LATHAM & WATKINS LLP

The BOOK *of* JARGON®

Healthcare & Life Sciences

The Latham & Watkins Glossary of Healthcare & Life Sciences Terminology and Acronyms

First Edition

The Book of Jargon®: Healthcare & Life Sciences *is one of a series of practice area-specific glossaries published by Latham & Watkins.*

The definitions contained in The Book of Jargon® *are designed to provide an introduction to the applicable terms often encountered in the healthcare and life sciences industry. These terms raise complex legal issues on which specific legal advice will be required. The terms are also subject to change as applicable laws and customary practice evolve.*

As a general matter, The Book of Jargon®: Healthcare & Life Sciences *is drafted from a US perspective. The information contained herein should not be construed as legal advice.*

If you have suggestions for additional terms or expanded or clarified definitions for the current terms, please send an email to hlsglossary@lw.com.

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3A List: the stage of the BPCIA Exchange process when the Reference Product Sponsor provides the biosimilar producer with a list of the Patents it believes could be reasonably asserted against the Biosimilar based on its aBLA. Reference 42 U.S.C. 262 (3)(A). See also Patent Dance.

3B Statement: the stage of the BPCIA Exchange process when the Biosimilar Product Applicant provides the Reference Product Sponsor with a list of any additional Patents that the applicant believes could reasonably be infringed and a detailed statement that explains on a claim-by-claim basis why the Patents contained in the 3A List are invalid, unenforceable, or will not be infringed by the Biosimilar Product or a statement that the Biosimilar will not begin to market its product until after the Patent(s) expire(s). Reference 42 U.S.C. 262 (3)(B). See also Patent Dance.

3C Statement: the stage of the BPCIA Exchange process when the Reference Product Sponsor provides the biosimilar producer with a detailed statement that explains on a claim-by-claim basis how the Patents included in the 3A List will be infringed by the Biosimilar Product and a response to the allegations made by the biosimilar producer in its 3(B) Statements. Reference 42 U.S.C. 262 (3)(C). See also Patent Dance.

30 month stay: the 30-month period provided for under the Hatch-Waxman Act during which the FDA presumptively may not approve the ANDA or 505(b)(2) NDA triggered by the timely filing of a lawsuit involving one or more Patents listed in the Orange Book following the provision of notice to the Branded Company of a Paragraph IV certification. See also Paragraph IV, Generic, Branded Company.

340B Drug Pricing Program: a program that allows certain hospitals and other healthcare Providers to obtain covered outpatient Drugs (Prescription Drugs and Biologics other than Vaccines) from drug manufactures at Discounted prices. The minimum Rebate percentage provided by the Manufacturer varies among brand name and Generic Drugs. Covered entities include disproportionate share hospitals (DSH), critical access hospitals (CAHs), rural referral centers, sole community hospitals, children's hospitals and freestanding cancer hospitals. Covered entities can purchase 340B Drugs for dispensing to eligible patients treated in an outpatient setting, including patients with Medicare or private insurance.

351(k) Pathway: an abbreviated licensure pathway, which permits a Follow-on Biological Product to be licensed under section 351(k) of the Public Health Service Act (PHSA) based on less than the full complement of product-specific preclinical and clinical Data otherwise required to support a Biological License Application. Pursuant to this pathway, a Follow-on Biologic may be licensed as either biosimilar to or interchangeable with an FDA-licensed Biological Product (Biologic).

505(b)(2): a 505(b)(2) application is a New Drug Application that contains full reports of investigations of safety and effectiveness but where at least some of the information required for approval comes from studies

not conducted by or for the applicant. This alternate regulatory pathway enables the applicant to rely, in part, on the FDA's findings of safety and efficacy for an existing product, or published literature, in support of its application. The FDA may then approve the new product candidate for all or some of the labeled Indications for which the referenced product has been approved, as well as for any new Indication the 505(b)(2) applicant is seeking.

510(k) Premarket Notification (510(k) Submission): Manufacturers of certain Medical Devices must submit to the FDA a premarket notification submission pursuant to Section 510(k) of the Federal Food, Drug, and Cosmetic Act (also referred to as a 510(k) Submission) requesting clearance of the Device for commercial distribution in the United States. To obtain clearance, the Manufacturer must demonstrate that the Device is "substantially equivalent" to a predicate Device, which is either a Device that was legally marketed prior to May 28, 1976 for which the FDA has not yet called for the submission of a Premarket Approval (PMA), or PMA, application, or another commercially available, similar Device that was cleared through the 510(k) process. In determining substantial equivalence, the FDA assesses whether the proposed Device has the same intended use as the predicate Device and either has the same technological characteristics as the predicate Device or, if the proposed Device has different technological characteristics, is as safe and effective as the predicate Device and does not raise different questions of safety and effectiveness. In addition to a substantial equivalence comparison, many 510(k) Submissions contain performance Data, which may — but need not always — include Data from clinical testing. 510(k) Submissions are subject to user fees unless a specific exemption applies.

8 + 2 + 1 (EU Data and Market Exclusivity): in the EU, the holder of an initial marketing authorisation is given eight years of Data Exclusivity during which generic companies cannot cross-refer to the registration dossier of the initial product.

Additionally, a generic marketing authorisation holder cannot place the generic product on the market (market Exclusivity) before an additional period of two years, even if the medicinal product has already received a marketing authorisation.

A product authorized for marketing may also benefit from one additional year of market Exclusivity if a new therapeutic Indication of the product bringing significant benefit in comparison with existing therapies is authorized within the first eight years of Data Exclusivity.

AAC: acronym for Average Acquisition Cost.

Abbreviated Biologics License Application (aBLA): an application to the FDA, requesting approval for a Biosimilar. The application does not have to contain full clinical trial Data to establish safety and efficacy — as is the case with BLAs. Instead, the aBLA must contain Data, including

human clinical Data, demonstrating that the Biosimilar is "highly similar" to the innovator Biological Product (Biologic) (notwithstanding minor differences in clinically inactive components) and demonstrating no clinically significant differences between the two in terms of safety, purity and potency. See BPCIA.

Abbreviated New Drug Application (ANDA): an application to the FDA, requesting approval for a generic Drug product. Section 505(j) of the Federal Food, Drug, and Cosmetic Act establishes an abbreviated approval process for generic versions of approved Drug products through the submission of an ANDA. An ANDA provides for marketing of a Drug product that has the same active ingredients in the same strengths and Dosage Form as the Reference Listed Drug and has been shown to be bioequivalent to the reference listed Drug. ANDA applicants are required to conduct bioequivalence testing to confirm chemical and therapeutic equivalence to the branded reference Drug. The application does not need to contain full Pre-Clinical and clinical Data to establish safety and efficacy — as is the case with NDAs. Instead, the ANDA must contain Data demonstrating that the Generic Drug is bioequivalent to the innovator Drug. See Hatch-Waxman.

aBLA: acronym for Abbreviated Biologics License Application.

Ablation: the surgical removal of body tissue. Cardiac Ablation is a procedure used to scar small areas of the heart that may be related to heart rhythm problems. This Ablation is usually done by inserting Catheters through a vein in a patient's groin and threading them to the patient's heart to correct structural problems that cause Arrhythmia. Endometrial Ablation is a procedure that destroys the uterine lining, or endometrium, to treat abnormal uterine bleeding. The endometrium heals by scarring, which usually reduces or prevents uterine bleeding.

ACA: acronym for Affordable Care Act.

Accelerated Approval: the FDA may approve an application for a Drug or Biologic for a serious or life-threatening disease or condition upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. The evidence to support that an endpoint is reasonably likely to predict clinical benefit may include epidemiological, pathophysiological, therapeutic, pharmacologic or other evidence developed using Biomarkers, for example, or other scientific methods or tools. Accelerated Approval may be subject to a requirement that the sponsor conduct appropriate post-approval studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit, and/or that the sponsor submit copies of all Promotional Materials during the pre-approval review

period and, following approval and for a period that the FDA determines to be appropriate, at least 30 days prior to dissemination of the materials.

Accessory: an article which — although not technically a Device — is intended specifically by its Manufacturer to be used together with a Device to enable the article to be used in accordance with the use of the Device intended by the Manufacturer of the Device (Art. 1 para. 2 lit. b) Directive 93/42/EEC).

Accountable Care Organization (ACO): groups of doctors, hospitals, and other healthcare Providers, who voluntarily participate in a payment and care delivery model that ties Reimbursement for services rendered to quality metrics with the goal of reducing the total cost of care for assigned populations of patients. As a concept, ACOs share three core principles: (1) provider-led organizations with a primary care focus that are collectively accountable for quality and total per capita costs across the full continuum of care for a defined population of patients; (2) Reimbursement and payments are tied to quality improvements that also reduce overall costs; and (3) subject to performance measurements to support improvement and provide confidence that savings are achieved through improvements in care.

Under the Medicare program, an ACO is defined as an organization of healthcare Providers that agrees to be accountable for the quality, cost and overall care of Medicare beneficiaries enrolled in the traditional Fee-For-Service program and assigned to the particular ACO. CMS offers several ACO programs, including the Medicare Shared Savings Program, Advance Payment Initiative and Pioneer ACO Model.

Accreditation: a process of review that healthcare organizations participate in to determine their ability to meet predetermined criteria and standards of Accreditation established by the Accreditation organization. Providers and Suppliers accredited by an approved national Accreditation organization (AO) are exempt from routine surveys by state survey agencies to determine compliance with Medicare conditions.

ACE: acronym for Angiotensin-Converting Enzyme.

ACE Inhibitors: ACE Inhibitors are compounds that block angiotensin, with potential utility in lowering blood pressure.

ACO: acronym for Accountable Care Organization.

Active Implantable Medical Devices (AIMDs): the Directive 90/385/EEC* defines Active Implantable Medical Devices as Medical Devices intended to be totally or partially introduced, surgically or medically, into the human body or by medical intervention into a natural orifice, and which is intended to remain after the procedure.

Reference: Council Directive 90/385/EEC of 20 June 1990 on the approximation of the laws of the Member States relating to active implantable Medical Devices.

Active Moiety: portion of Molecule responsible for causing a Drug to act the way it does. Active Moiety does not include appended portions of a Molecule that cause the Drug to be an ester, salt or other noncovalent derivative of the Molecule.

Active Pharmaceutical Ingredient (API): the chemically active ingredient in a Drug intended to cause the desired effect in the body, as opposed to the inactive ingredients in a Drug, sometimes referred to as expedients.

Active Substance Master File (ASMF): according to the EMA, the main objective of the ASMF is to allow valuable confidential active substance Manufacturer Intellectual Property or Know-How to be protected, while at the same time allowing the applicant or marketing authorisation holder to take full responsibility for the medicinal product and the active substance's quality and quality control. National Competent Authorities and EMA thus have access to the complete information necessary to evaluate the active substance's suitability in the medicinal product.

Acute Lymphocytic Leukemia (ALL): also known as acute lymphoblastic leukemia (ALL), a cancer of the blood and marrow that is the most common form of childhood cancer. The term "acute" means that the Leukemia progresses rapidly and creates immature blood Cells. The term "lymphocytic" refers to the white blood Cells called lymphocytes, which ALL affects. Acute leukemia tends to respond well to treatment, especially in children.

Acute Myeloid Leukemia (AML): also known as acute myelogenous leukemia, acute myeloblastic leukemia, acute granulocytic leukemia and acute nonlymphocytic leukemia, a cancer of the blood and bone marrow which is most common in older people. The word "acute" means the Leukemia progresses rapidly. The word "myeloid" refers to a group of white blood Cells called myeloid Cells, which AML affects.

Adequate and Well-Controlled Clinical Trial: a study in humans typically characterized by: a clear statement of objective and study protocol, a study design allowing for valid comparison with a control to assess efficacy, a proper method of subject selection to minimize biases, well-defined and reliable methods of assessment, and proper analysis of the study results. The FDA typically requires Data from at least two Adequate and Well-Controlled Clinical Trials to support a claim of effectiveness for a Drug.

ADME: acronym for "absorption, distribution, metabolism, and elimination," the process of administering a drug Molecule throughout a human or animal body.

ADR: an acronym for Adverse Drug Reaction.

Adulterated Product: an FDA-regulated product that fails to conform to standards of quality, strength or purity. Drugs and Devices that are not manufactured, processed, packed or held in conformance with current good manufacturing practice are deemed adulterated as a matter of law.

AdvaMed: abbreviation for Advanced Medical Technology Association.

AdvaMed Code: abbreviation for AdvaMed Code of Ethics on Interactions with Health Care Professionals.

AdvaMed Code of Ethics on Interactions with Health Care Professionals (AdvaMed Code): a code of ethics which AdvaMed developed that provides guidance to Medical Device companies on ethical interactions with healthcare professionals. The AdvaMed Code supports the adoption of effective compliance programs and sets forth guidance on such interactions to foster transparency and compliance with applicable laws, regulations and government guidance issuances. The AdvaMed Code addresses subjects including: sales, marketing and promotional activities, and financial arrangements with healthcare professionals. Adherence to the AdvaMed Code is voluntary; however, certain states have based regulations on the provisions of the AdvaMed Code or adopted the AdvaMed Code in its entirety by reference.

Advanced Medical Technology Association (AdvaMed): a voluntary trade organization primarily for organizations that develop, produce, manufacture and market medical products, technologies, and related services and therapies. AdvaMed advocates on behalf of its global membership to facilitate faster product approvals, appropriate Reimbursement, and access to international markets. AdvaMed has more than 300 members. The organization developed the Code of Ethics on Interactions with Health Care Professionals (known as the AdvaMed Code) that serves as a guide for the Medical Device industry on ethical interactions with healthcare professionals.

Advanced Therapy Medicinal Products (ATMPs): Advanced Therapy Medicinal Products (ATMPs) are biological medicinal products based on Genes or Cells and intended for human use.

ATMPs can be classified into four main groups:

- Gene-therapy medicines
- Somatic-cell therapy medicines
- Tissue-engineered medicines
- Combined ATMPs

Adverse Drug Reaction (ADR): see Adverse Event (AE).

Adverse Event (AE): US: the FDA defines an Adverse Event as any untoward medical occurrence associated with the use of a Drug in humans, whether or not considered drug related.

EU: defined by the Clinical Trials Regulation* as any untoward medical occurrence in a subject to whom a medicinal product is administered and which does not necessarily have a causal relationship with this treatment.

*Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on Clinical Trials on medicinal products for human use, and repealing Directive 2001/20/EC.

See Adverse Drug Reaction (ADR).

Advertising: an advertisement for an FDA-regulated product that appears in print materials (published journals, magazines, other periodicals, newspapers) or that is broadcast through media (radio, television or telephone communication systems).

Advisory Committee: a group that advises the FDA on whether to approve a Drug.

Advisory Opinion: a legal opinion which the OIG issues to one or more requesting parties about how the OIG will apply its Fraud And Abuse authorities, principally the AKS, to the requesting party's existing or proposed business arrangement. An OIG Advisory Opinion is legally binding on the Department of Health & Human Services and the requesting party or parties. It is not binding on any other governmental department or agency. A party that receives a favorable Advisory Opinion is protected from OIG administrative sanctions, so long as the arrangement at issue is conducted in accordance with the facts submitted to the OIG. No person or entity can rely on an Advisory Opinion issued to someone else. CMS also has a similar Advisory Opinion process addressing the Stark Law.

AE: acronym for Adverse Event.

AEMPS: acronym for Spanish Agency for Medicines and Health Products or Agencia Española de Medicamentos y Productos Sanitarios.

Affordable Care Act (ACA): also known as the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act (and colloquially referred to as "Obamacare"), a US statute enacted on March 23, 2010, that substantially changed the US healthcare system to increase the quality and affordability of health insurance, to lower the uninsured rate by expanding access to and enrollment in insurance Coverage, and to reduce the cost of healthcare for all stakeholders, by transforming the provision of healthcare in the United States. Among the ACA's healthcare reform provisions are:

- The prohibition on denial of Coverage due to pre-existing conditions
- Minimum standards for health insurance policies
- A mandate that all individuals not otherwise covered by an employer-sponsored health plan or a public health insurance program (such as Medicare, Medicaid or TRICARE) obtain an approved private-health insurance policy or pay a penalty

- The creation of health insurance exchanges to foster a market through which such individuals may compare and purchase health insurance

The ACA also included numerous provisions designed to assist the government to fight fraud, waste and abuse in the federal healthcare programs, including provisions amending the FCA's public disclosure bar for certain whistleblower/Relator complaints, reducing the intent standard necessary to prove a violation of the AKS to permit the government to take action against persons for violating the law, even if that person did not have actual knowledge of the law or the specific intent to violate it; and imposed a requirement obligating Providers and Suppliers to report and return Overpayments to the government within 60 days of identifying the Overpayment or face potential liability under the FCA for retaining the Overpayment.

Age-Related Macular Degeneration (AMD): the leading cause of vision loss among Americans aged 50 and older, AMD involves the degeneration of the macula, a small spot near the center of the retina responsible for the sharp, central vision needed to see objects that are straight ahead. Macular degeneration is defined as either dry (non-neovascular) or wet (neovascular). Neovascular refers to the growth of new blood vessels in an area where they are not supposed to be. Dry macular degeneration is more common and wet macular degeneration usually leads to more serious vision loss. AMD can only be detected by a comprehensive dilated eye exam.

AIFA: acronym for Italian Medicines Agency or Agenzia Italiana del Farmaco (the Italian drug agency).

AKS: acronym for Anti-Kickback Statute.

ALL: acronym for Acute Lymphocytic Leukemia.

Allele: one of a number of alternative forms of the same Gene. Humans are called diploid organisms because they have two Alleles at each genetic locus, with one Allele inherited from each parent. In the case of genetically inherited disease, a person inheriting two or sometimes just one of a disease-causing Allele, that person may or may not get the disease, but the individual is a carrier. Genetic testing companies will screen for many disease Alleles and CRISPR technology eventually may be able to edit out bad Alleles in humans. Research is currently underway to edit out Alleles during In Vitro fertilization to eliminate inheritance of particularly bad Alleles (where there are no cures). Examples include Alleles for breast cancer (BRCA1 and BRCA2) and Leukemia (BCR-ABL).

Allogenic: relating to or involving tissues or Cells that are genetically dissimilar and hence immunologically incompatible, even though they come from individuals of the same species.

Ambulatory Payment Classification (APC): the APC system is the Coding system which the CMS designed and maintains to reimburse hospitals for outpatient services provided to Medicare beneficiaries. This bundled payment system groups covered outpatient services, identified by HCPCS Codes, that are comparable clinically and with respect to cost. APCs form the basis for payment rates under the Medicare Hospital Outpatient Prospective Payment System, with services assigned to specific APCs and bundled payment amounts calculated for the APC group.

Ambulatory Surgery Center (ASC): a licensed healthcare facility that is dedicated to performing surgical procedures on an outpatient basis; that is, patients are admitted and discharged on the same day. ASCs may be either free-standing facilities or a dedicated part of a hospital. They may be owned by physicians, hospitals, publicly owned companies or various combinations of the foregoing. Also sometimes referred to as "outpatient surgery centers," "same day surgery" or similar variations.

Amino Acid: organic compounds that combine to form Proteins. The human body uses Amino Acids to make Proteins to help the body break down food, grow, repair body tissue and perform other bodily functions. There are 20 natural Amino Acids, and scientists are also making unnatural Amino Acids to create Molecules that are Protein-like, but with unique properties. Amino Acids are tethered to tRNA and are bound together with ribosomes as the tRNA reads the mRNA sequence during the Protein synthesis process.

Amplification: an increase in the frequency of a Gene or chromosomal region as a result of duplicating a DNA segment by an In Vivo or In Vitro process, such as gene duplication or PCR. Gene duplication refers to the duplication or replication of a portion of genetic material resulting in multiple copies of a region of DNA.

Anatomical Therapeutic Chemical (ATC) Codes: the Anatomical Therapeutic Chemical Codes are two classification codes used to classify approved medicines into different levels.

In the WHO (World Health Organization) classification system, the active substances are divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties. Drugs are classified in groups at five different levels. The Drugs are divided into 14 main groups (1st level), with pharmacological/therapeutic subgroups (2nd level). The 3rd and 4th levels are chemical/pharmacological/therapeutic subgroups and the 5th level is the chemical substance. The 2nd, 3rd and 4th levels are often used to identify pharmacological subgroups when that is considered more appropriate than therapeutic or chemical subgroups.

In the EphMRA (European Pharmaceutical Market Research Association) classification system, the approved medicines are classified into four different levels, from the most general to the most specific. In its antitrust

and merger control decisions the European Commission uses the third level (ATC3) of the EphMRA classification system as a starting point to define the relevant market in which to assess the effects on competition of investigated merger or conduct.

ANDA: acronym for Abbreviated New Drug Application.

Anesthesia: is a way to control pain during surgery or other procedures by using medicines called anesthetics. Local Anesthesia numbs a small part of the body during minor procedures while the patient remains conscious. Regional Anesthesia blocks pain to a larger part of the patient's body. General Anesthesia affects the patient's brain and the rest of the body and renders the patient unconscious.

Angiogenesis: the physiological process through which new blood vessels form from pre-existing vessels. This process is distinct from vasculogenesis, which is the de novo formation of blood vessels. The first vessels in a developing embryo form through vasculogenesis, after which Angiogenesis is responsible for most blood vessel growth.

Angiotensin-Converting Enzyme (ACE): an Enzyme which catalyzes the production of angiotensin, a hormone that causes narrowing of blood vessels.

Animal and Plant Health Inspection Service (APHIS): an agency of the U.S. Department of Agriculture responsible for protecting animal health and welfare and plant health.

ANSM: acronym for National Agency for Medicine and Health Products Safety or Agence Nationale de Sécurité de Médicament et des Produits de Santé (the French Drugs and Medical Devices agency).

Antibacterials: anything that destroys or suppresses the growth of Bacteria or their ability to reproduce. Heat, certain chemicals and antibiotic Drugs have Antibacterial properties.

Antibiotic and Antibiotic Resistance: antibiotics are natural or synthetic chemicals that kill Bacteria, but over- and misuse of Antibiotics has enabled some Bacteria to mutate their Genes in a way to resist the most common Drugs. As a result, super toxic alternatives must be used or no treatment is possible. More and more resistant Bacteria are showing up in society.

Antibody/Antibodies: Molecules the body makes in response to the detection of a foreign substance in order to target the foreign substance for destruction by the immune system. Antibodies can be used to diagnose a patient's exposure to something.

Antibody Construct: the particular molecular structure of an Antibody, which typically consists of two large and two small subunits, each of which can vary in structure.

Anticipation: a reason for finding a Patent claim is not patentable based on the prior Invention or disclosure of the claimed Invention by another, or based on the inventor's own disclosure of the claimed Invention by publication, prior sale or prior use. Anticipation requires that all claim elements appear in a single prior art reference.

Antigen: any substance (Bacteria, Protein, Virus or other harmful agent to which an Antibody binds) that causes an immune system to produce Antibodies against such substance.

Anti-Kickback Statute (AKS): a federal law prohibiting persons and entities from knowingly and willfully soliciting, receiving, offering or providing remuneration, directly or indirectly, if one purpose of the Remuneration is to induce either the referral of an individual, or the furnishing, recommending, or arranging for a good or service, for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs. In this context, the term "induce" generally means the intent to gain influence over the reason or judgment of the person making a referral decision or recommendation. The definition of "remuneration" has been broadly interpreted to include anything of value, including for example gifts, Discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash or cash equivalents, waivers of payments, ownership interests, and providing any item or service at an amount inconsistent with Fair Market Value. The penalties for violating the AKS include criminal penalties and civil sanctions, including fines, imprisonment and possible Exclusion from the Medicare and Medicaid programs.

Antisense DNA: the non-coding strand of DNA that complements a coding strand in a segment of double-stranded DNA. During RNA synthesis, this strand serves as a template, and binds to RNA polymerase.

Antisense RNA: the non-coding strand of RNA that complements a coding sequence of mRNA, in atypical circumstances when RNA forms a duplex. The presence of Antisense RNA impedes Translation because when RNA is in its duplex state, the ribosome cannot access the Nucleotides in the mRNA, or because the ribonucleases in the Cell quickly degrade the duplex RNA.

Antitrust Statutes: federal and state laws designed to protect trade and commerce from illegal restraint, monopolies, price fixing and price discrimination. The primary federal antitrust acts are the Sherman Antitrust Act (1890), the Clayton Act (1914), the Federal Trade Commission Act (1914) and the Robinson-Patman Act (1936).

