Site Master File (SMF)

Harmonized with
Pharmaceutical Inspection Co-operation Scheme (PIC/S)
PE 008-4, Annex 1, January 01, 2011

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An integrated QMS based on ISO 9001-2015 & 21 CFR Part 210 & 211 (cGMP)

Solésence, LLC / Nanophase Technologies Corporation

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Romeoville, Illinois 60446

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PREPARED AND MAINTAINED BY
QUALITY ASSURANCE DEPARTMENT

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0.1 APPROVALS

APPROVALS	DATE
_____ Prepared By	
_____ Reviewed By	
_____ Director, QA	

0.2 REVISION HISTORY

Quality Manual Revision #.	Date	Section	Page	Amendment	Authorization
000	08/20/19	all	all	Original .	MNA
001	03/04/21	4.1	12-18	Updated equipment/layout	MNA
002	10/20/2021	Appendix 3,5 & and 6a	32,35,36	Added ISO 22216 certification. Added updated Org chart. planning Updated Facility diagram.	MNA
003	11/22/2021	Section 1, 3. Appendix 6, 5, 8	4, 11, 36,38,39, 40,41,44	Added Appendix 6b-1, 6b2, 6c, and 6d. updated Org chart. Updated number of employees. Updated equipment list.	MNA
004	1/22/23	F/A, WH sections	various	Removed previous Warehouse maps and operations. Indicating move of F/A processes and WH	MNA
005	1/24/23	1.0	4, 34	Updated Customer Relations contact Information. Updated Org chart	MNA
006	1/2/2024	4.1 (e), 4.2	16, 17, 40	Added USP water system. Updated Appendix 8 (page 40)	MNA

1.0 GENERAL INFORMATION ON THE MANUFACTURER

1.1 Contact Information on the manufacturer

Corporate head office is located at Romeoville, IL in a standalone structure, building and its operation are not shared. The total covered area is roughly 35,000 SF with total premises are about 65,000 SF. Other location dedicated to Zinc Oxide API is located at 453 Commerce Street, Burr Ridge , IL 60527.

Solésence/Nanophase recent addition is located at Bolingbrook, IL in a standalone structure, the total covered area is roughly 265,000 SF, this facility is being constructed to house all Filling/Assembly, Dispersions/Lotions/API powders processes, laboratories, warehouse, and offices. Warehouse in operations, manages storage of Raw Material, Work -in-process (WIP) and Finished Goods along with all Shipping and Receiving processes.

Name and Address of Site
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24 hour number
Facility main number, 630-771-6700 is manned during business hours (8-5 M-F), CDT. Calls received after hours can be recorded on the voice mail. For emergencies related to the materials shipped, both domestic and international 24-hour contact information is provided on the relevant Safety Data Sheet (SDS).

1.2 Authorized pharmaceutical manufacturing activities of the site

Solésence/Nanophase produces Active Pharmaceutical Ingredients (API) in powder & liquid forms and semi-solid/solid dosage form of OTC-topical products for human use only. Other processes include packaging & assembly of finished sunscreens as "White Label Products" that are marketed under various Private Label Distributors (PLD). The site is registered with US FDA and annual renewal are kept current.

Solésence/Nanophase operates onsite QC laboratory and routinely performs USP tests as applicable to certain API. Method adopted from current USP are considered validated, however, suitability studies are performed on applicable. Non compendial methods are developed in house and method/instrument validation are executed. Nanophase managed all stability storage and testing based on ICH guidelines in-house. Microbial testing is performed at authorized FDA registered laboratories and the testing follows the USP methodologies.

1.3 Any other manufacturing activities carried out on the site

Under Nanophase name, several industrial grade metal oxides and dispersions are manufactured and distributed to both domestic and international customer.

2.0 QUALITY MANAGEMENT SYSTEM OF THE MANUFACTURER

2.1 The quality management system of the manufacturer

Solésence/Nanophase quality management system is based on and in compliance with ISO 9001-2015 and cGMP 21 CFR Part 210 and 211 and 21 CFR Part 11 as selected for specific requirements under cGMP. In addition, Solésence/Nanophase fully complies with all legal requirements related to the product and services it offers and any contractual/quality agreements mutually agreed with its suppliers and customers. Compliance to all applicable safety and environmental regulations is an integral part of the Solésence/Nanophase management system, processes and products.

With regards to cGMP compliance Solésence/Nanophase recognizes the importance of FDA guidance documents, such as Q7A and others and uses these guidance documents as applicable to its quality management system. Guidance documents are not regulations and should be consulted based on business needs, customer requirement and in cases where legal regulations do not provide an effective method for implementation of certain cGMP elements.

Solésence is Nanophase wholly owned subsidiary and it is operated under all applicable quality, safety, environmental, and legal requirements as established under Solésence/Nanophase Technologies Corporation.

Solésence/Nanophase on a routine basis, monitor and address internal and external issues related to its business. Example of external issues generally includes development of products and services based on current market trends and applicability of Solésence/Nanophase

technologies and products, IP, compliance to regulations related to domestic and international domains, and supporting current customer needs.

Internal issues are focused on employee retention (talent/knowledge), empowerment at departmental cross functional levels, performance monitoring and corrections based on KPI. Solésence/Nanophase is committed to establish, document, implement and maintain a quality management system, and continually improve its effectiveness, in conformance with requirements of ISO 9001-2015 International Standard and current Good Manufacturing Practices (cGMP) 21 CFR Part 210 and 211. Solésence/Nanophase QMS is documented in **QMS-000**.

2.2 Release procedure of finished products

Products are released for delivery only after all specified activities have been satisfactorily completed and conformity of the product has been verified. Operational Procedure **QP-825**, Final Inspection, defines the system for final product verification and release. QA/QC is authorized and responsible for all product releases, rejections, and management of delivery under quarantine (if applicable).

Director of Quality and Regulatory Compliance is responsible for setting, procedures, roles, and responsibilities of QA/EHS staff in compliance with 21 CFR Part 211.22 as listed below;

"Quality department and has the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging material, labeling, and drug products, and the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated. The quality control unit is responsible for approving or rejecting drug products manufactured, processed, packed, or held under contract by another company."

"The quality control unit has the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the drug product."

For decision affecting the release of materials for FDA application (as required under 21 CFR Part 211.22) only QA/QC staff is authorized to release product for distribution and use. There are cases when Engineering trail materials, R&D development batches, and/or industrial grade products may be evaluated, released, and distributed/used by respective departments as needed. Normally, any product with a defined specification and testing performed by Quality department is release by Quality staff. **(Ref SOP: QA-700)**

In any circumstance, manufacturing, R&D, and/or Engineering and any other department within the company are not authorized to assume a function of releasing.

QA/QC staff is competent and knowledgeable via work experience, training, and/or education. Minimum qualification for QA/QC staff is 4-year college in related scientific discipline.

An approved Master Batch Record is used for all drugs and API manufacturing with 2 level of supervisory review and approval by manufacturing followed by 2 level review and approval by QA/QC.

2.3 Management of suppliers and contractors

Solésence/Nanophase Technologies Corporation conducts a supplier partnership program that encourages high performance on the part of its suppliers. Augmented by sound receiving inspection practices, Solésence/Nanophase Technologies Corporation maintains high confidence that purchased product conforms to specified requirements.

Supplier evaluation

Critical new suppliers are evaluated with regards to their quality and process capability. Critical suppliers are defined as suppliers whose products are consumed in the process or have direct contact with finished products. Purchasing and Quality Assurance establish the criteria for selection of suppliers, and conduct supplier evaluation. Suppliers are rated APPROVED or PENDING. The Approved and Pending suppliers are entered on the approved supplier list. Existing suppliers with a satisfactory quality performance history are exempted from the initial evaluation and are initially rated as APPROVED or PENDING. Records of the initial supplier evaluation are maintained. Supplier evaluation process is governed by Procedure **QP-741**, Supplier Evaluation

Supplier quality performance monitoring

Quality performance of suppliers is monitored. Suppliers showing inadequate performance are notified annually and asked to implement corrective actions and are downgraded to the PENDING rating. If the requested corrective actions are not implemented and there is no improvement, the supplier is further downgraded to the NOT APPROVED rating and is discontinued. Records of suppler monitoring and reevaluations are maintained. The system for monitoring suppliers is defined in Procedure **QP-741.**

Outsource suppliers are located in the critical supplier category. They are evaluated on their ability to produce a product or provide service that is equal to the product or service provided by Solésence/Nanophase Technologies processes or services.

Approved supplier list

Purchasing maintains an approved supplier list for critical raw materials and supplies. Orders are only placed with vendors that are on the list.

Information for external provider (*Purchasing information*)

Solésence/Nanophase Technologies Corporation purchase orders require that the originator include where applicable:

a) precise identification of product ordered.

b) positively identified specifications, drawings or other technical documents required to establish full acceptability; and
c) pertinent standards and codes including quality system standards by title, number, and issue.

