

Appendix A

Master Glossary

% differences: %differences = (Result A – Result B) X 100% / Mean of A & B

% Relative Standard Deviation: % RSD (or coefficient of variation, % CV) = (Standard deviation/mean) x 100%

5S (Sort, Straighten, Shine, Standardize, and Sustain): a workplace discipline used to ensure reliable work practices and a clean working environment; used in the West but originally from Japan

Accuracy: demonstrates the closeness of test results obtained by the method to the true value (nominal) or an acceptable reference value

Act: the federal Food, Drug, and Cosmetic Act, as amended (21 U.S.C. 301 et seq.)

Action level: an established microbial or airborne particulate level that, when exceeded, should trigger appropriate investigation and corrective action based on that investigation

Active Pharmaceutical Ingredient (API): any substance or mixture of substances intended for use in the manufacture of a drug (medicinal) product; when used in the production of a drug it becomes an active ingredient in the drug product.

Addenda: a controlled addition to a post-execution approved protocol

Administrative controls: EHS control intended to modify human behavior so that exposure to hazards are either minimized or managed

Adulterated: drugs manufactured without following proper cGMPs

Agent: chemical agents (solid, liquid, or gas phase) and biological hazards that can potentially cause harm to humans and other living organisms, property, and the environment

Alert level: an established microbial or airborne particle level giving early warning of potential drift from normal operating conditions and triggering appropriate scrutiny and follow-up to address the potential problem; alert levels are always lower than action levels.

Ambient temperature: the temperature of the surrounding air; the range is 10–38 degrees Celsius (50–100 degrees Fahrenheit)

Amendment: a controlled change, prior to execution, to an approved protocol

Ampoule: a small sealed vial used to contain and preserve substances that must be protected from air and contaminants

Analyst: laboratory personnel performing the analytical method

Analytical method: a laboratory procedure used to measure a physiochemical entity or attribute of the entity

Andon: a visual management tool and component of the lean philosophy; these are lights placed on or adjacent to machines or production lines to indicate operation status.

Animal-derived materials: Animal Sourced/Animal-Derived Material is defined as a raw material that is created from or processed in part from animals. Materials of Special Consideration are not considered animal-derived; these include materials of animal origin defined as “Special considerations” as described in EMA/410/01. These are materials that are unlikely to be sources of TSE/BSE when produced in accordance with EMA/410/01 guidelines. Examples include collagen, gelatin, tallow derivatives, milk and milk derivatives, wool derivatives, amino acids, etc.

API: Active Pharmaceutical Ingredient

Aseptic: the absence of pathogenic (disease-causing) microorganisms

Aseptic processing: biomanufacturing methods for those sterile products that cannot be subjected to terminal sterilization; typically utilized for those products that are heat-labile (products that are damaged by heat sterilization methods)

Aseptic techniques: techniques that prevent contamination by unwanted microorganisms; used not only in biomanufacturing methods but also with medical procedures

Batch: a specific quantity of material produced in a process or series of processes that is expected to be homogenous within specified limits; may also be referred to as a “lot.”

Batch record: a record of all materials and proportions used to produce a batch

Biological hazard: living organism or non-living agent that can cause harm to humans and other living organisms and the environment; examples include bacteria, viruses, allergens, toxins, etc.

Biologics License Application (BLA): an application to the FDA for a license to market a biologic (biopharmaceutical)

Bioreactor: a device or system meant to grow cells in cell culture

Calibration (Metrology): a process/program that demonstrates that a measuring device produces results within specified limits of those produced by a reference standard device over an appropriate range of measurements

Capture/recovery: the rapid separation of the product of interest from the cells of the bioreactor

Cell Bank (working): cells grown from those maintained in a master cell bank with well-characterized stability and uniformity

Centers for Disease Control and Prevention (CDC): a United States government agency whose mission is to protect health and promote quality of life through the prevention and control of disease, injury, and disability

Centrifugation: the process of separating the lighter constituents of a solution, mixture, or suspension from the heavier constituents by centrifugal force

Certification: documented testimony by qualified authorities that a system qualification, calibration, validation, or revalidation has been performed appropriately and that the results are acceptable; personnel certification is proof that a person has achieved a certain level of qualification

Change Control: a formal, documented process used to ensure that changes to a product or system are introduced in a controlled and coordinated manner, thereby reducing the possibility that unnecessary and potentially harmful changes will be introduced; also provides a documentary record of the evolution of the product or system

Characterization method: a scientifically-sound analytical test method used to evaluate a specific quality attribute; they are used in support of cGMP manufacturing, process development, process characterization, formulation development/optimization/characterization, deviation investigations, comparability, reference standard qualification, process validation, or other studies required for regulatory submissions

Chemical hazard: substances in either a solid, liquid, or gas form that can cause health problems, death, and/or environmental pollution; examples include acids, solvents, cleaning agents, etc.