Antivirals: a class of medications used to treat viral infections. Most Antivirals are used for specific viral infections, whereas a broad-spectrum Antiviral is effective against a wide range of Viruses. Antivirals do not destroy the Target pathogen, but instead inhibit its development.

APC: acronym for Ambulatory Payment Classification.

APHIS: acronym for Animal and Plant Health Inspection Service.

API: acronym for Active Pharmaceutical Ingredient.

Applicable GPO (Sunshine Act): Applicable Group Purchasing Organizations (see GPOs) under the Sunshine Act are those GPOs that operate in the United States, that purchase or arrange for purchase, or negotiate the purchase of a Prescription Drug, or a Device, or medical supply that requires premarket approval or notification from the FDA, for which federal Reimbursement is available, on behalf of GPO members. Applicable GPOs must annually disclose physician ownership through the open payments reporting system.

Applicable Manufacturer (Sunshine Act): an entity with a physical location or which otherwise conducts activities within the United States, and engages in the production, preparation, propagation, compounding or conversion of a Covered Drug, Device, biological or medical supply, including entities under common ownership (5% ownership or more) that provide assistance or support with respect to the production, preparation, propagation, compounding, conversion, marketing, promotion, sale or distribution of a Covered Drug or Device for sale or distribution in the United States. Unless exempted or otherwise limited by the Act, an Applicable Manufacturer must report any payment or other transfer of value to a covered recipient, even if the payment is not related to a specific Covered Drug or Device.

Arrhythmia: an irregular heartbeat. Tachycardia refers to the heart beating too fast and bradycardia refers to the heart is beating too slow. Arrhythmias result from many causes including coronary heart disease, high blood pressure, electrolyte imbalances in the blood and other medical conditions.

Arzneimittel-zulassung (Drug Approval): the ultimate approval of a Pharmaceutical from the Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte) in Germany. Such approval in particular requires Proof of Concept (Wirksamkeitsnachweis), appropriate Pharmaceutical quality as well as harmlessness of the Pharmaceutical.

ASC: acronym for Ambulatory Surgery Center.

ASMF: acronym for Active Substance Master File.

ASP: acronym for Average Sales Price.

Assay: a generic term that refers to a method or experiment used to discover a new entity or to quantify the activity of a Molecule or organism.

ATMPs: acronym for Advanced Therapy Medicinal Products.

Authorized Representative: any natural or legal person who, explicitly designated by the Manufacturer, acts and may be addressed by authorities and bodies in the relevant country instead of the Manufacturer with regard to the latter's obligations.

Autologous: derived from the same individual; for example, incubated lymphoid Cells with Autologous tumor Cells.

AUC / Area Under the Curve: a Pharmacokinetic term denoting drug exposure over time and proportional to the total drug amount absorbed by the body. When plotting drug concentration in plasma against time, the quantification of the Area Under The Curve in such plot can then be used to describe the bioavailability of a given Drug.

Average Acquisition Cost (AAC): an amount typically derived from the purchase prices retail community pharmacies pay to acquire Drug products. In the context of Medicaid, the AAC is used by some state agencies as a pricing benchmark to reimburse pharmacy Providers for covered outpatient Drugs dispensed to Medicaid beneficiaries.

Average Manufacturer Price (AMP): the average price paid to the Manufacturer by wholesalers for Drugs distributed to retail community pharmacies, and by retail community pharmacies that purchase Drugs directly from the Manufacturer. AMP includes certain defined sales, nominal price sales, Discounts, Rebates, payments and other financial transactions. AMP may be used to calculate the Rebate amount Manufacturers must pay for Drugs under the Medicaid Drug Rebate Program (see, Medicaid Drug Rebate Program).

Average Sales Price (ASP): a price calculated by dividing the value of a Manufacturer's sales of a Drug to all purchasers in the United States in a calendar quarter by the total number of units of the Drug that the Manufacturer sold in that same quarter. The ASP is calculated net of price concessions, such as volume Discounts, prompt pay Discounts, cash Discounts, free goods contingent on purchase requirements, chargebacks and certain Rebates. Medicare pays for most Drugs covered under Medicare Part B using a methodology based on ASP.

BAA: acronym for Business Associate Agreement.

Bacteria: microscopic single-celled organisms. Bacteria can be harmful (causing infection) or beneficial (aiding in decomposition or fermentation) depending on the context.

Basal and Squamous Cell Skin Cancer: Basal Cell Skin Cancer is the most common form of skin cancer and consists of abnormal growths or lesions that arise in the skin's basal Cells, which line the deepest layer of the epidermis. Squamous Cell Skin Cancer is the second most common form of skin cancer and consists of uncontrolled growth of abnormal Cells arising in squamous Cells, which compose most of the skin's upper layers.

Bayh-Dole: this legislation deals with patentable Inventions that result from federally funded research. The Bayh-Dole Act establishes that research institutions can retain patent rights for Inventions that arise from federally funded research. The Act contains other provisions governing those rights, such as requirements that the institution utilize the Invention and grant the US government a License. 35 U.S.C. § 200–212.

B-Cell: also known as B lymphocytes, a type of white blood Cell that secretes Antibodies. In humans, B-Cells mature in the bone marrow.

Beneficiary: a person eligible to receive healthcare benefits paid for by a Third-Party Payor, such as Medicare, Medicaid, HMOs and indemnity insurance companies.

Beneficiary Inducement: the prohibited offer or transfer of Remuneration to a Medicare or Medicaid Beneficiary that the person offering or providing the Remuneration knows or should know is likely to influence the Beneficiary's selection of a particular Provider, practitioner or Supplier of Medicare or Medicaid payable items of services. Remuneration includes, without limitation, waivers of Copayments or Deductible amounts (or any part thereof) and transfers of items or services for free or for other than Fair Market Value. The person offering or providing such Remuneration to the Beneficiary may be liable for civil monetary penalties of up to US$10,000 for each wrongful act. A limited number of exceptions to the prohibition are set forth in the applicable statute and implementing regulations.

Best Price: with respect to a Manufacturer's single source Drug or innovator multiple source Drug, the lowest price available from the Manufacturer during a period of time to any entity in the United States in any pricing structure (including capitated payments). Best Price includes all sales and associated Rebates, Discounts and other price concessions provided by the Manufacturer to any entity unless the sale, Discount, price concession or entity is specifically excluded by statute or regulation. A Drug's Best Price may be used to calculate the Rebate amount a Manufacturer must pay under the Medicaid Drug Rebate Program.

BfArM: acronym for the German Federal Institute for Drugs and Medical Devices or Bundesinstitut für Arzneimittel und Medizinprodukte.

Biotechnology Innovation Organization (BIO): formerly known as the Biotechnology Industry Organization, BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO advocates for its members, focusing on critical issues and industry policies, and working with Congress, federal agencies and international organizations to encourage the development of new technologies.

Benign: the opposite of Malignant. A Benign tumor is one that is not recurrent, favorable for recovery with appropriate treatment and does not invade surrounding tissue or spread to other parts of the body.

Bioassay: a type of scientific experiment that involves the use of live animals or plants (In Vivo) or tissue or Cells (In Vitro) to determine the biological activity of a substance.

Biocatalyst: a substance, such as an Enzyme or hormone, that initiates or increases the rate of a chemical reaction.

Bioinformatics: a generic term that refers to quantifying and standardizing large amounts of biological Data; such Data sets are then collected in databases and mathematical algorithms are used to find trends and models within these Data sets.

Biological Product (Biologic): a Virus, therapeutic serum, toxin, antitoxin, Vaccine, blood, blood component or derivative, allergenic product, Protein (except any chemically synthesized polypeptide), or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings. Biological Products (Biologics) are regulated under the Public Health Service Act, as well as the Federal Food, Drug, and Cosmetic Act. See Biologics License Application (BLA).

Biological Target: see Target.

Biologics License Application (BLA): an application to the FDA, requesting permission to market a Biological Product (Biologic). Such products include Antibodies, Cytokines and other therapeutic Proteins. The BLA contains information about the product, the manufacturing process, Data from Pre-Clinical studies, Data from clinical studies and labeling information.

Biologics Price Competition and Innovation Act (BPCIA): the BPCIA was passed as part of the Patient Protection and Affordable Care Act to amend the Public Health Service Act (PHSA). It created an abbreviated FDA approval pathway (the 351(k) Pathway) for Biosimilar Products. Instead of completing a full BLA, Biosimilar Products now have a shortened approval pathway, as long as the applicant can establish that the Biosimilar Product is highly similar to the Reference Product, and that there are no clinically meaningful differences in terms of safety, purity and potency. The BPCIA also amended the PHSA to create periods of Exclusivity for certain Interchangeable Biological Products and FDA-licensed reference Biological Products (Biologics), and to create a framework for resolving Patent disputes involving Follow-on Biologics. See aBLA.

Biomanufacturing: the production of biologics-based therapeutic Drugs including protein-based Therapeutics, Vaccines, Gene Therapy and other Drugs that are so complex that they can only be made from living systems or are living systems.

Biomarker: a measurable substance in an organism, the presence of which indicates a condition, disease, infection or environmental exposure. Biomarkers can be used both for clinical research and diagnostic and therapeutic purposes.

Biosimilar / Biosimilar Product: a Biological Product (Biologic) that is approved based on a showing that it meets certain standards for similarity to an approved Biological Product. In the United States, a Biosimilar Product is a Biological Product that is approved pursuant to Section 351(k) of the Public Health Service Act, as amended by the BPCIA, based on a showing that it is highly similar to an FDA-approved Biological Product, known as a Reference Product, notwithstanding minor differences in clinically inactive components, and that it has no clinically meaningful differences in terms of safety, purity and potency from the Reference Product.

Biosimilar Product Applicant: the company that owns or has the rights in the Biosimilar Product. See Biosimilar.

Biological Product Sponsor: the company that owns or has the rights in the Biological Product (Biologic).

Biotechnology: the exploitation of biological processes for industrial and other purposes, especially the genetic manipulation of microorganisms for the production of Antibiotics and hormones.

BLA: acronym for Biologics License Application.

Bispecific Antibodies: artificial Proteins composed of fragments of two different antibodies that bind to two different types of Antigens. The most common use for Bispecific Antibodies is in cancer Immunotherapy; antibodies are engineered to simultaneously bind to a cytotoxic Cell and a Target such as a tumor Cell that is to be destroyed.

Blockbuster Drugs: an extremely popular Drug that generates annual sales of at least US$1 billion. Examples include Vioxx, Lipitor and Zoloft.

Blood Brain Barrier (BBB): the filtering mechanism of the capillaries that carry blood to the brain and spinal cord tissue, blocking the passage of certain substances.

Bovine Spongiform Encephalopathy (BSE): mad cow disease.

BPCIA: acronym for Biologics Price Competition and Innovation Act.

BPCIA Exchange: the process that occurs after a Biosimilar Product Applicant files an aBLA with the FDA, but before the Biological Product Sponsor sues the applicant for patent Infringement. The process includes the following steps in order: (1) the applicant provides its aBLA to the sponsor within 20 days of the FDA accepting the aBLA; (2) the sponsor provides a 3A List to the applicant; (3) the applicant provides its 3B Statements; and (4) the sponsor provides its 3C Statements. After this

exchange, the sponsor and applicant agree what Patents should be subject to patent infringement litigation, which is known as the Good Faith Negotiation stage. 42 U.S.C. § 262(l). See Patent Dance.

Brand Name Drug: a Drug that is marketed under a Trademark protected name, typically under an NDA, BLA, or 505(b)(2) application.

Branded Company (Branded Pharmaceutical Company): also known as brand name pharmaceutical companies. These companies file and/or maintain NDAs (21 U.S.C. 355(b)) and/or BLAs (42 U.S.C. 262(a)) with the FDA for approval of new Drugs, and such companies' Drugs are typically protected by Patents.

Breakthrough Therapy: pursuant to the Federal Food, Drug, and Cosmetic Act, a Breakthrough Therapy is a Drug that is intended, alone or in combination with one or more other Drugs, to treat a serious or life-threatening disease or condition, for which preliminary clinical evidence indicates that the Drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints (such as substantial treatment effects observed early in clinical Development). The FDA may take actions to expedite the Development and review of the Drug, including, as appropriate: holding meetings between the sponsor and the FDA review team; providing advice to, and interactive communication with, the sponsor regarding the Development of the Drug; involving senior FDA managers and experienced review staff; assigning a cross-disciplinary project lead to facilitate an efficient FDA review; and taking steps to ensure that the design of Clinical Trials is as efficient as practicable. The sponsor of a Drug may request that the Drug be designated as a breakthrough therapy concurrently with, or at any time after, submitting an Investigational New Drug Application.

BsUFA (Biosimilar User Fee Act) Date: the date by which the FDA expects to decide whether to approve a Biosimilar for licensure.

Bulk Product / Bulk Ware: products which have completed all processing stages except for blistering and/or final packaging and/or Labeling.

Business Associate: a person or entity, other than a member of a Covered Entity's workforce, that creates, receives, maintains or transmits PHI on behalf of a Covered Entity for a function or activity regulated by HIPAA. HIPAA requires Covered Entities to enter into Business Associate Agreements with any Business Associate. Under the HIPAA Omnibus Final Rule, Business Associates are directly liable for compliance with certain portions of HIPAA — including the HIPAA Security Rule — and are subject to enforcement for violations. Likewise, under HITECH and the HIPAA Omnibus Final Rule, Subcontractors of Business Associates who create, receive, maintain or transmit a Covered Entity's PHI are also considered Business Associates, and are also directly subject to HIPAA.

Business Associate Agreement (BAA): an agreement entered into by a Covered Entity and a Business Associate, or a Business Associate and its Subcontractor to ensure that the Business Associate or Subcontractor, as applicable, appropriately safeguards PHI. Among other duties, the BAA establishes the permitted and required uses and disclosures of PHI by the Business Associate or Subcontractor, and requires the Business Associate or Subcontractor to implement appropriate safeguards to prevent unauthorized use or disclosure of the information. Such safeguards include implementing requirements of the HIPAA Security Rule with respect to electronic PHI.

Business Combination: a transaction that results in the economic and legal combination of businesses and assets of two or more entities, whether by merger, asset purchase, stock sale or otherwise.

Cmax: a Pharmacokinetic term denoting the peak serum concentration of a Drug. The time at which Cmax occurs is known as Tmax.

Capsid: the Protein shell enclosing the genetic material of a Virus .

CAR: acronym for Chimeric Antigen Receptor.

Carcinogenicity: a cancer-causing substance or agent.

Cardiac Arrest: also known as sudden cardiac arrest (SCA), the sudden, unexpected loss of heart function, breathing and consciousness due to a sudden stop in effective blood circulation caused by the failure of the heart to contract effectively.

Cardiology: the branch of medicine that deals with diseases and abnormalities of the heart.

Cardiomyopathy: a disease causing the heart muscle to become enlarged, thick or rigid. As Cardiomyopathy worsens, the heart weakens, possibly leading to heart failure or Arrhythmias.

CAR T-Cell: acronym for Chimeric Antigen Receptor T-Cells.

Cas: CRISPR-associated Genes.

CAT: acronym for Committee for Advanced Therapies.

Catheter: a thin tube made from medical grade materials that can be inserted in the body to treat disease or perform surgical procedures. Catheters have cardiovascular, urological, gastrointestinal, neurovascular and ophthalmic applications.

CDC: acronym for Centers for Disease Control and Prevention.

CDR(s): acronym for Complementary Determining Region.

CDRH: acronym for Center for Devices and Radiological Health.

CE Marking: a compulsory conformity marking for a certain range of products sold – or manufactured or intended to be sold –within the European Economic Area (EEA), which was established in 1985. For a Manufacturer of Medical Devices, CE Marking certifies that a product meets fundamental requirements of relevant existing European Medical Device Directives. CE Marking is a legal requirement to place a Device on the market within the European Union.

Cell: the smallest structural and functional unit of an organism — consisting of cytoplasm and a nucleus enclosed in a membrane.

Cell Bank: a facility that stores Cells of a specific Genome for future use in a product or for medicinal needs.

Cell Line: a culture of Cells with uniform genetic makeup developed from a single Cell, used for research purposes.

Center for Biologics Evaluation and Research (CBER): a regulatory body within the FDA responsible for regulating Biological Products (Biologics) for human use under applicable federal laws, including the Public Health Service Act and the Federal Food, Drug and Cosmetic Act.

Center for Devices and Radiological Health (CDRH): a regulatory body within the FDA responsible for regulating Medical Devices and radiation-emitting products.

Center for Drug Evaluation and Research (CDER): a regulatory body within the FDA responsible for regulating over-the-counter and Prescription Drugs, including biological Therapeutics and Generic Drugs.

Centers for Disease Control and Prevention (CDC): a federal agency under the Department of Health and Human Services; a highly influential national public health institute in the United States. The CDC's main goal is to protect public health and safety through the control and the prevention of disease, injury and disability. Its areas of focus include, among other things, infectious diseases, pathogens, occupational safety, health education and promotion and injury prevention.

Centers for Medicare & Medicaid Services (CMS): an agency of the U.S. Department of Health and Human Services, formed in 1965 and previously known as the Health Care Financing Administration (HCFA), that administers the Medicare program, partners with state governments to administer the Medicaid program and Children's Health Insurance Program (CHIP), and has responsibility for health insurance portability standards, clinical laboratory quality standards under the Clinical Laboratory Improvement Amendments (CLIA), as well as other programs and standards.

Central Authorization of Medicinal Products in the European Union: a procedure that simplifies the marketing of medicinal products, enabling respective companies to place such products on the market in all states within the European Union.

Central Nervous System (CNS): the part of the nervous system consisting of the brain and the spinal cord. The CNS integrates information its receives from, and coordinates and influences the activity of, all parts of the bodies of all multicellular animals.

Central Reexamination Unit (CRU): a dedicated unit within the PTO that administers Ex Parte Reexaminations. The CRU was formed in 2005 and remains largely unchanged by the AIA.

Centralised Procedure: the Centralised Procedure, which came into operation in 1995, allows applicants to obtain a marketing authorisation that is valid throughout the EU. The Centralised Procedure is compulsory for human medicines derived from biotechnology processes Advanced Therapy Medicinal Products (such as Gene Therapy, somatic cell therapy and tissue engineered products), products that contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders, diabetes, autoimmune diseases and other immune dysfunctions, viral diseases and officially designated orphan medicines. The Centralised Procedure is optional for medicinal products containing a new active substance not yet authorized in the EEA, if the substance would be a significant therapeutic, scientific or technical innovation over existing therapies or if its authorization would be in the interest of public health in the EEA.

CEP: acronym for Certification of Suitability of Monographs of the European Pharmacopoeia.

Certification: a process by which an individual, an institution, or an educational program is evaluated and recognized as meeting prescribed standards. A nongovernmental agency usually makes the Certification, with the notable exception of Medicare or Medicaid which certify a Provider or facility under public reimbursement programs. The purpose of Certification is to assure that established standards are met in order to promote ethical and safe practice of a service or profession.

Certification of Suitability of Monographs of the European Pharmacopoeia (CEP): verifies by relevant monographs of the European Pharmacopoeia that the quality of a medical substance is adequately controlled and that pharmaceutical substances or Active Pharmaceutical Ingredients (API) are produced in accordance with such monographs. CEP is granted by the Certification Secretariat of the European Directorate for the Quality of Medicines & HealthCare (EDQM).

Checkpoint Inhibitor: also known as immune Checkpoint Inhibitors, Drugs, often made of Antibodies, that use the body's immune system to attack cancers. Checkpoint Inhibitors function by blocking normal Proteins on cancer Cells, or the Proteins on the T-Cells that respond to them, which prevent the body from realizing that a Cell is cancerous. By removing these "blinders," Checkpoint Inhibitors allow the immune system to recognize and fight the cancer.

Chemistry, Manufacturing, and Controls (CMC): refers to information regarding the composition, manufacture and specification of a drug substance and/or Drug product that is required to be included in various regulatory submissions to the FDA, including Investigational New Drug (IND) Applications, New Drug Applications (NDAs) and annual reports. The amount and depth of CMC information submitted may depend on the type of submission and, in the case of an IND, on the phase of the investigation, the proposed duration of the investigation, the Dosage Form, the amount of information otherwise available and the scope of the proposed clinical investigation. The CMC information may include: information regarding physical and chemical characteristics, stability, methods of synthesis and purification, procedures and process controls used during manufacturing and packaging, and Specifications necessary to ensure identity, strength, quality, purity and/or bioavailability, including tests, analytical procedures and acceptance criteria.

Children's Health Insurance Program (CHIP): a federal health insurance program jointly funded and administered by CMS and participating states that provides health insurance Coverage to eligible children. The program was intended to provide health insurance to children in families with modest incomes that exceeded the qualification limits for Medicaid eligibility. Certain states have expanded CHIP eligibility to include pregnant women, parents of children receiving benefits from CHIP and Medicaid, as well as other populations.

Chimeric Antigen Receptor (CAR): also known as artificial T-Cell receptors and chimeric immunoreceptors, special receptors on the surface of T-Cells which recognize a specific Protein/Antigen on tumor Cells. The word chimeric is used because the receptors are composed of parts from different sources. CARs are under investigation for cancer therapy, using a technique called adoptive cell transfer. See CAR T-Cell, Immuno-oncology, TCR or T-Cell Receptor.

China Food and Drug Administration (CFDA): China Food and Drug Administration (CFDA) is the Chinese equivalent to the U.S. FDA.

CHIP: acronym for Children's Health Insurance Program.

CHMP: acronym for Committee for Medicinal Products for Human Use.

Chromosome: thread-like structures inside the nucleus of animal and plant Cells consisting of Protein and a single Molecule of Deoxyribonucleic Acid (DNA). DNA contains the specific instructions that make each living creature unique. During most of a Cell's life cycle, a Chromosome consists of one long, double-stranded DNA Molecule (and Protein), but during the "S phase" of a Cell's life cycle, the Chromosome replicates, resulting in an "X" shape structure called a metaphase Chromosome.

Chronic Lymphocytic Leukemia (CLL): a type of a cancer that begins in the bone marrow in Cells that become certain white blood Cells called lymphocytes. The cancerous Cells move from the bone marrow into the blood stream. Typically, the cancerous Cells build up slowly over time and therefore people may remain asymptomatic for a prolonged period of time. The word "chronic" refers to the fact that most of the abnormal, cancerous Cells are partially mature, although they cannot fight infection like normal white blood Cells.

Chronic Myeloid Leukemia (CML): also known as chronic myelogenous leukemia, a type of cancer that starts in myeloid Cells, which make red blood Cells, platelets and most types of white blood Cells (except lymphocytes). CML is a slow-growing Leukemia, but can change into a fast-growing acute Leukemia that is difficult to treat. The word "chronic" refers to the fact that most of the abnormal, cancerous Cells are partially mature, although they cannot fight infection like normal white blood Cells.

Chronic Myelomonocytic Leukemia (CMML): a cancer that starts in the blood-forming Cells of the bone marrow and invades the blood. CMML patients usually have a high number of monocytes (white blood Cells that help protect against Bacteria) and enlarged spleens.

Chronic Obstructive Pulmonary Disease (COPD): a progressive disease that causes difficulty breathing. Smoking is the most common cause, but long-term exposure to other lung irritants, such as air pollution, chemical fumes or dust can also cause COPD. In patients with COPD, the airways and air sacs in the lungs lose their elasticity, the walls of the airways in the lungs become thick and inflamed and the airways produce more mucus than usual, all of which contribute to a patient's difficulty breathing.

CID: acronym for Civil Investigative Demand.

CIP: acronym for Clinical Investigation Plan.

Civil Investigative Demand (CID): a demand for production of documents and answers to interrogatories or to give oral or deposition testimony issued by the U.S. Department of Justice or other law enforcement entities, such as States Attorneys General. CIDs are similar to but distinct from Subpoenas, which are usually limited to requesting documents. In healthcare, CIDs are frequently used by the government during investigations in False Claims Act cases.

Claim Chart: typically a two-column chart providing an element-by-element comparison of a Patent's claims against an allegedly infringing product or the prior art. Invalidity Claim Charts are useful for visualizing which claim elements exist in the prior art (Invalidity Claim Chart).

Claim Construction: refers to the process an adjudicative body uses to determine the legal meaning of a patent claim term, or the actual meaning ascribed to the claim term after the Claim Construction process. The PTAB gives claim terms their Broadest Reasonable Interpretation, whereas district courts give claim terms their Ordinary and Customary Meaning.

