Entered between

ETABLISSEMENT FRANCAIS DU SANG ATLANTIC BIO GMP (CDMO)

- and –

subcontractor

DATE

This Quality Agreement (“Agreement”) shall become effective when signed by the last party (the “Effective Date”).

SUMMARY

[1. SCOPE 4](#_Toc190081417)

[2. GENERAL 4](#_Toc190081418)

[2.1. Priorities 4](#_Toc190081419)

[2.2. Quality Control sites concerned 4](#_Toc190081420)

[2.3. Duration 5](#_Toc190081421)

[2.4. Severability Clause 5](#_Toc190081422)

[2.5. Entire Agreement/Written form requirement 5](#_Toc190081423)

[2.6. Confidentiality 5](#_Toc190081424)

[2.7. Resolution of Quality Issues 5](#_Toc190081425)

[3. STANDARDS AND LICENSES 6](#_Toc190081426)

[4. AUDITS 6](#_Toc190081427)

[5. SERVICE(S) SUPPLIED 6](#_Toc190081428)

[6. COMPLIANCE – REQUIREMENTS 7](#_Toc190081429)

[6.1. Documentation 7](#_Toc190081430)

[6.2. Controls 7](#_Toc190081431)

[6.3. DELIVERABLES QUALITY NOTIFICATION 8](#_Toc190081432)

[6.4. COMPLAINTS 8](#_Toc190081433)

[6.5. VALIDATION/QUALIFICATION 8](#_Toc190081434)

[6.6. DOCUMENTATION AND RECORDS 8](#_Toc190081435)

[6.7. CHANGE CONTROL 9](#_Toc190081436)

[6.8. DEVIATIONS 10](#_Toc190081437)

[6.9. INSPECTION AND TEST EQUIPMENT CONTROL 10](#_Toc190081438)

[6.10. CERTIFICATE OF ANALYSIS 10](#_Toc190081439)

[7. APPENDICES TO THE AGREEMENT 11](#_Toc190081440)

[8. CHANGE LOG 11](#_Toc190081441)

[9. SIGNATURE 11](#_Toc190081442)

[APPENDIX 1 – OBLIGATIONS AND RESPONSIBILITIES 12](#_Toc190081443)

[APPENDIX 2 – CONTACTS AND ROLES/COMMUNICATION PLAN 13](#_Toc190081444)

This AGREEMENT made as of DATE,

BETWEEN:

**Etablissement Français du Sang Atlantic Bio GMP**

2 Rue Aronnax, 44800 Saint-Herblain

FRANCE

(hereinafter referred to as **« Customers »**)

- and -

**SUBCONTRACTOR**

XXXX

(hereinafter referred to as **« QC Lab »**)

Effective Date

The effective date of this Agreement is **DATE** (the **« Effective Date** »).

# SCOPE

This Agreement outlines the responsibilities and obligations of the SUBCONTRACTOR and the CUSTOMERS with respect to the Quality Assurance requirements of the service(s) XXX (the « SERVICE(S) ») supplied by XXX.

The general and specific responsibilities and obligations of the SUBCONTRACTOR and CUSTOMERS to assure that the SERVICE (S) is (are) performed in compliance with the relevant regulations and standards are outlined in the body of the Agreement and are tabulated in Appendix 1.

The contacts for communication between the parties on subject matters covered by this Agreement are listed in Appendix 2*.*

SUBCONTRACTOR will perform to CUSTOMERS the SERVICE(S) detailed in article 5. The SERVICE(S) will be used for ATMP batches certification by CUSTOMERS.

# GENERAL

## Priorities

The parties entered into a supply contract (“Supply Agreement”) DATE with regard to the SERVICE(S).

In the event of any conflict between the Supply Agreement and this Agreement with regard to quality issues, the requirements of this Agreement shall prevail. For all other issues, the terms and conditions of the Supply Agreement shall prevail.

## Quality Control sites concerned

Unless otherwise indicated in an amendment to this Agreement, all the SERVICE(S) will be carried out at one or more of the following SUBCONTRACTOR sites:

SUBCONTRACTOR Site 1:

XXX

SUBCONTRACTOR Site 2:

XXX

## Duration

This Agreement will commence on the Effective Date and will remain in effect for as long as SUBCONTRACTOR supplies the SERVICE(S) to CUSTOMERS or until terminated in writing by either party.

