STANDARD OPERATING PROCEDURE (SOP)

TECHNICAL AGREEMENTS

Version 1.4 Active

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Laboratory Manager

Cytogenex Ltd

Contents

Revision History

Name	Date	Reason For Changes	Version
C. J. Newton	8/4/08	SOP for the construction of Technical Agreements first described	1.0 Draft
C.J.Newton	6/6/08	Minor modifications to formatting	1.1 Draft
C.J. Newton	8/9/08	Modifications as per comments by QP, Colin Newbould, 10/6/08	1.2 Draft
C.J. Newton	12/9/08	Addition of Schedule for contract giver and conversion of SOP to active	1.3 Active
C.J.Newton	10/10/08	1. Removal of reference to Orange Guide; 2. On page 7 of Technical agreement Pro-Forma reference is now give to the use of validated methods; 3. Technical agreement now references the assays that are required by the customer.	1.4 Active

Introduction

Purpose	This document outlines the information that should be included in a Technical Agreement (TA).
Scope	A Technical Agreement (TA) describing the responsibilities of the contract giver and the contract acceptor should be in place before work commences. Either party can instigate the TA and both the contract giver and the contract acceptor have a responsibility to comply with current EU GMP. This document describes the format of the TA used by Cytogenex prior to the commencement of work that falls under the scope of EU GMP as it applies to a contract laboratory.

Expectations and Requirements.

1. General Expectations

To re-iterate the information provided in 'scope' on the previous page, a TA must be in place prior to analysis being conducted. The contract giver or the contract acceptor can instigate the technical agreement and ultimately the responsibility for the format and content of the technical agreement lies with the QP.

The TA should clearly identify the Company providing the contract and the contact details of key contact personnel and also the Company accepting the contract and key contact personnel. Although not necessarily stated in the contract, there should be provision for an annual review of the TA and this should be incorporated into the Self Inspection Process and should also be dealt with through the Change Control Procedure.

2. Requirements of Contract Giver (Client, customer, sponsor)

The contract giver should provide the contract acceptor (Cytogenex Ltd) with methods, specifications and other information required for the contract acceptor to perform the tasks required. It is incumbent on the contract giver to inform the contract acceptor as to changes in methods and/or specifications. The contract giver should make it their responsibility to assess the suitability of the contract acceptor for both the suitability of facilities and resources and the adequacy of the quality system with respect to GMP requirements. The contract giver should name the QC testing site on their license.

3. Requirements of Contract Acceptor (QC laboratory)

The contract acceptor should have a quality system in place that meets the requirements of EU GMP. Medicinal products should be tested according to the principal of EU GMP as outlined in the MHRA Orange Guide. The contract acceptor should not contract work out to a third party without the approval of the contract giver. The time frame within which OOS results and/or Deviations are communicated to the contract giver should be clearly stated in the TA with reference to the appropriate SOP for OOS Results and Deviations.

4. Requirements of both parties and Pro Forma TA

The Technical Agreement should be reviewed by both parties on a regular basis at a period of not greater than about 1 year.

A key representative of both the contract giver and the contract acceptor should sign the document before the Technical Agreement can be made active.

The Pro Forma TA used by Cytogenex is presented in Appendix 1 of this SOP.

5. Schedule of Raw materials for testing

The customer (contract giver) should provide Cytogenex Ltd (contract acceptor) with a list of all substance to be tested, the test that are required and the standard to which samples should be tested (eg. Category 3A and B European Pharmacopoeia).

This information should be provided as an Annex (Appendix 1) to the Technical Agreement.

TECHNICAL AGREEMENT

For Analytical Testing

Agreement between:

CONTACT ACCEPTOR: **Cytogenex Limited,** Unit 16 Argyl Street Unit Factory Estate, Kingston-upon-Hull HU3 1HD

CONTRACT GIVER:

Confidentiality

The Contractor (Contract Acceptor) and Customer (Contract Giver) agree not to disclose this Agreement or any part of it to any third party either in writing or verbally, without obtaining written consent of the other party.

Agreement signatures and dates:

FOR CONTRACT ACCEPTOR (CONTRACTOR)

Signed: ……/Job title: …… Date: …….

FOR CONTRACT GIVER (CUSTOMER)

Signed:…… /Job title:……..Date: ……..

Effective date: ……..

General Terms and Conditions

This is a general agreement giving detailed responsibilities for analytical testing of material or product samples. Any changes to these responsibilities must be agreed, documented and signed by both the Contract Acceptor (Contractor) and the Contract Giver (Customer). The agreement covers all testing performed by the Contractor for the Customer.

This agreement does not cover financial arrangements, which will be made separately depending on the analyses performed.

The Contractor will store and test material at conditions required by the Customer and will report any OOS results and/or deviations within one working day (or for a period defined by the contract giver) of occurrence to the Customer according to the Contractor's SOP for OOS results and Deviations.

The Customer will supply the Contractor with the required Methodological Procedures and the Specifications to be applied and these Procedures should be documented by the customer as Standard Operating Procedures that should be subject to Validation by the Contractor and to review (by both parties), on an annual basis, to ensure compliance of these Procedures with the principals of EU Good Manufacturing Practice.

Any changes to the agreed procedures or specifications, or to this technical agreement, may only be made by mutual agreement between the Contractor and Customer. Such changes must be subject to the Contactor's Change Control Procedure and must therefore be documented.

The Contractor will not sub-contract or assign any responsibilities to a third party without prior written approval from the Customer.

Services supplied by Contractor

Analytical testing of materials as requested by the Customer using methods agreed between the Contractor and Customer as follows:

	YES	NO
Stability storage of starting materials and product at ICH conditions		✓
Chemical analysis of starting materials and product		✓
Microbiological analysis of starting materials and product	✓	
Microbiological analysis of environmental monitoring samples	✓	
Analysis of biological samples from clinical trial or toxicology studies		✓
Other		✓

Initialed on behalf of Contractor……

Initialed on behalf of Customer……

Specific Responsibilities **Contract Acceptor** **Contract Giver**

ASPECT OF WORK	**Cytogenex**	**Customer**
Supply of material/product		✓
Material/product identification and labeling		✓
Supply of safety information		✓
Transport of material/product to contractor		✓
Data supporting storage conditions	✓	
Methodology to be applied		✓
Specifications to be applied		✓
Purchase of reference materials	✓	
Notification of Out Of Specification (OOS) result	✓	
O O S Investigation(s)	✓	
Notification of Deviation	✓	
Deviation Investigation(s)	✓	
Reporting of analysis to customer	✓	
Supply of hard copy of Certificate of Analysis	✓	
Decision on acceptability of product		✓
Destruction of unused material / product	✓*	
**Note: as determined with contract giver*		

Initialed on behalf of Contractor…….

Initialed on behalf of Customer……...

Designated Contacts

CYTOGENEX	CUSTOMER
Chris Newton (Laboratory Manager)	…….. (QP/ Laboratory Manager/QC Analyst)

Initialed on behalf of Contractor……..

Initialed on behalf of Customer……

Appendix 1 Schedule of Raw Materials and Samples to be tested by Contract Acceptor (Cytogenex).

For :

Products to be tested:	Assays required

TVC=Aerobic bacteria/Enterobacteriaceae/Anaerobic bacteria; Y+M =yeast and moulds; Pathogens= E. coli, Staphylococcus aureus, Salmonella species.

Samples to be tested to a Standard of Category 3b, European Pharmacopoeia.

Initialed on behalf of Contractor……..

Initialed on behalf of Customer……

Initialed on behalf of Contractor……..

Initialed on behalf of Customer…….