Clarification: the removal of small amounts of fine, particulate solids from liquids

Clean In Place (CIP): a method of cleaning the interior surfaces of pipes, vessels, process equipment, and associated fittings without disassembly

Clean room: a room or interconnected rooms maintained and controlled to prevent particle and microbiological contamination of drug products; they are assigned and reproducibly meet an appropriate air cleanliness classification

Coefficient of Variance (CV) or % Relative Standard Deviation: a statistical measure of variability

Commissioning: the process of bringing a new production facility or unit on-line; commissioning involves validation of the facility, facility infrastructure (e.g., utilities and HVAC systems), and production process to include IQ and OQ; the completion of the commissioning process results in a Turn Over Package (TOP) being presented to the plant operator

Conductivity: a measure of a material's ability to conduct an electric current

Contamination: the presence of any unwanted substance that will affect the purity, safety, identity, or strength of a drug product

Continuous Improvement (CI): recognizing that all products, processes, and systems can be improved, CI describes methodologies and management systems designed to enable ongoing improvement

Control Chart: a statistical trending tool that graphically represents whether a process is either in- or out-of-control by depicting a variable compared to established upper and lower control limits over time

Correlation: a statistical relation between two or more variables such that systematic changes in the value of one variable are accompanied by systematic changes in the other

Cpk (Process Capability Index – not centered): a calculated value used to compare process variation to a specification; this can also be used to compare processes.

Cryovial: a small vial designed for the storage of biological materials, cells, etc., under extremely low temperatures

Culture initiation: at the beginning of each batch of a campaign, a vial of cells is transported to an inoculum prep room; the culture is then initiated by thawing the vial

current Good Clinical Practice (cGCP): a guideline that describes a standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate and that the rights, integrity, and confidentiality of trial subjects are protected

current Good Laboratory Practice (cGLP): a set of guidelines published by various governments which describes general principles that must be complied with when planning, performing, monitoring, recording, reporting, and archiving preclinical laboratory studies; these studies generate data by which the hazards and risks to users, consumers, third parties, and the environment can be assessed for pharmaceuticals and other products

current Good Manufacturing Practice (cGMP): a set of guidelines published in the United States Code of Federal Regulations (CFR) that describes general principles that must be complied with in the manufacture of effective pharmaceutical products in order for the product to be safe; the term *current* indicates these are not static but evolve over time

Design Qualification (DQ): a process to ensure that equipment and systems are suitable for their intended use; an example of design qualification parameters would be checking that the water system has sufficient capacity to serve the needs of the facility (including production, testing, steam generation, and autoclave operations)

Detection Limit (also referred to as Limit of Detection or LOD): the lowest amount of analyte in a sample that can be detected but not necessarily quantitated as an exact value

Development Studies: studies that are performed prior to validation to determine the extent and scope of required validation testing; examples of development studies may include temperature mapping of autoclaves to identify cold regions as well as cleaning studies in dishwashers to identify hard to clean items

Deviation: any event occurring during validation of a system that is a departure or variation from a written procedure or acceptance criteria

Device Under Test (DUT): an object that is undergoing testing

Dewar: a storage vessel which provides thermal insulation by interposing a partial vacuum between the inside and the outside walls of the vessel; cell cryovials are stored in liquid nitrogen within a Dewar

Direct Flow Filtration (DFF): devices which allow the process fluid to cross the membrane in essentially a perpendicular flow direction; this provides little or no prevention of particulate build-up or the concentration of other elements that do not fit through the pore structure

Direct Impact System: a system that is expected to have a direct impact on product quality; these systems are designed and commissioned in line with Good Engineering Practice and are subject to Qualification Practices that incorporate the enhanced review, control, and testing against specifications or other requirements necessary for cGMP compliance

Disinfection: the elimination of most recognized disease-causing or harmful microorganisms but not necessarily all microbial forms; is a less lethal process than sterilization

Dissolved Oxygen (DO): the amount of oxygen gas that is dissolved in the media and is available to cells