Class I Medical Device: the FDCA classifies Medical Devices into one of three classifications based on the risks associated with the Device and the level of control necessary to provide reasonable assurance of safety and effectiveness. Class I Medical Devices are those for which reasonable assurance of safety and effectiveness can be provided by adherence to the FDA's general controls for Medical Devices, which include applicable portions of the FDA's Quality System Regulation, facility registration and device listing, reporting of adverse medical events and requirements for appropriate, truthful and non-misleading Labeling, Advertising and Promotional Materials. Many Class I Medical Devices are exempt from premarket review; however, some Class I Medical Devices require premarket clearance by the FDA through the 510(k) Premarket Notification process.

Class II Medical Device: the FDCA classifies Medical Devices into one of three classifications based on the risks associated with the Device and the level of control necessary to provide reasonable assurance of safety and effectiveness. Class II Medical Devices are subject to the FDA's general controls, which include applicable portions of the FDA's Quality System Regulation, facility registration and device listing, reporting of adverse medical events and requirements for appropriate, truthful and non-misleading Labeling, Advertising and Promotional Materials, and any other product-specific special controls, such as Performance Standards, postmarket surveillance and FDA guidance, that the FDA deems necessary to provide reasonable assurance of the Devices' safety and effectiveness. Unless exempt, the Manufacturer of a Class II Medical Device must submit to the FDA a 510(k) Premarket Notification submission requesting clearance of the Device for commercial distribution in the United States.

Class III Medical Device: the FDCA classifies Medical Devices into one of three classifications based on the risks associated with the Device and the level of control necessary to provide reasonable assurance of safety and effectiveness. Devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life-supporting or implantable Devices, or Devices deemed not substantially equivalent to a previously 510(k) cleared Device, are classified as Class III. Class III Devices generally require approval of a Premarket Approval application, or PMA, prior to marketing, in addition to compliance with the FDA's general controls, which include applicable portions of the FDA's Quality System Regulation, facility registration and device listing, reporting of adverse medical events and requirements for appropriate, truthful and non-misleading Labeling, Advertising and Promotional Materials.

CLFS: acronym for Clinical Laboratory Fee Schedule.

CLIA: acronym for Clinical Laboratory Improvement Amendments.

Clinical Data of a Device: the safety and/or performance information generated from the use of a Device (Art. 1 para. 2 lit. k) Directive 93/42/EEC).

Clinical Investigation Plan (CIP): the European Commission defines the Clinical Investigation Plan as a document stating the rationale, objectives, design and proposed analysis, methodology, monitoring, conduct and recordkeeping of the clinical investigation.

Clinical Laboratory Improvement Amendments (CLIA): the Clinical Laboratory Improvement Amendments (passed in 1988, updating the Clinical Laboratory Improvement Act of 1967) generally regulate laboratory tests performed on humans in the United States and require clinical laboratories to be certified by the state in which they operate, as well as by CMS, before the facility can accept human samples for diagnostic testing. There are various levels of Certification under CLIA, which are based on the type of Diagnostic tests a laboratory conducts.

CLIA Certification: CLIA Certification is based on the types of Diagnostic tests a laboratory conducts and includes the following five categories:

- Certificate of Waiver for laboratories conducting certain waived tests (*e.g.*, glucose meter tests)
- Certificate for Provider-Performed Microscopy Procedures for laboratories in which a physician, midlevel practitioner or dentist conduct no tests other than the microscopy procedures and waived tests
- Certificate of Registration enabling laboratories to conduct moderate- or high-complexity laboratory testing until the laboratory's compliance with CLIA regulations is determined
- Certificate of Compliance for laboratories determined by inspection to be in compliance with all applicable CLIA requirements
- Certificate of Accreditation for laboratories accredited by an organization approved by CMS

The process by which clinical laboratories obtain CLIA Certification involves an application (CMS Form 116) to the applicable state agency. CLIA Certification typically requires an existing state laboratory License and a laboratory director meeting certain qualifications.

Clinical Development Safe Harbor / 271(e) Safe Harbor: activity falling within a zone with respect to which otherwise potentially infringing activity is deemed "not ... an act of Infringement" because it is performed "solely for uses reasonably related to" development of information and its submission under federal law 35 U.S.C. § 271(e)(1).

Clinical Laboratory Fee Schedule (CLFS): promulgated by CMS, the Clinical Laboratory Fee Schedule sets forth payment rates for outpatient laboratory services. Each laboratory test is assigned a code with a corresponding reimbursement rate. Due to the Protecting Access to Medicare Act, as of January 1, 2018, payments under the CLFS will be based on the weighted median of private payor rates for each test as reported by applicable laboratories receiving a majority of their Medicare Reimbursement under the CLFS or Medicare Physician Fee Schedule and that meet a minimum threshold criteria.

Clinical Superiority: in the US regulatory context, the FDA defines Clinical Superiority to mean that "a Drug is shown to provide a significant therapeutic advantage over and above that provided by an approved Drug (that is otherwise the same Drug) in one or more of the following ways: greater effectiveness than an approved Drug (as assessed by effect on a clinically meaningful endpoint in Adequate and Well-Controlled Clinical Trials); greater safety in a substantial portion of the target populations; or in unusual cases, where neither greater safety nor greater effectiveness has been shown, a demonstration that the Drug otherwise makes a major contribution to patient care." In the context of EU regulation, "Clinically Superior" is a regulatory concept related to Orphan Drugs. In the EU, after an orphan designated product has been granted a marketing authorisation, for a period of 10 years, the EMA or EU Member State drug agencies cannot accept another application for a marketing authorisation, or grant a marketing authorisation or accept an application to extend an existing marketing authorisation, for a product that is similar and has the same therapeutic Indication as the orphan designated marketing authorised product. This Exclusivity can however be broken by applications that demonstrate that their product, although similar to the Orphan Medicinal Product already authorised, is safer, more effective or otherwise clinically superior.

Clinical Trial: a test or study conducted in human subjects.

Clinical Trial Exemption (CTX): an authorization to administer an investigational agent to patients or volunteer subjects under the specified conditions of a particular research study in a clinical setting.

Clinical Trials Registry or ClinicalTrials.gov: a government-run, publicly accessible database or registry information about certain Clinical Trials of FDA-regulated Drugs, Biological Products (Biologics) or Devices, and certain pediatric postmarket surveillance of Devices. Registration is required for trials that meet the definition of an "applicable Clinical Trial" under Section 801 of the Food and Drug Administration Amendments Act and that were either initiated after September 27, 2007 or initiated on or before that date and were still ongoing as of December 26, 2007. In addition to registration requirements, trial results must be submitted for applicable Clinical Trials that study Drugs, Biologics or Devices that are approved, licensed or cleared by the FDA. The website provides the public with easily accessible summary information about Clinical Trials — such as what intervention is being tested,

what disease or condition is being treated, the eligibility criteria if a patient wants to enroll in the study, contact information and locations for the study. For certain types of Clinical Trials, sponsors are also required to post study outcomes and Adverse Events.

CLL: acronym for Chronic Lymphocytic Leukemia.

Clone or Cloning: this usually refers to a genetically identical copy of a parent created by growing many individuals from the Cells of a single parent. The ability to secure patent protection over manufacturing technologies and a Clone is of value.

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR): when used with the Cas9 nuclease, CRISPR is a technique for highly specific editing of the Genome. This technique has made permanently changing the Genome of any organism very easy compared to past technologies and is being tested in human disease applications. The American Association for the Advancement of Science awarded this technology as the 2015 Breakthrough of the Year.

CMC: acronym for Chemistry, Manufacturing and Controls.

CML: acronym for Chronic Myeloid Leukemia.

CMML: acronym for Chronic Myelomonocytic Leukemia.

CMS: acronym for Centers for Medicare & Medicaid Services.

Co-Branding: also referred to as "brand partnership," Co-Branding involves a variety of marketing partnerships involving two or more brands aiming to combine the strengths of the two brands in the market. Such arrangements typically involve cooperative marketing, but may also involve combined or joint products or the joint services of a Supplier and a physician.

Co-Marketing: an arrangement between two or more parties for the joint marketing of each party's product or service (*e.g.*, a Drug or Medical Device), or the joint advertisement of each party's business (*e.g.*, joint marketing between a Manufacturer and a healthcare professional who uses the Manufacturer's products) while each party maintains its own sales and distribution networks. Co-Marketing aims to increase the commercial strength, and accelerate the adoption or implementation of a product or service. These arrangements may implicate state and federal fraud and abuse laws.

Co-Promotion: an arrangement between two or more parties for the joint promotion of a single product or service (*e.g.*, a Drug or Medical Device) wherein the companies share a single sales force that promotes that product to improve the promotion effort. These arrangements may implicate state and federal fraud and abuse laws. Co-Promotion agreements are commonly used by pharmaceutical companies to improve marketing and product penetration in particular industries or geographic areas.

Coding: Coding is the process through which healthcare Providers identify diagnoses, procedures, services, and certain Drugs, Medical Devices and equipment as numeric or alphanumeric codes as part of the billing process. Codes correspond to the Reimbursement that Providers receive for healthcare items and services rendered to patients. Current Coding systems used by providers are the 10th version of the International Statistical Classification of Disease and Related Health Problems (ICD-10), a medical classification list published by the World Health Organization; the Current Procedural Terminology (CPT), a widely used code set for reporting medical procedures and services, published by the American Medical Association; and the Healthcare Common Procedure Coding System, a Coding system utilized by CMS that is based on CPT and other codes. Improper or erroneous Coding can lead to an Overpayment that must be refunded and potential violations of the False Claims Act.

COGS: acronym for Cost of Goods Sold.

Coinsurance: the portion of the cost of covered healthcare items or services for which an insured is financially responsible. The amount is typically determined as a fixed percentage of the allowed cost of the item or service under the insured's healthcare insurance plan. Often, Coinsurance applies after the Beneficiary has satisfied a specified Deductible.

Collaboration Agreement: an agreement between two or more researchers or entities engaged in a joint research project that governs their working relationship. The most important terms of a Collaboration Agreement govern copyright ownership. A Collaboration Agreement also usually specifies the intent of the parties to share Data, research materials, and facilities as well as to publish research findings. Other important terms govern confidentiality as well as consequences where one or more parties chose to terminate its involvement in the joint project.

Collagen: the main structural Protein found in animal connective tissue.

Combination Product: According to the FDA, "a product may constitute a Combination Product if it satisfies one of the following four conditions: it is comprised of two or more FDA-regulated components, *i.e.*, Drug/Device, Biologic/Device, Drug/Biologic, or Drug/Device/Biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity; it involves two or more separate products packaged together in a single package or as a unit and comprised of Drug and Device products, Device and Biological Products, or Biological and Drug products; it is a Drug, Device, or Biological Product packaged separately that according to its investigational plan or proposed Labeling is intended for use only with an approved individually specified Drug, Device, or Biological Product, where both are required to achieve the intended use, indication, or effect, and where upon approval of the proposed product the Labeling of the approved product would need to

be changed; or it is an investigational Drug, Device, or Biological Product packaged separately that according to its proposed Labeling is for use only with another individually specified investigational Drug, Device, or Biological Product, where both are required to achieve the intended use, indication, or effect."

Commercial Reasonableness: a standard applicable to various healthcare fraud and abuse laws under which financial or business arrangements must be sensible and prudent, be for reasonable and necessary services, and make commercial sense from the perspective of the involved parties even in the absence of any potential referrals.

Commercial Success: one of the so-called "Secondary Considerations" that can be used to help establish that a Patent is not obvious. In order to be relevant, there must be a "nexus" (causal connection) between the patented Invention and the product's Commercial Success. Evidence of high volume of early sales, extensive licensing of the technology and increasing market share can all be used to counter an argument that the patented Invention was obvious.

Commercialization: the marketing, promotion, sale and distribution of a product.

Commercially Reasonable Efforts: a defined term found in many License and Collaboration Agreements setting forth a standard to which a party must perform certain obligations. Also commonly defined as Diligent Efforts.

Committee for Advanced Therapies (CAT): a scientific committee within the EMA responsible for assessing the quality, safety and efficacy of Advanced Therapy Medicinal Products (ATMPs) and following scientific developments in the field.

Committee for Medicinal Products for Human Use (CHMP): scientific committee within the EMA responsible for all questions relating to medicines for human use and for the initial assessment in the Centralised Procedure. Formerly, the CPMP — Committee for Proprietary Medicinal Products.

Committee for Orphan Medicinal Products (COMP): a scientific committee within the EMA responsible for all questions related to Orphan Medicinal Products, including reviewing the application for Orphan Designation.

Committee for Veterinary Medicinal Products (CVMP): a scientific committee within the EMA responsible for all questions relating to medicines for veterinary use and the initial assessment in the Centralised Procedure.

Committee on Herbal Medicinal Products (HMPC): a scientific committee within the EMA responsible for all questions related to herbal medicinal products.

COMP: acronym for Committee for Orphan Medicinal Products.

Companion Diagnostic: a Medical Device, often an in vitro Device, which provides information essential for the safe and effective use of a corresponding Drug or Biological Product (Biologic). The Companion diagnostic test helps medical professionals determine whether the Drug or product's benefits to patients will outweigh any potential serious side effects or risks.

Compassionate Use: the use of an IND outside a Clinical Trial by patients with serious or life-threatening conditions who do not meet the enrollment criteria for the Clinical Trial in progress. See also Expanded Access Program.

Competent Authorities of the Member States of the EEA: for medicinal products, a Member State's governmental body which supervises and delivers marketing authorisation.

for Medical Devices, a Member State's governmental body which enforces the provisions of the EU Medical Devices Directives as transposed into the laws of their country. Unlike the medicinal product Competent Authorities, Medical Devices Competent Authorities do not authorize Medical Devices in the EU.

Competing Product: a product that competes for market share with another product that is the subject of the agreement. Generally, a "Competing Product" term will be highly customized to suit the specific agreement and products contemplated thereunder.

Complementary Determining Region (CDR): a portion of an Antibody that recognizes the Antigen.

Complete Response Letter: a communication from the FDA that informs a company that a NDA cannot be approved in its present form.

Compliance Program Guidance (OIG): voluntary Compliance Program Guidance materials developed by OIG (occasionally in conjunction with industry organizations) and directed at various segments of the healthcare industry, such as hospitals, pharmaceutical Manufacturers, nursing homes, third-party billers, and durable medical equipment Suppliers, to encourage the development and use of internal controls to monitor adherence to applicable statutes, regulations, and program requirements. OIG also issued compliance resource materials to assist healthcare entity Boards of Directors exercise their oversight role, determine the adequacy and effectiveness of the organization's compliance program and make compliance a responsibility for all levels of management.

Composition of Matter: in US patent law, one of the four principal categories of things that may be patented. The other three categories are a process, a machine and an article of manufacture.

Conditional Marketing Authorisation (CMA): are marketing authorisations granted by the EMA on the basis of less complete Data than is normally required but subject to certain conditions. Conditional Marketing Authorisations are only available for products to treat, prevent or diagnose seriously debilitating diseases or life threatening diseases, products used in emergency situations in response to public threats, or orphan designated products. CMAs are valid for only one year and are renewable on a year by year basis. The obligations attached to a CMA typically involve completing on-going studies or conducting new studies or the collection and monitoring of specific pharmacovigilance Data.

Confidential Disclosure Agreement: see Non-Disclosure Agreement.

Confidential Information: any non-public information pertaining to a company's business, generally consisting of Trade Secrets, Know-How, and other information.

Confidentiality Agreement: see Non-Disclosure Agreement.

Conforming/Non-Conforming: refers to whether a product manufactured or supplied under a manufacturing or supply agreement meets or does not meet the Specifications for that product. Generally, a customer will be obligated to accept Conforming product but not Non-Conforming product, and there will be procedures in place for disposing of products, based on whether the product is Conforming or Non-Conforming.

Congenital Heart Disease: a malformation of the heart, aorta or other large blood vessels present since birth.

Contingent Value Rights (CVR): rights given to shareholders of an acquired company that entitle them to additional benefits if a specified event occurs. CVRs are similar to options in that they often have an expiration date that relates to the time by which the contingent event must occur. An example of a CVR is the right of shareholders of an acquired company to receive additional shares of the target company in the event the target company's share price falls below a certain level by a specified date.

Continuations: a patent application that claims Priority to another patent application that pursues additional claims to an Invention disclosed in the priority patent application, but relies on the same disclosure as in the priority application.

Continuations in Part: a continuation application that includes new subject matter in the disclosure.

Contract Research Organization (CRO): CROs provide specialized research services to drug, biologic and medical device companies, including clinical outsourcing and the conduct of preclinical and Clinical Trials on behalf of Manufacturers.

Control, Controls or Controlled: a term used to define the level of interest triggering certain rights. In terms of an entity, Control means the power to direct or cause direction of the management and policies of another entity, whether through ownership of voting securities, by contract or otherwise. In terms of Intellectual Property or information, Control means the ability to grant rights under such Intellectual Property or information as provided in the agreement without breaching or violating third-party rights.

Cooperative Research and Development Agreement (CRADA): an agreement between a governmental agency and a private company or university to work together on research and Development.

Coordination Group for Mutual Recognition and Decentralised Procedures (human/veterinary) (CMDh/v): a regulatory body responsible for questions relating to the EU's Decentralised and Mutual Recognition Procedures for medicinal products for human and veterinary use.

Copayment: a fixed amount paid by an insured to the healthcare Provider or Supplier, usually at the time a healthcare item or service is furnished to the insured. The amount, determined under the insured's healthcare insurance plan, typically varies based on the type of service.

COPD: acronym for Chronic Obstructive Pulmonary Disease.

Corporate Integrity Agreement (CIA): an agreement entered into between OIG and an individual or entity as a component of a civil or administrative settlement of a federal healthcare program investigation arising under a variety of false claims statutes, including the FCA and Civil Monetary Penalties Law. The individual or entity agrees to comply with the obligations imposed by the CIA in exchange for OIG agreeing not to seek the Exclusion of the individual or entity from participation in Medicare, Medicaid or other federal healthcare programs. CIAs have many common elements, but each CIA is intended to address the specific facts underlying the settlement and often attempts to accommodate and recognize elements of the individual's or entity's preexisting voluntary compliance program. A comprehensive CIA typically lasts for five years and includes requirements to:

- Hire a compliance officer, appoint a compliance committee, and develop written standards and policies
- Implement a comprehensive employee training program
- Retain an Independent Review Organization to conduct annual reviews and audits
- Establish a confidential disclosure program
- Restrict employment of ineligible persons

- Report Overpayments, reportable events, and ongoing investigations/ legal proceedings to OIG
- Provide an implementation report and annual reports to OIG on the status of the individuals or entity's compliance activities

Corporate Practice of Medicine: refers to a doctrine that generally prohibits corporations (other than licensed professional corporations or associations) or other unlicensed persons from owning, Controlling, or employing physicians or a medical practice, or from otherwise engaging in conduct for which a medical License is required. Prohibitions of the Corporate Practice of Medicine exist in various states and range from prohibiting the practice of medicine without a License or sharing fees between licensed and unlicensed individuals (see, Fee Splitting), to prohibitions on the ownership of a medical practice or employment of professionals by non-professionals. Some states have carved out exceptions to the prohibition for certain employers, such as hospitals, health maintenance organizations and professional corporations.

Cosmeceuticals: a cosmetic that has or claims to have medicinal properties, for example, anti-aging properties.

Cost of Goods Sold (COGS): used in calculating the cost to produce products.

Covenant Not to Sue: a legal agreement in which one party agrees not to assert against another party an intellectual property right. Conceptually, a Covenant Not to Sue can be thought of as equivalent to a nonexclusive License, though there are nuanced legal distinctions.

Cover, Covering or Covered: a product or service will be Covered by a Patent if the making, using, or sale of such product or service would otherwise infringe such Patent without a valid License thereto.

Coverage: the amount of liability covered under an insurance plan for a specific item, service or event. In the healthcare context, Coverage refers to the availability of payment by a particular Third-Party Payor for defined healthcare items or services. Coverage for a healthcare item or service typically means that the item, service or event is eligible for Reimbursement by the insurer, such as Medicare, Medicaid or other Third-Party Payors, so long as the item, service or event meets the Medical Necessity criteria established by such payors' policies.

Covered Drug, Device, Biological or Medical Supply (Sunshine Act): under the Sunshine Act, a Covered Drug, Device, Biological or Medical Supply is one for which payment is available under Medicare, Medicaid or Children's Health Insurance Program (CHIP) — either separately or as part of a bundled payment such as the inpatient or Outpatient Prospective Payment Systems (IPPS and OPPS) — and which requires a Prescription to be dispensed (in the case of a Drug or Biological) or Premarket Approval by or notification to the FDA (in the case of a Device or a medical supply that is a Device).

Covered Entity: a health plan (*e.g.*, health insurance companies, HMOs, company health plans), healthcare clearinghouse or healthcare Provider that engages in certain electronic standard transactions, such as insurance claims transactions or equivalent encounter information.

Covered Recipient (Sunshine Act): under the Sunshine Act, Covered Recipients of payment from Manufacturers are physicians, other than those who are bona fide employees of the Applicable Manufacturer reporting the payment, and teaching hospitals. Physicians are defined to include doctors, dentists, optometrists, podiatrists and chiropractors. Applicable Manufacturers must publicly report their payments to Covered Recipients on or before March 31 of each calendar year.

CPT CODE: acronym for Current Procedural Terminology Code.

CRISPR: acronym for Clustered Regularly Interspaced Short Palindromic Repeats.

CRISPR-Cas9: a method for editing and inducing Mutation in a target Cell. A pre-designed segment of guide RNA binds to the targeted sequence of DNA, and guides a Cas9 Enzyme to cut the DNA at a specific location along both strands of the DNA sequence. When the Cell's break repair machinery attempts to fix the break, it does so imperfectly, introducing errors in the form of lost or missing nucleotide bases. These permanent changes are Mutations which inactivate a Gene or prevent it from functioning properly. The CRISPR-Cas9 technology has been recognized as high-potential technology that can be used to target and mutate Genes with a high degree of precision.

Cross License: an agreement between two or more parties in which each party grants rights to their Intellectual Property to the other parties.

Cross-Walking: the process of mapping one set of Data to one or more other sets of Data and may be used for a variety of purposes. For example, CMS may Cross-Walk payment amounts for existing clinical laboratory tests to a similar, new clinical laboratory test to establish the Clinical Laboratory Fee Schedule (CLFS) payment amount for the new test. In another example, CMS used Cross-Walking to assist Providers and other relevant parties during the ICD-10 transition by creating General Equivalence Mappings or GEMs as a tool to Cross-Walk diagnoses from ICD-9-CM to ICD-10-CM and vice versa.

CRU: acronym for Central Reexamination Unit.

CTX: acronym for Clinical Trial Exemption.

Current Procedural Terminology Code (CPT Code): CPT Codes are primarily numeric codes published and maintained by the American Medical Association (AMA) used to identify medical services and procedures furnished by physicians and other healthcare professionals on claims submitted to Third-Party Payors for Reimbursement.

Decisions regarding the addition, deletion or revision of CPT Codes are made by the AMA, with permanent CPT Code updates published annually. CPT Codes are divided into three categories:

- Category I codes consist mainly of five-digit numeric codes describing procedures widely performed
- Category II codes consist of four-digit numeric codes followed by a single alphabetical character utilized for performance measurement, not Reimbursement
- Category III codes consist mainly of temporary five-character codes (four numeric digits followed by a "T") describing new and emerging technologies

The CPT Code set represents Level I of the Healthcare Common Procedure Coding System (HCPCS), while Level II HCPCS Codes are alphanumeric and primarily describe medical items, supplies or non-physician services See, HCPCS Code.

Custom-Made Device: any Device specifically made in accordance with a duly qualified medical practitioner's written Prescription which gives, under the practitioner's responsibility, specific design characteristics and is intended for the sole use of a particular patient (Art. 1 para 2 lit. d) Directive 93/42/EEC).

CVMP: acronym for Committee for Veterinary Medicinal Products.

Cytokine: a small Protein released by Cells that has a specific effect on the interactions between Cells, on communications between Cells or on the behavior of Cells. Cytokines are produced by a broad range of Cells and a given Cytokine may be produced by more than one type of Cell. Cytokines act through receptors and are especially important in the immune system.

Cytology: the branch of biology concerned with the structure and function of plant and animal Cells.

Data: in the context of life sciences agreements, often a defined term meaning Data and information related to the Development of a Drug, including clinical trial Data.

Data Breach: a compromise of security that leads to the accidental or unlawful destruction, loss, alteration, unauthorized disclosure of or access to protected Data. Typically the protected Data is Sensitive Personal Data subject to state Data Breach notification laws, or PHI subject to the HIPAA Breach Notification Rule.