Verification of Purchased Product

Solésence/Nanophase Technologies Corporation's purchasing policies provide that a decision not to inspect incoming material or the failure to detect a supplier-generated nonconformity before receipt does not relieve the supplier of responsibility for quality of the supplied goods.

Critical key purchased products are inspected by quality control. This includes verification of product identity and quantity, visual inspection and, where applicable, verification that all requested certificates and quality records are available. Designated products are further inspected or tested by QC.

QC inspection or testing is not necessary when products are supplied with records or certificates demonstrating conformity; or when the supplier is qualified based on their quality system certification or supplier audits, and a satisfactory quality performance history.

Supplier Verification at Subcontractors

Solésence/Nanophase Technologies Corporation may stipulate in any contract that purchased material is subject to source inspection. When electing to do so, the details for such an inspection and subsequent release of accepted material is stated in the purchase agreement.

Quality Assurance is responsible for selecting appropriate methods for purchased product verification and acceptance. Operational Procedure **QP-743**, Verification of Purchased Products, sets forward detailed rules for selecting product verification methods and for performing receiving and QC inspections.

When verification of purchased product is to be performed at supplier's premises, purchasing documents specify the intended verification arrangements and method of product release.

Outsourced processes

When processes that affect product conformity are outsourced, special controls are implemented to ensure that these processes meet specified requirements. Such controls may include, as appropriate: evaluation and pre-qualification of suppliers; assessment of supplier realization processes and quality system; monitoring of supplier quality performance; requirements for inspection, testing or other records demonstrating product conformity; or containment and verification of the supplied product. Section 8.4 of this quality manual and the corresponding operational procedures define such a purchasing control system.

Supporting services

Supporting services required by Solésence/Nanophase Technologies include transportation, communication, and IT services:

Transportation services are usually purchased from parcel delivery and courier services, and from trucking or other transportation companies or consolidators. Purchasing of these services is managed by Shipping and is conducted in accordance with operational procedures **QP-741**, Supplier Evaluation, and **QP-742**, Purchasing.
Communication services are provided by various telephone, wireless, and internet access companies. Purchasing and Human Resources is responsible for administrating and coordinating these contracts.
IT systems are designed and implemented by internal IT group and are operated internally by Human Resources. If external IT support is necessary, IT consultants are selected, and are contracted with, in accordance with applicable purchasing procedures (**QP-741 and QP-742**).

2.4 Quality Risk Management

General

Assessment of Risk and opportunities are integral part of product, processes and service provisions (when applicable). Risk assessment is normally carried out during product development, change control, management review process and by other mechanism for elements that are critical to Solésence/Nanophase business, Risk Assessment process is defined under **SOP NTC-300**.

Improvements and risk based approach

Solésence/Nanophase Technologies Corporation deploys continual improvement philosophy throughout the entire organization. The quality and EH&S systems are designed to incorporate all elements necessary to identify opportunities for improvement and to implement improvement projects. An approach for improvements is provided in **QP-851** while maintaining a balance between risk and reward. Risk assessments activities are carried through **NTC-300** and review of risk and opportunities are presented in Management Review (**QP-561).**

2.5 Product Quality Reviews or Annual Product Reviews (APR)

On an annual basis, quality records related to all components, containers, closures, and labeling are used for evaluating, at least annually, the quality standard of each drug product to determine the need for changes in product specification, manufacturing, or control procedures. This review is recorded in form **QP-562A & B** by complying with cGMP 211.180 requirements.

The following criteria is utilized to complete form **QP-562A**;

- "*A review of representative number of batches; whether approved or rejected, each product must have at least one batch included in the annual review." (21 CFR 211.180 (e) (1).* ***NOTE****: Different products are not grouped by "similar processes" or any other similar approach.*
- *"A review of complaints, recalls, returned or salvaged products, and investigation conducted under 211.192 for each product." (21 CFR 211.180 (e)(2).*
- *Any investigation conducted under 21 CFR 211.198, 211.204, 211.208, and any recalls, reports of inspectional observation issued by the FDA, or any regulatory actions relating to cGMP brought by FDA are submitted to the Senior Leadership Team*
- *A summary report is generated (****QP-562B****) to record various elements as related to a specific drug product(s).*

3.0 PERSONNEL

3.1 Organization Chart

The organizational chart in **Appendix 5** provides for the independence of all who manage, perform, and verify work affecting quality. That work includes the following activities:

- preventive action for the products, the processes and the quality system.
- detection of any problems in the products, the processes and the quality system.
- problem-solving participation.
- verification of corrective actions; and stop shipment.

Attachment 1 reflects the most current version of Solésence/Nanophase Technologies Corporation functional organizational chart. Departmental organization charts are the extended version of this attachment and are not included with SMF.

Employee

Solésence/Nanophase Technologies Corporation employees a permanent staff of +40 at this site, with the breakdown for each departments as listed below;

- Manufacturing: +12
- Quality Control/Quality Assurance: +10
- Shipping/Warehouse: None
- Engineering & Maintenance: +7
- Research and Development: +12
- Sales/Marketing/Business Development: +10
- Finance/HR/Administration: +6
- Note-All disciplines Excludes off-site staff

4.0 PREMISES AND EQUIPMENT

4.1 Premises

Solésence, LLC/Nanophase Technologies Corporation is situated on four acres at 1319 Marquette Drive, Romeoville, Illinois. Approximately 36,000 square feet of the facility is under one roof, and there is 126,000 square feet of impervious surface on site. This is a manufacturing facility that produces metal oxide powders and dispersions, API surface treated powders, metal oxide dispersions, and sunscreen formulation in solid, and semi-solid forms. Solésence, LLC/Nanophase Technologies Corporation operates under the regulatory requirements as mandated by FDA, IEPA, OSHA, and DOT.

The site is registered with FDA as API Manufacturer, Manufacturer, and Packaging and drug products are notified under Drug Product Listings of FDA.

Facility layout is shown in **Appendix 6,** which includes areas used for metal oxide manufacturing, API manufacturing, bulk sunscreens, dispersions manufacturing, S&H, Offices, R&D and QC laboratories, storage of flammables, secured access points for entry to the site, location of EHS related equipment.

REGULATORY STATUS

Nanophase Romeoville sites is registered with FDA and applicable products are submitted to FDA under Drug Product Listing. The white label lotions (bulk sunscreens) are produced under private label for various customers.

All air emission sources have been identified and permitted according to the IEPA rules and regulations and reporting requirement of state and federal EPA.

Nanophase practices and promotes a safe work environment for its employees by following the OSHA requirements and applicable Best Industry Practices.

Comprehensive ingredients review and approval program (**SP-02-1500**) is in place to authorize only safe, effective, and regulatory suited ingredients to final formulations.

REACH (Registration, Evaluation, Authorization and Restriction of Chemical substances) compliance is followed for EU market, as applicable. Nanophase has secured "LTS" as REACH "***Only Representative (OR)***" in Europe. Nanophase has completed and/or secured via downstream suppliers, the registrations of selected metal oxide and other solvents, monomers, and dispersants.

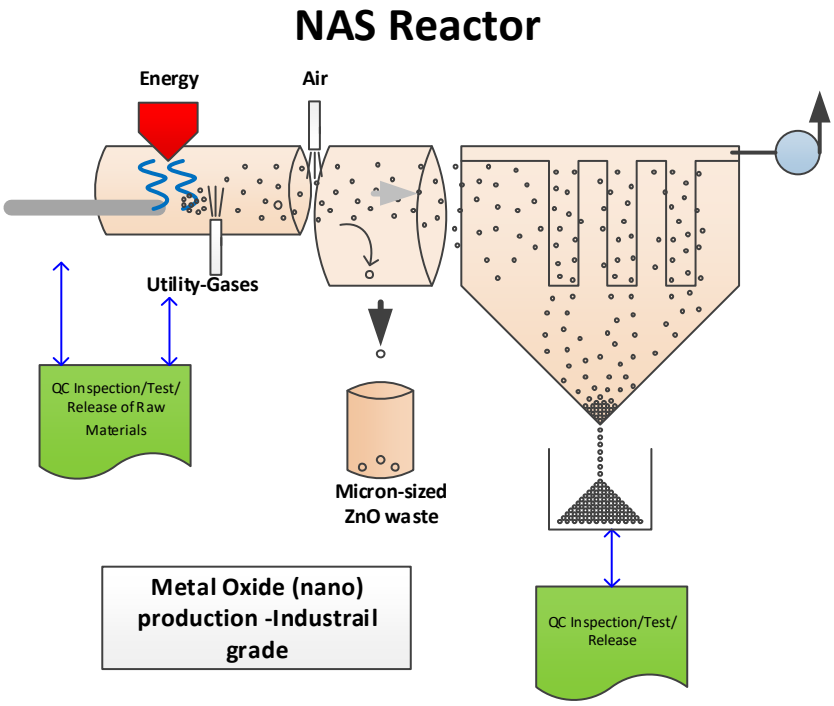
Key registration information

- FDA DUNs# **623502044**
- FDA Labeler code# **063931**
- FDA establishment ID# **3003574860**

DESCRIPTION OF CORE MANUFACTRING

(a) NanoArc® Synthesis (NAS)

Two NAS production lines are located in central plant 1200 SF area, the NanoArc® Synthesis (NAS) method employ transferred and non-transferred electric arcs to vaporize precursor materials, which are then carefully condensed to produce nanoparticles with desired properties. These methods have been used to produce both simple and complex, multi-component mixed metal oxides. NAS reactors are operated in a closed system fashion and do not allow generation of fugitive dust. This process is not validated for API and drug products.



