QUALITY AGREEMENT

Exhibit of the Services Agreement reference ....

Between

Reference & Version Number: CES - 51703

This quality agreement (hereinafter referred to as "Agreement") is entered into by and between:

Zentiva, k.s.
Whose registered office is: U kabelovny 130, 10237 Praha 10 – Dolní Měcholupy, Czech Republic
Represented by: Thomas Koene
ID Number:49240030
hereafter referred to as "the **Contract Giver**".

And
Univerzita Palackého v Olomouci
Whose registered office is: Křížkovského 8, 77147 Olomouc, Czech Republic
Represented by: Prof. Mgr. Jaroslav Miller, M.A., Ph.D. rector
ID number: 61989592
hereafter referred to as "the **Contract Acceptor**".

The **Contract Giver** and the **Contract Acceptor** are hereafter referred to individually as a "**Party**" and collectively as the "**Parties**".

WHEREAS, the **Contract Acceptor** supplies analytical services to the **Contract Giver,** for the pharmaceutical needs of the **Contract Giver**.

WHEREAS, the Parties accept that conformance with generally accepted pharmaceutical principles and rules (cGMP) in Manufacturing Operations are the basic prerequisites for all activities described in this agreement.

WHEREAS, the Parties intend to determine their obligations and responsibilities with regard to their cooperation in the Manufacturing Operations, as outlined in this Agreement.

NOW, THEREFORE, the Parties agree as follows:

(1) 'Affiliates' shall mean any company, which directly or indirectly, controls, is controlled by or is under common control with SANOFI by means of ownership or more that fifty percent (50%) of the voting stock or similar interest in said company.

CONTENTS:

1. PURPOSE

1.1. Scope

This Agreement defines the quality aspects between the entities of the **Contract Giver** and the **Contract Acceptor** with regard to the analytical services provided by the **Contract Acceptor,** hereinafter called "SERVICE", and performed at the facilities of the **Contract Acceptor** as referenced in this Agreement to the exclusion of any other site, for the pharmaceutical needs of the **Contract Giver**.

The **Contract Acceptor's** and the **Contract Giver's** references are detailed in Appendix 1: Administrative information. This section lists each **Contract Giver** entity that is concerned by this Agreement, at its date of issuance; if additional entities need to be added after the signature of this Agreement, this will be managed as an extension through a separate "**Extension Form**" that will be approved by both the **Contract Acceptor** and the **Contract Giver**.

Should a Service Agreement exist, this Agreement is considered as an addendum to the Service Agreement between the **Contract Giver** and the **Contract Acceptor**, and it shall not supersede the terms of the Service Agreement, except when contradictions relating to Quality issues exist (if any), in which case, this Agreement will prevail.

1.2. Duration

This Agreement shall be effective as the date hereof and shall remain into force for an indefinite period of time. This Agreement shall replace and supersede any previous quality agreement(s) on the same subject matter. This Agreement shall be periodically assessed for continued applicability.

Either Party may terminate this Agreement at any time by registered letter with acknowledgement of receipt with a three (3)-month prior notice. The termination of this Agreement shall not affect the rights and obligations of the Parties which have accrued before such termination.

1.3. Confidentiality - Restriction of Use

All matters regarding confidentiality and restriction of use may be defined in a separate confidential disclosure agreement.

2. SERVICES

For each SERVICE supplied by the **Contract Acceptor** to the **Contract Giver**, a separate "SERVICE TECHNICAL SPECIFICATION" or "Work Order" document must be approved by both the **Contract Giver** site(s) which order the concerned activities, and the **Contract Acceptor**'s site(s) which will be involved in the SERVICE.

The corresponding "SERVICE TECHNICAL SPECIFICATION" describes the activities to be completed by the **Contract Acceptor**, quality and technical referential to be applied, acceptance criteria, stability protocol and all other technical information needed to ensure the consistency and reliability of the quality of the activities provided.

The "SERVICE TECHNICAL SPECIFICATION" must be considered as amendment of this Agreement.

The **Contract Acceptor** shall not subcontract any agreed work related to the SERVICE unless authorized in writing by the **Contract Giver**.

