R&D Quality Terms and Conditions

These “R&D Quality Terms and Conditions” (“Quality Terms”) are entered into as of the effective date of the services agreement (“Agreement”) which incorporates these Quality Terms by reference and which is entered into by and between the Menarini Group entity (“Company”) engaging you or your company (“Service Provider”) for the provision of R&D services. In the event of a conflict between these Quality Terms and the Agreement, the former will prevail. Company is part of the Menarini Group of companies. For purposes of these Quality Terms, Menarini Group entities engaged in R&D activities are referred to herein as “Menarini Group R&D.”

SERVICE PROVIDER AGREES, AS FOLLOWS:

1. **Definitions:**

1.1 Audit Trail: the automatic logging/documentation of changes and deletions if data in a computer system

1.2 Data Integrity: the attributability, legibility, contemporaneousness, originality, accuracy, completeness, consistency, availability and durability of data (both electronic and paper) over the entire lifecycle of the data, from initial creation to destruction.

1.3 Retention: the application to all records and information, regardless of the medium or location, including but not limited to physical documents and records., electronic documents, and records, business applications, databases, websites, and mobile devices. This also includes documents, records and information managed by subcontractors on behalf of the Service Provider.

1.4 Services: the services the performance of which Service Provider is being engaged by Company under the Agreement.

1.5 Subcontractor(s): Any third-party suppliers, subcontractors, or service providers of the Service Provider, as approved by Company in accordance with the Agreement.

2. **About the Services.**

2.1 Safety and Quality Reporting. Service Provider acknowledges that Menarini Group R&D, including the Company, is required to comply fully and promptly with all regulatory and safety reporting requirements regarding its products. If the Service Provider receives information or inquiries relating to serious adverse events [SAE], product quality complaints [PQC]), or other Menarini Group R&D product safety matters in connection with its performances of Services under the Agreement, Service Provider shall refer any such information or inquires to Menarini Group R&D via email at adverseevents@menarinistemline.com or productcomplaints@menarinistemline.com, respectively. Without limiting the foregoing, Service Provider shall notify Menarini Group R&D within one (1) business day (using the contact set forth above) of learning of any SAE concerning any Menarini Group R&D product of which Service Provider becomes aware including but not limited to experiences reported in clinical trials, experiences reporting in connection with marketed products, and experiences reported in scientific literature, where or not the SAE is consider related to the Menarini Group R&D product.

A “SAE” is defined as any untoward medical occurrence in a patient or clinical trial participant administered Menarini Group R&D medicinal product, which does not have to have a causal relationship with this treatment. A SAE can therefore be any unfavorable and unintended sign (e.g., an abnormal laboratory finding), symptom, or disease temporally

associated with the use of a medicinal product, whether or not considered related to the medicinal product. In addition, the following scenarios are managed as a SAE: overdose, medication error occupational exposure, abuse or misuse, lack of efficacy, unexpected therapeutic benefit, transmission of an infectious agency via the medicinal product, use during pregnancy/breastfeeding, and off-label use including reports of use in pediatric or elderly populations not included in the prescribing information. Service Provider further agrees to participate at its own expense, in any training programs required by Menarini Group R&D concerning product safety reporting as directed in future correspondence by Menarini Group R&D. If the Service Provider is contracted to fulfill specific Pharmacovigilance responsibilities and/or has the probability to receive safety information, additional Pharmacovigilance terms, including a separate Pharmacovigilance Agreement (PVA), may be required; terms pertaining to Pharmacovigilance requirements are set forth in the Agreement.

If the Service Provider is contracted to fulfill specific human clinical trial sample processing responsibilities normal ranges shall be established for safety tests prior to the start of analysis. If clinically significant deviations from the ranges are recorded, a mechanism shall be in place to communicate this information to Menarini Group R&D as quickly as possible. It is always appropriate to consider the need to expedite the reporting of results, regardless of the nature of analysis or evaluation that is being conducted. In all cases, results and observations shall be revered by a qualified person to identify any anomalous or out of specification data and this review shall be performed in a timely manner. In situations where the Service Provider and Menarini Group R&D clinical trials are operating in different time zones in countries with different public holiday allocations, consideration shall be given to how the laboratory would expedite reporting of issues that may impact participant safety or wellbeing. In such situations, the laboratory shall consider the implementation of an agreed out-of-hours communication policy.

2.2 Standard Operating Procedures (SOPs and Facility Policies). Service Provider shall have written procedures that are designated to assure quality and integrity of the data it generates as necessary to execute agreed upon tasks in each Work Order. In the event that procedures or templates of the Menarini Group R&D company sponsoring a clinical trial are to be used, this shall be specified in the relevant Planning Document.