Distributed Control System (DCS): a series of computer-based devices that operate in conjunction with each other on a variety of applications; these are usually widely separated throughout the system being controlled

DMAIC (Define, Measure, Analyze, Improve, and Control): a method which can be considered as a continuous improvement process in its own right; based upon statistical analysis, it aims for systematic elimination of all non quality sources

Downstream: another term for the purification process in biomanufacturing

Downstream Processing: typically includes 2–3 chromatographic steps; Tangential Flow Filtration (TFF) steps for buffer exchange and product concentration

DOWNTIME: an acronym to remember the different sources of waste to be eliminated through lean manufacturing practices

Drug product: also known as a medicinal product; a formulated dosage form that contains the drug substance, normally (but not always) in combination with one or more inactive ingredients (excipients), that is ultimately used by the patient via a tablet, injection, ointment, etc.

Drug substance: also known as an API (Active Pharmaceutical Ingredient); a material that is intended to be used in the manufacture of a drug product and when so used becomes an active ingredient of the drug product; provides the therapeutic effect of the drug product used by the patient; most biopharmaceutical drug substances are protein in nature.

Efficacy: effectiveness of the product in achieving its medicinal purpose

Electronic record: any combination of text, graphic, data, audio, pictorial, or other information representation in digital form that is created, modified, maintained, archived, retrieved, or distributed by a computer system

Electronic signature: an electronic symbol attached to a record for the purpose of signing the record; electronic signatures are conceptually the computerized equivalent of handwritten signatures; an electronic signature provides a unique basis for confirming the identity of the person who made the signature

Engineering control: EHS control intended to either eliminate the need for human interaction or physically impede human exposure to a hazard by employing a facility or equipment design; engineering controls include barrier guards, shielding, ventilation, etc.

Environmental Protection Agency (EPA): a United States government agency whose mission is to protect human health and the environment

EOR: Edge of Operating Range

Ergonomic hazard: stresses created on the human body by repetitive tasks, improperly designed or adjusted workspaces, incorrect use of tools/equipment, etc.; also referred to as a biophysical hazard

Eukaryote: an organism whose cells contain complex membrane-enclosed structures called organelles

European Medicines Agency (EMA): the legal agency in the European Community that administers the regulation of medicines in the community and associated nations

Expiry period: the period of time from the date of manufacture that the product or substance is considered to be fit for use

Expression system: protein expression consists of the stages after DNA has been translated into a polypeptide chain, which ultimately folds into a functional or native state.

Facility Management and Control System (FMCS): a building management system capable of controlling, monitoring, alarming, trending, and reporting operations of building utility systems

Failure Modes and Effects Analysis: a systematic approach to risk identification and analysis of identifying possible modes of failure and attempting to prevent their occurrence

Feed stream: consists of cells and culture media; the feed stream is cooled and microfiltered at a temp of 4 degrees Celsius

Fermentation: biopharmaceutical fermentation involves the culture of mammalian, yeast, or microbial cells for the purposes of protein drug production; most fermentations are aerobic; this is not to be confused with biochemical fermentation, which is the breakdown of complex carbon compounds into simpler compounds of water, carbon dioxide, etc.

First Order Kinetics: chemical reactions that proceed at a rate that is directly proportional to the concentration of one of the reaction ingredients

Fishbone Diagram: a problem-analysis tool that derives its name from its shape, which resembles the skeleton of a fish; also known as a Cause and Effect diagram or Ishikawa diagram, named for its inventor, Kaoru Ishikawa

Flow Chart: a pictorial summary that illustrates with symbols and words the steps, sequence, and relationship of the various operations involved in the performance of a function or a process

Food and Drug Administration (FDA): the governmental agency in the United States responsible for oversight of the foods and drugs made available to consumers

F-Test: a method to test statistical hypotheses' distributional variance from where the samples have been collected

Gemba: the Japanese word for "actual place" or the place where real action occurs—where products or services are performed; in a manufacturing environment the gemba often refers to the shop floor, since it is there that products are transformed.