(b) Surface Treatment (aka coating) processes

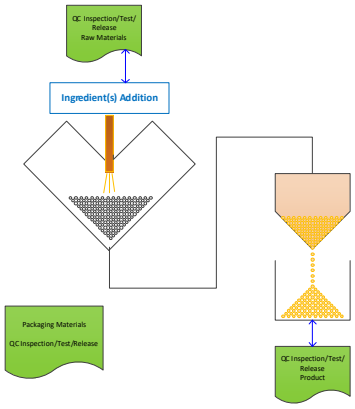
Surface treatment (aka coating) processes are carried out in PK-100 and LD-600 solids processors. PK-100 solids processor, 100CF capacity, is installed in two levels segregated brick walled room with steel ceiling, room is approximately 1100 SF in area. Room is kept under positive pressure *(+0.05 In.w.g*) to limit contaminants from general plant side. PK-100 is housed in Class1 DIV 2 classified.

LD-600 Plow blender/solids processor, 600L capacity, is installed in dispersion Room alongside with P-098, Dispersion Room also housed P-097, P095, and P-099.

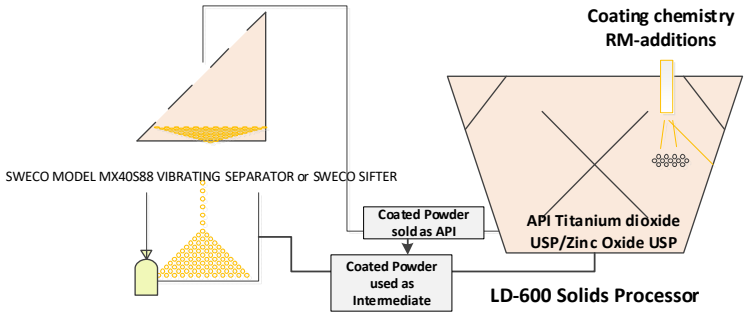
Nitrogen gas is brought inside from the liquid nitrogen bulk tank located outside the building Steam heating unit is located in a separate room within the plant. Solvents (process waste) are pulled through the condenser and collected in solvent vessel.

PK-100 and LD-600 have been validated (IQ/OQ) with process validations in place for API manufacturing. This equipment are NOT shared with industrial grade products.

PK-100 Surface Treatment Process



Surface Treatment Process LD-600



(c) White Label Cosmetics, Topical Drug Products process (bulk sunscreen/skin protectant manufacturing) and dispersion processes for API and Industrial grade) products

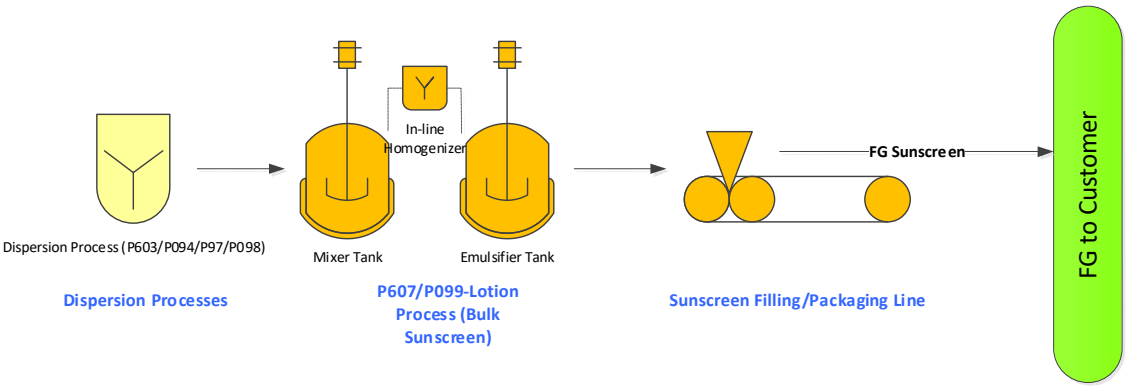
Small scale lotion production (P607) is located adjacent to the main dispersion area. The lotion room housed several 20-80 jacketed tanks fitted with mixers and in-line homogenizer. The room is approximately 400 SF in area and it is constructed of dry wall, semi reinforced with poly panels with drop ceiling. Floors are epoxy coated.

Large scale lotion or cream production (P099) is located within the main dispersion room, which is classified as CLASS 1 DIV 1. Lotion process includes several 20–300-gallon jacketed tanks fitted with mixers, in-line homogenizer, pumps and other processing equipment. Other processing equipment includes several 150-300 Gallon jacketed tanks, centrifuges, and associated chemical processing equipment. All processes are designed to prevent cross contamination and mix up of products. Powder drug products are also produced in dispersions room using LD-600 or other powder processing equipment as applicable.

The dispersion room is approximately 3100 SF in area and it is constructed of bricked wall, semi reinforced with poly panels with drop ceiling. Floors are epoxy coated.

Large scale lotion line, installed at west wall of the Dispersion room, supported by powder coated steel frame (pharma grade paint) with elevated walkways.

Lotion equipment has been validated (IQ/OQ) with process validations in place for API or drug manufacturing. This equipment is not shared with industrial grade products. Rooms are kept under positive pressure *(+0.03 In.w.g*) to limit contaminants from the general plant side.



(d) Heating, ventilation, and air conditioning (HVAC) systems

Office and lab areas maintained by several rooftop units. Process areas are serviced by air handlers with filters, chilled water cooling and steam heat. Lotion room is fitted with 14 ton capacity and high efficiency filters; Surface Treatment Area (PK-100) and Dispersions area supplied with 4,000 cfm air handler with chilled water cooling.

Densely populated work areas within the facility are recently outfitted with MERV 13 filters with inline ionizers to guard against the spread of the COVID-19 virus.

SOP MFG-02-021 is used to address HVAC Filter Monitoring and Change schedule.

(e) Water systems

Facility operates a validated EVOQUA DIRS10PPUV43x PURIFIED WATER SYSTEM – DIRS Recirc Skid to support cosmetic, drug and API manufacturing processes. Purified Water meets USP Purified Water (non-sterile). Measurements that are critical to final water quality include the following:

Parameter	Sampling Mode	Reference
Conductivity	inline	USP <645>
TOC	inline	USP <643>
Bioburden	Grab and Rapid Micro-inline	USP

After the PWS has been placed into operational use, monitoring of the water quality attributes and the system process parameters are performed on a routine frequency to ensure that the PWS remain within a state of control during long-term variability from seasonal variations in source water quality, unit operation maintenance, system sanitization processes, and established Alert and Action Levels. The PWS is continuously monitored and evaluated following a life cycle approach using online instruments and process automation technology, for conductivity, TOC, Rapid Microbiological Method (RMM), flow rate, and pressure to facilitate operational control of the attributes and parameters and for process release.

The Rapid Microbiological Method (RMM) – 7000RMS microbial detection analyzer offers a real-time microbial monitoring solution, providing continuous results every two seconds for better control of your water system. The 7000RMS rapid bioburden analyzer uses advanced, laser-induced fluorescence and Mie scattering technology to provide immediate detection and quantification of microorganisms. The real-time analyzer helps in identifying the root cause of contamination events. Rapid micro is selected to monitor bioburden and the alert and action limits are established per USP <1223> criteria.

In addition, to PWS controls (UV lamp, 0.2 µ Filters and continuous recirculation), the PWS is chemically sanitized every week using Minncare. System sanitization is performed by the manufacturing department.

(f) Steam, compressed air, compressed gases

A small boiler (exempt from EPA air permitting) is used on a daily basis to provide steam to various processes, steam is used as a non-contact utility. The boiler is inspected by State of Illinois on an annual basis.

The site maintains 3 oil free compressor to provide air to the various processes within the facility.

Compressed gases are used as contact utility for certain industrial and API manufacturing. The site is equipped with 3 (+10,000Lb) storage tanks for Liquid Argon, Liquid Nitrogen, and Liquid Oxygen. Compressed gases, from the liquid phase, are USP/NF grade and each lot (delivery) is traced and recorded on approved specification.

4.2 Equipment

All Manufacturing equipment is selected based on the application type, business demand, and any regulatory constraints.

Equipment and Material flow diagrams are included under Appendix 7.

Equipment types and uses based on core processes are shown in Appendix 8.

The Quality Control laboratory is equipped with many instruments to facilitate in-house testing of raw materials, in-process and finished products and analyses of R&D formulations. Compendial testing is performed by Quality Control per USP methods.