Data Safety Monitoring Board: the FDA defines at Data Safety Monitoring Board as "an independent data monitoring committee that may be established by the sponsor to assess at intervals the progress of a Clinical Trial, the safety Data, and the critical efficacy endpoints,

and to recommend to the sponsor whether to continue, modify, or stop a trial." The Data Safety Monitoring Board advises the sponsor regarding the continuing safety of trial subjects and those yet to be recruited to the trial, as well as the continuing validity and scientific merit of the trial.

De novo Classification: the De novo Classification process provides a pathway to classify a low to moderate risk Medical Device for which there is no legally marketed predicate Device, such that the Device cannot obtain clearance through a 510(k) Premarket Notification and therefore is automatically classified as a Class III Medical Device, but for which general controls or general and special controls provide reasonable assurance of safety and effectiveness. De novo Classification is a risk-based and evidence-based classification process. Devices that are classified into Class I or Class II through the de novo process may be marketed and used as predicates for future premarket notification 510(k) submissions.

Decentralised Procedure: used by a Manufacturer which has not received any marketing authorisation in the EU and seeks, as in the Mutual Recognition Procedure, to obtain an MA in two or more Member States. The applicant simultaneously submits an identical application to all the Member States in which the applicant wants to market its product and choses a Reference Member State. The Reference Member State will make the assessment which will be submitted for approbation by the other Member States, the Concerned Member States.

Declaration of Helsinki Procedure: a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and Data developed by the World Medical Association (WMA). The principles of the Helsinki declaration are recognized by EU clinical trial regulations and applied by EU competent authorities and Ethics Committees supervising Clinical Trials.

Declaratory Judgment: a legal determination by a court resolving an issue affecting the rights of the parties to a dispute. Declaratory Judgments are common in Patent litigation because they allow alleged infringers to seek judicial determination of, for example, validity, non-infringement or enforceability of an Asserted Patent before the patent owner brings suit. A Declaratory Judgment action may allow the alleged infringer to determine the forum of the lawsuit.

Deductible: the portion of an individual's insured healthcare expenses that the insured must pay before payment from the insurer commences.

Deferred Prosecution Agreement (DPA): a voluntary agreement under which the government grants amnesty in exchange for the defendant individual or entity agreeing to fulfill certain enumerated requirements, generally including the admission of guilt or responsibility, payment of fines, implementation of corporate compliance obligations, agreement to fully cooperate in the investigation, and occasionally, appointment of an independent compliance monitor, over a defined period of time, usually

several years. DPAs typically involve filing criminal charges against the defendant, but the government agrees to drop the charges, provided the defendant complies with the enumerated requirements. DPAs are frequently a tool of the U.S. Department of Justice (DOJ), the U.S. Securities and Exchange Commission (SEC) and other law enforcement agencies, for resolving allegations of corporate criminal wrongdoing, including healthcare fraud and abuse allegations.

Definiteness: a requirement for patentability. To satisfy Definiteness, a Patent claim must particularly point out and distinctly claim the subject matter of the Invention. 35 U.S.C. § 112(b).

Deoxyribonucleic Acid (DNA): the double-stranded helix made up of Nucleotides that encode our genetic information and make up an organism's Chromosome.

Derivation Claim: when a party with a later-filed Patent application seeks to establish that an earlier-filed Patent application on the same Invention was derived from the later-filed application and that the earlier-filed application was filed without authorization.

Dermal: relating to the skin, especially the dermis.

Dermatology: the branch of medicine concerned with the diagnosis and treatment of skin disorders.

Designated Health Services (DHS): for purposes of the Stark Law, DHS include clinical laboratory services; physical and occupational therapy services; outpatient speech-language Pathology services; Radiology and certain other imaging services; radiation therapy services and supplies; Durable Medical Equipment and supplies; parenteral and enteral nutrients; equipment and supplies; prosthetics, orthotics, and prosthetic Devices and supplies; home health services; outpatient Prescription Drugs; and inpatient and outpatient hospital services.

Development: the Development stage of a Drug product, from preclinical activities through Clinical Trials and the filing for Regulatory Approval of the product.

Development Costs: the costs associated with Development, calculated on a Full-Time Equivalent and Out-of-Pocket Cost or other basis.

Device Intended for Clinical Investigation: any Device intended for use by a duly qualified medical practitioner when conducting investigations in an adequate human clinical environment (Art. 1 para. 2 lit. e) Directive 93/42/EEC).

Device Master File: an optional, confidential document submitted to the FDA by Manufacturers of components or materials for Medical Devices. The Device Master File is confidential, and accessible only when a submission is made by approved customers of the component Manufacturer who wish to file related medical device applications.

Device / Medical Device: Section 201(h) of the Federal Food, Drug and Cosmetic Act defines a Medical Device as an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or Accessory, which is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease in man or other animals, or intended to affect the structure or any function of the body of man or other animals, and that does not achieve its principal intended purposes by chemical action or by being metabolized.

DHS: acronym for Designated Health Services.

Diagnosis Code: a standard numerical representation of a disease, injury, impairment, or other health-related problem and its manifestation or cause. The standard medical data code set CMS uses is the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM). ICD-10-CM codes are used to classify diagnoses and procedures submitted to Medicare and private insurance payors. The ICD-10-CM code set, which replaced ICD-9-CM on October 1, 2015, is significantly more granular than the ICD-9-CM code set, with nearly five times as many Diagnosis Codes.

Diagnosis Related Groups (DRGs): a classification system CMS uses to determine payments by Medicare for hospital inpatient services. Assignment of the DRG to a patient is based on a variety of factors, including the patient's primary and secondary diagnoses, procedures performed during the hospitalization, age and length of hospitalization. Medicare uses the DRG system to establish prospective, per-discharge bundled payment rates intended to reimburse the hospital for operating and capital expenses related to the patient's care. In 2007, CMS revised the DRG system, now known as Medicare-Severity DRGs (MS-DRGs), to better reflect the severity of the patient's condition.

Diagnostic: a kit, test, or Device that tests for disease or condition of a patient to diagnose disease or monitor treatment. Examples include gene testing for disease Alleles, presence of Bacteria, levels of Antibodies in the blood, etc.

Diagnostic Kit: products that produce Data regarding the presence, absence or level of a particular substance in a sample.

Dialysis: a treatment for kidney failure that uses a machine to filter out harmful wastes, salt and excess fluid from a patient's blood because the patient's kidneys are unable to filter blood on their own. Dialysis returns the blood to a normal, healthy balance.

Diligence: in the context of life sciences Licenses and Collaboration Agreements, a functional provision of such agreement imposing an obligation on a party to perform certain development and/or commercialization activities. Diligence provisions often will include a timeline for achieving certain Milestones with respect to such activities.

Diligent Efforts: see Commercially Reasonable Efforts.

Discount/Rebate: reductions in price taken at the time of sale or a later point in the transaction. Under the Anti-Kickback Statute, a Discount or Rebate (defined as a Discount given after the time of sale) is a reduction in price, typically between a Manufacturer and a distributor or healthcare Provider or entity, and may be considered Remuneration under the law. Discounts and Rebates may be protected under the Anti-Kickback Statute Safe Harbor for Discounts, but certain types of price reductions are excluded from the Safe Harbor, such as cash payments or equivalents.

Divisionals: a Patent application that claims Priority to another Patent application, but differs from a Continuation, in that a divisional claims a distinct or independent Invention from subject matter in the parent application. A divisional application is often filed after the Examiner issued a "restriction requirement," because a Patent can only claim a single Invention.

DME: acronym for Durable Medical Equipment.

DMEPOS Competitive Bidding Program: a nationwide program CMS implemented to establish Medicare payment amounts for certain Durable Medical Equipment, prosthetics, orthotics and supplies (DMEPOS) through a competition among Suppliers who operate in specific geographic bidding areas. CMS evaluates bids based on the Supplier's eligibility, financial stability and bid price. Contracts are awarded to Medicare Suppliers that offer the Best Price and meet applicable quality and financial standards. The DMEPOS Competitive Bidding Program replaces the prior DMEPOS fee schedule payment methodology for certain DMEPOS.

DNA: acronym for Deoxyribonucleic Acid.

Doctrine of Equivalents: if a product does not literally satisfy every element of a Patent claim, but comes substantially close, the product may still be found to infringe under the Doctrine of Equivalents. Under this doctrine, if an accused Device performs substantially the same function as a Patent claim in substantially the same way to yield substantially the same result, the accused Device may infringe the Patent, even if not all of the elements of the Patent claims are literally satisfied.

Domain Name: a unique address on the internet that, when entered into a web browser, directs the user to a company's website.

Dosage Form: the FDA defines Dosage Form as, "the physical form or appearance of a Drug product or the way a Drug is administered to a patient, *e.g.*, aerosol, injectable, patch, tablet."

Drug: The Federal Food, Drug, and Cosmetic Act defines a Drug as an article recognized by an official pharmacopoeia or formulary; an article intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; an article (other than food) intended to affect the structure or any function of the body of man or other animals; or an article intended for use as a component of any of the aforementioned articles.

Drug Development: the process of bringing a new pharmaceutical Drug to the market once a lead compound has been identified through the process of Drug Discovery. There are three phases in the FDA's Investigational New Drug (IND) process. The first phase tests the Drug on healthy individuals to determine its basic properties and safety profile. The second phase tests the Drug for efficacy in the target population. The third phase is large-scale testing for safety and effectiveness, with one to three thousand study subjects. After the third phase, the developer files a New Drug Application (NDA), which, is reviewed by the FDA and expert Advisory Committees. If the NDA is approved, the Drug may be put on the market.

Drug Discovery: the process by which a Drug candidate or lead compound is identified and partially validated for the treatment of a disease.

Drug-Eluting Stent: a peripheral or coronary stint placed into a diseased peripheral or coronary artery that slowly releases a Drug to block Cell proliferation.

Drug Master File: an optional, confidential document submitted to the FDA to support a drug application. The Drug Master File contains detailed information about the chemical processes, facilities, or articles used in the manufacture and storage of a Drug or drug component.

Drug Price Competition and Patent Term Restoration Act: see Hatch-Waxman Act.

Dual Eligible Beneficiaries: individuals (commonly referred to as Dual Eligibles) who are entitled to Medicare Part A and/or Part B, and are eligible for either full Medicaid benefits in the state in which they reside or certain Medicare Shared Saving Programs for low income or disabled beneficiaries. For Dual Eligibles, Medicare-covered services are paid first by Medicare. Medicaid may pay for applicable Medicare premiums, Coinsurance, Deductibles or Copayment amounts. Medicaid may also cover the cost of prescription Drugs or other care not covered by Medicare, such as certain long-term care facilities.

Durable Medical Equipment (DME): reusable or long-lasting (*i.e.*, an expected lifetime of at least three years) medical equipment, like a walker, wheelchair, or hospital bed, prescribed by a healthcare Provider for certain medical conditions and/or illnesses that is intended for use in a person's home or in daily activities. Medicare Part B covers DME as long as the equipment is medically necessary.

E. coli, or Escherichia coli: E. coli, or Escherichia coli, is a well characterized bacterium that has been harnessed by scientists to do recombinant DNA work, or the splicing together of different types of Genes.

EAP / Expanded Access Program: according to the FDA, "expanded access, also called 'Compassionate Use,' provides a pathway for patients to gain access to investigational Drugs, Biologics, or Medical Devices

for serious diseases or conditions." In the Drug and Biologic context, expanded access may be authorized by the FDA for individual patients, including for emergency use; for intermediate-size patient populations; and for widespread treatment use.

Ear, Nose and Throat (ENT): also known as otolaryngology, an ENT specialist is a physician trained in the medical and surgical management and treatment of patients with diseases and disorders of the ear, nose, throat and related structures in the head and neck.

Earn-out: a contractual provision stating that the seller of a business is to obtain additional future compensation based on the business achieving certain goals, typically financial.

EDMA: acronym for European Diagnostic Manufacturer's Association.

EDMA Code: the European Diagnostic Manufacturer's Association (EDMA) represents national associations and major companies engaged in the research, Development, manufacture and distribution of in vitro diagnostic Medical Devices. The EDMA Code of Ethics is intended to provide guidance on the interactions of EDMA members with Healthcare Professionals in Europe.

On December 2, 2015, Members of Eucomed and EDMA adopted a new common MedTech Europe Code of Ethical Business Practice which will become binding to the members of EDMA and Eucomed on January 1, 2017. This code will replace the Codes of Ethical Business Practice issued by EDMA and Eucomed and set the minimum standard across the EEA.

EDQM: acronym for the European Directorate for the Quality of Medicines & HealthCare.

EFPIA: acronym for European Federation of Pharmaceutical Industries and Associations.

EFPIA Code: The EFPIA Code sets out the minimum standards companies must follow to comply with the European legislation that the member associations must adopt as a minimum into their national codes. The EFPIA Code provides for disclosures of transfers of value to healthcare professionals, whether directly or indirectly.

Electrocardiogram (EKG): a test that checks for problems with the electrical activity of a patient's heart by showing the heart's electrical activity as line tracings on paper. An EKG is performed to find the cause of unexplained chest pain or other symptoms of heart disease, to see how well medicines or implanted Medical Devices, such as pacemakers, are working in a patient and to check on the health of a patient's heart when other diseases or conditions are present, such as high blood pressure or diabetes.

Elements to Assure Safe Use (ETASU): mandatory medical interventions or other actions health professionals must execute prior to dispensing or prescribing a Drug to a patient.

EMA: acronym for European Medicines Agency.

Embryology: the branch of biology and medicine that is concerned with the study of embryos and their development.

Embryonic Stem Cells: Embryonic Stem Cells, or ESCs, are Cells that are derived from embryos and that are pluripotent (*i.e.*, they have the potential to become many or all of the different types of Cells in a mature organism). As a result, such Cells could have utility in creating healthy Cells and tissues to replace damaged or cancerous tissues in adults. Isolating such Cells in humans (hESCs) is controversial because isolation destroys or manipulates an embryo, current research may allow extraction from placenta and amniotic fluids as well.

Enablement: a requirement for patentability, distinct from the Written Description requirement. To satisfy Enablement, a Patent specification must contain sufficient information such that a Person of Ordinary Skill in the art could make or use the Invention from the disclosures in the Patent together with information known in the art without undue experimentation. 35 U.S.C. § 112(a).

Encumbered: with respect to Intellectual Property, any right, interest in or legal liability attached thereto. Typically, liens or security interests on Intellectual Property (often times in connection with a loan) will cause such Intellectual Property to be encumbered.

End-of-Phase I Meeting: a meeting that may occur between the Drug or Biologic sponsor and the FDA staff once data from Phase I testing are available, to discuss the design of Phase II trials.

End-of-Phase II Meeting: a meeting between the Drug or Biologic sponsor and the FDA — after completing the Phase II clinical program and before a sponsor enters into Phase III — to obtain feedback from the FDA on the proposed Phase III program in light of the Data obtained through Phase II.

Endogenous: produced within, or originating from within, the body or one of its parts.

Endoscopy: a visual examination of the interior organs and structures of the body using a visualization tool, often referred to as an endoscope. Endoscopy can also be used to obtain samples for cytological and histological examination or to follow the course of a disease.

Enforcement Discretion: a decision by a regulatory agency, such as the FDA or Department of Justice, to selectively enforce or decline to enforce a particular legal requirement.

Enzyme: a generic term for Proteins that catalyze or speed up biochemical reactions or Protein degradation in Cells. Enzymes work by binding Molecules so that they are held in a particular geometric

configuration that allows the reaction to occur. In some cases, companies may try to customize enzymes for targeted, unique or faster reactions. Enzymes are often given names ending in -ase.

Epidemiology: the branch of science that deals with the incidence, distribution and control of disease or health-related states or events in a specific population.

Epigenetics: Epigenetics refers to modification of Gene Expression in contrast to modification of the Genes themselves. Methylation of specific DNA sequences is one way that an organism can modulate a Gene's expression without changing the sequence of the Gene. The organism's environment may result in such modification, and in theory some Epigenetic modifications may be passed to the organism's progeny.

Erythropoietin: a hormone secreted by the kidneys that increases the rate of production of red blood Cells in response to decreasing oxygen levels in tissue.

Ethics Committee: ICH describes an independent Ethics Committee — sometimes known as an Institutional Review Board (IRB) — as "a group formally designated to protect the rights, safety, and wellbeing of humans involved in a Clinical Trial by reviewing all aspects of the trial." The group approves the initiation of the trial and ensures that Clinical Trial participants are exposed to minimal risks in relation to any benefits that might result from the research.

Etiology: a cause or set of causes of a disease or condition.

EU: the European Union, which currently consists of 28 Member States, including: France, Germany, Italy, the United Kingdom and Spain. Following the Brexit vote, the United Kingdom presumably will be leaving the EU in the coming years.

EU Data Protection Directive: the protection of Personal Data is set out in the Directive 95/46/EC* which aims at balancing the free movement of Personal Data within the EU with a high level of protection for the privacy of individuals. In accordance with this Directive, each Member State set up an independent national body responsible for supervising any activity linked to the processing of Personal Data. The collection and use of Personal Data can only take place within strict limits defined by the Directive.

*Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of Personal Data and on the free movement of such Data.

Eucomed Code: the European Confederation of Medical Devices Associations (Eucomed) represents the interests of European medical technology/device Manufacturers. Eucomed represents the interests of its members before various European-level authorities.

Eucomed issued guidelines intended to provide guidance on the interactions of Eucomed members with individuals (clinical or Non-Clinical, including but not limited to, physicians, nurses, technicians and research co-ordinators) or entities (such as hospitals or group purchasing bodies) that directly or indirectly purchase, lease, recommend, use, arrange for the purchase or lease of, or prescribe Eucomed members' Medical Devices.

On December 2, 2015, Members of Eucomed and EDMA adopted a new common MedTech Europe Code of Ethical Business Practice which will become binding to the members of EDMA and Eucomed on January 1, 2017. This code will replace the Codes of Ethical Business Practice issued by EDMA and Eucomed and will set the minimum standard across the EEA.

Eukaryote: an organism that consists of one or more Cells containing a membrane-bound nucleus with Chromosomes of DNA, RNA and Proteins, that divides through a process called mitosis. Eukaryotes include fungi, animals and plants as well as some unicellular organisms.

European Directorate for the Quality of Medicines & HealthCare (EDQM): a group that plays an important role in the current regulatory framework for Pharmaceuticals in the EU and aims to protect public health by enabling the development, supporting the implementation, and monitoring the application of certain quality standards for safe Pharmaceuticals and their safe use.

European Drug Master File (EDMF): a document containing complete information on an Active Pharmaceutical Ingredient (API) or finished drug Dosage Form. EDMF is the European equivalent of the Active Substance Master File (ASMF) in the United States and the US-Drug Master File (US-DMF). The EDMF includes information on the Manufacturer, the Drug product's manufacturing method, specification, chemistry, impurity and stability.

European Economic Area (EEA): the European Economic Area (EEA) is the internal market of the 28 EU Member States and the three EEA EFTA States (Iceland, Liechtenstein and Norway). The objective of the EEA internal market is to enable goods, services, capital and people to move freely across the whole Territory of the EEA in an open and competitive environment.

European Federation of Pharmaceutical Industries and Associations (EFPIA): a trade association founded in Brussels in 1978 that represents the research-based pharmaceutical industry operating in the European Union.

European Medicines Agency (EMA): the London-based EU agency responsible for the scientific evaluation of the safety, efficacy and quality of human and veterinary medicines to be used in the EU. The EMA is

composed of scientific committees (CHMP, CVMP, COMP, CAT, HMPC, PDCO, PRAC), an Executive Director supported by the Agency's staff and a Management Board.

European Patent Office (EPO): an institution of the European Patent Organization responsible for granting and examining European Patents for the Member States to the European Patent Convention. Further, EPO is responsible for examining Oppositions filed against previously granted European Patents.

European Public Assessment Report (EPAR): a public version of the CHMP opinion on granting or refusing a marketing authorization for a specific medicinal product that excludes all commercially sensitive information.

Examiner: a Patent office employee, usually a civil servant with a scientific or engineering background, who reviews Patent applications to determine if the Patent application should be allowed to issue as a Patent.

Excipient: an inactive ingredient intentionally added to a therapeutic or diagnostic product that is not intended to exert a therapeutic effect (though it may improve product delivery, such as by enhancing absorption or controlling Drug substance release). According to the FDA, Excipients may include fillers, extenders, diluents, wetting agents, solvents, emulsifiers, preservatives, flavors, absorption enhancers, sustained-release matrices and coloring agents, but do not include process- or product-related impurities such as degradation products, leachates or residual solvents or extraneous contaminants.

Excluded Parties List System: a web-based system maintained by the Federal General Services Administration (GSA) containing the names and other information of persons who are ineligible for participation in federal grants and agreements. Exclusion, debarment, suspension and ineligibility are part of the FAR, and some contracts with the government are required to include this and other FAR provisions. A federal agency can exclude, *i.e.*, suspend or debar, businesses or individuals from receiving contracts or assistance for various reasons, such as a conviction of or indictment for a criminal or civil offense, or a serious failure to perform to the terms of a contract. A suspension temporarily excludes a party, pending the completion of an investigation. A debarment is a fixed-term Exclusion. Generally, the period of debarment does not exceed three years, though some are indefinite.

Exclusion from Program: penalty through which OIG can ban entities from all Federal Health Care Programs including Medicare, Medicaid and all other programs for which the US provides funding directly or indirectly. Federal Health Care Programs will make no payment to excluded entities for items or services furnished, ordered or prescribed.

Exclusive Provider Organization (EPO): a managed care plan consisting of a network of individual medical care Providers, or groups of medical care Providers, who have entered into written agreements with an insurer to provide health insurance to subscribers.

Exclusivity: a provision in a contract in which one party agrees to refrain from specified activities during a stated time period. For example, Exclusivity in a supply agreement may mean that a Supplier will supply a product only to the other party. Similarly, in a License agreement, a party may agree not to develop or sell a specified product in a particular field or Territory during a specified time period.

Fab Fragment: the region on an Antibody that binds to Antigens, with the binding regions located at the two top portions of the Y-shaped Molecule.

Fair Market Value: the price of an asset or compensation for a service, determined as the result of an arm's-length negotiation by well-informed parties in a transaction, who are not otherwise in a position to generate business for the other party and not determined, directly or indirectly, in a manner that takes into account the volume or value of referrals or other business generated between the parties. With respect to leases of space, fair market value is the value of rental property for general commercial purposes (not taking into account its intended use) that is not adjusted to reflect the additional value that either party would attribute to the property as a result of its proximity or convenience to potential sources of patient referrals. Transactions presumptively based on Fair Market Value also assume that both buyer and seller are rational and have a reasonable knowledge of facts pertinent to the transaction.

False Claim / False or Fraudulent Claim: under the FCA, a claim, request or demand for money or property that is presented to the US government, or a contractor, grantee or agent of the US government (*e.g.*, a Medicare contractor), that is false or fraudulent; or the retention of all or a portion of money or property to which one is not entitled (a "reverse false claim"). A False Claim may also arise from false records and statements material to such a claim. In the healthcare context, a False Claim may arise under various circumstances, including a claim for medically unnecessary items or services, a claim for items or services not provided as claimed or at all, or from the false Certification of compliance with certain requirements such as the AKS or the Stark Law.

False Claims Act (FCA): a federal statute that prohibits knowingly presenting or causing the presentation of a false or fraudulent claim for payment to the US government. The FCA also prohibits the knowing retention of property or money owed to the US government (*e.g.*, the retention of an Overpayment). To violate the FCA, a party must have actual knowledge that the information is false, act in deliberate ignorance of, or recklessly disregard, the truth or falsity of the information. Actions under the FCA may be brought by the Attorney General or by a private individual in the name of the government as a Qui Tam (whistleblower) action. Violations of the False Claims Act can

result in significant monetary penalties (between US$10,781 and US$21,563 for each false claim and adjusted each year for inflation) and treble the amount of damages sustained by the US. Numerous states have comparable statutes. In addition, there is a separate criminal FCA statute, a violation of which may result in additional penalties and/or imprisonment.

FAR: acronym for Federal Acquisition Regulations.

Fast Track Product: according to the FDA, "a fast track product is a Drug that is intended, alone or in combination with one or more other Drugs, for the treatment of a serious or life-threatening disease or condition and that demonstrates the potential to address unmet medical needs for such a disease or condition," or that has been designated as a Qualified Infectious Disease Product under the FDCA, and for which the FDA has determined to expedite Drug Development and review. If the FDA determines after a preliminary evaluation of clinical Data that a fast track product may be effective, the FDA will evaluate the product's marketing application for filing and may commence a review of portions of the application before the sponsor submits a complete application. The sponsor of a Drug may request that the Drug be designated as a fast track product concurrently with, or at any time after, the submission of an Investigational New Drug Application.