Generation number: the population-doubling level of the cell bank

Glycoproteins: proteins with specific sugar residues attached by a series of enzymatic reactions

Glycosylation: oligosaccharide attached to the N of asparagine results in N-linked glycosylation and to the O of tyrosine, threonine and serine results in O-linked glycosylation; N-glycosylation is common in mammalian cells; O-glycosylation is rare in humans but common in yeasts

Good Manufacturing Practice (GMP): a set of guidelines published by various governments which describes general principles that must be complied with in the manufacture of safe and effective pharmaceuticals

Gross Human Error: a type of error caused by a person making a mistake, misusing equipment, blunders, or other similar occurrences

Heating, Ventilation, and Air Conditioning (HVAC): a critical utility used to distribute, recirculate, and exhaust, while meeting air temperature, relative humidity, supply, differential pressure, and cleanliness requirements

Heijunka: leveling the type and quantity of production over a fixed period of time; this enables production to efficiently meet customer demands while avoiding batching; it results in minimum inventories, capital costs, manpower, and production lead time through the entire value stream.

HEPA: a commonly used acronym for High Efficiency Particulate Arrestance filters

HVAC: a commonly used acronym for Heating, Ventilation, and Air Conditioning used for indoor environmental control

Identity: a test confirming the identity of a component

Identity assay: an analytical procedure that confirms the presence of the active product ingredient

Impurity detection assay: an analytical procedure that indicates the presence of degradants and other impurities present with the active product ingredient

Impurity quantitation assay: a quantitative analytical procedure that measures the amount of degradants or other impurities present with the active product ingredient

Indirect Impact System: a system that is not expected to have a direct impact on product quality but will typically support a Direct Impact System; these systems are designed and commissioned following Good Engineering Practice only

Installation Qualification (IQ): documented verification that the equipment or systems, as installed or modified, comply with approved design, manufacturer's recommendations, and/or user requirements

Installation Verification (IV): the verification or checkout that all equipment and/or systems are installed as designed and specified; the IV is performed during commissioning and as equipment and/or systems are installed over the life of the installation (construction) phase; all installation is verified and documented to reflect as-built conditions; IV is executed by making a complete field verification of all trade contractors' work and vendors' deliverables by performing line-by-line checks using purchase orders, design documents, P&IDs, specifications, electrical drawings, instrument & control drawings, testing procedures, SOPs, and all other available tools

Intelligent Resistant Temperature Device (IRTD): a temperature measurement device that relies on changes in electrical resistance between dissimilar metals; IRTDs are used to record the temperature during equipment operations and relay those temperature measurements to external recording devices; IRTDs must be calibrated before and after use with a traceable standard

Intermediate precision: expresses the precision of a method, under the same operating conditions, when there are intra-laboratory variations involving different days, different analysts, and different equipment

Intermediate purification: the removal of bulk contaminants, including host cell proteins and adventitious viruses as well as any potential contaminating leachates from other in-process materials

Investigational New Drug application (IND): an application to the FDA for permission to test the drug substance for safety and effectiveness in humans

Issued For Construction (IFC): the stage of design for specifications, drawings, and/or other design documents when the design document is deemed acceptable to use for construction

Kaizen Event: the application of kaizen techniques in an accelerated manner that focuses on a specific improvement area; tracked as an event rather than an ongoing process

Kanban: a communications tool in the "just-in-time" production and control system; A Kanban, or signboard, is attached to specific parts in a production line and signifies the delivery of a given quantity

Lean Manufacturing: a business philosophy and/or strategy that focuses on eliminating waste—all steps or processes that do not add value to the final product or service; usually employed in conjunction with the concept of kaizen, or continuous improvement

Limit of Detection (LOD): the lowest amount of analyte that can be detected in a sample but not necessarily quantified

Limit of Quantification (LOQ): the lowest amount of analyte in a sample that can be quantified with suitable precision and accuracy

Linearity: demonstrates a method's ability (within a given range) to obtain test results directly proportional to the concentration (amount) of analyte in the sample

Loading (working) range: an interval of the linear range targeted for sample loading; this range is determined during method development and should provide a proportionate response to main analyte and appropriate sensitivity to other analytes that may be present.

Lot: a specific quantity of material produced in a process or series of processes that is expected to be homogenous within specified limits; may also be referred to as a "batch"

Manufacturing campaign: an extended run of batch processes in which only one product is being manufactured during one campaign

Master Validation Plan (Validation Master Plan): a document that pertains to the entire facility and describes which equipment, processes, systems, and methods will be validated and under what conditions; the Master Validation Plan should include a format for the IQ, OQ, and PQ protocols and include the types of information to be found in each document

Material Safety Data Sheet (MSDS): a vital document that provides information about the properties of a particular chemical, describing details about associated hazards such as first aid measures, accidental measures, exposure controls and personal protection, toxicological information, ecological information, etc.