In case the **Contract Acceptor** has received approval from the **Contract Giver** to subcontract parts of SERVICE, the **Contract Acceptor** is the ultimate responsible for the fulfilment of the obligations of this Agreement by its subcontractors.

3. CGMP GUIDELINES

The premises, equipment, methods and systems used to supply SERVICE must be in compliance with the principles detailed in (*add / delete, as appropriate*):

- ❑ EU Current Good Manufacturing Practices
- ❑ Applicable local GMPs and Regulations
- ❑ Pharmacopoeias (Ph. Eur., USP)
- ❑ ICH Guidelines

Each **Contract Acceptor** site must have an authorization from its local Health Authority to perform analytical testing on raw materials as well as finished products, for pharmaceutical use.

4. QUALITY MANAGEMENT SYSTEM

A clearly defined Quality management system integrating cGMP requirements shall be designed, documented and implemented by the **Contract Acceptor**.

The **Contract Acceptor** shall maintain and comply with a quality system when performing the SERVICE. The quality system must address, but is not limited to, the following activities:

- Sample receipt, handling, storage and destruction
- Testing
- Analytical validation
- Management of analytical reference standards and reagents
- Management of laboratory documents and records
- Personnel training and qualification
- Equipment/instrument calibration, qualification and maintenance program
- Equipment and instrument cleaning
- Change control management
- Deviation management, out of specification and out of trend investigation
- Management of analytical results, reliability and integrity of the data generated
- Subcontractors and suppliers management
- Risk management.

5. PERSONNEL, HEALTH & SAFETY

5.1. Personnel

The **Contract Acceptor** shall ensure it maintains, in accordance with the cGMP requirements, sufficient qualified staff to support the concerned SERVICE during the whole duration of Service Agreement.

5.2. Health, Safety & Environment

The **Contract Acceptor** shall operate in accordance with all applicable current Health, Safety and Environmental legislation at all sites providing the concerned SERVICE.

6. PREMISES & EQUIPMENT

The **Contract Acceptor** shall perform SERVICE at its site(s) as detailed in the SERVICE TECHNICAL SPECIFICATION.

The premises and equipment used must be in compliance with cGMPs and current local regulatory requirements. The **Contract Acceptor** guarantees the **Contract Giver** that all administrative authorizations necessary to provide the SERVICE have been granted and will be maintained accordingly.

Premises and equipment must be located, designed, constructed, adapted and maintained to suit the operations to be carried out. Premises and equipment layout and design must minimize the risk of errors and permit effective cleaning and maintenance in order to avoid mix-up and contamination of analytical samples. Steps must be taken to prevent the entry of unauthorized people.

In case of microbiological, biological activities and use of highly sensitizing products, toxic materials, cytotoxics, highly active drugs or those related to development, the design and validation of the premises must include the risk related to the material handled.

Lighting, temperature, relative humidity and ventilation must be appropriate to the need. Temperature and ventilation, when required by the analytical work involved, must be monitored and controlled.

A quality agreement must cover any sub-contracted analytical operation related to the SERVICE and any sub-contracted operation such as qualification, maintenance, cleaning or sanitation.

The **Contract Acceptor** and its subcontractors, if any, shall be responsible for ensuring that all equipment is properly maintained and calibrated and that appropriate qualification has been conducted. Equipment should be qualified following IQ (Installation Qualification), OQ (Operational Qualification) and PQ (Performance Qualification) methodology.

Computerized systems generating GMP related data shall comply to both the EU-Good Manufacturing Practices Annex 11.

The **Contract Acceptor** shall maintain a list of equipment. Each item of equipment shall be identified and qualified and the related documentation shall be properly managed by duly qualified people. Adequate controls shall be in place to ensure the integrity of electronic raw data generated by all computerised systems to conduct SERVICE and to prevent unauthorized manipulation of raw electronic data generated by the laboratories.