Instrument used in QC laboratory are listed below;

- Static Light Scattering (SLC)
- Dynamic Light Scattering (DLS)
- X-ray Diffraction (XRD)
- X-ray Florescence, *energy dispersive* (EDXRF)
- Inductively Coupled Plasma (ICP-OES)
- Atomic Absorption (AA)
- Surface Area analyzer (BET),
- Helium Pycnometer
- Fourier-transform infrared spectroscopy (FTIR)
- Thermal gravimetric analyzer (TGA)
- Gas chromatography (GC)
- Ion chromatography (IC)
- Karl Fischer analyzer (KF)
- Photospectrometer
- Viscometer
- Rheometer
- UV-VIS Spectrophotometer
- Laboratory scales and balances
- Oven and furnaces

4.3 Cleaning and sanitation

Equipment used in production is cleaned manually with validated cleaning methods. Equipment is used for non-sterile applications only. Cleaning Acceptance criteria is based on MAC calculation and are specific to product grouping and/or equipment type.

QA-125 General Cleaning and Housekeeping for Production Facility and Equipment outlines the general requirement. Equipment cleaning is performed according to their specific cleaning SOP or MBR. Equipment cleanings are verified on MBR or on QC forms and status of cleaning is posted on the equipment.

A metered approved soap/city water solution station provides consistent chemistry to mop water. An active Pest Control program is followed via SOP, MFG-05-510 Pest Control, pest control inspections are performed on monthly basis.

Line Clearance procedure and inspections are outlined in associated Master Batch Record, which is designed and intended to control cross confirmation and mix-up of prodcuts and materials. Manufacturing, formulations, and processes do not use or intentionally add any allergens, such as penicillin and peanut.

4.4 Critical computerized systems

None present, expect some equipment are semi driven by PLC. The PLC is not intended to replace the required elements for MBR, which is paper based.

5.0 DOCUMENTATION

5.1 Paper vs Electronic

To follow up with the FDA recommendation (5.10.1 (II), Nanophase has reviewed cGMP regulation to determine records required under predicate rule of 21 CFR Part 210 and 211. **TABLE 1** is used to show the list of Predicate and non-predicate records that are used by Nanophase QMS. Table 1 documents the applicability of records that must comply with 21 CFR Part 11 when used electronically.

TABLE 1

Review and Determination of data/records for 21 CFR Part11 compliance

Record Name	*Predicate Rule? (per 211, subpart J)	Regulatory Reference	Record Format	Compliance to "CFR Part 11" Required?
Training Records	No	211.25	Electronic/ Paper	No
Equipment cleaning and use log, including maintenance	Yes	211.182	Paper	No
Component, drug product container, closure, and labeling records	Yes	211.184	Paper	No
Master production and control records	Yes	211.186	Paper	No
Batch production and control records	Yes	211.188	Paper	No
Production record review	Yes	211.192	Paper	No
Laboratory records	Yes	211.194	Paper	No
Distribution records	Yes	211.196	Paper	No
Complaint files	Yes	211.208	Paper	No

*A predicate rule is any FDA regulation that requires companies to maintain certain records and submit information to the agency as part of compliance. For example, 211.180 of 21 CFR Part 211 (subpar J) lists records requirements that are considered Predicate Record.

5.2 In March 2021, Nanophase/Solesence started a process to migrate from paper to electronic document system including Qx (QMS) and Mx (eBR). It is anticipated that the project will be completed by mid-2022.

Documentation Scheme

A formalized SOP, **QP-421** is used to outline the system for the complete documentation of all required procedures, records, logs, and instructions defining the quality management system, EH&S management system, production processes, and products: and assign responsibilities for establishing and maintaining the documentation.

The scope and extent of quality system documentation is determined on the basis of the complexity and interaction of processes, elements, and activities, and on competence of personnel. The documentation is sufficient to ensure the effective planning, operation, and control of the quality and EH&S systems, processes, and products.

Documents related to this policy document include:

Documents are divided in several different categories based on their scope and their relation to specific operations function. Documentation categories of quality system are defined below;

Level 1, System and Policies Documents
This includes Level 1, System and Policies Documents and Operational or Quality and EH&S System Procedures

Level 2, Work Instructions and Departmental Procedures
This includes, Master Batch Records, QC Test Records, Process and EHS work instructions, and Departmental procedure

Level 3, Product realization and control plans
Documents under this category are the output of product realization and verification planning, as defined in Section 7.1 of the quality manual.

Level 4, Product specifications
Specifications are developed for raw materials, in-process, and finished products. Each specific product defines by a name and a specification number. Specifications are issued and authorized by QA Assurance

Level 5, External standards and reference documents
The company maintains a set of standards and other reference materials required to design and manufacture its products and to operate the quality and EH&S system. Quality Assurance maintains the regulatory and quality standards. Examples, use of, US Pharmacopeia, ANSI Z.14 ISO 9001, ISO14001, etc.

6.0 PRODUCTION

6.1 Type of products

Site managers 5 core processes to produce metal oxide powders, dispersions, sunscreen lotion, and finished sunscreens.

- As made Nonhazardous metal oxide powder via NAS process
- Surface treated Zinc Oxide (API) and Titanium dioxide (API)
- Metal oxide dispersion as API and industrial grade
- Sunscreens lotions, sticks, powders in bulk manufacturing levels
- Finished Sunscreens (Packaged and assembled)

For sunscreen, the dosage form is Topical. API does not require dosage form determination, but they are used for topical application as well.

Solésence, LLC/Nanophase Technologies Corporation does not prodcuce any drug prodcuts for oral and injectable use, nor a prescription drug is manufactured. Formulation are free from BSE/TSE and use of pestiside inside the facility is prohibited.

List of regulated products are shown in **Appendix 2.**

6.2 Process validation

Solésence, LLC/Nanophase Technologies Corporation understands validation as, "a documented program which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality attributes." To this end, validation of all processes, equipment and analytical methods becomes necessary.

The requirement of process validation is implicit in the language of 21 CFR 211.100 of the Current Good Manufacturing Practice regulations which states: "*There shall be written procedures for production and process control designed to assure that the drug products have the identity, strength, quality and purity they purport or are represented to possess*."

The key element of validation program practiced by this site are outline below;

- Validation Master Plan
- Validation Program
- Equipment validation (IQ/OQ) for API and drug process equipment
- Process validation for PQ for API and drug processes
- Method validation and/or Method suitability
- Instrument Validation (IQ/OQ/PQ)

All processing equipment new or used, when utilized for any regulated product are validated (IQ/OQ) prior to commercial marketing of a regulated product. At least 3 commercial batches are used to perform Process validation related to API or drug product. In limited cases, process validation may include <3 batches due to business demand.

All validations protocols are issued and approved by QA, other approval, such as related R&D, Engineering, Manufacturing are part of the approval process. Validation schedule outlines the past and current protocol development and execution status. The status of validation activities is recorded and presented in each Management Review meeting on a quarterly basis.

6.3 Materials management and warehousing

Solésence, LLC/Nanophase Technologies Corporation, uses several SOP to manage and control of starting raw materials, packaging componants, bulk and finished prodcuts, including sampling, release, and storage.

Receipt of Materials

Critical key purchased products are inspected by quality control. This includes verification of product identity and quantity, visual inspection and, where applicable, verification that all requested certificates and quality records are available.

Designated products are further inspected or tested by QC. QC inspection or testing is not necessary when products are supplied with records or certificates demonstrating conformity; or when the supplier is qualified based on their quality system certification or supplier audits, and a satisfactory quality performance history.

Quality Assurance is responsible for selecting appropriate methods for purchased product verification and acceptance. Operational Procedure **QP-743**, Verification of Purchased Products, sets forward detailed rules for selecting product verification methods and for performing receiving and QC inspections.

When verification of purchased product is to be performed at supplier's premises, purchasing documents specify the intended verification arrangements and method of product release.

Inspection, Quarantine, Release

Following every inspection or test, products are identified to indicate whether they have passed or failed the inspection. This is to prevent nonconforming products from being used or dispatched. Physical location of product is only used as inspection status identification when the location is designated and contained.

QC inspectors and production personnel authorized to carry out inspections and testing are responsible for identifying product inspection status. All personnel handling products are responsible for maintaining the identification.

Products that have passed the receiving inspection are tagged in place to show their status. Detailed rules for identifying inspection status of purchased products are provided in procedure **QP-743** Verification of Purchased Products and QA-070 Quarantine Control.

Status of an in-process inspection is usually identified by a sign-off in the batch record and/or in-process quality document. The status is also identified by tagging or labeling or holding products in designated containers. Operational procedure **QP-824**, In-process Inspections, provides more detailed instructions.

Final inspections of Nanophase Technologies Corporation products are carried out in conjunction with final inspection and testing and the applicable quality plans. The product is released only after evidence is available that all requirements of all applicable documents have been achieved. Controls assure that all requirements are met before product is dispatched.