Microfiltration: the first step in process recovery; separation of the biomass and the culture filtrate is carried out by a filtration process

New Drug Application (NDA): an application filed with the FDA for permission to market a new drug substance

Non-Animal-Derived Materials: materials used in the manufacture of biopharmaceuticals that are accompanied by a Certificate of Origin (COO) stating that the material was not derived from animal sources

Occupational Safety and Health Administration (OSHA): a United States government agency whose mission is to assure safe and healthful working conditions for working men and women

Operational Qualification (OQ): the documented verification that the system or subsystem operates as expected according to the manufacturer's specification and/or the user functional requirements

Operator Interface Terminal (OIT): a graphic display panel serving as the interface between an operator and a control system

OPs: Operating Parameters

OR: Operating Range

Out of Specification Results (OOSR): results of any measurement that differ from predetermined specifications

Overkill Approach: a cycle that provides a minimum 12-log reduction of a resistant biological indicator with a known D-value of not less than one minute; this approach assures a reduction of the bioburden that is substantially greater than a 12-log reduction; therefore only minimal information on the bioburden is required

Pareto Chart: named for Vilfredo Pareto, a type of chart containing both bars and a line graph; it displays the values in descending order as bars and displays the cumulative totals of each category, left to right, as a line graph

Percent differences: measure of the difference from two separate results

Performance characteristics: attributes of a method that are evaluated to assure that an analytical method is suitable for its intended use

Performance Qualification (PQ): documented verification that the system or subsystem performs as intended, meeting predetermined acceptance criteria under actual production conditions; establishes confidence through appropriate testing that the process is effective and reproducible

Permeate: product (including media and other proteins similar in size) smaller than the filter pore size that passes through the hollow fiber cores of the filter and enters the filter housing where it can be collected

Personal Protective Equipment (PPE): EHS control intended to provide protection to a worker against potential hazards; PPE consists of specialized clothing and gear, such as lab coats, aprons, gloves, safety goggles, respirators, etc.

pH: a measure of the acidity or alkalinity of a solution

Pharmacopeia: a pharmaceutical reference that contains directions for the identification of samples and the preparation of medicines and functions; pharmacopeias are typically published under the authority of a government or a medical/pharmaceutical society

Physical hazard: environmental factors such as temperature, pressure, noise, trips/falls, Electromagnetic Radiation (EMR), mechanical forces, and motive forces (electricity, pneumatics); OSHA defines a physical hazard as one that relates to a chemical for which there is valid evidence that it is a combustible liquid, compressed gas, or oxidizers such as organic peroxides, as well as explosive, flammable, pyrophoric (liable to spontaneously ignite in air), unstable (reactive), or water-reactive substances

Piping & Instrumentation Diagram (PID): engineering drawings that specify all of the piping in a facility, including the sequence of branches, valves, equipment, instruments, and control interlocks; the PID is used in the actual operation of the process; PIDs should include all instrumentation, equipment, size of process piping, vents, sampling lines, and flow directions.

Poka Yoke: a Japanese term which translates roughly to “mistake proofing;” it is a manufacturing technique of preventing errors from occurring by designing the

manufacturing process, equipment, and tools in such a way that an operation literally cannot be performed incorrectly

Polishing: the elimination of trace contaminants and impurities, including inactive or unwanted isoforms of the desired therapeutic, or common impurities, including fragments or other chemical modifications thereof

Post-translational modification: a step of following protein synthesis where the polypeptide chain is modified; the most common type is the enzymatic addition of sugar residues, resulting in a glycoprotein

Potency: the specific ability or capacity of the product to produce a strong physiological or chemical effect

PPs: Performance Parameters

Precision: the closeness of agreement between repeated measurements of the same quantity under the same conditions; also referred to as **repeatability**

Process Flow Diagram (PFD): a basic, standard drawing that depicts the flow of a product through a process

Process or Production Qualification (PQ): establishing confidence through appropriate testing that the process is effective and reproducible

Process Validation: the scientific study of a process conducted in order to: prove that the process works as intended (process is under control); determine the process-critical variables and their acceptable limits; and set up appropriate in-process controls

Product Lifecycle: the complete life of a product, from early planning through sales build-up, maximum sales, declining sales, and withdrawal of the product; product life cycle lengths and types can vary depending on the type of product, the frequency of replacement, and other factors