The **Contract Acceptor** shall maintain the list of persons authorized to use equipment on the basis of records of training and evaluation by relevant management. All access levels for computerised systems must be clearly defined and documented in a written procedure. **Contract Acceptor** must have a list of all employees and their access levels; the list needs to be maintained and kept up-to-date.

The **Contract Acceptor** shall be responsible for keeping records of equipment usage, qualification, maintenance and calibration, reference standards and reagents batch numbers and certification, results and parameters. Such documentation shall be retained by the **Contract Acceptor** (see section 7 Documentation).

Calibration and maintenance of instruments and equipment shall be regularly executed in accordance with standard operating procedures and be under control of the Quality Assurance department.

Any equipment problem must be reported to and the severity assessed by the qualified and authorized person. All equipment must be labelled to indicate the current operational status as per standard operating procedures of the **Contract Acceptor**, such as "Out of order", "being tested" or "not in use".

7. DOCUMENTATION

Documentation package to be provided by the **Contract Acceptor** depending on the service is detailed in the SERVICE TECHNICAL SPECIFICATION agreed document.

The **Contract Acceptor** shall supply the **Contract Giver** with any testing, development, validation or stability data within five (5) business days, if requested as a result of a regulatory inspection, a regulatory submission, an audit by the **Contract Giver**, or a potential exposure such as a recall or a complaint.

The **Contract Acceptor** shall retain at minimum original reports if not provided to the **Contract Giver** and all analytical raw data for the concerned SERVICE, for ten (10) years, unless otherwise longer required by local legislation. The original reports, if any, and raw data, will thereafter be provided upon request within three (3) business days to the **Contract Giver**.

8. MATERIALS

Materials are defined as the products to be tested, the reagents and reference standards needed to conduct the SERVICE, as well as laboratory equipment dedicated to the SERVICE such as chromatographic column.

In view of section 16 – Conflict Resolution of this Agreement, sample quantity should be sufficient to allow three (3) repeat analyses to be done.

8.1. Safety

Both parties will freely communicate any Safety Data Sheets (SDS) or other safety information in its possession regarding possible hazards incurred in handling the products to be tested. Every effort will be made to address the safety of the individual and the environment with regards to the products to be tested.

8.2. Materials procured by the Contract Acceptor

The **Contract Acceptor** shall be responsible for ensuring that all materials procured for use in SERVICE are in full compliance with the agreed SERVICE TECHNICAL SPECIFICATION at the time of use in the SERVICE for the **Contract Giver.**

8.3. Materials provided by the Contract Giver (e.g. reagents, analytical standards) *(If Applicable)*

The **Contract Giver** shall be responsible for ensuring that all materials provided by the **Contract Giver** for use in SERVICE are in full compliance with the SERVICE TECHNICAL SPECIFICATION. The **Contract Acceptor** shall verify the Certificate of Analysis upon receipt, transportation conditions being met and also the identity of the concerned material. The **Contract Acceptor** shall be responsible for ensuring that materials provided by the **Contract Giver** are used correctly.

8.4. Sampling and Sample Management of the product to be tested

The **Contract Giver** will provide the laboratory of the **Contract Acceptor** with samples properly labelled and coded and shipped in adequate conditions for transport.

An identified zone shall be available in the **Contract Acceptor** laboratory, dedicated to the receipt and storage of samples, in accordance with the storage conditions required.

Upon receipt of sample, the **Contract Acceptor** laboratory shall inspect the shipment for damage or loss of environmental control. If any damage or loss of environmental control appears to have taken place, the **Contract Acceptor** will consult with the **Contract Giver** prior to commencing any work on the impacted samples.

A unique unchangeable sample number shall be used for identifying each sample. This unique sample number shall appear on all documentation used to document the required data/information and shall be utilized to track, trend or investigate any quality related issues.

Reconciliation of the sample and the analysis request as described in the SERVICE TECHNICAL SPECIFICATION shall be performed by qualified staff. An analysis number shall be assigned to each sample/test run and properly recorded on each package and working sheet.

The **Contract Acceptor** laboratory shall send an acknowledgement of receipt, which confirms the type of the received sample, the analysis to be performed, feasibility and delays, and comments when necessary.