FBMC: acronym for Fully Burdened Manufacturing Costs.

Fc Region: the region of an Antibody that interacts with Cell surface receptors and allows the Antibody to signal immune response to the Antigen.

FCA: acronym for False Claims Act.

FCA / Free Carrier Alongside (Incoterms): a commonly used term for delivery of products that obligates a seller to deliver product to a carrier at a named place specified by the buyer. Risk of loss passes to the buyer when the seller has delivered product to the carrier at the named place. FCA is a seller-favorable term both in relation to delivery costs and risk of loss.

FCPA: acronym for the Foreign Corrupt Practices Act.

FDA: see U.S. Food and Drug Administration (FDA).

Federal Acquisition Regulations (FAR): federal regulations that set forth policies, procedures and standard contract clauses applicable to nearly all federal executive agency procurements, including the acquisition of Drugs, Medical Devices and medical services.

Federal Circuit: a federal appellate court that has exclusive jurisdiction to hear patent cases. Both District Court decisions on patent Infringement/invalidity and Final Written Decisions of the PTAB are appealable directly to the Court of Appeals for the Federal Circuit, which has exclusive jurisdiction over appeals for PTAB Proceedings and patent litigations in federal district court. 35 U.S.C. § 141.

Federal Food, Drug, and Cosmetic Act (FDCA): the Federal Food, Drug, and Cosmetic Act is the overarching statute pursuant to which the FDA regulates products and activities subject to its jurisdiction.

Federal Health Care Programs (FHCP): any plan or program providing healthcare benefits, whether directly through insurance or otherwise, that is funded directly, in whole or in part, by the US government (other than the Federal Employees Health Benefits Plan — insurance Coverage provided to federal employees) or any state healthcare program; including the Medicare and Medicaid programs, the Children's Health Insurance Program (CHIP); TRICARE; and the Department of Veterans Affairs.

Federal Institute for Drugs and Medical Devices or Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM): The German Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM) is an independent federal authority within the Federal Ministry of Health. Its core missions are licensing, improving the safety of medicinal products, detecting and evaluating the risks of Medical Devices, and monitoring the legal traffic in narcotic drugs.

Federal Supply Schedule (FSS): a listing of commercial supplies and services at stated prices for given periods of time that federal agencies may use to purchase commercial supplies and services. The FSS Program uses the buying power of the government to obtain volume Discounts from Suppliers, Manufacturers, and service Providers. The Federal Acquisition Service (FAS) negotiates fixed prices for the supplies and services each contractor proposes to offer under the schedule (or hourly rates for some services), and then publishes the prices on the FSS so agencies can place orders for the discounted supplies and services directly with the schedule contractors. Being included on a federal supply schedule does not guarantee that contractors will receive any orders; the government is under no obligation to order any supplies or services under a federal supply schedule contract. The General Services Administration (GSA) has delegated authority to the Department of Veterans Affairs (VA) to establish its own schedules for medical supplies.

Federal Trade Commission (FTC): the federal agency with jurisdiction over interstate and foreign commerce, including enforcement of federal Antitrust Statutes. Section 5 of the Federal Trade Commission Act provides that the purpose of the FTC is to "promote free and fair competition in interstate commerce in the interest of the public through prevention of price-fixing agreements, boycotts, combinations in restraint of trade, unfair methods of competition, and unfair and deceptive acts and practices."

Fee Splitting: the practice of sharing professional fees with other professionals and non-professionals, typically in order to generate referrals from the other licensed or unlicensed individual or entity. Various states have laws prohibiting healthcare professionals (typically physicians) from sharing professional fees with other professionals and/or non-professionals. See Corporate Practice of Medicine.

Fee-for-Service (FFS): a Reimbursement methodology by which physicians or other healthcare Providers and Suppliers receive a fee for each item or service provided to a patient, such as an office visit, diagnostic test or procedure. Payment for such services is made by the patient, a Third-Party Payor, or a combination of the two. The Medicare program traditionally reimbursed Providers and Suppliers through the FFS model, but new payment models and initiatives (some required by statute) are shifting Reimbursement for Medicare-covered services to other payment models, such as bundling of related services, pay-for-performance and coordinated care.

Femoral Catheterization: often associated with cardiac catheterization, a diagnostic procedure which comprehensively examines how the heart and its blood vessels function, by means of a central venous Catheter inserted through the femoral artery or vein. A Catheter is a tubular, flexible instrument, passed through body channels for withdrawal of fluids from (or introduction of fluids into) a body cavity.

Field: a provision in a License that limits the scope of allowed use of the licensed technology. Generally, Field of use limitations will be carefully crafted to suit the needs of the agreement.

Fill & Finish: the last stage in the production process of Pharmaceuticals and implies the filling of the bottle/packaging, and any post-filling processes (*e.g.* Labeling).

First Commercial Sale: the First Commercial Sale of a therapeutic product or Medical Device, usually following receipt of Regulatory Approval for that product or Device in a given country. A First Commercial Sale can be used to define the term of royalties or trigger payment obligations.

First to Invent (FTI): a system of granting Patents where Priority is given to the first person to invent the subject matter of the Patent. The US Patent system used an FTI system until March 16, 2013, when the FTF (First to File) system under the AIA went into effect. Issued Patents that claim Priority before March 16, 2013 are considered FTI patents. 35 U.S.C. § 100.

FTI: acronym for First to Invent.

Flow Cytometry: a technology used for identifying and sorting Cells and their components to measure cell size, number, viability and nucleic acid content by analyzing the physical and chemical characteristics of particles in a fluid as it passes through at least one laser. Staining the Cell components with fluorescent dyes and detecting the fluorescence by laser beam to activate the dyes is a common Flow Cytometry process.

Fluorescence-activated Cell Sorting (FACS): a type of Flow Cytometry in which individual Cells in a Heterogeneous mixture are organized. The Cells are separated into individual drops through vibration and scanned one at a time by passing them through a laser. The Cells are then given an

electrical charge based upon the scatter and fluorescence Data scanned by the laser. The charged Cells are then sorted into collection tubes by a positively or negatively charged deflection plate.

Follow-on Biologic: similar to a Generic Drug in the traditional pharmaceuticals context, a Follow-on Biologic is intended to provide an alternative, potentially lower-cost Biological Product (Biologic) to compete with a brand-name or "reference" Biological Product. Follow-on Biologics may be either biosimilar to or interchangeable with the reference Biological Product. See 351(k) Pathway, Biosimilar, Interchangeable Biologic.

Food and Drug Administration Safety and Innovation Act (FDASIA): the Food and Drug Administration Safety and Innovation Act (FDASIA) was signed into law on July 9, 2012. Among other powers, FDASIA gave the FDA authority to collect user fees from industry to fund reviews of innovator Drugs, Medical Devices, Generic Drugs and Follow-on Biologic products; established the FDA's Breakthrough Therapy designation; created incentives for the Development of new Antibiotic products; gave the FDA new authorities to address the challenges posed by an increasingly global Drug supply chain; and included significant provisions affecting the Medical Device regulatory framework.

Force Majeure: a circumstance beyond the control of the parties to a contract that prevents a party from fulfilling its obligations under the contract. A Force Majeure event will result in a party being excused from performing its obligations and in some cases allows a party to terminate the agreement if the event continues for a defined time period.

Foreign Corrupt Practices Act (FCPA): a US federal law aimed at preventing the bribery of foreign government officials in an effort to obtain business. International agreements that involve a heavy regulatory component, such as research and Collaboration Agreements, will often include a provision obligating the parties to comply with the FCPA.

Form 483: According to the FDA, a Form 483, "is issued to firm management at the conclusion of an inspection when an investigator has observed any conditions that in his or her judgment may constitute violations of the FDCA."

Formulary: a list of all Drugs covered by a drug benefit plan. Formularies often feature a tiered structure in which Drugs are assigned to tiers that indicate the level of cost-sharing of the covered Drug. See Formulary Tier.

Formulary Tier: categories of Drugs on a Formulary that indicate Beneficiary cost-sharing obligations for the covered Drugs. Tier 1 is generally considered the lowest cost-sharing tier, and subsequent tiers will be higher cost-sharing tiers in ascending order. For example, Drugs in Tier 3 typically will be a higher cost-share for patients than Drugs in Tier 2.

Formulation: the combination of (or act of combining) an Active Pharmaceutical Ingredient (API) (or active Drug) with other compounds to produce a final medicinal product.

Fraud and Abuse (F&A): the intentional deception or misrepresentation of facts with the purpose of inducing or receiving greater Reimbursement than is owed or obtaining services or benefits for which the recipient is not eligible. F&A also applies to violations of certain federal laws and regulations, such as the FCA, AKS and the Stark Law, as well as analogous state laws. Conduct consisting of F&A in the context of the Federal Health Care Programs may expose such individuals and entities to criminal and civil liability, as well as Exclusion from participation in federal healthcare programs.

Free Sales Certificate: Free Sales Certificate, or a Certificate of Free Sale refers to the various classes of export certificates issued by the FDA for various categories of products requiring FDA approval. These export certificates are often required by foreign customers or governments for companies exporting such products to foreign markets.

FTE: acronym for Full-Time Equivalent.

FTE Costs: an amount equal to the number of FTEs to be dedicated to a particular activity under an agreement, multiplied by the FTE Rate, which is used to calculate the amounts to be paid to the party whose employees are performing such activities.

FTE Rate: a defined term in an agreement that sets forth the amount owed to an FTE employee on an hourly basis.

Full-Time Equivalent: the number of hours worked by one employee of a party working on a full-time basis, for use in calculating the overall number of hours to be contributed by a party to a particular activity.

Fully Burdened Manufacturing Costs (FBMC): a term used to define the type of costs to be included in the calculation of a payment due to a party for providing services or products.

Fully Integrated Medical Group (FIMG): a medical group practice organized as a single legal entity that: practices under a common name; possesses governance and centralized management with complete authority over the management of the organization and its business; has fully unified administrative, business and clinical systems; and distributes income among its physicians through a single allocation system. As distinguished from a Partially Integrated Medical Group (PIMG).

GAAP: acronym for Generally Accepted Accounting Principles.

GAIN Act: the Generating Antibiotics Incentives Now (GAIN) Act was passed as part of the Food and Drug Administration Safety and Innovation Act in an attempt to create incentives for the Development of new Antibacterial or antifungal products designated as qualified infectious disease products. See Qualified Infectious Disease Product.

Gapfilling: a technique CMS may use to determine fee schedule amounts for certain items or services when the Data that would otherwise be used to determine the fee schedule amount is insufficient or unavailable. For example, CMS may use Gapfilling to establish payment amounts under the CLFS for new or substantially revised HCPCS Codes of clinical diagnostic laboratory tests when there is no comparable test on the CLFS upon which to base payment for the new or substantially revised HCPCS Code. Similarly, CMS will "gap-fill" the fee schedule amounts of DMEPOS for which charge Data is unavailable during the fee schedule Data base year. Under Gapfilling, payment amounts for items may be based on various sources of information available to CMS.

Gastrointestinal Stromal Tumor (GIST): a type of tumor that usually begins in the Cells in the wall of the gastrointestinal tract. Nearly all of these tumors are found in the stomach or the small intestine, and can be Benign or Malignant.

Gene: a specific sequence of Nucleotides in DNA or RNA usually located on a Chromosome, and that is the functional unit of heredity controlling the transmission and expression of one or more traits by specifying the structure of a particular polypeptide and Protein or controlling the function of other genetic material. Genes make up segments of the complex DNA Molecule that controls cellular reproduction and function.

Gene Expression: the Translation of information encoded in a Gene into Protein or RNA structures that are present and operating in the Cell. More commonly known as the appearance of an inherited trait, or the detectable effect of a Gene.

Gene Fragment: portions of a Gene that actually encode the Protein sequence.

Gene Synthesis: the artificial construction of a Gene by chemical means using Oligonucleotides.

Gene Therapy: a generic term for modifying diseasing-causing Genes using viral Vectors, RNAi, CRISPR, antisense or zinc finger Proteins.

Generally Accepted Accounting Principles (GAAP): a framework of accounting rules, procedures and standards adopted by the professional accounting industry and used to calculate amounts due to a party under agreements. Another such framework is the IFRS.

Generic Drug or Generic Product: Generic Drug Products are versions of reference-listed Drugs that are identical to the innovator Drug product (branded product) in active ingredient(s), Dosage Form, strength, route of administration and conditions of use, except that conditions of use for which approval cannot be granted because of Exclusivity or an existing Patent may be omitted. A Generic Drug product can receive approval after filing an ANDA which references the branded product rather than the NDA system, and avoid duplicative Clinical Trials, if the Generic Drug can show bioequivalence to the branded product.

Generic Product Applicant: the company that owns or has the rights in the generic product. See Generic Product.

Genetic Engineering: scientific alteration of the structure of genetic material in a living organism using recombinant DNA technology.

Genetic Variation: the phenotypic and genotypic differences among individuals in a population, often referring to the diversity in Gene frequencies.

Genetically Modified Organism (GMO): usually plants or microorganisms that have their genetic code permanently modified. Examples include pesticide resistant crops and soy beans that express higher levels of oleic fatty acid. CRISPR technology will enable the GMO market to expand quickly.

Genetics: the branch of biology that deals with the heredity and variation of organisms.

Genome: all of the genetic information possessed by any organism, or the complete set of Genes and hereditary factors contained in a set of Chromosomes.

Genome Sequencing: the technique that allows researchers to read and decipher the genetic information found in the DNA of any living organism.

Genomics: the study of Genes and their function. Genomics is a branch of biology concerned with applying the techniques of Genetics and molecular biology to the genetic mapping and DNA sequencing of sets of Genes or the complete Genomes of selected organisms.

Genotype: the genetic constitution of an organism or Cell; also refers to the specific set of Alleles inherited at one or more specific loci.

Geriatrics: the branch of medicine concerned with the diagnosis, treatment and prevention of disease in older people and the problems specific to aging. Related to the science of Gerontology.

Gerontology: the study of the social, psychological and biological aspects of aging.

GIST: acronym for Gastrointestinal Stromal Tumor.

Glaucoma: a group of eye diseases characterized by damage to the optic nerve due to excessively high intraocular pressure (IOP). Several different types of glaucoma, if left untreated, could lead to damage to the optic nerve, causing loss of vision or blindness.

Glucose Monitoring: also known as blood glucose monitoring, the periodic testing of serum glucose, or blood sugar, in patients known to have diabetes.

GMO: acronym for Genetically Modified Organism.

Good Laboratory Practices (GLP): FDA regulations codified at 21 CFR Part 58 regarding the conduct of nonclinical laboratory studies that support or are intended to support applications for research or marketing permits for products regulated by the FDA, including food and color additives, animal food additives, human and animal Drugs, Medical Devices for human use, Biological Products (Biologics) and electronic products.

Good Clinical Practices (GCP): an international 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. In the United States, GCPs are codified at various parts of Title 21 of the Code of Federal Regulations, including 21 C.F.R. Part 50 (Protection of Human Subjects) and Part 56 (Institutional Review Boards).

Good Clinical Practices (GCP) Inspection Findings: any good Clinical Trial inspection which the EMA requests can generate the following findings:

- Critical findings – Conditions, practices or processes that adversely affect the rights, safety or wellbeing of the subjects and/or the quality and integrity of Data.
- Major findings – Conditions, practices or processes that might adversely affect the rights, safety or wellbeing of the subjects and/or the quality and integrity of Data.
- Major observations are serious deficiencies and are direct violations of GCP principles.
- Minor findings – Conditions, practices or processes that would not be expected to adversely affect the rights, safety or wellbeing of the subjects and/or the quality and integrity of Data.

Good Distribution Practice (GDP): a set of guidelines published by the European Commission on good distribution practice of medicinal products designed for human use which define appropriate tools to help Wholesale Distributors conduct their activities and prevent falsified Pharmaceuticals from entering the legal supply chain.

Good Faith Negotiations: the stage during the BPCIA Exchange when the parties negotiate about which Patents should be part of a Patent litigation suit under 42 U.S.C. 262 (l)(6). This stage occurs after the parties have exchanged their respective Infringement and validity positions. Reference 42 U.S.C. 262 (l)(4). See Patent Dance.

Good Manufacturing Practices/Current Good Manufacturing Practices (GMP/cGMP): FDA regulations that establish minimum requirements for methods to be used in, and facilities or controls to be used for, the

manufacturing, processing, preparing, packing, and/or holding of, and record-keeping regarding, foods, dietary supplements, Drugs, Devices and other FDA-regulated products. In the case of Devices, cGMP requirements are referred to as the Quality System Regulation.

Good Pharmacovigilance Practice (GVP): good pharmacovigilance practices (GVP) are the standards of Pharmacovigilance elaborated in compliance with EU laws and regulations. These standards apply to the marketing authorisation holders and the regulatory agencies.

Governmental Authority: a defined term in many licensing and Collaboration Agreements that refers to all applicable governmental and regulatory authorities in relevant jurisdictions (*e.g.* the FDA in the United States) whose laws and regulations apply to a party's activities under an agreement.

GPO: acronym for Group Purchasing Organization.

Graham Factors: questions of fact used to resolve the issue of Obviousness as set forth by the Supreme Court in *Graham v. John Deere Co.*, 383 U.S. 1 (1965). Graham Factors include: (1) the scope and content of the prior art, (2) the differences between the claimed Invention and the prior art and (3) the level of ordinary skill in the prior art. Further objective evidence may also be relevant to Obviousness and is often referred to as Secondary Considerations.

Group Contract: an agreement between an HMO and a subscriber group (*e.g.*, a group of policyholders) specifying rates, performance, covenants, relationships among parties, schedule of benefits and other conditions. The term of the contract is generally limited to a 12-month period.

Group Model HMO: an HMO contracting for professional services with a single multi-specialty physician group practice or network of group practices that are closely related to but legally separate from the HMO. The contracting relationship is typically substantially (or totally) exclusive.

Group Purchasing Organization (GPO): an entity that helps healthcare Providers, such as hospitals, nursing homes and home health agencies, realize savings and efficiencies by aggregating purchasing volume and using that leverage to negotiate Discounts with Manufacturers, distributors and other vendors. GPOs rely, in part, on fees vendors pay to finance the services the GPOs offer healthcare Providers. These administrative fees are generally based upon the purchase price that the healthcare Provider pays for a product purchased through a GPO contract.

Gynecology: the branch of medicine concerned with diseases unique to women, especially those of the genital tract and breasts, as well as endocrinology and reproductive physiology of women.

Hart-Scott-Rodino Antitrust Improvements Act of 1976 (HSR): a federal statute requiring prior notification to the Federal Trade Commission of a prospective merger of parties that together have total market assets of US$100 million or more, or total annual sales in excess of US$10 million.

The HSR filing to the FTC must be made in considerable detail, subsequent to which the FTC has 30 days in which to request additional information or allow the merger to proceed. Additional information will be requested if the FTC believes that the transaction could substantially reduce competition in the market. The scope of the inquiry and information requested will then be greatly expanded.

Hatch-Waxman Act: a federal law that provides the framework for the approval of generic products and that established the ANDA process. The Hatch-Waxman Act also established procedures for patent term extensions. Also referred to as the Drug Price Competition and Patent Term Restoration Act.

HCPCS: acronym for Healthcare Common Procedure Coding System.

HCPCS Code: a code used to identify items and services related to the provision of healthcare. The HCPCS coding system is divided into two principal subsystems, referred to as HCPCS Level I and HCPCS Level II. HCPCS Level I is comprised of CPT Codes. HCPCS Level II is a standardized Coding system that is used primarily to identify products, supplies and services not included in the CPT Codes, such as ambulance services and DMEPOS when used outside a physician's office. While the CPT Code set is maintained by the AMA, the HCPCS Level II code set is updated and maintained by CMS. Because Medicare and other insurers cover a variety of services, supplies and equipment that are not identified by CPT Codes, the Level II HCPCS Codes were established for submitting claims for these items. Level II codes are also referred to as alpha-numeric codes because they consist of a single alphabetical letter followed by four numeric digits, while CPT Codes are identified using five numeric digits.

Health and Human Services (HHS): US agency tasked with protecting the health of Americans and providing essential human services; also known as the Health Department.

Health Claims Act: the regulation of the European Parliament on nutrition and health claims made on foods (Regulation (EC) No. 1924/2006). Health claims are details on food packaging or labels used by food business operators when they intend to highlight beneficial effects of their products (normally for Advertising purposes). The act provides the legal framework for such use and is designed to ensure that any claim an operator makes in/on presentation, Labeling or Advertising in the European Union is clear, accurate and based on scientific facts.

Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH): the American Recovery and Reinvestment Act of 2009, which was signed into law on February 17, 2009, included the HITECH Act. The act (1) extended the reach of HIPAA to apply directly to Business Associates and their Subcontractors, (2) imposed breach notification requirements on Covered Entities and Business Associates; (3) imposed restrictions on marketing communications

and generally prohibited Covered Entities or Business Associates from receiving Remuneration in exchange for PHI; and (4) increased the civil and criminal penalties that may be imposed for HIPAA violations, increasing the annual cap for civil money penalties from US$25,000 to US$1.5 million per year per standard violation.

Health Insurance Portability and Accountability Act (HIPAA): the Health Insurance Portability and Accountability Act of 1996 establishes uniform standards governing the conduct of certain electronic healthcare transactions and protecting the security and privacy of individually identifiable health information maintained or transmitted by certain Covered Entities. In the early 2000s, HIPAA was implemented by the HIPAA Privacy and Security Rules, which were promulgated by the U.S. Department of Health & Human Services (HHS). In 2009, HIPAA was amended by HITECH. In 2013, the HIPAA Omnibus Final Rule modified and amended the HIPAA Privacy and Security Rules. The HHS Office for Civil Rights (OCR) is responsible for implementing and enforcing HIPAA, HITECH and the HIPAA Rules.

HIPAA also created federal statutes to prevent healthcare fraud and false statements relating to healthcare matters. The healthcare fraud statute prohibits knowingly and willfully executing a scheme to defraud any healthcare benefit program, including Private Payors. A violation of this statute is a felony and may result in fines, imprisonment or Exclusion from government-sponsored programs such as the Medicare and Medicaid programs. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. A violation of this statute is a felony and may result in fines, imprisonment or Exclusion from government-sponsored programs.

Health Maintenance Organization (HMO): an organization that provides both financing for, and the delivery of, physician and hospital services to an enrolled population for a fixed sum of money, paid in advance, for a specified period of time. These health services may include a wide variety of medical treatments, inpatient and outpatient hospitalization, home health services, ambulance services, and sometimes dental and pharmacy services. The HMO arranges for the provision of health services through contracts with Providers, who may be organized as a group model, an independent practice association (IPA) model, a network model or a staff model. Enrollees are typically required to use the services of participating Providers, except in point-of-service (POS) HMO plans, under which the enrollee identifies an in-network primary care Provider, but seeks care outside the network (similar to a PPO).

Healthcare Professional / Healthcare Practitioner (HCP): an individual who is qualified by education, training, licensure or regulation and facility privileging, when applicable, to perform a professional healthcare service such as preventative, curative, or rehabilitative services within his or

her scope of practice. Such individuals include physicians, dentists, pharmacists, physician assistants, nurses, advanced practice registered nurses, surgeons, surgeon's assistants, surgical technologists, midwives, psychologists, pathologists, occupational and physician therapists and speech-pathologists, among other professionals. Although actually more expansive, the term is frequently used in reference to only individuals who are in a positon (by training, licensure or otherwise) to refer or recommend patients for healthcare items or services.

Hematology: the branch of medicine concerned with the diagnosis, treatment and prevention of diseases of the blood and bone marrow as well as the immunologic, hemostatic and Vascular systems.

Heterogeneous: comprising elements with various and dissimilar properties.

HHS: acronym for Health and Human Services.

HIPAA: acronym for Health Insurance Portability and Accountability Act.

HIPAA Breach: the acquisition, access, use or disclosure of PHI in a manner not permitted under the HIPAA Privacy Rule which compromises the security or privacy of the PHI. An impermissible use or disclosure of PHI is presumed to be a breach, unless the Covered Entity or Business Associate, as applicable, demonstrates that there is a low probability that the PHI has been compromised based on a risk assessment of at least the following factors: (1) the nature and extent of the PHI involved, including the types of identifiers and the likelihood of re-identification; (2) the unauthorized person who used the PHI or to whom the disclosure was made; (3) whether the PHI was actually acquired or viewed; and (4) the extent to which the risk to the PHI has been mitigated. Once an entity determines that a breach has occurred, notification must be made pursuant to the requirements of the HIPAA Breach Notification Rule, or, in the case of a breach by a Business Associate, the BAA.