Programmable Logic Controller (PLC): a specialized industrial computer used to program and automatically control production and process operations by interfacing software control strategies to input/output devices

Prokaryote: an organism whose cells are lacking a membrane-bounded nucleus or membrane-bounded organelles

Purity assay: a quantitative analytical procedure used to determine the purity of the active product ingredient

Purity method: a qualitative analytical procedure used to determine the purity of the active ingredient

Qualification: an experimental study demonstrating that an analytical method performs as expected, providing consistent and meaningful data under a defined set of conditions

Qualification Result: the result calculated for a particular performance characteristic tested during a Qualification; the reportable Qualification Result is usually determined by statistical analysis of a specified number of reported values

Quality Assurance (QA): all aspects of the systematic monitoring and evaluation of the various activities being performed during pharmaceutical manufacture to verify that appropriate standards of quality are attained and to assure that the products are of the required quality for their intended use

Quality by Design (QbD): a systematic approach to development that begins with predefined objectives and emphasizes product/process understanding and process control based on sound science and quality risk management

Quality Control (QC): all testing that is performed during pharmaceutical manufacture on the associated products and intermediates in order to verify that appropriate standards of quality are attained

Quality Risk Management (QRM): a systematic process for the assessment, control, communication, and review of risks to the quality of the drug (medicinal) product across the product lifecycle

Quality System (QS): management system to direct and control a pharmaceutical company with regard to quality

Quantitation Limit (also referred to as Limit of Quantitation or LOQ): the lowest (Lower Limit of Quantitation or LLOQ) and highest (Upper Limit of Quantitation or ULOQ) amount of analyte in a sample that can be quantitatively determined with suitable precision and accuracy; the upper and lower limits define the endpoints of the range

r (the correlation coefficient): R^2 is the coefficient of determination which will be used in validation reports

Random Error: a type of error that causes scatter in the results of a sequence of readings; this is a measure of dispersion

Range (also referred to as linear or assay range): the interval between the upper and lower concentration (amounts) of analyte in the sample (including these concentrations) for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy, and linearity

Relative Standard Deviation (RSD): $\%RSD = \text{Standard Deviation} \times (100\%) / \text{mean}$ —it is the absolute value of the coefficient of variation

Repeatability: expresses the precision of a method under the same operating conditions over a short interval of time, such as performing the test by the same analyst, on the same day, and using the same experiment set ups—measures inherent method variability (short time between measurements)

Replicate: the determination of a single reported value as prescribed by the method Standard Operating Procedure (SOP); multiple replicates are treated as individual samples during Qualification studies

Reported value: the result obtained by following the testing scheme outlined in the method SOP; most often the reported value is the average result calculated from a specified number of replicate or individual measurements

Reproducibility: expresses the precision between laboratories; demonstrates the measurement of inter-laboratory method variability

Re-Qualification (RQ): documented verification that the system or subsystem remains in a validated state; this can apply to a specific function or the entire operation of a system and/or equipment

Retentate: consists of rejected species (cell debris, proteins larger than the filter's pore size, etc.) that remain in the recirculation loop until removed

Retrospective Validation: validation of a process or piece of equipment for a product already in distribution based upon accumulated and statistical reviews of production, testing, and control data; these reviews are primarily accomplished by graphic representation of the data in chronological order; the review is limited to quantitative results that are indicative of product quality

Reverse Traceability: the ability to identify and recall, if necessary, all measuring instruments that were calibrated according to a given measurement standard

ROB: Process Robustness

Robustness: demonstrates the method's ability to remain unaffected by deliberate variations in the method procedure and provides an indication of its reliability under normal operating conditions

Second Order Kinetics: chemical reactions that proceed at rates that are proportional to the square of the concentration of one of the reaction ingredients; reactions that proceed by second order kinetics decrease faster than reactions that proceed through first order kinetics

Six Sigma: a systematic method for improving the operational performance of an organization by eliminating variability and waste ("sigma" refers to standard deviation from the mean in a normal distribution)

Spaghetti Diagram: a map depicting the movement of people, product, or materials and total distance traveled; able to depict multiple people

Specification: an explicit set of requirements or limits to be satisfied by a product when subject to testing

Specificity: demonstrates the ability of the method to measure an analyte in the presence of components that may be in the sample, including impurities, degradants, and matrix components

Spinner flask: a flask used to culture cells; the side arms of the flask are used for drawing samples from the culture and transferring the culture from one vessel to another.