## Severability Clause

In case any provision of this Agreement is or becomes invalid or unenforceable in whole or in part, such provision shall be invalid without affecting the validity of the remaining provisions unless the invalid provision is of such essential importance to this Agreement that it cannot reasonably be assumed that the parties would have concluded this Agreement in its absence. The parties shall attempt to replace the invalid provisions with valid provisions as closely as possible in line with the original intent of the parties.

## Entire Agreement/Written form requirement

This Agreement, with the exception of the Supply Agreement, constitutes the entire understanding and agreement between the parties with respect to the subject matter hereof and supersedes and is a substitute for all other agreements, contracts and communications between the parties relating to the subject matter hereof, including, without limitation, the previous version of this Agreement, if any.

This Agreement may be modified only by a written instrument duly executed by an authorized representative of each party. Any amendments and/or modifications to this Agreement shall be agreed upon and signed by the parties hereto.

Notwithstanding the foregoing, nothing in this Agreement shall exclude or limit either party’s liability for any untrue statement (whether written or oral) made to it upon which it relied in entering into this Agreement made by either party knowing it to be untrue.

## Confidentiality

The parties agree to keep the terms of this Agreement, the PRODUCT(S) specifications as well as any technical documentation exchanged during the Agreement confidential, except information that is in the public domain or is required to be disclosed pursuant to regulations, authorities or jurisdiction order.

## Resolution of Quality Issues

Quality-related disagreements between SUBCONTRACTOR and CUSTOMERS that are not resolved in the normal course of business shall be brought to the attention of the appropriate Key Contacts, in writing. If both parties agree that a resolution of the disagreement is reasonably possible, then SUBCONTRACTOR and CUSTOMERS shall agree to work jointly to develop a strategy for such resolution. SUBCONTRACTOR and CUSTOMERS further agree to record such resolution in writing.

# STANDARDS AND LICENSES

The regulations and/or standards to be applied as basis for the Quality Management System for the PRODUCT(S) supplied are:

* EU Volume 4, Good Manufacturing Practice for Medicinal Products principles
* European Pharmacopeia; US Pharmacopeia (USP)
* ICH Q2(R2) Validation of analytical procedures

The standards are defined according to the SERVICE(S) supplied.

# AUDITS

1. SUBCONTRACTOR shall maintain an internal audit or self-inspection program.
2. CUSTOMERS has the right to audit SUBCONTRACTOR’s facilities and systems and review documents as they relate to the SERVICE(S). Such inspections and document review shall be conducted by CUSTOMERS at a time, date, and duration mutually agreeable to the SUBCONTRACTOR and CUSTOMERS. Audit frequency shall be no more than 1 routine audit per 2 years, no more than two (2) auditor days per audit (1 auditor, 2 business days or 2 auditors, 1 business day).
3. CUSTOMERS retain the right to conduct reasonable "for cause" audits.
4. Specific goals/scope of the audit, proposed dates and names of the auditors will be agreed upon mutually by CUSTOMERS and the SUBCONTRACTOR.
5. CUSTOMERS will issue SUBCONTRACTOR a confidential written audit report summarizing audit findings within 30 business days of conducting such audit.
6. As requested, SUBCONTRACTOR will issue responses to findings documented in the issued audit report in writing to CUSTOMERS within 30 business days.
7. SUBCONTRACTOR shall notify CUSTOMERS within 2 business days of all regulatory agency inspections that are potentially connected to CUSTOMERS’ SERVICE(S).
8. Additionally, the respective inspection reports or observations that impact CUSTOMERS shall be provided to CUSTOMERS within 2 business days.
9. CUSTOMERS may request documentation for review as part of an audit.

# SERVICE(S) SUPPLIED

ATMP Quality Control testing : XXX.

# COMPLIANCE – REQUIREMENTS

## Documentation

1. Supply of the SOP followed for each analytical method
2. Supply of the validation report of the analytical method for each analytical method.
3. A Certificate of Analysis is required for each sample shipped to CUSTOMERS.