It is expected that these procedures shall be periodically reviewed and approved by a qualified person(s). Revisions to procedures shall be controlled, documented, and approved. If new procedures are issued, or existing ones revised, the need to provide additional training shall be considered, and where appropriate, addressed and documented. The Service Provider agrees to conduct an impact assessment of new/revised procedures as they relate to product/services provided to Menarini Group R&D and notify designated Menarini Group R&D Representatives of any impact of Menarini Group R&D prior to implementation of the procedure. Service Provider agrees to notify Menarini Group R&D of any change, proposed change of physical location of Service provider activities in writing.

Service Provide controlled procedures shall clearly define what constitutes a source document, which must always be archived and retained, and be sufficiently detailed to ensure they can be used to reconstruct any analysis and any subsequent operation performed on the data, during or after analysis.

2.3 Operational Plans. If applicable to the Services being provided, project-specific planning documents (hereinafter referred to as “Planning Documents”) shall be created as deemed necessary by the Service Provider and Menarini Group R&D as required and defined in a written procedure. Plans are to be authorized prior to initiating the specific contracted service(s). Menarini Group R&D shall provide timely review and approval of the Planning Documents, as well as all revisions. Once effective, Menarini Group R&D and Service Provider shall ensure that operational personnel are trained and ensure processes to monitor compliance with Planning Documents are available and followed; and documentation of training and adherence to the Planning Documents shall be retained.

2.4 Personnel. Both Service Provider and Company agree to provide notification of changes of any essential personnel as defined in a Planning Document within 30 days of the change being identified, but no later than the date of change for unforeseen changes.

2.5 Training. It is appropriate for the Service Provider staff to receive periodical GCP training.

2.6 Transfer of Responsibilities. For clinical development services involving transfer of sponsor regulatory obligations, Service Provider shall be responsible for those obligations of a sponsor of a clinical study transferred or delegated by Menarini Group R&D to the Service Provider in the Service Provider’s role as the designated organization as set forth in the Transfer/Delegation of Responsibilities (a “TORO”) under the relevant Work Order.

2.6.1 Clinical Trial Sample Processing. If the Service Provider is contracted to fulfill specific human clinical trial sample processing responsibilities, the Service Provider shall ensure samples are labeled in such a way as to allow their unequivocal identification. A mechanism to track the movement of each sample from arrival to analysis or evaluation shall be implemented and maintained by the Service Provider. Samples shall be transported in such a way that their integrity and viability remain unaffected. This requirement shall apply to all samples whether they are being transported over long distances or between different departments within the same organization. All samples received by the Service Provider shall be assessed on arrival to check their physical integrity. If samples have been compromised in transit Menarini Group R&D shall be notified within five (5) business days. If samples are poorly labeled, missing or if unexpected samples are received, Menarini Group R&D shall be contacted in order to investigate and resolve the issue(s). If the identity of the samples cannot be established, the results shall not be reported.

If information is recorded on the label which compromises the participants right to privacy, the Service Provider shall redact only the necessary details and care shall be taken not to obliterate other details which are needed to identify the sample. It would not be appropriate to permanently delete information on the label if there was no other way of identifying the sample. Service Provider shall monitor storage conditions to provide evidence the samples have been stored in a way that ensures they remain fit for purpose.

Analysis shall be performed using validation methods with defined acceptance criteria, where appropriate. The validation of methods shall be documented by the Service Provider, and on completion, this documentation shall be archived. Relevant storage stability data must be available if samples are to be stored prior to analysis. It is never acceptable to selectively report data; consequently, the rationale for performing the repeat analysis and the reason for the selection of the data points that shall be reported shall be transparent and documented by the Service Provider.

It is particularly important that the Service Provider personnel know to whom they should report anomalous results, which may impact the trial participant safety. The analysis or evaluation of clinical trial samples shall be overseen by a named individual(s) who assumes responsibility for the conduct and reporting of the work.

Service Provider management shall ensure that the staff are competent to perform the techniques required by the protocol, work instructions or associated methods. There shall be a mechanism to ensure that the laboratory is informed in a timely manner of what actions to implement if informed consent of a clinical trial participant is withdrawn.

2.6.2 Clinical Trial Sample Equipment. Equipment shall be regularly maintained by a qualified person and any maintenance documented. Prior to the use, analytical equipment shall be subject to an appropriate level of user acceptance testing, by a qualified person to demonstrate that the equipment is fit for purpose. The requirement shall be periodically inspected, clearned, maintained and calibrated according to a controlled procure or the manufacturer's manual and records of these activities shall be maintained. Equipment calibration shall, wherever appropriate, be traceable to national and international standards of measurement and calibration frequency shall be determined by the Service Provider.

2.6 Risk Management. The Service Provider and Company agree to document risk and issues and agree to develop a risk management plan to oversee and communicate. The parties agree to periodically review, and, as necessary, amend the risk assessment and the mitigation management plans and to communicate such plans to all relevant personnel.