Stakeholders: departments with a vested interest in facility, system, and/or equipment validation

Standard Deviation: measure of how widely values are dispersed from the average value (mean) of a sample

Standardization: the process by which a user adjusts an instrument or measurement system to a defined reading at the beginning of the day/shift or just before use by comparison with one or more certified, traceable calibration standards

Standard Operating Procedure (SOP): a written and approved procedure that is version controlled and used consistently for current Good Manufacturing Practices (cGMPs)-related testing or operations

Statistical Process Control (SPC): the application of statistical methods to the monitoring and control of a process to ensure that it operates at its full potential to produce conforming product

Steam In Place (SIP): the introduction of steam to sanitize or sterilize a piece of equipment without disassembling the equipment

Sterile: the complete absence of viable (living) microorganisms

Sterilization: the act or process, either physical or chemical, that destroys, inactivates, or eliminates all forms of life, including bacterial endospores (the most resistant of all microorganisms)

Sterilizing grade filtration: direct flow filtration (oftentimes involving the use of *nanofiltration* cartridges) that eliminates microbial organisms and insoluble proteins; removes adventitious and endogenous viruses; and sterile filters the product in preparation for final formulation

Systematic Error: a type of error that causes the average of the readings to be offset from the true value; also referred to as bias

Tangential Flow Filtration (TFF): devices that orient the membrane so that process flow sweeps across the active filtration surface, which minimizes pore plugging and surface fouling by concentrated reject elements of the feed

Terminal Sterilization: a process whereby a product is sterilized in its final container, permitting the measurement and evaluation of quantifiable microbial lethality

Test Uncertainty Ratio (TUR): the ratio of the stated accuracy of the measurement standard to the stated accuracy of the measuring instrument under test

Tolerance: the maximum allowable deviation or error from a specified value (exemplified by the phrase *plus or minus* used after a given value) to indicate the allowable error

Total Organic Carbon (TOC): a measure of carbon-containing chemical compounds; often used as a quality control assay to measure the presence of potential chemical contamination (e.g., product, media, etc.); units typically used in TOC analysis are ppb (parts per billion); TOC does not distinguish among compounds.

Traceability: a process that demonstrates a chain of unbroken measurements (calibrations or comparisons) from the device being calibrated, to the calibration standard, to national, international, or available intrinsic standards of measurement

Transgenic expression: protein is expressed by an organism whose genome has been altered by the transfer of a gene from another species

TRIZ: the Russian acronym for Theory of Inventive Problem Solving; a technique that attempts to define a specific problem as a system and identify elements in the system that need correction to reach the desired solution

T-test: a statistical test used to determine if the scores of two groups differ on a single variable; for instance, a t-test could be used to determine whether writing ability differs among students in two classrooms

Turn Over Package (TOP): data package(s) consisting of critical data and documentation to support system validation; documentation of the design basis, fabrication, assembly, installation, and testing of equipment and facilities, which provides the basis for validation, operation, and maintenance; the documentation package that is provided with each qualified system is typically supplied by the facility or equipment provider/installer

Ultrafiltration: filtration used between chromatography steps to concentrate the product and change the buffer conditions in order to prepare it for subsequent chromatography steps

United States Pharmacopeia (USP): a non-governmental, official, public standards-setting authority for prescription and over-the-counter medicines and healthcare products sold or manufactured in the United States; sets standards for the quality, purity, strength, and consistency of these products, which are critical to public health; also sets widely recognized standards for food ingredients and dietary supplements

Upstream: fermentation process incorporating dispensing, media preparation, and cell culture

VAC: Validation Acceptance Criteria

Validation Protocol: a written plan describing the process to be validated, including production equipment and how validation will be conducted; this includes the kind and number of samples and replicates, the tests to be used, and acceptance criteria for the test results; the validation protocol addresses objective test parameters, product and process characteristics, predetermined specifications, and factors which will determine acceptable results

Value Stream Map: Value Stream Mapping is a lean manufacturing technique used to analyze the flow of materials and information currently required to bring a product or service to a consumer; at Toyota, where the technique originated, it is known as "material and information flow mapping"

Water For Injection: high quality water made by filtering and distilling potable water; this purification process results in a significantly lower microbial action level than tap water

WC: inches water column; a measurement of pressure

Work Instruction (WI): WIs are similar to SOPs and are also the more commonly accepted terminology in ISO 9001 certified sites; typically SOPs are more general in nature than WIs