Rules for identifying inspection status of finished products are provided in procedure **QP-825**, Final Inspection.

Products that fail any inspections or tests are labeled with REJECTED stickers or tag and are segregated and/or quarantined. Whenever a nonconforming product is identified, the nonconformity is documented using a product nonconformity report. Procedure **QP-831**, Control of Nonconforming Product, instructs on how to identify and process nonconforming products.

Product in doubt is segregated using QUARANTINE, MRB QUARANTINE, or QC HOLD tag until final disposition or decision has been assigned.

7.0 QUALITY CONTROL (QC)

7.1 The quality and EHS management systems of the manufacturer

Solésence, LLC/Nanophase Technologies Corporation practices an integrated QMS based on ISO 9001 and FDA cGMP requirements. EHS elements based on ISO14001, EPA, OSHA and DOT are merged in a singular set of requirements and many elements are shared with QMS.

Quality and EHS management systems are designed to be integral part of daily operations allowing seamless integration with routine business.

- A detailed Quality Management System is documented in QSM-000
- A detailed Environmental, Health, and Safety management system is documented in EHS-000

Key regulatory/statutory along with voluntary elements are outlined below;

Regulatory Elements (mandatory in nature)

- ❑ FDA – Food and Drug Administration, *Registered since 2001*
- ❑ EPA – Environmental Protection Agency (Air, Water, Land, TSCA)
- ❑ OSHA – Occupational Health and Safety (workplace safety)
- ❑ DOT – Department of Transportation (shipments)
- ❑ IEMA – Radiation Safety (X-ray instruments)
- ❑ ECHA – REACH (EU- import/manufacturing of chemicals)
- ❑ REACH- European Regulation on Registration, Evaluation, Authorization and Restriction of Chemicals

Voluntary Elements (proactive in nature)

- ❑ ISO 9001-2015 *Registered since 1997, Recertification, 2018*
- ❑ ISO 14001-2015 *Registered since 2006, Recertification, 2017*
- ❑ Nanotechnology Standardization Initiatives (ASTM, ANSI, NMSP etc.), *active voting member since 2006*
- ❑ Implementation of advanced Industrial Hygiene (IH) tools for chemical exposure
- ❑ Implementation of advanced PPE at workplace
- ❑ Active member of PCPC

Activities on site

Quality Control/ Quality Assurance is solely responsible for inspection, release, and rejection as related to product and processes. QC/QA operates a QC laboratory that is capable of performing all in-process and finished products per established specification. Lab is equipment with various analytical instruments/tools to facilitate physical and chemical-based testing of products.

An onsite stability study function housed several stability chambers to facilitate stability studies of products under Accelerated and Long term storage conditions, the data from stability study is used to establish either the Expiry date or Retest date as relevant to a product type.

Microbial testing is performed at FDA registered approved laboratory that is experienced and qualified to perform many microbial test protocol including but not limited to USP<60>, USP <61>, USP<62>, USP <51>. A microbial suitability study is an integral part of all microbial testing.

8.0 DISTRIBUTION, COMPLAINTS, PRODUCT DEFECTS AND RECALLS

8.1 Distribution

Solésence, LLC/Nanophase Technologies Corporation stores and distribute large quantity bulk API and finished prodcuts products from an off-site wharehouse located in Bolingbrrok, IL. Products at this location are stored at ambient conditions with temperature and humidity are recorded but not controlled.

In-process and staged Storage areas are maintained in good condition to prevent damage or deterioration of stored products. Inventory levels of stock are monitored by Rootstock MRP software. Products are stored on heat treated wood or plastic pallet on floors and racks. Solésence, LLC/Nanophase Technologies Corporation practices FIFO system for lot selection.

Prodcuts are shipped from Bolingbrook site based on customer selection (as indicated by the written agreement) or Solésence, LLC/Nanophase Technologies Corporation prefffered carriers. Shipments mode includes, Air, Sea, and ground via LTL and FTL. Small orders and samples are normally shipped via FedEx, DHL, or UPS. Reference MFG-04-080.

Solésence, LLC/Nanophase Technologies Corporation employs trained and certified personnel for supporting Air, Sea, and Ground shippment of both naohazarous and hazardous types.

Prodcut names, customer informtion, PO number, Lot numbers and other informtion is listed on shipping documents, such as Packaging Slip, Bill of Lading etc. A copy of SDS and COA is provided with each shipment, as applicable.

Orders are inspected and released for shipping by following SOP QA-151, *Finished Products Inspection and Release for Shipping*. Only orders that have been verified and signed off by the QA can be released for shipment. Release of orders for shipment is evidenced by a sign-off on QA-151 form.

Unless required by the customer, placement of more than one lot or batch is not allowed on a single pallet or in a single container.

8.2 Complaints, product defects and recalls

Complaints

Customer Service department is responsible for receiving and processing customer feedback and complaints. All received customer communication is recorded in the customer feedback and complaints log.

Customer feedback and complaints are classified into categories to allow for better tracking of trends and evaluating improvement in specific aspects. Every complaint is communicated to relevant functions within and outside the organization. Customer Service, the responsible department, and Quality Assurance decide how to respond to the customer and, when appropriate, what corrective or preventive actions are implemented internally.

Procedure **QP-723,** Customer Feedback and Complaints, provides detailed instructions on how to receive, process, and respond to customer feedback and complaints.

Out of Specification Investigation (OOS)

Non- conformity due to specification is investigated by following cGMP requirements. Procedural details are defined in Operational procedure **QA-385** OOS Results.

Deviation Reports (OOS)

Deviation reporting process applies to all steps and phases of production, packaging, labeling, sampling, and Quality Control testing. To be used when any deviation from the normal operating procedure has occurred or is planned, either by mistake, planned act, equipment failure, etc., with or without prior approval. Deviations are recorded and approved on **QA-190A** and logged on **QA- 190B**.

Product returns and recalls

When product nonconformity is detected by the customer after delivery or use has started, the customer may be instructed to return the product, or a part, on a return authorization number issued by customer service. When product nonconformity is detected internally after delivery or use has started, customers are informed and instructed what to do with the product. In situations when the nonconformity creates a safety or other hazard, the product is recalled. Only the President of the company is authorized to make recall decisions. All returns are processed according to **NTC-050**, whereas **QA-211** is used to handle recall issues.

Nonconforming Products (NCR)

QC staff, Engineering, R&D and Production personnel are responsible for identifying nonconforming products or situations in the course of their normal work activities. In addition, all other personnel are encouraged to watch for, and identify, nonconforming events and products, regardless of their other responsibilities. Nonconforming IP and intermediate products are placed in Quarantine in MRP until a disposition is determined. Not all IP products are regraded or

scraped by completing **QP-831A** form, due to the complexity of the use but the decision is made jointly with QA based on the testing and/or use in other processes. API intermediate are always requires initiation of **QP-831A**.

9.0 SELF INSPECTION (INTERNAL AUDITS)

10.1 The Quality Director or assignees is responsible for planning and scheduling the internal audits. Each main activity comprising the quality and environmental management systems is audited at least once every two (2) years. ISO 9001 and 14001 audits are scheduled based on previous audit results as determined by the score for the audit. **Audit scores** are calculated from the number of concerns and nonconformances found during the audit (# of concerns + [2 X # of nonconformances]). Audit(s) with a score of 5 and above are given priority in the next audit period. Process and cGMP audits are conducted annually. EH&S audits are conducted based on operations schedule. Reference **SOP QP-822, Internal Audits.**

Planning and scheduling

The Quality Director establishes an internal audit plan and schedule in accordance with Procedure **QP-822**, Internal Quality Audits. Every activity and area is audited as required by the procedure. Selected activities are audited more frequently, depending on their importance and quality performance history.

Audit team and preparation for audit

Only personnel independent of the audited activities are assigned to conduct internal audits. Auditors prepare for audits by reviewing applicable standards and procedures, analyzing quality records, and establishing questionnaires and checklists. Selection of auditors and preparation for the audit are explained in Procedure **QP-822**, Internal Quality Audits.

Conducting the audit

Conducting the audit, auditors seek objective evidence indicating whether the audited activities comply with the requirements of the documented quality system and ISO 9001, and whether the quality system is effective. The evidence is collected by observing activities, interviewing personnel, and examining records.

Nonconforming conditions are documented and recorded using the audit findings report form. A model of the form and instructions on how to use it are provided in Procedure **QP-822.**

Audits are conducted in a way that minimizes disruption of the audited activities.

Corrective action and follow up

When nonconforming conditions are identified, the manager responsible for the affected area or activity is requested to implement corrective action. Implementation and effectiveness of the action are verified by a follow-up audit. The CAPA form (**QP-852A**) is used for monitoring and recording the implementation of the corrective actions.

Reporting

All finding reports established during the audit are compiled and analyzed, and a summary is presented at the management review meeting.

Appendix 1
Copy of valid manufacturing authorization

"None available or applicable in USA" Sites are registered with FDA for API and OTC drugs for human use.