2.7 Management of Subcontractors. Service Provider shall maintain a supplier qualification program and shall be responsible for qualifying all Subcontractors and for reviewing and overseeing the activities of those Subcontractors. The service agreements with Subcontractors shall be maintained and periodically reviewed. A list of approved Subcontractors as well as the subcontracted activities shall be pre-approved in writing by Menarini Group R&D and provided prior to any changes.

2.8 Serious Non-Compliance Notification. Service Provider agrees that in the event of identification of a suspected misconduct, potential fraud, or any non-compliance related to applicable regulations.

Service Provider will inform Menarini Group R&D of any non-compliances that have an impact or potential impact on participant’s rights, safety, data integrity or regulatory compliance during the conduct of any Menarini Group R&D project-related activities.

Service Provider will monitor deviations for trends, conduct root cause analyses, take appropriate action to prevent recurrences, and verify effectiveness of corrective actions taken. Service Provider will follow its internal procedures for investigation and documentation of any noncompliance; and any corrective or preventive actions (CAPA) identified by Service Provider will be documented, traceable, available for audit, and made available for review by Menarini Group R&D prior to finalization. Menarini Group R&D shall have final assignment of criticality. Menarini Group R&D will internalize major and critical non-compliances and the vendor shall promptly provide evidence to support event closure.

Following any verbal communications, a written report that provides a detailed explanation of the issue, activities that have been done to date, and any current action plan being discussed shall be submitted to Menarini Group R&D Quality Assurance (QA) representative. Menarini Group R&D and the Service Provider QA representatives shall assess whether a serious breach of GCP or other reportable event has occurred and shall determine the course of action. Service Provider management shall provide follow-up status reports on a mutually agreed cycle until the conclusion of the issue. The Service Provider shall not report Serious Breaches on behalf of Menarini Group R&D.

2.9 Inspections by Health Authorities and Audits. Service Provider agrees to full disclosure and communication of any regulatory inspection/inquiries directly related to the services performed for Menarini Group R&D. Service Provider shall notify Menarini Group R&D within one (1) business day of the initiation of a regulatory agency inspection directly related to Menarini Group R&D product or service. Service Provider agrees if a FORM 483, Warning Letter or similar regulatory document, having a regulator compliance effect on a Menarini Group R&D product/service is received the Service shall notify Menarini Group R&D within one (1) business day.

Service Provider shall notify Menarini Group R&D of audit observations related to Menarini Group R&D activities from internal audits or observations identified by external parties that are relevant to the services provided to Menarini Group R&D. All critical or major observations shall include an assessment of impact to Menarini Group R&D activities. This includes Corrective and Preventive actions (CAPAs), quality events, proactive initiatives, investigations, or issues.

2.9.1 Menarini Group R&D Audits. Menarini Group R&D reserves the right to audit Service Provider's facilities and processes at the beginning of an engagement, and then routinely. The right to audit includes any subcontractors utilized by Service Provider. "For Cause" audits can also be conducted in addition to regular audits (e.g., in response to identification of a known or potential quality issue) with expedited scheduling. Service Provider will allow Menarini Group R&D auditors and technical subject matter experts (SMEs) to review all data generated in support of Menarini Group R&D studies, including raw (source) data, processed data, and all metadata including audit trails and will not delay, deny, limit, or refuse to provide Menarini Group R&D auditors or SMEs access to complete source data, metadata, and/or records that support Menarini Group R&D studies.

2.10 Key Quality Indicators (KQIs) and Metrics. If requested, the Service Provider and Menarini Group R&D representative shall identify applicable KQIs and metrics to be reported

and define the frequency of reporting in the Work Order. Penalties and the escalation process for failure to meet KQIs and metrics shall be specified in the Work Order. Changes to the individual KQI or metric, or changes to the reporting requirements shall be identified in the Work Order. Both parties shall review KQIs to evaluate where target goals have been achieved. If target goals were not achieved,or if the metrics suggest significant risk of non-achievement, Menarini Group R&D and Services Provide shall investigate. Once the evaluation has been completed on a periodic basis Service Provider shall forward KQIs and documentation of review to Menarini Group R&D. Should any issues be identified through KQI review that require immediate attention, the Service Provider shall escalate to Menarini Group R&D as described in this document. Documentation of KQI review and with any pertinent documentation related to the evaluations and actions shall be maintained and filed by Menarini Group R&D or Service Provider.

Service Provider and Menarini Group R&D shall track agreed quality metrics and issues within and across Menarini Group R&D work orders to identify patterns or trends. Service Provider and Menarini Group R&D shall undertake necessary investigations to determine the root cases(s) of identified quality issues and shall ensure that appropriate actions are taken proactively to prevent further recurrence. Proactive corrective and preventive actions may include organization wide team communications, Menarini Group R&D/Service Provider system process improvements, further training/retraining of staff, or other measures. Service Provider and Menarini Group R&D shall perform effectiveness checks to ensure that the issues are mitigated and have not recurred.