HIPAA Breach Notification Rule: requires Covered Entities and Business Associates to provide notification following a HIPAA Breach of unsecured PHI. In the case of ePHI, unencrypted ePHI is considered unsecured. Once a HIPAA Breach is determined to have occurred, Covered Entities must notify affected individuals within 60 days following discovery. If a HIPAA Breach affects 500 or more individuals, Covered Entities must notify HHS within 60 days. If 500 or more affected individuals reside in the same state or jurisdiction, the Covered Entity must also provide notice within 60 days to prominent media outlets in the state or jurisdiction. If the HIPAA Breach has affected fewer than 500 individuals, HHS must still be notified, but it may be on an annual basis. If the HIPAA Breach is also considered a state Data Breach, then Covered Entities must also notify the state Attorney General under many states' laws. If a Business Associate has experienced a HIPAA Breach, then under the HIPAA Breach Notification Rule, the Business

Associate must notify the Covered Entity whose PHI was breached within 60 days. However, in practice, BAAs almost universally impose a much shorter timeframe for notifying the Covered Entity. If a BAA imposes stricter contractual obligations than the obligations imposed by the HIPAA Rules, the BAA controls.

HIPAA Omnibus Final Rule: published in 2013, the HIPAA Omnibus Final Rule implements HITECH and amends and modifies the HIPAA Privacy, Security, and Breach Notification Rules. The most notable change was to apply the HIPAA Security Rule and certain portions of the HIPAA Privacy Rule directly to Business Associates. The Omnibus Final Rule also strengthened the Breach Notification Rule by creating a presumption that any breach of unsecured PHI is reportable, unless the Covered Entity or Business Associate can demonstrate a low probability that the PHI has been compromised (see, HIPAA Breach). Further changes expanded individual rights by permitting patients to request a copy of their electronic medical record in electronic form, or to request that a copy of their medical record be sent directly to a third party. The Omnibus Final Rule also prohibited the sale of PHI without an individual's permission and set new limitations on how PHI may be used for marketing and fundraising purposes.

HIPAA Privacy Rule: as distinct from the HIPAA Security Rule, the HIPAA Privacy Rule regulates the use and disclosure of PHI held by Covered Entities and Business Associates in any form, and sets standards for individuals' privacy rights to understand and control how their PHI will be used. As a general rule, the HIPAA Privacy Rule prohibits a Covered Entity from using or disclosing an individual's PHI without an authorization, except in certain defined circumstances. The main permitted uses and disclosures of PHI without an authorization are either to the individual, or for purposes of treatment, payment or healthcare operations. A Covered Entity may also use and disclose PHI without an authorization in certain other circumstances, such as for research purposes if certain requirements are met (such as the use of a limited Data set or with Institutional Review Board approval of a waiver of the authorization requirement). Covered Entities are required to give notice to their patients of how they use and disclose PHI through a Notice of Privacy Practices, and must give individuals rights with respect to their health record, such as access and an opportunity to amend the record. The Privacy Rule also imposes certain administrative requirements on Covered Entities, such as having privacy policies, procedures, and personnel, and training their workforce on Privacy Rule obligations.

HIPAA Security Rule: as distinct from the HIPAA Privacy Rule, the HIPAA Security Rule establishes a national set of security standards for protecting PHI held in electronic form only, by requiring Covered Entities and Business Associates to implement certain defined administrative, technical and physical safeguards to protect the confidentiality, integrity and availability of electronic PHI (ePHI). Key administrative safeguards include conducting a risk analysis and risk management plan that evaluates

the likelihood and impact of potential risks to ePHI, implementing appropriate security measures to address the risks identified in the risk analysis, documenting the chosen security measures, and maintaining continuous, reasonable, and appropriate security protections. Technical safeguards include access controls and encryption that is a reasonable and appropriate safeguard in the environment, when analyzed with reference to its likely contribution to protecting ePHI. Physical safeguards include facility access controls and workstation and Device security.

HMPC: acronym for Committee on Herbal Medicinal Products.

Hodgkin's Disease: also known as Hodgkin's Lymphoma, a type of cancer that develops in the lymph system and is marked by the presence of Reed-Sternberg Cells. Hodgkin's Disease can start in almost any part of the body, and can spread to any organ or tissue in the body. Hodgkin's Disease is one of two common types of cancers of the lymphatic system. The other type, Non-Hodgkin's Lymphoma, is far more common.

Hospital Outpatient Prospective Payment System (OPPS): a payment system used by Medicare for hospital outpatient services, certain Part B services furnished to hospital inpatients without Part A Coverage, and several other categories of services provided to Medicare beneficiaries. The OPPS assigns a status indicator to every HCPCS Code that identifies whether the service is paid under the OPPS or another payment system or fee schedule, and if paid under OPPS, whether payment is made separately or packaged into payment for another separately paid service. Each HCPCS Code for which a separate payment is made under the OPPS is assigned to an Ambulatory Payment Classification (APC) group for which CMS calculates a corresponding bundled payment rate on an annual basis.

Howard Hughes Medical Institute (HHMI): non-profit medical institution headquartered in Maryland dedicated to biomedical research and education founded by aviator-industrialist Howard Hughes. HHMI investigators, who are provided flexible long-term funding (as opposed to specific research grants), are based in over 60 research institutions across the United States and research areas including, but not limited to, developmental biology, Genetics, Immunology, Neuroscience and computational biology. HHMI invested more than US$650 million in research and US$85 million in support for science education in FY 2015.

Human Leukocyte Antigens (HLA): Gene complex in the human Genome that controls the Major Histocompatibility Complex Proteins in humans, which allow the immune system to distinguish the body's own Proteins from foreign Proteins.

Hybrid Marketing Authorisation Application: when applying for a Marketing Authorisation, if the product does not entirely fit into the definition of a Generic Product, the applicant must provide additional results of clinical and/or Non-Clinical research.

There are three circumstances in which such additional Data is required:

- If the strict definition of a generic medicinal product is not met
- If bioavailability studies cannot be used to demonstrate bioequivalence (for example if the new product is supra-bioavailable)
- If there are changes in the active substance(s), therapeutic Indications, strength, Pharmaceutical form or route of administration of the generic product compared to the Reference Product.

Hyperkalemia: a medical term used to describe a potassium level in a patient's blood that is higher than normal.

Hyperphosphatemia: a medical term used to describe an excess of phosphates in a patient's blood.

Hypertension: a term used to describe high blood pressure, which is a sustained high level of force exerted against the walls of arteries as a person's heart pumps blood through the body.

ICH: acronym for International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, formerly International Conference on Harmonisation.

ICH Guidelines: agreed-upon scientific guidance issued by the ICH for meeting technical requirements for registration, aimed at eliminating duplication in the development and registration process. Each ICH Regulatory Party implements the guidelines according to its national/regional requirements.

ICH Regulatory Party: the ICH Regulatory Parties include representatives of the US (represented by the FDA), the European Union (represented by the European Commission and the EMA), Japan (represented by the Ministry of Health, Labour and Welfare), Canada (represented by the Health Products and Food Branch) and Switzerland (represented by Swissmedic).

IFRS: acronym for International Financial Reporting Standards.

Immunology: the science that deals with all aspects of the immune system, including the structure and function, disorders of the immune system and the humoral aspects of immunity and immune response.

Immuno-oncology: a treatment or therapy that uses the body's immune system to fight cancer. Immuno-oncology therapies activate a person's immune system, making it able to recognize cancer Cells and destroy them. See Chimeric Antigen Receptor (CAR), CAR T-Cell, T-Cell, TCR or T-Cell Receptor.

Immunotherapy: a treatment to stimulate or restore the ability of the immune system to fight infection and disease. The passive immunization of a person by administration of preformed Antibodies actively produced in another individual.

In Silico: also known as computational medicine, referring to analysis or experimentation carried out in a computer environment, rather than in the laboratory or in a living organism.

In Vitro: the technique of performing a given procedure in a controlled environment outside of a living organism, such as in a glass or plastic vessel or test tube. The opposite of In Vivo.

In Vitro Diagnostic (IVD): according to the FDA, "In Vitro Diagnostic products are those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body."

In Vitro Diagnostic Medical Device: any Medical Device which is a Reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, whether used alone or in combination, intended by the Manufacturer to be used In Vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information (i) concerning a physiological or pathological state, or (ii) concerning a congenital abnormality, or (iii) to determine the safety and compatibility with potential recipients, or (iv) to monitor therapeutic measures (Art. 1 para. 2 lit. c) Directive 93/42/EEC).

In Vivo: in the living body, or the technique of performing a given procedure or experimentation in a whole, living organism as opposed to a partial or dead organism.

Incident: an EU Medical Device vigilance concept that is defined by the Medical Device Directive (Council Directive 93/42/EEC of 14 June 1993 concerning Medical Devices) as any malfunction or deterioration in the characteristics and/or performance of a Device, as well as any inadequacy in the Labeling or the instructions for use which, directly or indirectly, might lead to or might have led to the death of a patient, or user or of other persons or to a serious deterioration in their state of health.

Incoterms: short for International Commercial Terms, Incoterms are a set of standard commercial rules determined by the International Chamber of Commerce and used in many manufacturing and supply agreements. Using Incoterms helps to efficiently delineate each parties' responsibilities with respect to shipping, receiving, packaging, risk of loss, and similar terms, and helps decrease ambiguity in contracts.

IND: acronym for Investigational New Drug.

IND Enabling Studies: Pre-Clinical animal pharmacology and toxicology studies that generate Data required to allow an assessment of whether an IND should be accepted by a Regulatory Authority.

Independent Review Organization (IRO): a third-party entity that provides independent, objective reviews and assessments of the subject for which the IRO is engaged. An entity subject to a CIA may be required to engage an IRO to review claims, cost reports, Medical Necessity and appropriateness determinations, or financial arrangements and transactions with healthcare Providers and Suppliers, to assess compliance with applicable laws and regulations.

Indication: a particular disease or condition for which a therapeutic product is used.

Induced Pluripotent Stem Cells (iPSCs): Pluripotent Stem Cells that are generated from adult Cells, and thus do not require destruction or manipulation of an embryo. Another advantage of this technology is that iPSCs generated from a patient's tissue should be well tolerated by the patient's immune system. Research is underway to determine if iPSCs have the same properties and potential as Embryonic Stem Cells.

Inducement: indirect form of patent Infringement that can trigger liability for an entity that knowingly aids and abets patent Infringement, even though the entity is not making, using, selling, or offering to sell an infringing product or method. 35 U.S.C. § 271(b). Inducement may arise if a Drug is indicated for use in a method Covered by a Patent. To establish Inducement, a patentee must prove there has been an act of direct Infringement and that the induced acts constitute patent Infringement. Commil USA, *LLC v. Cisco Systems*, Inc., 575 US __, 135 S. Ct. 1920 (2015).

Inflammation: a localized protective response elicited by injury or destruction of tissues, which serves to destroy, dilute or wall off both an injurious agent and the injured tissue. May be external or internal, and often produces redness, warmth, swelling and pain as a result of infection, irritation or injury.

Infringement: the act of making, using, selling, or offering to sell a patented Invention, or importing into the United States a product Covered by a claim of a Patent without the permission of the Patent owner.

Institutional Review Board (IRB): also known as the independent Ethics Committee or the ethical review board, a type of committee used in medical research in the United States that has been formally designated to approve, monitor and review biomedical and behavioral research. The IRB is a committee within a hospital charged with responsibility for ensuring the safety and well-being of human subjects involved in research.

Intellectual Property: government-conferred or legally conferred rights in non-tangible property. Common forms of Intellectual Property include Patents, copyrights, Trademarks, Trade Secrets and Know-How.

Intercellular: located between or among Cells.

Interchangeable Biologic: according to the FDA, an Interchangeable Biological Product is a product that is biosimilar to an FDA-approved reference Biological Product (Biologic) and meets additional standards for interchangeability. Specifically, an Interchangeable Biologic can be expected to produce the same clinical result as the reference Biological Product in any given patient; and for a Biological Product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between the Interchangeable Biological Product and the reference Biological Product is not greater than the risk of using the reference Biological Product alone.

Interference Proceeding: a US Patent proceeding conducted by the CRU to resolve which of several parties first invented an Invention commonly claimed in two or more FTI Patents or Patent applications. As a form of inter partes proceeding, Interferences are conducted among the PTO and several parties.

International Council on Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH): an international body that brings together the ICH Regulatory Parties as well as representatives of the Pharmaceutical industry to discuss scientific and technical aspects of drug registration.

International Financial Reporting Standards (IFRS): a set of accounting standards developed by the International Accounting Standards Board (IASB).

International Non-Proprietary Names (INNs): the World Health Organization (WHO) issues International Non-proprietary Names (INN), also known as a generic names, to identify Pharmaceutical substances or Active Pharmaceutical Ingredients (API). Each INN is unique.

Inter Partes Review (IPR): a PTAB proceeding for challenging the validity of any issued Patent. IPR may be requested on the basis of Novelty and Obviousness, and only Patents and printed publications may be used as prior art. 37 C.F.R. § 42.104(b).

The PTAB will not institute a petition for IPR if the Petitioner previously filed a Declaratory Judgement action challenging the Patent's validity. But a Declaratory Judgement action filed as a counterclaim to an infringement suit does not bar instituting an IPR. 37 C.F.R. § 42.101.

IPR may be requested at any time for first-to-invent Patents. But for first-to-file Patents, IPR may only be requested nine months after the issuance or later (the period when a Petition for post- grant review could be filed). 37 C.F.R. § 42.102. And if Petitioner has been served with a patent infringement complaint, then the Petition must be filed in the PTAB within one year after service. 35 U.S.C. § 315(b).

Intervened Case: when the government decides to prosecute a whistleblower or Relator's private action against an entity engaging in potentially fraudulent conduct. After a private citizen files a False Claims Act complaint against an entity, the complaint will remain sealed for at least 60 days, during which time the government will investigate the underlying allegations and determine whether to intervene, continue to investigate or decline intervention.

Intracellular: located within a Cell or Cells.

Intravenous (IV): into or within a vein. Intravenous medications are solutions administered directly into the vein via a syringe or Intravenous Catheter.

Invention: a novel idea, technology, machine, manufacture, composition or method.

Investigational New Drug Application (IND): an IND is an application that must be submitted to the FDA prior to any clinical investigation of a Drug or Biological Product (Biologic) in the United States, subject to certain exemptions. An Investigational New Drug or Biological Product for which an IND is in effect is exempt from the premarketing approval requirements that are otherwise applicable and may be shipped lawfully for the purpose of conducting clinical investigations of that Drug or Biological Product.

In-vitro Fertilization (IVF): a complex series of procedures used to treat fertility or genetic problems and assist with the conception of a child. During IVF, mature eggs are collected from a woman's ovaries and fertilized by sperm in a lab, and then the fertilized egg (embryo) is returned to the woman's uterus.

IPR: acronym for Inter Partes Review.

Italian Medicines Agency or Agenzia Italiana del Farmaco (AIFA): the Italian Medicines Agency (AIFA) is the Italian drug agency. Among other things, the AIFA's responsibilities include: granting Marketing Authorisations for medicinal products; authorizing Clinical Trials; monitoring adverse effects and other drug-related safety information; and monitoring and controlling (*e.g.*, through inspections) medicinal products commercialized and used in Italy to ensure they comply with applicable laws.

J-Code: a subset of the HCPCS Level II code set used to identify certain Drugs and other items. J-Codes typically describe Drugs that are administered in the Provider's office, clinic or by a home health agency through injection or Intravenous administration, in addition to certain orally administered chemotherapeutic agents, and certain Drugs administered through DME.

Japanese Ministry of Health, Labour and Welfare (Koseisho): the Pharmaceutical and Food Safety Bureau of the Japanese Ministry of Health, Labour and Welfare states that one of its missions is to ensure the quality, efficacy and safety of Drugs/Medical Devices manufactured and sold in Japan by examining whether they can be safely used or not and how effective they are in treating diseases before approving them. The Japanese equivalent of the FDA.

JDC: acronym for Joint Development Committee.

Joint Commercialization Committee (JCC): a governing body formed pursuant to a Collaboration Agreement that has representatives from each party, who perform defined tasks with respect to the Commercialization of product.

Joint Commission: a private, non-governmental organization composed of representatives from the American College of Physicians, American College of Surgeons, American Dental Association, American Hospital Association and American Medical Association. The Joint Commission establishes standards for hospital operations and conducts survey and Accreditation programs to determine whether a healthcare facility meets those standards.

Joint Development Committee (JDC): a governing body formed pursuant to a Collaboration Agreement that has representatives from each party, who perform defined tasks with respect to the Development of products.

Joint Invention: an Invention reduced to practice jointly by agents of both parties to an agreement.

Joint Steering Committee (JSC): a governing body formed pursuant to a Collaboration Agreement that has representatives from each party, who perform collaboration oversight activities, including resolution of disputes on the JDC and JCC.

Kaplan-Meier Analysis: a form of survival analysis calculated over a period of time, or a method of calculating survival of a patient population in which the increments are the actual survival times of the patients.

Key Opinion Leader (KOL): in the healthcare context, certain physicians (also known as thought leaders) perceived as experts in their field whose opinions and practices may influence their peers' medical practice, including but not limited to prescribing behavior. KOLs may be engaged by pharmaceutical and medical device companies as part of the early product Development process to advise on research and Development, and to conduct Clinical Trials. KOLs are also often engaged for marketing activities, such as lectures, advocacy and marketing feedback.

Kickback: the transfer of anything of value, directly or indirectly, overtly or covertly, in cash or in kind given to encourage or induce service Providers to prescribe certain Drugs or services for patients or to refer a patient to a physician or facility for receipt of services. Federal law prohibits Kickbacks.

Know-How: ideas, knowledge, technology, information, materials or other items that are not themselves the subject of Patent rights. Trade Secrets may be included in Know-How.

Label: FDA-approved, non-promotional material provided with the retail package of a Drug that describes the Drug, including what Indications the Drug is approved for, instructions regarding how to use the Drug, side effects and safety information.

Labeling: the physical overlabel in accordance with certain packing specifications or the design to be printed directly onto the product packaging, as applicable.

Laboratory Developed Test (LDT): according to the FDA, an In Vitro Diagnostic intended for clinical use and designed, manufactured and used exclusively within a single laboratory.

Large Molecule Drug: also known as Biological Products (Biologics) or biopharmaceutical Drugs, a large and complex Drug often consisting of Heterogeneous mixtures. Large Molecule Drugs are generally made in genetically engineered Cells that impose their own variabilities on the processes used to make such Drugs.

Latham & Watkins: also known as global law firm with leading practice in the healthcare & life science industry.

Lauer-Taxe (Germany): an information database of pharmacy software products (Große Deutsche Spezialitätentaxe or ABDA-Artikelstamm), which contains economic, social and medical law information and which is to a great extent supplied with Data by the Informationsstelle für Arzneispezialitäten (IFA).

LDT: acronym for Laboratory Developed Test.

Leahy-Smith America Invents Act: a US federal statute that represented a significant shift in the US Patent system from the previous first-to-invent system to a first-inventor-to-file (FITF) regime, effective for all Patent applications with effective filing dates on or after March 13, 2013. The Act also expanded prior art to include foreign offers and sale and public uses, among other notable changes.

Legal Privilege: legal protection against compelled disclosure afforded to communications between attorneys and their clients (Attorney-Client Privilege), or afforded to documents and communications undertaken at the direction of an attorney and in anticipation of litigation (Work Product Privilege). The Attorney-Client Privilege is held by the client, not the lawyer, and the lawyer has a legal duty to keep such information confidential. Whether the attorney or client holds the Work Product Privilege varies by jurisdiction, but the majority of federal jurisdictions recognize that the client holds this privilege as well.

Leukemia: an acute or chronic disease of unknown cause that involves a progressive, malignant Neoplasm of the blood-forming organs, and is characterized by an abnormal increase in the number of white blood Cells in tissues of the body, with or without a corresponding increase of those in the circulating blood. Leukemia is classified clinically in several ways, most commonly by the predominant proliferating Cells, such as myelocytic, granulocytic or lymphocytic.

Leukocytes: white blood Cells that help the body fight infections and other diseases.

License: an agreement that grants to a party certain rights to practice under Intellectual Property rights. A License can be exclusive (which means the Licensee receives the sole right to practice the Inventions Covered by the License, even as to the Licensor) or non-exclusive (which means that the Licensee can grant similar rights to other third parties and reserves for itself the same rights it has granted to the Licensee).

License Fee: the fee to be paid by the Licensee in consideration for the grant of a License by the Licensor. The fee can be a one-time lump sum or a recurring payment.

Licensed Know-How: the Know-How that is licensed to the Licensee by the Licensor pursuant to a License.

Licensed Patents: the Patents and patent applications that are licensed to a Licensee by the Licensor pursuant to a License.

Licensed Product: a product that is the subject of a Licensee.

Licensee: the recipient of a License.

Licensor: the grantor of a License.

Ligand: a Molecule that binds to another. Typically a ligand is binding to and modulating a receptor Molecule.

Lipid: any of a large group of organic compounds such as fats and fatlike substances, including fatty acids, neutral fats, waxes and steroids, which are not soluble in water, but are soluble in fat solvents such as alcohol. Lipids are stored in the body as energy reserves and are also important components of Cell membranes.

List of Excluded Individuals and Entities (LEIE) Database: a list the OIG maintains of all individuals and entities currently excluded from participation in federally funded healthcare programs. Excluded individuals must apply to the OIG for reinstatement and receive notice that reinstatement has been granted to be removed from the LEIE and permitted to participate in federally funded healthcare programs. Anyone who hires an individual or entity on the LEIE may be subject to civil monetary penalties (CMP).

Local Coverage Determination (LCD): a Coverage determination by a Medicare Administrative Contractor (MAC) regarding whether a particular service or item is reasonable and necessary under Medicare within such MAC's geographical jurisdiction. MACs publish LCDs to provide guidance to the public and medical community within the MAC's jurisdictions on the terms and conditions of Coverage for services and items. Contractors develop LCDs by considering medical literature, the advice of local medical societies and medical consultants, public comments, and comments from the provider community.

Lock Ups: a window of time during which investors are not allowed to redeem or sell shares of a company.

Lymphoma: a type of cancer that develops as a tumor of the lymphoid tissue. The major types of lymphoma include Hodgkin's Lymphoma and Non-Hodgkin's Lymphoma.

Magnetic Resonance Imaging (MRI): a non-invasive diagnostic technique that uses magnetic fields and radio waves to produce a detailed image of the body's soft issues and bones that cannot be seen with other radiologic techniques. The MRI image gives information about the chemical makeup of tissues, thus making possible the distinction between normal, cancerous, atherosclerotic and traumatized tissue masses in the image.

Major Histocompatibility Complex (MHC): series of Genes that code for Proteins on Cell surfaces. MHC Molecules bind to Peptide fragments on foreign pathogens, signaling to the T-Cells in the body's immune system to destroy foreign pathogens.

Malignant: tending to become progressively worse and to result in death, often having the properties of anaplasia, invasiveness and metastasis. In oncology, this term is used to describe tumors that are cancerous, meaning that they have the ability to multiply uncontrollably and to spread to other parts of the body. In contrast, a Benign tumor is a growth of abnormal Cells confined to one area of the body.

Management Services Organization (MSO): a for-profit or non-profit corporation, general or limited partnership, or limited liability company providing a variety of services for or on behalf of one or more medical practices (or other healthcare entities such as a hospital). Generally, the services include a broad range of management, financial and administrative services, often the entire administrative requirements or "back office" of a healthcare Provider. In many cases, the MSO acquires the tangible assets of the medical practices and leases them back to the practice as part of a management services fee. The MSO may also perform services such as marketing (where permitted under state law), contract procurement and administration, and purchase of capital assets. MSOs are often established by hospitals or by hospitals in conjunction with physicians, to assist in the consolidation of medical

practices and the business development of the resulting group practice. An MSO created by a hospital and physicians is not an integrated organization, as no merger or consolidation directly occurs between the hospital and medical practice.

Manufacturer: the natural or legal person with responsibility for the design, manufacture, packaging and Labeling of a Device before it is placed on the market under the natural or legal person's own name, regardless of whether these operations are carried out by that person or by a third party of behalf of that person (Art. 1 para. 2 lit. f) Directive 93/42/EEC).

March-in Rights: rights retained by the federal government under the Bayh-Dole Act under any Inventions developed using federal funding. March-in Rights allow the federal government to have Licenses to such Inventions and related Intellectual Property rights on behalf of the federal government or to grant Licenses to such Inventions and Intellectual Property rights to other third parties without the permission of the Licensor in limited situations (*e.g.* a threat to public safety the Licensee is not equipped to handle). In practice, federal March-in Rights have rarely been exercised.