Appendix 2

List of products Manufactured

Scope of Manufacturing Processes Nanophase Technologies /Solésence LLC			
Manufacturing Site	**Operation**	**Drug Products**	**Notes**
Romeoville	Bulk API Powder Surface Treatment	ZL15000(aka ZO-S1), TE15000, TE5000, ZL6000	Surface treatment (excipient registered in TGA by Akeroyd and Associates)
Romeoville	Bulk API Powder Surface Treatment	Z-Cote HP1, Z-Cote LSA, TE17000	Surface treatment with Triethoxycaprylylsilane or dimethicone (Dimethicone 10 TGA name)
Romeoville	Bulk API Dispersion Manufacturing	+20 products (see validation list)	Dispersed surface treated API in cosmetic carrier fluids
Romeoville	Bulk Sunscreen Lotion Manufacturing	+25 products (see validation list)	Emulsion (W/O, O/W) and anhydrous bulk drug sunscreen products. White label products manufactured for brand partners.
Romeoville	Bulk Sunscreen Powder Manufacturing	3 products	Bulk drug powder format sunscreen products. White label products manufactured for brand partners.
Romeoville	Bulk Sunscreen Stick Products Manufacturing	2 products	Hot pour/hot fill
Romeoville	Metal Oxide Manufacturing	+3 products	Non-Hazardous metal oxide for polishing and medical device ingredient use.
Romeoville	Dispersion Manufacturing	+5 products	Non-Hazardous metal oxide dispersions for polishing and other industrial applications.

Appendix 3

Copy of valid GMP certificate (if applicable)

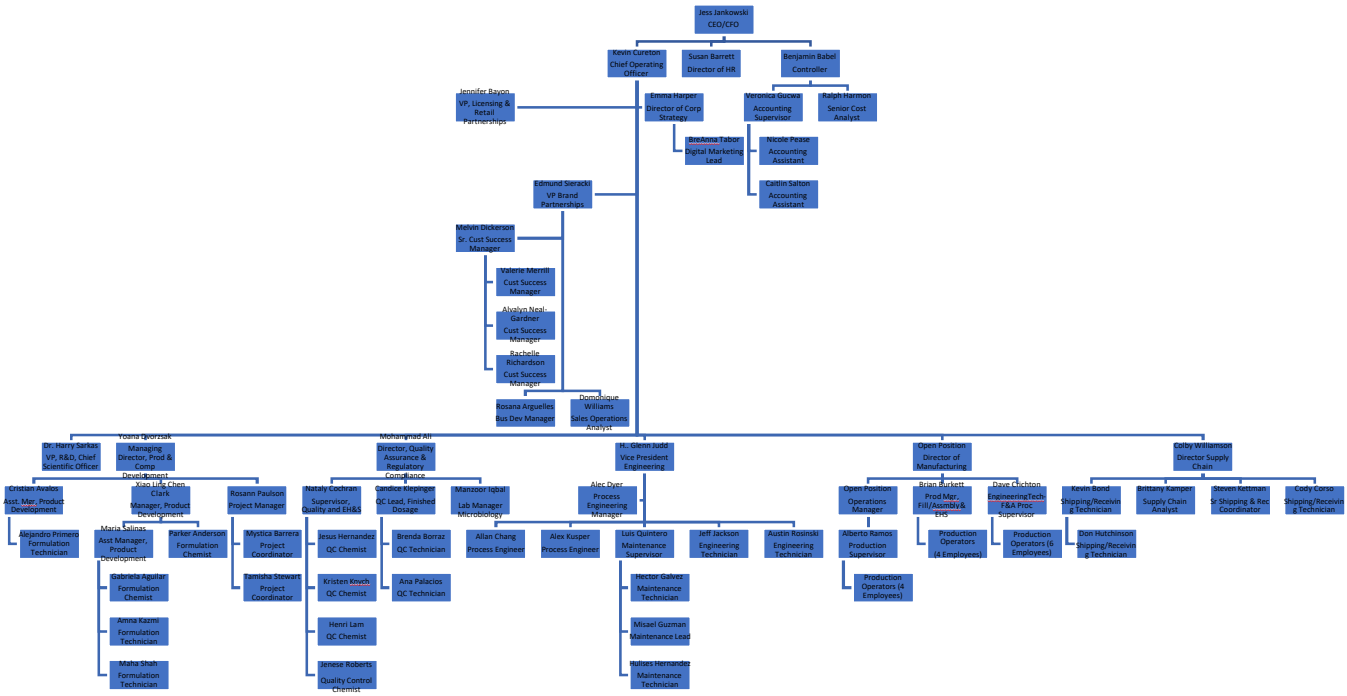
ISO 22716 has been implemented.

Appendix 4

List of contract manufacturers and laboratories

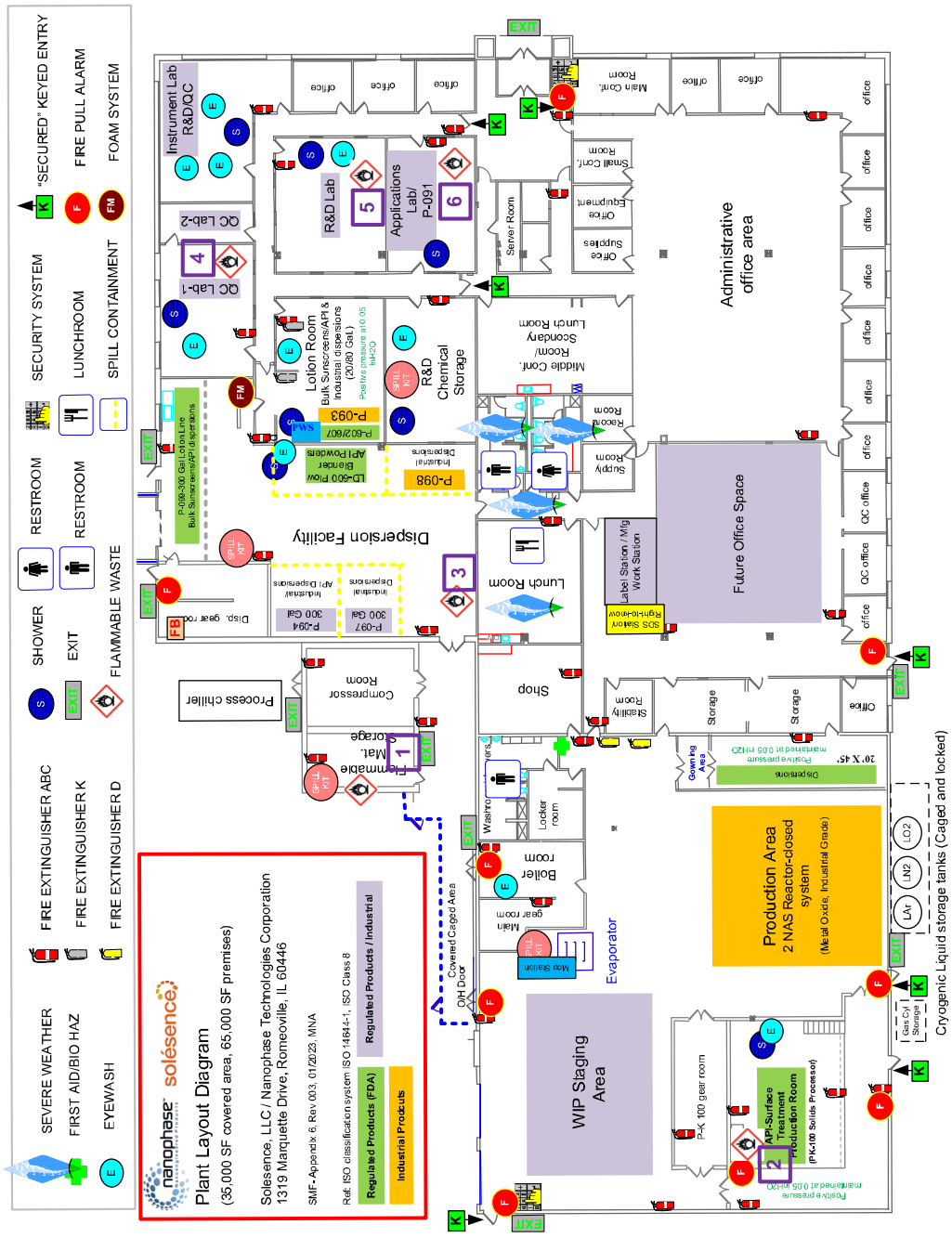
Business Name	Address	Contact Information	Type of Service	FDA Registered?
Amcol Health & Beauty Solutions, Inc. (MTI)	301 Laser Ln Lafayette, LA 70507	337-354-1061 Fax: 337-354-1055 www.amcolhpc.com	API Manufacturing	Yes
MPL Laboratories	12 Wilson Drive, Sparta, NJ, 07871	(973) 300-9715, 1-800-548-1874, Fax: (973) 300-9830 pgriffin@mpllaboratories.com	Microbial Testing	Yes
Accugen Laboratories, Inc.	2121 W. Army Trail Road, Addison, IL 60101	800-282-7102 Fax: 630-812-2219 info@accugenlabs.com	Microbial Testing	Yes
Microbiological Testing & Consulting, LLC	10401 S Kenzie Ave, Suite 2, Chicago, IL 60065	773-253-2929 www.mtcresearch.com	Microbial Testing	Yes
Amri (former name; Whitehouse Laboratories)	291 US Highway 22 East, Lebanon, NJ 08833	908.823.9300	Stability Storage	Yes
Florida Skincare Testing	101 N Bay St, Bunnell, FL 32110	(386) 492-2959	SPF Testing UVA Testing (Primary)	Yes
CPT Labs	70 New Dutch Lane, Fairfield, NJ 07004	(973) 957-3250	HET-CAM Testing Toxicological Assessments Phototoxicity testing	Yes
Essex Testing Clinic	799 Bloomfield Avenue, Verona NJ 07044	(973) 857-9541	HRIPT Testing Phototoxicity testing	Yes
Eurofins CRL	371 Hoes Ln #100, Piscataway, NJ 08854	(732) 981-1616	Phototoxicity testing Comedogenicity Testing SPF and UVA Testing	Yes
Bioscreen	3904 Del Amo Blvd Suite 801 Torrance, CA 90503	(310) 214-0043	Moisturization testing HRIPT testing SPF testing	Yes
Cantor Research Labs	630 Route 303 Blauvelt, NY 10913	(845) 727-4100	SPF and UVA Testing (recently qualified) Comedogenicity Testing	Yes