The Certificate of Analysis must include – as a minimum:

* SUBCONTRACTOR name and address, including telephone number
* Sample identification : name of the product, batch number, sample number
* Name of the analytical method and reference of the SOP used to perform the analysis
* Date of the analysis performed
* Validity of result
* Test results (numerical, where applicable) and result interpretation for each test performed

1. Raw data could be supply by customer on demand

## Controls

SUBCONTRACTOR shall:

1. Follow applicable Standards related to the control, and documentation of the SERVICE(S).
2. Operate in compliance with applicable environmental, occupational health and safety laws and regulations.
3. Maintain a quality control unit ("Quality Unit").
4. Involve the Quality Unit in all quality related matters and have them review and approve all quality-critical related documents.
5. According to its quality system employ appropriate facilities, qualified equipment (including softwares) and the required know how and trained personnel to perform the SERVICE(S).
6. Have in place a supplier qualification process for reagent and consumable suppliers.
7. Notify CUSTOMER of the use of subcontractor for any part of the activity subcontracted.
8. Have in place a follow-up policy for its subcontractors in the case where SUBCONTRACTOR subcontracts any part of its activity.
9. Review and approve testing records and certificate of analysis by Quality Unit

## DELIVERABLES QUALITY NOTIFICATION

SUBCONTRACTOR will notify CUSTOMERS of any significant adverse findings that relate to the SERVICE(S) or the facilities used to perform the service(s). A significant adverse finding is herein defined as conditions, practices, or processes that adversely affect or may adversely affect service(S) or results generated by the subcontractor.

SUBCONTRACTOR shall notify CUSTOMERS within 2 business days if SUBCONTRACTOR finds a significant adverse finding.

## COMPLAINTS

SUBCONTRACTOR:

1. Will have written procedures to document, investigate, and respond to all quality-related complaints.
2. Agrees to respond to quality-related complaints in writing within 1 business day.
3. Will assist in investigations as reasonably requested by CUSTOMERS for complaints associated with SERVICE(S) within 30 business days

## VALIDATION/QUALIFICATION

SUBCONTRACTOR shall :

1. Determine, according to SERVICE(S) lifecycle and guidance documents, when process / systems validation is required.
2. Have a written master validation/qualification plan for the facilities, equipment/instruments, analytical procedures and computerized systems, as appropriate. Plan will be approved by the Quality Unit.
3. Develop, prepare, and maintain validation documentation and associated documentation.
4. Qualify as necessary all critical systems and equipment used (installation qualification (IQ), operational qualification (OQ), and/or performance qualification (PQ)).

## DOCUMENTATION AND RECORDS

SUBCONTRACTOR shall:

1. Maintain a controlled system to initiate, review, revise, approve, declare obsolete, and archive all quality documentation
2. Retain all control records for at least 5 years after the end of the clinical trial
3. Have written procedures for the review and approval of all testing documentation
4. Maintain a document control system for specifications and test methods.
5. Provide all the relevant documentation related to the SERVICE(S) to CUSTOMERS for archiving in addition of a complete Certificate of Analysis.
6. Notify CUSTOMER before discarding or returning any vial after CUSTOMER’S decision.

## CHANGE CONTROL

SUBCONTRACTOR shall:

1. Have established written procedures for control of any SUBCONTRACTOR changes that have an impact on the SERVICE(S),
2. Major Changes that could impact the Services require advance notification and CUSTOMERS’ approval prior to implementation. The following list includes (but is not limited to) Major Changes that are likely to require CUSTOMERS’ approval. Where there is any doubt clarification must be sought from SUBCONTRACTOR :

* Change of incoming reagent needed to perform the service(S)
* Change of suppliers of critical reagent
* Change of quality control site of the SERVICE(S)
* Change of test methods and associated equipments

1. Notify CUSTOMERS in writing within 30 business days of intent to make changes that could affect the SERVICE(S).
2. Issue to CUSTOMERS a written evaluation of the change including change justification so that CUSTOMERS can assess the impact of the change.
3. Have a change control process that requires changes to be reviewed and approved by the subcontractor’s Quality Unit.

Other notifications to be reported:

* Company/subsidiary name changes
* Changes in attachments to this Agreement
* Significant administrative changes.

For those changes required to comply with applicable laws and regulatory authority requirements concerning SERVICE(S), SUBCONTRACTOR shall notify CUSTOMERS of such requirements after SUBCONTRACTOR becomes aware of the need for such changes, and vice versa.

## DEVIATIONS

SUBCONTRACTOR shall:

1. Follow procedures for the identification, investigation, and reporting of deviations and out-of-specification (OOS) results.
2. Notify CUSTOMERS of any deviation.
3. Document and explain all deviations, investigate OOS results and all deviations within 14 days. Extend the investigation to other analyses that may have been associated with the failure as appropriate, and include preventive and corrective actions and track these to completion.