Marketing Authorisation Application (MAA): the application submitted to (an) EU Member State(s) for a Decentralized or Mutual Recognition Procedure or to EMA for the Centralized Procedure seeking permission to place a new medicinal product on the market. The equivalent in the US is called a New Drug Application.

Markman: a pretrial hearing conducted by the district court for the purposes of Claim Construction. The district court hears evidence and arguments about how to interpret key claim language. Also referred to as a Claim Construction hearing.

Mass Spectrometry (MS): a method to identify and quantify Molecules in simple and complex mixtures by measuring their mass-to-charge ratio. The Mass Spectrometer ionizes individual Molecules so they can be manipulated by external magnetic fields, accelerates the ionized Molecules and then measures the distance the ionized Molecules travel after being deflected by a magnetic field. This distance is used to determine the Molecule's mass-to-charge ratio. The Data output is in the form of a bar graph or "stick diagram" showing the relative abundance of each Molecule in the mixture.

Master Batch Record / Batch Record: written instructions for the conduct of a specific manufacturing process, documentation of which the FDA requires for the manufacture of a Therapeutic.

Master Cell Bank: a storage facility for frozen tissue samples or Cell Lines held for research purposes and for surgical reconstruction of damaged body structures.

Maximum Tolerated Dose (MTD): the largest dose of a remedy that can be accepted without the production of injurious symptoms. Characterized by a dose that produces grade 3 (severe) or grade 4 (life-threatening) toxicity in 30% or fewer of the patients tested. The maximum tolerated dose is determined in Clinical Trials by testing increasing doses on different groups of people until the highest dose with acceptable side effects is found.

Mayo: in *Mayo Collaborative Services v. Prometheus Labs.*, Inc., 566 U.S. ___, 132 S. Ct. 1289 (2012), the Supreme Court held unpatentable claims applying natural laws in the context of determining whether a drug dose would be harmful or ineffective by looking at blood metabolite concentrations. Natural laws themselves are unpatentable, and the Court announced that, to be patentable, a process focused on the use of such a law must include other elements or "an inventive concept."

Means-Plus-Function: Patent claims may include terms that are expressed as a means for performing some function. When a patentee uses this Means-Plus-Function format, the term is construed to Cover the structure — as described in the Patent specification — that corresponds to that function. 35 U.S.C. § 112(f).

Mechanism of Action: the means by which a Drug exerts its effect on Cells or tissues, or the means by which a therapeutic agent acts. Examples of Mechanisms of Action include the blocking of receptors, Enzymes, stimulating hormone production, etc.

Medicaid: a federal health insurance program authorized by Title XIX of the Social Security Act that is jointly funded by the federal and respective state governments, and administered by the state. The program provides health insurance and other services to persons of all ages whose income and resources meet means-tested eligibility criteria determined by each state and approved by CMS. Recipients of Medicaid must be US citizens or permanent residents. The scope of Coverage provided by the various state Medicaid programs must meet certain minimum criteria established in federal law and regulations; however, payment methodologies and other administrative aspects of the Medicaid program are left to the respective state. The ACA significantly expanded both eligibility for and federal funding of Medicaid.

Medicaid Drug Rebate Program: a program that requires participating drug Manufacturers to pay Rebates to state Medicaid agencies to partially offset federal and state costs of outpatient Prescription Drugs dispensed to Medicaid patients. The program requires a drug Manufacturer to enter into, and have in effect, a national Rebate agreement with the Secretary of the Department of Health and Human Services (HHS) in exchange for state Medicaid Coverage of the Manufacturer's Drugs. Manufacturers are required to report to CMS certain prices for all covered outpatient Drugs identified under the

Manufacturers' labeler codes and to pay a Rebate to state Medicaid agencies on those Drugs for which payment was made under the state Medicaid plan. The amount of the Rebate due for each unit of Drug is based on statutory formulas for different types of Drugs.

Medical Device: any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its Manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the Manufacturer to be used for human beings for any of the following purposes:

- Diagnosis, prevention, monitoring, treatment or alleviation of disease
- Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap
- Investigation, replacement or modification of the anatomy or of a physiological process
- Control of conception

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means (Art. 1 para. 2 lit. a) Directive 93/42/EEC).

Medical Necessity: the requirement that healthcare services must be in accordance with generally accepted standards of medical practice, clinically appropriate, and not for an economic or other benefit of the healthcare Provider. The Medicare program will not cover services that are not medically necessary to diagnose, treat or improve a patient's condition.

Medicare: a federal healthcare insurance program authorized by Title XVIII of the Social Security Act for all persons age 65 years or older who have been legal residents of the United States for at least five years, as well as younger people with disabilities, end-stage renal disease and amyotrophic lateral sclerosis (also known as Lou Gehrig's disease). Medicare is administered by CMS through contracts with private insurance companies, known as Medicare Administrative Contractors (MACs), to operate as claims process and payment intermediaries between CMS and medical Providers and Suppliers. Medicare is comprised of four Parts:

- Part A (generally, inpatient hospital, home health, skilled nursing and hospice insurance)
- Part B (generally, medical and outpatient care insurance)
- Part C (Medicare Advantage plans — optional capitated health insurance plans)
- Part D (Prescription drug insurance)

Medicare Access and Chip Reauthorization Act Of 2015 (MACRA): signed into law in April 2015, MACRA repealed the Sustainable Growth Rate methodology for determining updates to the Medicare Physician Fee Schedule and established annual positive or flat fee updates for 10 years. MACRA also established a Merit-Based Incentive Payment System that consolidates existing Medicare Fee-For-Service physician incentive programs and created a pathway for physicians to participate in alternative payment models. MACRA also extended the CHIP for two years.

Medicare Administrative Contractor (MAC): a private healthcare insurer that has been awarded a geographic jurisdiction to process Medicare Part A and Part B claims or Durable Medical Equipment (DME) claims for Medicare Fee-For-Service Beneficiaries. CMS relies on a network of MACs to serve as the primary operational contact between the Medicare FFS program and the healthcare Providers enrolled in the program.

Medicare Part A: also known as hospital insurance, a part of the Medicare program that pays for certain inpatient hospital, skilled nursing facility, hospice and home health services for eligible individuals.

Medicare Part B: also known as medical insurance, a part of the Medicare program that reimburses certain healthcare items and services that are not covered under Part A , such as certain physician services, outpatient services, DMEPOS, ambulatory surgery services, certain home health services and certain diagnostic tests.

Medicare Part C (Medicare Advantage): also known as Medicare Advantage, and formerly known as Medicare+Choice, a type of Medicare health plan offered by a private insurance company, such as an HMO, PPO, private Fee-For-Service plan, special needs plan, or Medicare Savings Account Plan, that contracts with CMS to provide enrolled beneficiaries with all Medicare Part A and Part B benefits. Many Medicare Part C plans offer some form of prescription drug benefit.

Medicare Part D: an optional Prescription Drug benefit program created through the U.S. Medicare Prescription Drug, Improvement and Modernization Act of 2003, designed to subsidize the costs of Prescription Drugs and Prescription Drug premiums for Medicare Beneficiaries. Medicare Part D gives Medicare recipients four basic choices: stay in traditional Medicare without signing up for the Prescription Drug benefit outlined in the Act, stay in traditional Medicare and enroll in a Medicare Drug plan, enroll in other Medicare plans, or enroll in a comprehensive private health plan (which may or may not cover Prescription costs).

Medicare Payment Advisory Commission (MedPAC): an independent congressional agency that advises the U.S. Congress on issues affecting the Medicare program. MedPAC advises Congress on payments to Providers and Suppliers in Medicare's traditional Fee-For-Service program and private health plans participating in Medicare through

Part C or Part D. MedPAC also analyzes access to care, quality of care and other issues affecting Medicare. MedPAC meets publicly to discuss policy issues and formulate its recommendations to Congress.

Medicare Physician Fee Schedule: a schedule of Medicare payment rates for individual physician services, including office visits, surgical procedures, Anesthesia services, and a range of other diagnostic and therapeutic services. The schedule sets payment rates for physician services provided in offices, hospitals, ambulatory surgical centers, skilled nursing facilities and other post-acute care settings. Payment rates are assigned to each CPT Code and are based on relative value units, a conversion factor and geographic practice cost indices.

Medicare Shared Savings Program: a program that facilitates coordination and cooperation among Providers to improve the quality of care for Medicare Fee-For-Service (FFS) beneficiaries and reduce unnecessary costs by requiring coordinated care for all services provided under Medicare FFS and encouraging investment in infrastructure and redesigned care processes. Eligible Providers, hospitals, and Suppliers may participate in the Medicare Shared Savings Program by creating or participating in an Accountable Care Organization (ACO). The Medicare Shared Savings Program rewards ACOs that lower their respective growth in healthcare costs while meeting Performance Standards on quality of care.

Medicines and Healthcare Products Regulatory Agency (MHRA): the Medicines and Healthcare Products Regulatory Agency regulates medicines, Medical Devices and blood components for transfusion in the UK. MHRA is an executive agency, sponsored by the Department of Health. The agency ensures that medicines, Medical Devices and blood components for transfusion meet applicable standards of safety, quality and efficacy; and assesses and grants authorizations for marketing of medicinal products in the UK.

Medizinisches Versorgungs-zentrum (MVZ) (Medical Care Center) (Germany): an association of different medical specialists in one place. An MVZ is used to create synergies in ambulant treatment based on the proximity of multiple specialists; legal requirements, *e.g.* with regard to limited group of possible shareholders, regulated in German Social Book (Book V, Para 95 and Para 140 b).

MedTech Code: MedTech Europe is an alliance of EDMA and Eucomed. On 2 December 2015, Members of Eucomed and EDMA have adopted a new common MedTech Europe Code of Ethical Business Practice which will become binding to the members of EDMA and Eucomed on January 1, 2017. This code will replace the Codes of Ethical Business Practice issued by EDMA and Eucomed and set the minimum standard across the EEA.

Melanoma: the most serious type of skin cancer, a Benign or Malignant tumor arising from the melanocytic system of the skin (the Cells that produce melanin) and other organs.

Mesothelioma: a type of cancer that causes Malignant cancer Cells to form within the thin layer of tissue that covers the majority of a person's internal organs, such as the lining around the chest, abdomen or heart. Its primary cause is believed to be exposure to asbestos.

Messenger RNA (mRNA): an RNA produced by Transcription that carries the code for a particular Protein from the nuclear DNA to a ribosome in the cytoplasm and acts as a template for the formation of that Protein.

Metastasize: the process by which cancer spreads from the place at which it arose as a primary tumor to distant locations in the body. The transfer of disease from one organ to another not directly connected with it.

Methylation of DNA: an epigenetic mechanism Cells use to inactivate Genes by adding a methyl group to the DNA, which inhibits Transcription.

Micro-RNAs: Micro-RNAs, or miRNAs, are small segments of RNA (~22 Nucleotides) that are involved in regulation of Gene Expression.

Microbiome: a term referring to all of the different micro-organisms co-habitating in a human's gastrointestinal tract. It is thought that people have a symbiotic relationship with one pound of micro-organisms, which can influence everything from disease to obesity, immunity to personality. Characterization and manipulation of individual Microbiomes is a hot area of research.

Milestone: in the context of life sciences Licenses and Collaboration Agreements, a future event that generally triggers an obligation of one party to pay the other party for the achievement of that event or is required to be achieved by a party to comply with Diligence objectives. Generally, Milestones can be conceptualized into two categories: (1) research/Development/regulatory Milestones, such as filing an IND, completing a certain phase of a clinical study, or Regulatory Approval of a Drug; and (2) sales Milestones, such as Milestones payable on achievement of aggregate Net Sales of certain amounts in any given time period. Milestones are similar to the concept of an earnout in mergers and acquisitions.

Milestone Payment: a financial payment paid during the course of a Drug's Development after a company achieves defined goals or Milestones, such as in Phase 2 or Phase 3 trials, or meeting certain sales goals.

Ministry of Food and Drug Safety (MFDS): formerly known as the KFDA, is the South Korean equivalent to the US FDA.

Misbranded Product: an FDA-regulated product with Product Labeling that is false or misleading in any particular, that lacks required information or that otherwise fails to conform with FDA requirements.

Mitochondria: any of various round or long cellular organelles found in a Cell's cytoplasm that are responsible for energy production through cellular respiration. Mitochondria are rich in fats, Proteins and Enzymes, and not only convert nutrients into energy but also perform many other specialized tasks.

MolDx: abbreviation for Molecular Diagnostic Services.

Molecular Diagnostic Services (MolDx) Program: a program designed and operated by a Medicare Administrative Contractor (MAC) to identify and establish Coverage on existing tests, newly developed Laboratory Developed Tests (LDTs), tests using Pathology not otherwise classified (NOC) codes, and other Molecular Diagnostic Tests that fall within the scope of the Molecular Diagnostic Test Local Coverage Determination (LCD).

Molecular Diagnostics / Molecular Diagnostic Tests: a broad term describing a class of Diagnostic tests that assess a person's health at a molecular level, using techniques designed to analyze biological markers in the Genome and Proteome by applying molecular biology to medical testing. Molecular Diagnostic Tests detect specific sequences in DNA or RNA that may or may not be associated with disease.

Molecule: a group of atoms joined by chemical bonds. The smallest possible quantity of a substance that retains the chemical properties of the substance.

Monoclonal: produced by, being or composed of Cells derived from a single Cell or Cells identical to that Cell.

Monoclonal Antibody: an Antibody produced by a single Clone of Cells. A Monoclonal Antibody is made in a laboratory for the purposes of binding to a specific substance in the body, such as cancer Cells.

Monogenic Disease: a genetic disorder or disease that is the result of a single defective Gene occurring in all Cells of the body.

Most Favored Nation (MFN) Provision: an agreement between a buyer and a seller that guarantees the buyer the lowest price for a product or service during the contract period. In healthcare, MFNs typically manifest as a provision within a health network plan contract in which a dominant health plan obtains a promise that the Provider (Supplier of healthcare services) will not give an equal or more favorable price to any other plan. MFNs have received close scrutiny lately as federal and state payors seeks to reduce healthcare costs.

mRNA: abbreviation for Messenger RNA.

Mutation: a permanent transmissible change or structural alteration in the DNA (for humans and many other organisms) or RNA (for retroviruses).

Multiple Ascending Dose (MAD): refers to an approach in phase 1 of Clinical Trials. Multiple Ascending Dose studies investigate the pharmacokinetic and pharmacodynamic properties of multiple doses of a target experimental Drug, with the goal of determining its safety and tolerability. The experimenter gives subjects multiple doses of the Drug, starting at the lowest possible dose, working up to a predetermined

dosage level. Throughout the study, the experimenter collects Data and blood and fluid samples from the subjects to analyze how the Drug is processed by the human body. See Single Ascending Dose (SAD).

Multiple Myeloma: a type of cancer that develops in the bone marrow and forms in a type of white blood Cell called a plasma Cell. In Multiple Myeloma, normal plasma Cells transform into Malignant myeloma Cells and produce large quantities of an abnormal immunoglobulin called Monoclonal Protein, which interferes with normal blood Cell production. Multiple Myeloma is the most common type of plasma Cell Neoplasm.

Mutual Recognition Procedure: used by a Manufacturer who already received a national marketing authorisation (MA) from at least one Member State and is seeking to extend this MA to one or more additional Member States. The applicant choses one Member State in which it already received the MA as its Reference Member State. The Member States where the product would be marketed if approved are called the Concerned Member States.

Myocardial Infarction (MI): the medical term for a heart attack. The death of the Cells of an area of the heart muscle as a result of oxygen deprivation, which in turn is caused by obstruction of the blood supply. Heart attacks most commonly occur when one or more of the coronary arteries become blocked.

Myriad: in Association for *Molecular Pathology v. Myriad Genetics, Inc.*, 596 U.S. ___, 133 S. Ct. 2107 (2013), the Supreme Court announced that naturally occurring Gene sequences are not Patent eligible.

Nanotechnology: generically refers to synthetic materials that operate on the 1-100 nanometer scale (75,000 times smaller than a human hair). From small fluidic chambers, to sensors, to biochemical switches, to labels, nanotechnology is an active area of therapeutic research.

National Agency for Medicine and Health Products Safety or Agence Nationale de Sécurité de Médicament et des Produits de Santé (ANSM): formerly, the French Agency for the Safety of Health Products (Agence française de sécurité sanitaire des produits de santé or AFSSAPS), the ANSM is the French Drug and Medical Device agency. Among other things, the ANSM's responsibilities include: assessing and granting of French marketing authorisations of medicinal products; monitoring adverse effects of Drugs and Medical Devices; approving Clinical Trials; and monitoring and controlling Medical Devices and Drugs commercialized and used in France to ensure the Drug or Device complies with applicable laws and regulations.

National Cancer Institute (NCI): part of the National Institutes of Health (NIH), which is one of 11 agencies that compose the Department of Health and Human Services. The National Cancer Institute was established in 1937 as the principle agency for cancer research and training.

National Coverage Determination(NCD): a Coverage policy established by CMS setting forth the extent to which Medicare will cover specific services, procedures, or technologies on a national basis. NCDs are published in the Medicare National Coverage Determinations Manual. Medicare contractors are required to follow NCDs. If an NCD does not specifically exclude/limit an Indication or circumstance, or if the item or service is not mentioned at all in an NCD or in a Medicare manual, the Medicare contractor makes the Coverage decision. An NCD becomes effective as of the date listed in the transmittal that announces the manual revision.

National Health Surveillance Agency of Brazil (ANVISA): the Brazilian equivalent to the US FDA.

National Institutes of Health (NIH): the principal federal agency for health research in the United States, which is one of the 11 agencies that compose the Department of Health and Human Services.

National Provider Identifier: a unique identification number issued to healthcare Providers in the United States by CMS. The National Provider Identifier is a 10-position numeric identifier, and must be used in HIPAA standard transactions.

Needs Assessment: a typically internal evaluation of an entity's bona fide, commercially reasonable need or business justification for entering into or continuing an arrangement with a physician or other healthcare Provider or Supplier, such as a consulting arrangement. A Needs Assessment is intended to ensure the entity engages only in financial transactions with healthcare Providers and Suppliers that fulfill the entity's bona fide medical, clinical, training, education, and research and Development needs in compliance with healthcare fraud and abuse laws.

Neoantigens: an Antigen that is present in a tumor Cell.

Neoplasm: any new and abnormal growth, specifically one in which Cell multiplication is uncontrolled and progressive beyond normal growth. Neoplasms may be Benign or Malignant.

Net Sales: a defined term found in many License agreements that will generally be defined as the gross revenues from sales of Licensed Products minus certain deductions. Often used to define Royalty and Milestone Payments.

Neuroblastoma: a type of cancer that usually originates either in the tissues of the adrenal gland or in the ganglia of the abdomen or nervous system. Tumors develop in the nerve tissue in the neck, chest, abdomen or pelvis and most commonly affect children age five or younger.

Neurology: the branch of medicine concerned with the diagnosis and treatment of disorders of the nervous system, which includes the brain, the spinal cord and the nerves.

Neuropathy: a term used to describe an abnormal and usually degenerative state of the nervous system or nerves, usually the peripheral nerves. Neuropathy is seen underlying a number of different medical conditions.

Neuroscience: the branch of science that deals with the anatomy, physiology, biochemistry or molecular biology of nerves and nervous tissue and their relation to behavior and learning.

New Chemical Entity (NCE) Exclusivity: a new chemical entity (NCE) is a Drug that contains no Active Moiety that has been approved by the FDA in a New Drug Application. An NCE is eligible for five years of Exclusivity from the date of approval during which time no ANDA or 505(b)(2) application that references the NCE may be submitted, except that ANDAs and 505(b)(2) applications may be submitted after four years with a Paragraph IV notification.

New Drug Application (NDA): an application submitted to the FDA for approval to market a new Drug. An NDA generally must contain information regarding nonclinical Pharmacology and Toxicology, Pharmacokinetics and bioavailability, Chemistry, Manufacturing and Controls, clinical Data and proposed Labeling, among other information. The FDA will approve an NDA if it determines that the Drug meets the statutory standards for safety and effectiveness, Chemistry, Manufacturing and Controls, and Labeling.

New Molecular Entity (NME): The FDA classifies certain Drugs and Biological Products (Biologics) as New Molecular Entities (NMEs) for purposes of FDA review. These products may contain Active Moieties that have not previously been approved by the FDA, either as a single ingredient Drug or as part of a Combination Product, or may be characterized as NMEs for administrative purposes but nonetheless contain Active Moieties that are closely related to Active Moieties in previously approved products, such as Biological Products submitted under a Biologics License Application even when the FDA has previously approved a related Active Moiety in a different product. The FDA's classification of a product as a NME for review purposes is distinct from the FDA's determination of whether a product is a new chemical entity within the meaning of the Federal Food, Drug, and Cosmetic Act.

New Technology APC: a designation under the Medicare Hospital Outpatient Prospective Payment for comprehensive services or procedures that CMS has determined cannot: (1) be appropriately reported by an existing HCPCS Code assigned to a clinical APC, or (2) be appropriately reported by a new HCPCS Code that could be appropriately assigned to a clinical APC. Neither assignment of an HCPCS Code nor approval of a service for assignment to a New Technology APC assures Coverage of the specific item or service in a given case. To receive payment, a new technology service must be considered reasonable and necessary; and each use of a new technology service is subject to medical review for determination of whether its use was reasonable and necessary.

NIH: acronym for National Institutes of Health.

Non-Clinical: in respect to a study, an experiment in which experiments on a test article, such as a Drug, Biological Product (Biologic) or Medical Device, are performed under lab conditions and not on human subjects. See Preclinical Studies.

Non-Compete: a provision in an employment agreement or offer letter that prevents an employee from working for a competitor of the employer. A Non-Compete may not be enforceable under certain circumstances.

Non-Disclosure Agreement: not to be confused with the other NDA (New Drug Application), Non-Disclosure Agreements are contracts designed to protect Confidential Information, like Trade Secrets, of one or more parties. Also known as Confidentiality Agreements or Confidential Disclosure Agreements, Non-Disclosure Agreements can be unilateral, bi-lateral or multi-lateral.

Non-Hodgkin's Lymphoma: a type of cancer that develops in the lymph system. A malignancy of a family of white blood Cells known as lymphocytes. Non-Hodgkin's Lymphoma is one of two common types of cancers of the lymphatic system. The two most common types of cancers of the lymphatic system are Hodgkin's Lymphoma and Non-Hodgkin's Lymphoma. Non-Hodgkin's lymphoma are more common than Hodgkin's Lymphoma. There are a variety of Non-Hodgkin's Lymphomas, which vary significantly in terms of aggressiveness of growth and patient survivability. Chemotherapy is a common method of treatment for Non-Hodgkin's Lymphoma.

Non-Small Cell Lung Cancer (NSCLC): a group of lung cancers that are named for the type of Cells found in the cancer and how the Cells look under a microscope. NSCLC may arise anywhere in the tissue that lines the air passages in the lung. The three main types of Non-Small Cell Lung Cancer are squamous cell carcinoma, large cell carcinoma and adenocarcinoma. Non-Small Cell Lung Cancer is the most common kind of lung cancer.

Notice of Commercial Marketing: the notice that a Biosimilar Product Applicant provides to a Reference Product Sponsor before the date of the applicant's first commercial marketing. This notice can only be provided after the FDA has licensed the biosimilar Drug and it must be provided at least 180 days before the date of the first commercial marketing. Reference 42 U.S.C. 262 (l) (8).

Notified Bodies: as defined by the European Commission, an organisation designated by an EU country to assess the conformity of Medical Devices before being placed on the market. The European Commission publishes a list of the certified Notified Bodies.

Novelty: the legal requirement that a patented Invention be new. An Invention cannot be patented if the claimed Invention was already patented, described in a Printed publication, or in public use (prior use), on sale (prior sale) or otherwise available to the public before the effective

filing date of the claimed Invention. If an Invention was available to the public before the filing date, then it is considered anticipated by the prior art. Reference 35 U.S.C. § 102. See Anticipation.

Nucleotides: there are four naturally occurring nucleotides that encode our DNA; adenine, guanine, cytosine and thymine. The order in which they are bound together is referred to as the genetic sequence and is unique for each individual. Current research aims to create unnatural Nucleotides that can incorporate into DNA sequences for research and possibly therapeutic use.

Nutraceuticals: a combination of the terms nutrition and Pharmaceutical, Nutraceuticals are broadly defined as a dietary supplement or any food product claiming to confer beneficial health or medicinal effects.