The **Contract Acceptor** shall retain all remaining samples within adequate storage conditions for a period of three (3) months after the analytical results (unless otherwise specified) are approved and sent to the **Contract Giver**.

In case the **Contract Acceptor** performs sampling on behalf of the **Contract Giver**, specific conditions of this operation must be described in the SERVICE TECHNICAL SPECIFICATION.

9. ANALYTICAL METHOD DEVELOPMENT AND VALIDATION

Analytical method validation or qualification should be conducted according to ICH-Q2 Guidelines, except if different methodology is specified in the SERVICE TECHNICAL SPECIFICATION.

The **Contract Giver** shall approve validation protocol before its implementation by the **Contract Acceptor.**

The **Contract Acceptor** shall provide the **Contract Giver** with a detailed validation report including all individual data, calculation and statistical data if any, as well as summary and conclusions.

All documented evidence of development works, shall be kept by the **Contract Acceptor** for the same time period as the final report (see section Documentation).

10. CHANGE CONTROL

The **Contract Acceptor** must have documented procedures to address change control.

The **Contract Acceptor** is not allowed to implement any change without the prior and written agreement of the **Contract Giver** in the following areas:

- The **Contract Acceptor**'s site in charge of the SERVICE
- Subcontractor used for the SERVICE, if any
- Analytical methods
- Defined SERVICE TECHNICAL SPECIFICATIONS
- Critical characteristics of premises and major equipment

The **Contract Acceptor** must notify the **Contract Giver** in writing of any change in the following areas, as soon as the **Contract Acceptor** obtains definite knowledge that such a change will occur:

- Key positions and organizational chart for Qualified Person or head of Quality Assurance.
- Ownership of **Contract Acceptor** laboratory

Change notifications must be sent to Zentiva via email.
Each notification shall contain a detailed description and evaluation of the effects of the pending change to the SERVICE and the target date for the change. Sufficient time must be allowed for Contract Giver to implement the change and Contract Acceptor needs to consider this when notifying the Contract Giver of changes.

In case of change implemented by the **Contract Acceptor** despite the **Contract Giver** disagreement, the **Contract Giver** will decide whether to maintain or revoke the **Contract Acceptor**'s partnership accreditation, as approved service provider.

11. DEVIATION & INVESTIGATIONS

All deviations from the SERVICE requirements or any out-of-specifications (OOS) or suspect abnormal test results (i.e. OOT out- of-trend) during the testing related to the provided SERVICE shall be fully documented and investigated by the **Contract Acceptor** according to the **Contract Acceptor**'s standard operating procedures.

The investigation must document the impact of any failure on the quality of the provided SERVICE. Each investigation must give rise to a root cause and corrective and/or preventive action which must be reviewed and approved by a person qualified and responsible for quality assurance of the **Contract Acceptor**.

Out-of-specifications (OOS) or suspect abnormal test results (i.e. out-of-trend) related to the concerned SERVICE shall be investigated and documented according to a specific procedure agreed by both **Parties.**

The **Contract Acceptor** must inform the **Contract Giver** within forty-eight (48) hours of any observed OOS or OOT result, identified by the **Contract Acceptor** as non-obvious laboratory error and in every case before initiating a "Full Scale" investigation. The **Contract Giver** may be involved in the OOS or OOT investigation and conclusion.

The **Contract Acceptor** must notify the **Contract Giver** immediately, when problems that may impact the SERVICE previously provided to the **Contract Giver** are discovered.

12. DEFECTS DISCOVERED AFTER SERVICE DELIVERY

Upon discovery that any SERVICE previously delivered fails to conform to Specifications or the Dossier (if any) or has in any way been adulterated, the **Contract Acceptor** shall promptly notify the **Contract Giver** of such failure and of the nature thereof in detail, including, but not limited to, supplying SANOFI with all investigation reports, data, communications, and out of specification reports, and the results of any outside laboratory testing.

Contract Acceptor shall investigate all such failures without delay, at its expense, and co-operate with **Contract Giver** in determining the cause for the failure and the corrective action required.