Appendix 5 (subject to change)



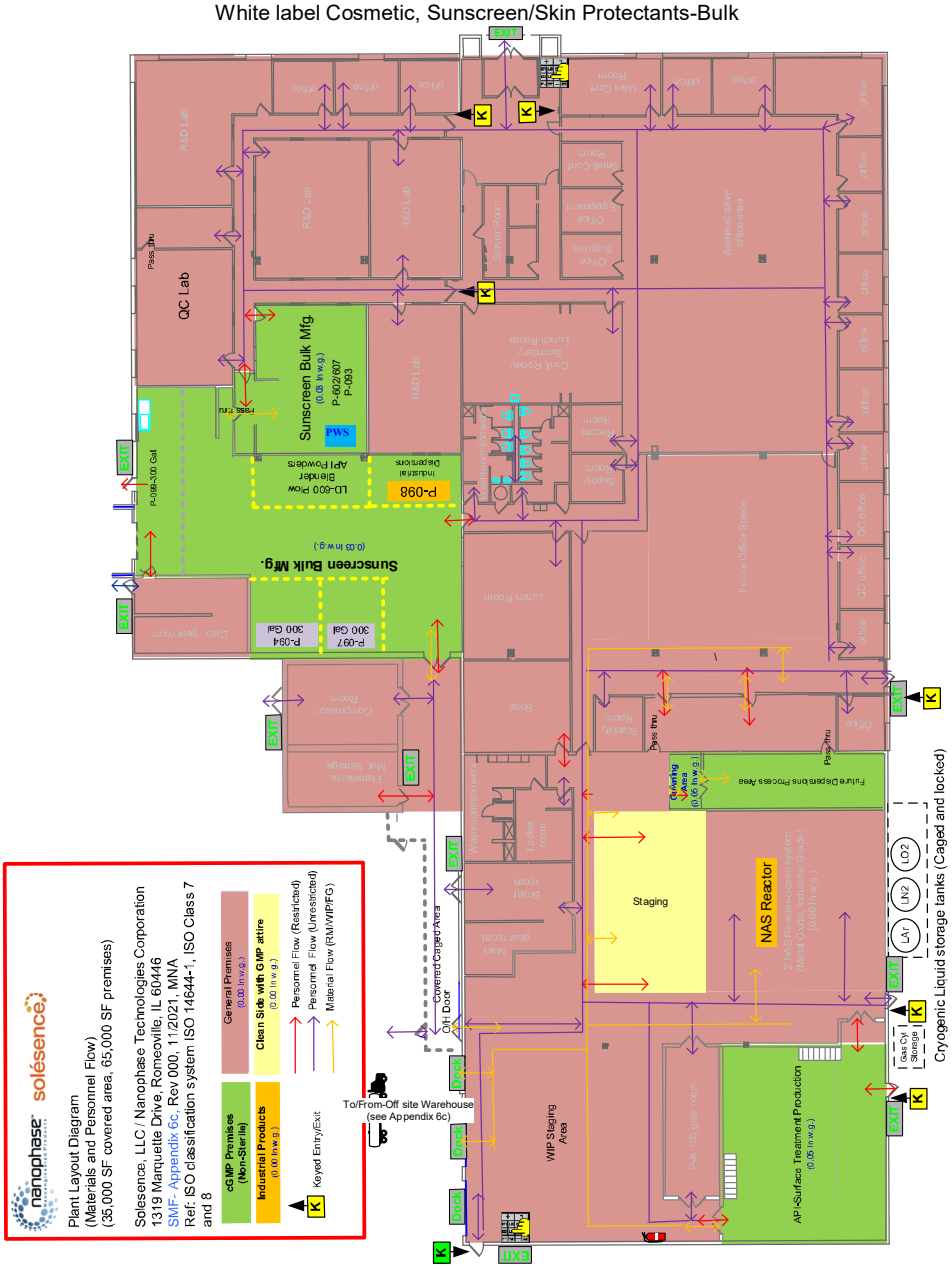
Appendix 6a

Products at this location are stored at ambient conditions with temperature and humidity are recorded but not controlled.