2.11 Records Storage. Service Provider's controlled procedures shall clearly define what constitutes a source document and data, which must always be archived and retained and be sufficiently detailed to ensure that it can be used to reconstruct any activities or analysis and any subsequent operations performed.

2.12 Computerized System. Computerized systems used for the capture, processing, reporting, and storage of data by Service Provider shall be developed, validated and maintained in ways which ensure the validity, integrity and security of the data. Service Provider shall maintain Part/Annex 11 compliance and controls to safeguard the authenticity, integrity and where appropriate the confidentiality of electronic records. Controls shall include audit trails, audit trail review, access management, integrity and security controls, incident management and escalation processes, configuration and patch management, archiving and migration of data systems, disaster recovery, and data backup and restoration.

Prior to use, computerized systems used at the Service Provider for Menarini Group R&D activities shall be validated to demonstrate that the computerized systems is fit for its intended use and can produce reliable and consistent data. Validation shall be performed in accordance with a documented plan and all key aspects of the validation process shall be documented. For each computerized system, the components (e.g., hardware and software) which contribute to the system shall be clearly defined. This information shall be documented with the associated validation package. If additional functionality is utilized beyond the scope of the original validation, the need to perform additional validation shall be required and documented. Once a computerized system is deemed fit for use, the decision shall be documented and approved by the Service Provider, with any limitations of the

systems clearly documented. The Service Provider shall provide Menarini Group R&D a description or diagram of the electronic data flow between computerized systems.

If changes are needed to a computerized system, such as a system upgrade or installation of ”patches”, the need to revalidate the computerized systems shall be determined. The Service Provider shall perform a documented risk assessment, when needed, to determine what level of re-validation is required. Following any re-validation activities, if it is deemed that the computerized system remains fit for use, the decision shall be documented and approved by the Service Provider.

If the computerized system has been in use for some time, but has never been subject to any formal validation, a retrospective assessment of the suitability shall be justified, performed, and documented. If the computer system is made obsolete, the system and its associated validation documentation shall be archived.

Logical and physical access to Service Provider’s computerized systems shall be controlled, tracked, and managed. Computerized systems shall be sited in locations with controlled environmental conditions. The identity of those with specific access rights to computerized systems shall be documented and subject to periods of review to ensure that the access restriction remains correct and appropriate. Also, there shall be external security safeguards in place to prevent, detect, and mitigate effects of computer viruses, worms and other potentially harmful software code on data and software. The Service Provider agrees to conduct impact assessments of information technology infrastructure changes and notify Menarini Group R&D of any potentially significant findings prior to implementation.

The Service Provider shall provide Menarini Group R&D with access to documentation related to computerized system validation, audit trails, user access control, issue management, and change notifications. If the Service Provider uses documentation within a Subcontractor’s validation package as evidence of computer system validation, the Service Provider shall provide Menarini Group R&D access to Subcontractor’s documentation used as evidence.

If a computerized system is discontinued or supplanted by a newer (possibly incompatible) computerized system, the Service Provider shall retain the ability to retrieve and review the data recorded by the older system. If a computerized system is discontinued, the Service Provider shall provide Menarini Group R&D with access to the archived validation documentation.

If Menarini Group R&D data is migrated from one computerized system to another computerized system, the Service Provider shall notify Menarini Group R&D of the change and provide the data migration plan prior to implementation. Once implemented, the Service Provider shall provide evidence of successful migration.

2.13 Qualification and Validation of SaaS Tools. Menarini Group R&D shall provide written requirements to Service Provider for Menarini Group R&D instance configuration (to be implemented in the relevance implementation service order) and validate against such requirements prior to use. Menarini Group R&D shall establish, implement and maintain written procedures for the account authentication and authorized services to enable and

disable accounts. Menarini Group R&D shall perform documented validation to support the performance qualification of service during the preview period provided as part of the service release.

2.14 Business Continuity Plan/Disaster Recovery Plan (BCP/DRP). Disaster recovery and business continuity-controlled procedures shall be implemented and periodically tested for all Service Provider infrastructure and computerized systems. It is necessary for Service Provider to maintain documented policies, which shall describe the procedure that would be followed in the event of a system failure including description of the measures that would be taken by Service Provider to recover data. Service Provider agrees to notify Menarini Group R&D no later than one (1) business data after the need to implement a BCP or DRP in the case of natural disaster or other business disruption. Service Provider agrees to keep current and updated such plans and make them available to Menarini Group R&D during audits. In the event that Service Provider and Company stipulate business continuity terms for purposes of another agreement pertaining to the Services (e.g., a PVA) and those terms are in conflict with the terms above, the stricter terms will prevail with respect to the subject matter of this section.