13. REGULATORY INSPECTIONS

In case of regulatory inspection that involves the concerned SERVICE supplied to the **Contract Giver**, products or related SERVICE, the **Contract Acceptor** shall promptly inform the **Contract Giver** in order to allow, at the **Contract Giver's** option, **Contract Giver** Quality Assurance personnel to be present.

The **Contract Acceptor** shall promptly inform the **Contract Giver** if, following a regulatory inspection, conclusion can impact the quality of SERVICE supplied to the **Contract Giver**, or agreed SERVICE TECHNICAL SPECIFICATION.

The **Contract Giver** will promptly notify the **Contract Acceptor** if during any regulatory inspection of the **Contract Giver** negative comments are made relating to the **Contract Acceptor** or SERVICE.

In either of the above cases, a certified copy of all relevant excerpts of any regulatory report, or letter shall be provided to the other Party within fifteen (15) business days of receipt, if it relates in any way to SERVICE, or the quality systems of the **Contract Acceptor**. The Parties agree to co-operate on any response, as appropriate or required.

14. RIGHT TO AUDIT

The **Contract Acceptor** shall allow representatives from quality assurance of the **Contract Giver** and/or any of its Affiliates to have access to its premises and to the associated records with prior written, reasonable notice for audit purposes.

The frequency of these audits will be periodically realized each two years. The **Contract Giver** will inform the **Contract acceptor** about planned audit minimal two month in advance..

Where significant quality issues are detected, the **Contract Giver** shall be allowed to carry out specific audits designed to lead to resolution of these issues.

The **Contract Giver** shall follow the **Contract Acceptor** systems and procedures to ensure the safety, confidentiality and security of the **Contract Acceptor** processes, facilities and personnel during any audit.

The **Contract Acceptor** shall use a diligent approach to correct any defects identified during audits by the **Contract Giver** and/or any of its Affiliates. A corrective action plan should be provided and approved by the **Contract Giver** in a timely manner. This approach will require a time schedule with defined corrective/preventive actions, which shall be approved by the **Contract Giver** quality assurance where there is an impact on the **Contract Giver** products.

15. COMPLAINTS ABOUT SERVICE

The **Contract Giver** shall be responsible for coordinating the investigation of any complaints related to SERVICES provided by the **Contract Acceptor** and shall notify the **Contract Acceptor** of any complaints, which may impact the quality of the SERVICE and its conformity with cGMP.

The **Contract Acceptor** shall investigate and provide a rapid initial response (i.e. within two (2) business days) and a full report as soon as possible and in any event, to enable the **Contract Giver** to meet any required regulatory timeframes.

If the **Contract Acceptor** receives any complaint directly it shall promptly notify the **Contract Giver** and forward such complaint to the **Contract Giver**.

16. CONFLICT RESOLUTION

In the event that a dispute arises due to analytical SERVICE issues between both **Parties**, resolution efforts will proceed in stages.

In the case of disputes relating to analytical issues, the first stages requires direct communication between analysts from both **Parties** to determine that methods of analysis are the same and are being executed in the same manner at both sites.

Second, carefully controlled and split sub-samples originated from the failed sample should be sent from one site to another in an attempt to reach an agreement. Should there be a failure to achieve resolution, analysts from both **Parties** will be required to meet to work through the analysis of a mutually agreeable sample.

If these actions fail to achieve resolution, and only after these avenues have been exhausted, a qualified referee laboratory will be used to resolve the issue. This laboratory must be agreeable to both **Parties** prior to use. The results from this referee laboratory will be used to determine the final outcome.

The results from this referee laboratory shall be used to determine responsibilities for the costs of the failure, and this shall include costs of external review.