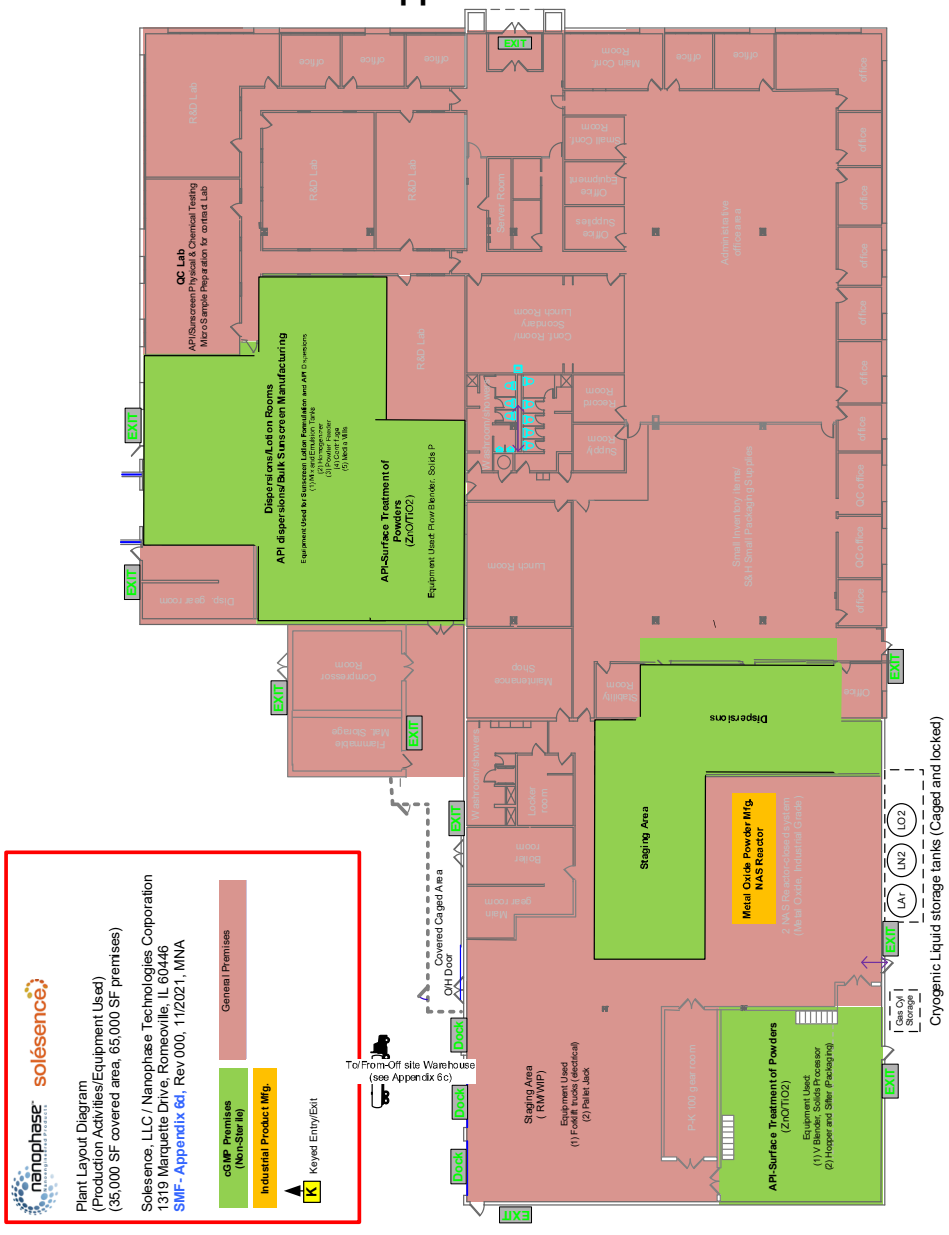


Appendix 6c

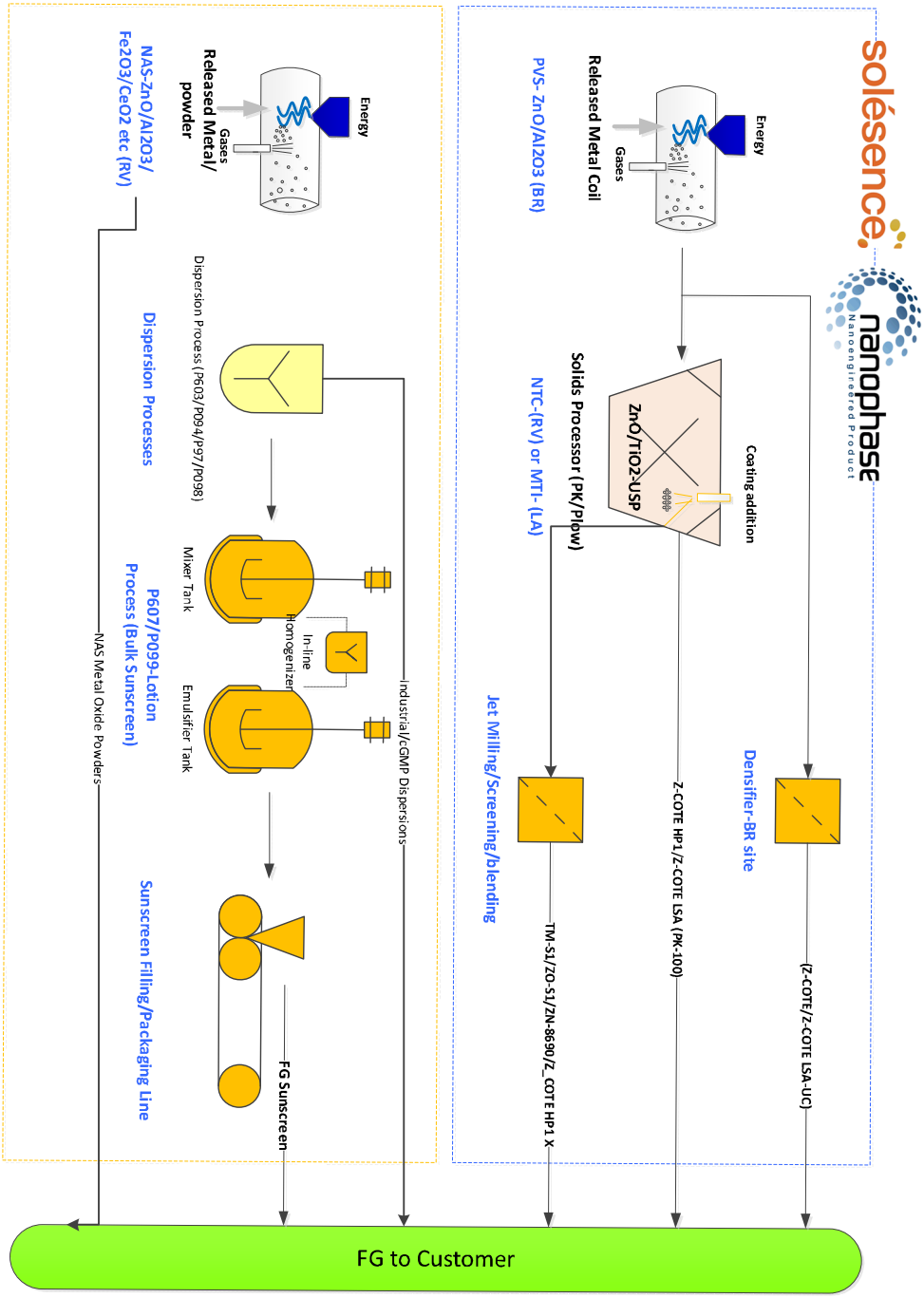
White label Cosmetic, Sunscreen/Skin Protectants-Bulk



Appendix 6d


Plant Layout Diagram
(Production Activities/Equipment Used)
(35,000 SF covered area, 65,000 SF premises)
Solesence, LLC / Nanophase Technologies Corporation
1319 Marquette Drive, Romeoville, IL 60446
SMF- Appendix 6d, Rev 000, 11/2021, MNA
Genesis Premises
cGMP Premises (Non-Sterile)
Industrial Product Mfg.
K Keyed Entry/Exit
To/From-Off site Warehouse (see Appendix 6c)
Covered Caged Area
O/H Door
Staging Area
Dispersions
Metal Oxide Powder Mfg. NAS Reactor
Staging Area (RM WIP)
Equipment Used (1) Forklift trucks (electrical) (2) Pallet Jack
API-Surface Treatment of Powders (ZnO/TiO2)
Equipment Used (1) V Blender Solid Processor (2) Hopper and Sifter (Packaging)
Cryogenic Liquid storage tanks (Caged and locked)
LO2
LN2
LA1
Gas Cyl Storage
Dock
EXIT

Appendix 7a


solésence
nanophase
Nanoengineered Product
PVS- ZnO/Al2O3 (BR)
Released Metal Coil
Energy
Gases
Solids Processor (PK/Plow)
ZnO/TiO2-USP
Coating addition
NTC-(RV) or MTI- (LA)
Densifier-BR site
Jet Milling/Screening/blending
Z-COTE HP1/Z-COTE LSA (PK-100)
TM-51/ZO-51/ZN-8690/Z_COTE HP1 X
(Z-COTE/Z-COTE LSA-UC)
NAS-ZnO/Al2O3/
Fe2O3/CeO2 etc (RV)
Released Metal/
powder
Energy
Gases
Dispersion Processes
Dispersion Process (P603/P094/P97/P098)
P607/P099-Lotion
Process (Bulk Sunscreen)
Mixer Tank
In-line
Homogenizer
Emulsifier Tank
Industrial/cGMP Dispersions
NAS Metal Oxide Powders
Sunscreen Filling/Packaging Line
FG Sunscreen
FG to Customer

Appendix 8

Core Process	Equipment/ Process Name	Intended Purpose	Contact Surfaces / Type	Sterile (Y/N)
Metal Oxide Mfg.	1. NanoArc Synthesis Plasma reactor 2. Power Supply 3. Powder Feeder 4. Dust Collector Process ID: NAS Reactor #1 NAS Reactor #2	Industrial grade metal oxide powders	Stainless steel Plasma reactor/classifier/baghouse	N
Surface Treatment-API Mfg.	1. V-Blender, PK-100 Solids Processor 2. Plow Blender: LD-600 Solids Processor 3. Sifter Process ID 001, 011	Surface treatment of API (powder)	Stainless steel	N
Dispersions Mfg.	1. Mix and Emulsion Tanks 2. Homogenizer 3. Powder Feeder 4. Media Mills 5. Centrifuge Process ID P093, P602, P603, 611, 612, 613P094, P097, P098	Industrial or API semi-liquid phase intermediates or products	Stainless steel, plastic 20-300 Gal. tanks equipped with mixers, mills, centrifuge, other processing equipment	N
Lotion / Cream / Powder / Stick / Balm Mfg.	1. Mix and Emulsion Tanks 2. Homogenizer 3. Mixer/Drum 4. Solids Processor Process ID: P607, P608, P094, P097, P099, LD-600, other	White label Cosmetic, Sunscreen/Skin Protectants-Bulk	Stainless steel (mirror finish), plastic 80-300 Gal. tanks equipped with mixers and homogenizer Stainless Steel equipment Powder based formulations	N
USP Purified Water System (non-sterile)	EVOQUA DIRS10PPUV43x PURIFIED WATER SYSTEM – DIRS Recirc Skid	Ingredients for White label Cosmetic, Sunscreen/Skin Protectants-Bulk, API	Stainless steel, other	N

Signature Manifest

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Title: Site Master File-Romeoville Site
Effective Date: 22 Nov 2024

All dates and times are in Central Time Zone.

Site Master File-Romeoville Site

Originator

Name/Signature	Title	Date	Meaning/Reason
Nataly Cochran (NCOCHRAN)	Quality Assurance Manager	22 Nov 2024, 12:06:36 PM	Approved

Department Head

Name/Signature	Title	Date	Meaning/Reason
Nadir Ali (MALI)	Director, EH&S and Quality	22 Nov 2024, 04:23:19 PM	Approved

QA

Name/Signature	Title	Date	Meaning/Reason
Nadir Ali (MALI)	Director, EH&S and Quality	22 Nov 2024, 04:23:31 PM	Approved