)</u> Date: <u>16-04-2020</u>
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Appendix I

This Appendix I may be amended upon the written agreement of the Parties.

List of Fisher Clinical Subsidiaries and Affiliates

<u>Legal Entity</u>	<u>Facility Address</u>
Fisher Clinical Services – AMERICAS	
Fisher Clinical Services Inc.	7554 Schantz Road, Allentown, PA 18106-9032, USA
	700 Nestle Way, Breinigsville, PA 18031, USA
	699 North Wheeling Road, Mount Prospect, IL 60056, USA
Fisher Clinical Services Mexico, S. de R.L. de C.V.	Michoacan No. 20 Nave 9D, Parque industrial FINSA, Col. Renovación, 09209 México, D.F.
Fisher Clinical Services S. A. S.	TV 21 98-05, Bogota, Colombia
Thermo Fisher Scientific Brasil Servicos de Logistica Ltda	Av. Jaquaré, 818 Unidade 29, Sao Paulo, SP CEP: 05346-000, Brazil
Fisher Clinical Services Peru S. R. L	Avenida Paz Soldan No. 170, Int. 203, San Isidro, 27 Lima, Peru
Fisher Servicios Clinicos Chile Limitada	Almirante Latorre 617, Santiago, Chile
Fisher Clinical Services Latin America S.R.L.	Heredia 563, C1427CNG, Buenos Aires, Flr 1, Argentina
Fisher Clinical Services – EUROPE / MIDDLE EAST / AFRICA (EMEA)	
Fisher Clinical Services U.K. Limited	Langhurstwood Road, Horsham, West Sussex RH12 4QD, United Kingdom
	Logistics House, Sussex Manor Business Park, Manor Royal, Crawley, RH10 9NH, United Kingdom
	Aurora House, Fleming Way, Crawley, RH10 9NL, United Kingdom
Fisher Clinical Services GmbH (Switzerland)	Steinbühlweg 69, 4123 Allschwil, Switzerland
	Ringstrasse 9, 4123 Allschwil, Switzerland
Fisher Clinical Services GmbH (Germany)	Im Wörth 3, 79576 Weil am Rhein, Germany
Fisher Clinical Services Limited Liability Company	142184 Russia, Moscow Region, Podolsk (mkr. Klimovsk), 23A Kommunalnaya St.

Southern Trials (Pty) Ltd. d/b/a Fisher Clinical Services	36 Parkview Street, Unit 1, Highway Business Park, Centurion, South Africa 0157
Fisher Clinical Services – ASIA / PACIFIC	
Fisher BioPharma Services (India) Private Limited	PHARMEZ, SEZ PLOT No 22, NH 8A, Village Matoda, Ahmedabad - 382213, Gujarat, India
Fisher Clinical Services (Beijing) Co., Ltd.	3rd Floor of No. 1 Plant Mauhwa Industrial Park, No. 1 Caida 3 Jie, Caiyuan Industrial Zone, Nancai Shunyi District, Beijing, China 101300
Fisher Clinical Services (Suzhou) Co., Ltd.	Unit B & C Building no. 5, 1 Qiming Road, Shengpu Town, Suzhou Industrial Park, Suzhou, 215000 Jiangsu, China
Fisher Clinical Services (Korea) Co., Ltd.	32, Geumnanghwa-ro 16-gil, (Banghwa-dong 451-5,451-23), Gangseo-gu, Seoul, Korea
Fisher Clinical Services Japan K.K.	AMB Shinkiba, Distribution Center, 1-12-10 Shinkiba, Koto-ku, Tokyo 13-0082, Japan
Fisher Clinical Services Pte Ltd	10 Toh Guan Road, #03-11/12, Singapore 608838
Fisher Clinical Services – Clinical Labeling Services Affiliate	
Clintrak Clinical Labeling Services, LLC	2800 Veterans Highway, Bohemia, NY 11716

Appendix II

This Appendix II may be amended upon the written agreement of the Parties.

Contact List

The University of Oxford		
	(Primary)	(Secondary)
Name	Christopher C Butler	Richard Hobbs
Title	Professor of Primary Care	Nuffield Professor of Primary Care Health Sciences
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Fisher Clinical Services Inc. (Allentown PA)		
	Quality Assurance (Primary)	Quality Assurance (Secondary)
Name	Chenita T. Brooks	Ann (Bonnie) Bartkowski
Title	FCS Regulatory Compliance Manager	Sr. Manager, Quality Assurance
Phone	+1 (610) 871-8399	+1 (610) 871-0151
Email	Chenita.brooks@thermofisher.com	bonnie.bartkowski@thermofisher.com
Fisher Clinical Services Inc. (Mt Prospect IL)		
	Quality Assurance (Primary)	Quality Assurance (Secondary)
Name	Asiya Imam	Bruce Heath
Title	Director, Quality Assurance	Quality Assurance Manager
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Fisher Clinical Services UK Ltd. (Horsham UK)		
	Quality Assurance (Primary)	Quality Assurance (Secondary)
Name	Wolfgang Zauner	Harry Berlanga
Title	Senior Qualified Person	Quality Director & Qualified Person
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Email	Wolfgang.Zauner@thermofisher.com	Harry.Berlanga@thermofisher.com
Fisher Clinical Services, GmbH (Allschwil Switzerland / Weil am Rhein Germany)		
	Quality Assurance (Primary)	Quality Assurance (Secondary)
Name	Tillmann Lindenblatt	Joanne Kruettli
Title	Director QA and Responsible Person (RP)	Director, Quality Assurance
Phone	+41 (0)61 485 28 60	+41 (0) 61 485 24 59
Email	tillmann.lindenblatt@thermofisher.com	Joanne.kruettli@thermofisher.com
Fisher Clinical Services UK Ltd. (Facilities and Depot Network)		
	Quality Assurance (Primary)	Quality Assurance (Secondary)
Name	Marianne Haslam	Julio Carrasco
Title	Global Quality Director of Logistics	Global Sr. QA Manager
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Email	marianne.haslam@thermofisher.com	julio.carrasco@thermofisher.com

Appendix III-Version Control

Version Number	Effective Date	Changes
0	Effective Date	New Document