17. RESPONSIBILITIES

RESPONSIBILITIES	Contract Acceptor	Contract Giver
Analytical, Laboratory, Sampling & Testing		
Provide reference standards and/or reagents for laboratory analysis	✓	
Analysis of the PRODUCT	✓	
Retain and store samples of all materials, components and products	✓	
Quality Assurance Activities		
Approval of Analytical Protocols (Stability)		✓
Approval of master documents	✓	✓
Approval to engage the Product concerned by SERVICE in the contract giver manufacture		✓
Sample numbering and traceability	✓	✓
Qualification of any subcontracted facilities	✓	
Approval of any subcontracted facilities		✓
Assurance of correct storage conditions for samples	✓	✓
Testing records and associated documents	COPY as defined	ORIGINAL retained
Approval of OOS and Out Of Trend (OOT) procedure	✓	✓
Failure investigation in case of OOS or OOT	✓	✓
Change control	Request for Approval (SOP Defined)	Approval where required by SOP
Provide data sheet and SDS	✓	✓
Supply all necessary technical and regulatory documentation	✓	✓
Develop and validate/qualify test methods	✓	(✓, if applicable)
Calibrate and Maintain all equipment for SERVICE	✓	
Qualification of all equipment for SERVICE	✓	
Regulatory Documentation		
Establish and update contact with registration agencies		✓
CMC section	Input and data provision	Review and submission
Pre-Approval and cGMP Inspections	✓	✓
DMF, Plant registration licenses		✓
Annual Report (changes, stability data, etc.)	Data provision and review. Final stability report	✓

18. CODICIL

The following are additional provisions or modifications to existing provisions in this Agreement main text.

19. HISTORY OF THE PRESENT DOCUMENT

Date	Quality Agreement reference	Version Nb.	Summary of Changes
10/2017	New document	1.0	---

20. SIGNATURES

IN WITNESS WHEREOF, this Agreement has been duly executed in 2 (two) original editions.

For and on behalf of the Contract Acceptor

Approver	Approver
Name: prof. Mgr. Jaroslav Miller, M.A., Ph.D. [redacted]	Name: .....
Position: Rector [redacted]	Position: .....
Date and signature*: [redacted] 27. 11. 2017	Date and signature**:

For and on behalf of the Contract Giver

Approver	Approver
Name: [redacted]	Name: [redacted]
Position: Quality Director & Distribution QP	Position: Analytical Development Director
Date and signature*: [redacted] 16.11.2017	Date and signature**: [redacted] 16.11.2017
Approver	
Name: Thomas Koene	
Position: Head of Industrial Operations Zentiva	
Date and signature* [redacted] Member of the board of directors of Zentiva Group, a.s.	

* To be signed by the Qualified Person or Delegate or the Quality Representative when the QP function does not exist

** If appropriate, to be signed by the General Manager or Delegate

21. APPENDICES

21.1. Appendix 1: Administrative information

Detail of the **Contract Acceptor**'s legal entity name, the **Contract Acceptor** site name, with corresponding addresses and Quality representative person name(s) and contact information

For Contract Acceptor :	
Site name :	Univerzita Palackého v Olomouci
Address :	Křížkovského 511/8 Olomouc 771 47
Contact person	Name of the **Contract Acceptor**'s Responsible of Quality Assurance: [redacted]
Contact person	[redacted]

Contract Acceptor's site(s) and subcontractor(s) involved in the SERVICE:

Legal Entity	Site name and full address	Health Authority Authorization Reference
To be completed by the **Contract Acceptor**	*Univerzita Palackého v Olomouci, Přírodovědecká fakulta, Regionální centrum pokročilých technologií a materiálů (RCPTM), Katedra analytické chemie, budova RCPTM, R-lab, místnosti č. 228, 324, 325, 326, Šlechtitelů 27, 783 71 Olomouc*	

List each **Contract Giver** site concerned by this Agreement, with corresponding addresses and Quality representative person name(s) and contact information

For the Contract Giver: Zentiva k.s.	
Site name:	Zentiva k.s.
Address:	U Kabelovny 130, Prague, 102 37
Contact person	[redacted]

21.2. Appendix 2: SERVICE TECHNICAL SPECIFICATION

Scope
Analytical analysis of drug product according ICH Q3D

Specific Cautions - NA

Analytical Service - *Analysis of drug product according ICH Q3D,*

Supplies - NA

Specifications – *According order*

Documentation – *CoA, Validation protocols, Validation reports*