## INSPECTION AND TEST EQUIPMENT CONTROL

SUBCONTRACTOR shall establish and maintain a calibration system for control of inspection and test equipment. Calibration standards shall be traceable to National lnstitute for Standards and Technology (NIST), or other recognized bodies recognized by national or international standards. Where this is not possible, SUBCONTRACTOR shall use an independent, reproducible standard.

## CERTIFICATE OF ANALYSIS

A Certificate of Analysis is required for each sample shipped to CUSTOMERS.

The Certificate of Analysis must include – as a minimum:

* SUBCONTRACTOR name and address, including telephone number
* Sample identification : name of the product, batch number, sample number
* Test results (numerical, where applicable) for each test performed
* Reference of the SOP used to perform the analysis

# APPENDICES TO THE AGREEMENT

|  |  |
| --- | --- |
| **APPENDIX n°** | **Description** |
| 1 | Obligations and Responsibilities |
| 2 | Contacts and Roles/Communication Plan |

# CHANGE LOG

|  |  |  |
| --- | --- | --- |
| **Version** | **Reason for update** | **Valid from** |
| 1 | First edition of the Quality Agreement |  |

# SIGNATURE

This Agreement has been made in three original copies with equal validity, whereof the parties take one each.

The Quality Agreement and the related Attachments are signed by the authorized signatures below:

|  |  |  |
| --- | --- | --- |
| **EFS-ABG** | | |
| **Signee** | **Signature** | **Date** |
| Name: K. TERTRAIS  Function : Qualified Person |  |  |
| Name: P Souêtre  Function : QC Manager |  |  |
| **SUBCONTRACTOR** | | |
| **Signee** | **Signature** | **Date** |
| Name:  Function : |  |  |
| Name:  Function : |  |  |

**APPENDIX 1 – OBLIGATIONS AND RESPONSIBILITIES**

**Responsibility matrix**

The following table is outlining the specific obligations and responsibilities when applying the defined regulations and quality standards outlined in this Agreement. Indicate with N/A if not applicable.

|  |  |  |
| --- | --- | --- |
| SERVICE(S) description | EFS ABG | Titulaire |
| Commande | | |
| Purchasing Order | ⌧ | 🞏 |
| Samples –Reagents-Consumables | | |
| Sample shipment | ⌧ | 🞏 |
| Sample Receipt | 🞏 | ⌧ |
| Acknowledgment of receipt | 🞏 | ⌧ |
| Storage condition | 🞏 | ⌧ |
| Testing | | |
| Carrying out analyzes < 1 week from sample receipt | 🞏 | ⌧ |
| Carrying out analyzes in accordance with the study plan | 🞏 | ⌧ |
| Verification of the correct execution of the analyzes | 🞏 | ⌧ |
| Verification of raw data | 🞏 | ⌧ |
| Approval of results | ⌧ | ⌧ |
| Archiving of raw data | 🞏 | ⌧ |
| Sending of CoA by email < BPU | 🞏 | ⌧ |
| Deviation | | |
| Notification in the event of sample receipt delay <24 hours | 🞏 | ⌧ |
| Notification in the event of Deviation – Out of specification result <48H | 🞏 | ⌧ |
| Preliminary investigation in case of OOS result <14 days | 🞏 | ⌧ |
| Notification of change requests related to the service before implementation within 30 business days of intent to make changes | 🞏 | ⌧ |
| Approval of change requests related to the service before implementation | ⌧ | 🞏 |

**APPENDIX 2 – CONTACTS AND ROLES/COMMUNICATION PLAN**

|  |  |
| --- | --- |
| Main Contacts | |
| EFS-ABG | |
| QUALITY ASSURANCE | MANAGEMENT |
| Name: Laurence Trillaud  Address: Rue Arronax 44800 SAINT Herblain FRANCE  Tel. N°: 02 40 44 28 80  Mobile N°:  Email: Laurence.trillaud@efs.sante.fr | Name: Fanny Montoya  Address: Rue Arronax 44800 SAINT Herblain FRANCE  Tel. N°: 02 40 44 28 80  Mobile N°:  Email: Cpdl.AbgCq <cpdl.abgcq@efs.sante.fr> |
| Main Contacts | |
| SUBCONTRACTOR | |
| QUALITY ASSURANCE | MANAGEMENT |
| Name:  Address:  Tel. N°:  Mobile N°:  Email: | Name:  Address:  Tel. N°:  Mobile N°:  Email: |