Obstetrics: the branch of medicine that deals with childbirth and the care of women before, during and after childbirth.

Obviousness: a Patent for a claimed Invention may not issue, even if the claimed Invention is not identical to prior art, if the differences between the claimed Invention and the prior art are such that the claimed Invention as a whole would have been Obvious before the effective Filing Date of the claimed Invention to a person having ordinary skill in the art to which the claimed Invention pertains. A court considers the Graham Factors when determining whether an Invention is Obvious. Reference 35 U.S.C. § 103.

Off-Label Promotion: any promotional communication by a drug or device Manufacturer regarding uses of the product that have not received FDA approval or clearance. The introduction of a Drug or Device into interstate commerce for an intended use that is not approved or cleared. While neither the FDCA nor FDA regulations prohibit Off-Label Promotion per se, the FDA has traditionally interpreted the adulteration and misbranding provisions as categorically banning Off-Label Promotion, with certain limited safe harbors. The FDA's ban of Off-Label Promotion has come under First Amendment challenge when applied to truthful and non-misleading communications.

Office of the Inspector General (OIG) of HHS: an agency of the U.S. Department of Health and Human Services (HHS), whose mission is to protect the integrity of HHS's programs, such as the Medicare and Medicaid programs, as well as the well-being of the Beneficiaries of those programs. OIG has jurisdiction over a variety of statutes, including Medicare and Medicaid fraud and abuse laws. The agency consists of six components, including:

- Office of Investigations, which conducts criminal, civil and administrative investigations associated with HHS programs and program Beneficiaries
- Office of Audit Services, which audits the performance of HHS programs, grantees and contractors (including healthcare Providers and Suppliers)

- Office of Evaluation and Inspections, which conducts management and program evaluations focused on areas for improvement and issues of concern to HHS, the Congress and the public
- Office of Counsel to the Inspector General, which represents the OIG in all civil and administrative fraud cases, negotiates and monitors Corporate Integrity Agreements (CIAs), and provides guidance to the healthcare industry to promote compliance with applicable laws and regulations
- Office of Management and Policy, which provides mission-support to the OIG

OIG: acronym for Office of the Inspector General.

Oligonucleotide: Polymers made up of a short sequence of Nucleotides that readily bind, in sequence, to complementary Oligonucleotides in DNA or RNA. Oligonucleotides can be lab-synthesized in specified sequences for applications in genetic testing, research and forensics. Oligonucleotides are frequently used for artificial Gene Synthesis, DNA and RNA detection, DNA sequencing, library construction and Polymerase Chain Reaction (PCR).

Oligonucleotides: also called oligos, are usually ~15-30 nucleotide synthetic chains of nucleic acid produced to modulate Gene Expression or for research applications. Oligonucleotides are usually made using multistep chemical reactions.

Oncology: the branch of medicine that deals with the diagnosis and treatment of cancer. Subdivisions of oncology include medical, radiation and surgical oncology, which cover different methods for studying and treating cancer.

Opposition (Patent): an administrative process that allows third parties to challenge the validity of a pending Patent application, an issued Patent, or a Trademark.

Opthalmology: the branch of medicine that deals with the study of the anatomy, function and diseases of the eye. Opthalmologists are specialist medical physicians who specialize in the medical and surgical care of the eyes.

Optogenetics: a technique whereby light is used to activate light-sensitive Molecules in living tissue, and the technique is typically used to study the functions of specific Proteins. Science magazine described this technology as a breakthrough of the decade.

Orange Book Listing: all Drug products approved by the FDA on the basis of safety and effectiveness and that have not been withdrawn for safety or effectiveness reasons, including both innovator and Generic Drug Products, are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, also known as the Orange Book.

Orange Book listings include therapeutic equivalence evaluations for approved multisource Prescription Drug products as well as Patent and Exclusivity information as applicable to each product.

Org Meeting / Organizational Meeting: in a securities offering, the initial meeting among the Issuer, the investment banks that are serving as underwriters or initial purchasers, the auditors and the lawyers. This is where the agenda for the deal is set and the initial due diligence with management is performed. Generally considered the beginning of the quiet period in public offerings.

Orphan Designation: in the United States, pursuant to the Orphan Drug Act, the sponsor of a Drug or Biological Product (Biologic) intended for an Orphan Disease may request that the FDA designate the Drug or Biological Product as a product for a Rare Disease or condition, referred to as Orphan Designation. Orphan Designation qualifies the sponsor of the Drug for various Development incentives, including tax credits for qualified clinical testing and potential Orphan Exclusivity.

EU: To qualify for Orphan Designation in the EU, a medicine must meet a number of criteria:

- The Drug must be intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating.
- The prevalence of the condition in the EU must not be more than five in 10,000 or it must be unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its Development.
- No satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorised, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

Orphan Disease: in the United States, the FDA defines an Orphan Disease as a Rare Disease or condition that "affects less than 200,000 persons in the United States, or affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug."

Orphan Drug / Orphan Medicinal Product: a drug that is under Development for (or has been approved for) an Orphan Disease. See Orphan Designation.

Orphan Exclusivity: in the United States, if a product that has Orphan Designation receives the first FDA approval for the disease for which it has such designation, the product is entitled to Orphan Exclusivity under the FDCA pursuant to which the FDA may not approve any other applications to market the same Drug for the same Indication for seven years, except in limited circumstances such as a showing of clinical superiority to the product with Orphan Drug Exclusivity or where the Manufacturer is unable to assure sufficient product quantity.

Orthopedics: the branch of medicine that deals with preventing and correcting deformities or impairments of the skeletal system and associated structures, such as tendons and ligaments.

Osteoarthritis (OA): the most common type of arthritis, Osteoarthritis is a joint disease that mostly affects cartilage, causing joint pain and reduced motion, usually in the hands, knees, hips and spine. Osteoarthritis generally occurs when protective cartilage covering bones wears down over time; most frequently occurring in older people and young people who have suffered joint injuries.

Out-of-Network: in the insurance context, Out-of-Network refers to Providers and Suppliers who do not have agreements with an insurance company to provide items and services to plan members. Although there are some exceptions, in many cases, insurance companies pay less or nothing at all for items or services provided by Out-of-Network Providers or Suppliers. Out-of-Network Providers and Suppliers may nonetheless, in certain circumstances, obtain higher total Reimbursement for rendered items and services, because after collecting any available Reimbursement from the insurer, the Provider or Supplier may be able to bill the patient for the remainder of any amount due, if permissible under state law. By contrast, in-network Providers typically accept a lower Reimbursement rate in exchange for the certainty of payment for services provided to the insurance company's plan members.

Overpayment: amounts that a person or entity receives or retains to which the person is not entitled. The ACA requires Medicare and Medicaid Providers, Suppliers, and other entities to report and return any overpayment of Medicare or Medicaid funds within 60 days of identifying the overpayment or face potential False Claims Act liability.

Paediatric Committee (PDCO): scientific committee within the EMA in charge of assessing the content of paediatric investigation plans (PIPs) and providing opinions on paediatric medicines.

Paediatric Investigation Plan (PIP): research and Development plan intended to determine whether a specific product could be authorised to treat a paediatric condition. All Marketing Authorisation Applications for new products must contain the result of the studies carried out in accordance with the PIP pre-agreed with the EMA. The result of the PIP, *i.e.* whether the medicine is suitable for a paediatric condition is irrelevant; what matters is the compliance with the pre-agreed PIP. Compliance with the PIP extends by six months the Supplementary Protection Certificate of a medicine authorised in all Member States and grants two additional years to the market Exclusivity of an orphan product.

Paragraph IV: under the Hatch-Waxman Act, when submitting its ANDA application, a Generic Drug Manufacturer must make a Certification to the FDA about whether or not its product will infringe a valid Patent covering the branded product. A Paragraph IV Certification is one in

which the applicant certifies that the Patent either is invalid or will not be infringed by the ANDA product. Paragraph IV refers to 21 U.S.C. § 355(j)(2)(A)(vii)(IV). A Paragraph IV Certification in an ANDA is considered an artificial act of patent Infringement; that is, once the generic company makes a Paragraph IV Certification, the patentee/branded drug company can sue the generic company for Infringement even though the generic company has not made, used, sold, or offered for sale an infringing Drug. Reference 35 U.S.C. § 271(e)(5).

Parallel Import Restrictions: restrictions on the buying of medicinal products in one country for resale in a different country, generally with the purpose of benefiting from price differentials. These restrictions can, under certain circumstances, be considered as unlawful restrictions of competition and trade between the Member States of the EU under EU law.

Pass-Through Payment Status / Transitional Pass-Through Payment Status: a temporary Medicare payment status for certain innovative Devices, Drugs and Biological Products (Biologics), under which CMS makes an additional payment to ensure the availability of such items to Medicare beneficiaries. Manufacturers must apply to CMS to obtain pass-through payment status for their products. Eligibility for a pass-through payment is limited to at least two years but no more than three years. CMS makes Transitional Pass-Through Payment for certain Drugs and Biologicals furnished as part of an outpatient hospital service, including Orphan Drugs, cancer therapy Drugs and Biologicals, and radiopharmaceutical Drugs and Biological Products.

Patent: a right or title conferred by a government authority for a set period, to exclude or prevent others from making, using or selling an Invention.

Patent Dance: refers to the exchange of Patent information under section (l) of the BPCIA 42 U.S.C. § 262(l). After a Reference Product Sponsor receives confidential access to a Biosimilar Product Applicant's application, the Reference Product Sponsor provides a list of Patents to the Biosimilar Product Applicant. That first list of Patents, referred to by its statutory section, is known as the 3(A) List. It contains the Patents the Reference Product Sponsors owns or exclusively Licenses which it believes could reasonably be asserted against the biosimilar applicant, were the Biosimilar Product Applicant to make, use, sell or offer to sell its Biosimilar Product. The next stage of the Patent Dance involves the Biosimilar Product Applicant providing a second list of additional Patents it believes could be asserted as well as a detailed statement about why Patents on the 3A List would be invalid, unenforceable or not infringed by marketing the Biosimilar Product. Further exchanges of information and negotiation determine what Patents should be subject to immediate patent infringement litigation. 42 U.S.C. § 262(l). See 3(B) List; 3(C) List; BPCIA Exchange; Good Faith Negotiations.

Patent Term Extension: refers to various mechanisms available under US patent law to extend the life of a Patent. Typically, extensions may be available for delays in Patent Prosecution at the patent office and delays in obtaining FDA approval for Patents Covering qualifying Drug products.

Patent Trial and Appeal Board (PTAB): a statutorily created administrative board within the PTO, which includes the Administrative Patent Judges that preside over all PTAB proceedings. The PTAB renders decisions on appeals from adverse examiner decisions involving patent applications, PTAB Proceedings and Interferences Proceedings. The PTAB replaced the Board of Patent Appeals and Interferences after the AIA passed in 2012. 35 U.S.C.§ 6(a).

Patentable Subject Matter: to be patentable, a claimed Invention must: (1) be directed to a process, machine, manufacture or Composition of Matter and (2) not be directed to laws of nature, physical phenomena, abstract ideas or another judicially recognized exception. 35 U.S.C. § 101. If only part of the Patent claim is directed to such subject matter, the Supreme Court has established a two part "Alice" test to determine whether the claim is patent eligible: (1) determine which part of the claim is directed to the unpatentable subject matter and (2) determine whether the claim's other elements "transform" the claims into a patent-eligible application.

Pathology: 1. the study of disease. 2. the anatomic and physiological deviations that constitute or characterize a particular disease.

Patient Assistance Programs (PAPs): programs, often operated by independent charitable organizations (*e.g.*, patient advocacy support organizations), intended to assist with patient cost-sharing obligations (*i.e.*, Copayments) associated with Drugs and medical visits, health insurance premiums and insurance Deductibles, genetic testing used in therapeutic management of a disease, and medical supplies and equipment. PAPs may be organized and funded through charitable contributions from Pharmaceutical Manufacturers or other Providers or Suppliers of healthcare items or services. OIG has raised concerns that such charitable contributions and PAP assistance to federal healthcare program beneficiaries may violate certain federal laws, including the AKS, the FCA, and the prohibition on providing Beneficiary Inducements.

Patient Registry: a system that uses observational study methods to collect standardized clinical or nonclinical Data to evaluate specified outcomes for a patient population that shares a particular condition, disease or exposure. Traditionally researcher-generated, patient registries are used for various purposes including learning about a particular disease, the Development of Therapeutics and the Development and study of best practices.

Paul-Ehrlich-Institut: the Paul-Ehrlich-Institut is the Federal Institute in Germany in charge of Vaccines and biomedicines. Its core missions are assessing and monitoring the benefit-risk balance through all the steps of the Marketing Authorisation process of biomedicines for human use and of immunological medicines for veterinary use.

Pay for Delay: patent settlement agreements (commercial agreements to settle patent-related disputes between originator and generic companies) that result in delayed market entry of generic medicine in exchange for benefits transferred from the originator to the generic company. The U.S. Supreme Court decided in *FTC v. Actavis* (2013) that a payment from an originator to a generic company to resolve patent-related disputes should be analysed considering the rule of reason test. The European Commission Directorate General for Competition has imposed several fines on pharmaceutical companies for delaying market entry of generic products. See Reverse Payment.

PCSK9: PCSK9 (acronym for proprotein convertase subtilisin/kexin type 9) is an Enzyme that prevents the low-density lipoprotein (LDL) cholesterol receptors from removing LDL cholesterol from the blood. PCSK9 thus makes a potentially useful target for inhibition by pharmaceutical compounds if the goal is to reduce circulating cholesterol in the patient.

PCR: acronym for Polymerase Chain Reaction.

PDCO: abbreviation for Paediatrics Committee.

Pediatrics: the branch of medicine that deals with the development and care of children and the treatment of diseases in children.

Peptide: a chain of two or more Amino Acid Molecules linked by covalent chemical bonds (a peptide bond). Proteins, also formed of chains of Amino Acids, are generally distinguished from peptides by being comparatively more complex and containing longer chains. Peptide Drug Development is considered promising but peptide manufacturing is currently time-intensive.

Performance Standards: a performance standard for a Device is a standard that includes provisions to provide reasonable assurance of the Device's safe and effective performance. According to the FDA, Performance Standards may include provisions regarding the "construction, components, ingredients and/or properties of the Device, the Device's compatibility with power systems, Device testing, measurement of Device performance characteristics and/or other provisions."

Periodic Safety Update Report (PSUR): US: Periodic safety update reports are Pharmacovigilance documents intended to provide a safety update resulting in an evaluation of the impact of the reports on the risk-benefit balance of a medicinal product. PSURs shall be submitted by Marketing Authorization holders at defined time points during the post-authorization phase.

EU: holders of Marketing Authorisations granted by the EMA must submit to the EMA PSURs at defined points in time following a medicine's authorisation. PSURs summarise Data on the benefits and risks of a medicine and include the results of all studies carried out with this medicine, both in its authorised uses and in unauthorised uses. The EMA uses the information in PSURs to determine if there are new risks identified for a medicine or whether the balance of benefits and

risks of a medicine has changed. The EMA can then decide if further investigations need to be carried out or it can take action to protect the public from the risks identified, such as updating the information provided for healthcare professionals and patients.

Peripheral Artery Disease: a disease in which plaque (commonly formed of calcium, cholesterol and calcium deposits) builds up and hardens in the arteries, narrowing the space for blood flow to the body's extremities, including the legs, arms and head. Peripheral Artery Disease can cause pain and numbness, and in more serious cases, can raise the risk of infection, gangrene, heart disease and stroke.

Person of Ordinary Skill / Person Having Ordinary Skill in the Art: a fictional person in patent law having normal skill and knowledge in the technology area of a given Patent. This hypothetical person serves as the reference for determining how a patent claim is defined (Claim Construction), whether a patent claim is obvious, and whether the patent specification is adequate to support the claims (Enablement and Written Description).

Personal Data: under the EU Data Protection Directive (95/46/EC) (the Directive) and the General Data Protection Regulation (the GDPR), Personal Data is any information relating to an identified or identifiable natural person (the data subject). An identifiable person is a person who can be identified, directly or indirectly, in particular by reference to an identification number or to one or more factors specific to the person's physical, physiological, mental, economic, cultural or social identity. Such factors can include name, address, telephone number, fax number, email address or other contact information, social security or insurance numbers, bank account number or credit card numbers, online identifiers such as IP addresses, cookie strings, mobile device IDs and location data.

Personal Data is often referred to as personally identifiable information, or PII, in the United States. The involvement of personal data or PII triggers the application of privacy laws, but in the US such laws are sectoralized, meaning that different laws apply to different types of personal data. For example, Protected Health Information (PHI) is one type of personal data, and PHI is governed by HIPAA. If Personal Data does not fall into a particular sector, then in the US the Federal Trade Commission (FTC) has jurisdiction to enforce privacy obligations under their authority to investigate unfair and deceptive trade practices.

Personalized Medicine: a practice of medicine focused on using information about a patient's unique profile, and in particular the patient's Genetics, to tailor medical diagnoses and treatments to better respond to individual patient needs. See Precision Medicine.

Pharmaceutical: see Drug and Biological Product (Biologic).

Pharmacodynamics (PD): the study of the effects and actions of Drugs on a living organism. Includes the study of how well Drugs bind to receptors at the site of introduction, the organism's reaction to the Drug and the duration and magnitude of the organism's response to the Drug.

Pharmacogenomics: a combination of the terms Pharmacology and Genomics, pharmacogenomics involves the study of how a person's Genetics affect their response to Drugs, with the goal of providing patients with access to effective medication in appropriate doses.

Pharmacokinetics (PK): the study of what happens to a Drug administered to a living organism. Includes the study of Drugs from the course of administration into the body, absorption and distribution through the body and excretion from the body.

Pharmacology: the study of the sources, properties, nature and uses of Drugs.

Pharmacovigilance: the monitoring and identification of Adverse Events to assess the safety of a Therapeutic.

Pharmacovigilance Risk Assessment Committee (PRAC): a committee of the EMA. The PRAC is in charge of monitoring and evaluating the risk management of human medicines.

Pharmaceutical Research and Manufacturers of America (PhRMA): a voluntary trade organization, established in 1958, representing primarily pharmaceutical, biopharmaceutical and biotechnology companies. PhRMA advocates on behalf of its global membership on public policies relevant to the discovery and Development of new medicines and treatments. The organization developed the Code on Interactions with healthcare Providers (known as the PhRMA Code) that serves as a guide for the industry participants on interactions with healthcare professionals.

Pharmacy & Therapeutics Committee (P&T Committee): committees typically composed of physicians, pharmacists, nurses and medical staff, who recommend to the administrations of the organizations that they serve which medications should be added to the formularies and where on the formularies the medications should be placed in relation to one another.

Pharmacy Benefit Manager (PBM): a third-party administrator of prescription drug benefits under the various insurance programs, such as Medicare Part D and numerous employer sponsored health plans, that is intended to maintain or reduce pharmacy expenditures while concurrently trying to improve healthcare outcomes. A PBM may provide services such as developing and maintaining prescription drug formularies, contracting with pharmacies, negotiating Discounts and Rebates with drug Manufacturers, and processing and paying prescription drug claims.

Phase I Clinical Trial: a trial in which a Drug or Biological Product (Biologic) is initially introduced into healthy human subjects or patients with the Target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, elimination and/or, if possible, to gain an early indication of the product's effectiveness. During Phase I, sufficient information about the Drug's Pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase II studies. The total number of subjects and patients included in Phase I studies varies with the Drug, but is generally in the range of 20 to 80. Phase I is sometimes sub-divided into Phase Ia and Ib, for example when the first set of Phase I studies (Phase Ia) is performed in healthy volunteers and a second set (Phase Ib) is performed in patients with the disease or condition under investigation.

Phase II Clinical Trial: a trial in which a Drug or Biological Product (Biologic) is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and/or to determine dosage tolerance and optimal dosage. Phase II Clinical Trials typically follow Phase I Clinical Trials, and typically involve no more than several hundred subjects. A Phase II Clinical Trial may be designated as a Phase IIa clinical trial or a Phase IIb clinical trial. Phase IIa clinical trials generally involve the first set of exposure response trials in patients, while Phase IIb clinical trials generally involve patient dose-ranging trials. In some cases, the FDA may approve a marketing application on the basis of Data from a Phase IIb Clinical Trial.

Phase III Clinical Trial: a trial in which a Drug or Biological Product (Biologic) is administered to an expanded patient population, usually from several hundred to several thousand subjects, generally at geographically dispersed Clinical Trial sites. According to the FDA, Phase III Clinical Trials "are performed after preliminary evidence suggesting effectiveness of the Drug has been obtained, and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the Drug and to provide an adequate basis for physician labeling."

Phase IV Clinical Trial: in some cases, the FDA may condition approval of a product candidate on the sponsor's agreement to conduct additional Clinical Trials after approval. In other cases, a sponsor may voluntarily conduct additional Clinical Trials post-approval to gain more information about the product. Such post-approval trials are typically referred to as Phase IV Clinical Trials.

Phenotype: a person's observable characteristics or traits, which result from the interactions between a person's Genes and their environment.

PHI: acronym for Protected Health Information.

Phillips Standard: the Claim Construction standard used in federal district court and established in *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-18 (Fed. Cir. 2005). Words of a claim are generally given their Ordinary and Customary Meaning as understood by a Person of Ordinary Skill in the art at the time of the Invention. In determining the ordinary meaning, the intrinsic evidence (claims, specification and file history) is of primary importance.

PhRMA: acronym for Pharmaceutical Research and Manufacturers of America.

PhRMA Code on Interactions with Health Care Professionals (PhRMA Code): a code of ethics promulgated by PhRMA to provide guidance to pharmaceutical, biopharmaceutical and biotechnology companies on ethical and legal interactions with healthcare professionals. The PhRMA Code supports the adoption of effective compliance programs and sets forth guidance on such interactions to foster transparency and compliance with applicable laws, regulations and government guidance issuances, for companies with marketed and premarket products. Adherence to the PhRMA code is voluntary; however, certain state laws and regulations require the adoption of the PhRMA Code by pharmaceutical and similar companies operating within the state.

PHSA: acronym for Public Health Service Act.

Physician Consulting Agreement: financial arrangements between an entity and a physician for research, product Development, Development and/or transfer of Intellectual Property, marketing, participation on advisory boards, presentations at company-sponsored training and other services. Such arrangements with physicians in a position to generate business for the entity, directly or indirectly through arranging or recommending the entity or its products, may implicate the AKS, the Stark Law (if the contracting entity also performs services that are billed as DHS or presented a claim to Medicare for DHS), and other laws. Payment for the item or service offered by the entity is payable in whole or in part by a federal healthcare program.

Physician Payment Sunshine Act: the ACA enacted physician sunshine provisions that require Applicable Manufacturers to report ownership and any payments or transfers of value made to Covered Recipients . Applicable GPOs must report physician ownership. The Physician Payment Sunshine Act provides that Applicable Manufacturers of a Covered Drug, Device, Biological or Medical Supply that provides a payment or other transfer of value to a physician or a teaching hospital must submit annually to the Department of Health and Human Services certain information regarding the transfer. That required information includes the name and address of the covered recipient, the amount of value paid, the date of the transfer, whether the payment was tied to a specific product, and the nature and form of the payment. The purpose of the law is to create transparency

and shed light on the nature and extent of the relationships between Manufacturers, GPOs and physicians, as well as to dissuade inappropriate relationships from forming. Failure to submit required information may result in civil monetary penalties of up to an aggregate of US$150,000 per year (or up to an aggregate of US$1 million per year for knowing failures), for all payments, transfers of value or ownership or investment interests not reported in an annual submission. Certain states also require Medical Device and/or pharmaceutical companies to track and report gifts, compensation and other Remuneration to physicians.

Physician-Owned Distributor (POD): an entity with complete or partial physician ownership that derives revenue in significant part from selling, or arranging for the sale of, products ordered by the physician-owners for use in procedures the physician-owners perform on their own patients at hospitals or Ambulatory Surgical Centers (ASCs). OIG has raised significant concerns regarding PODs in Special Fraud Alerts and other guidance due to the perceived strong potential for improper Inducements between and among physician investors, entities, vendors and product purchasers. Such ventures are typically subject to close scrutiny by law enforcement under the fraud and abuse laws.

Physiology: branch of biology focused on living organisms and their parts

PIP: acronym for Paediatric Investigation Plan.

Pivotal Clinical Trial/Registration Trial: a clinical study in which evidence is gathered to support the safety and effectiveness evaluation of a product for its intended use in order to support Regulatory Approval of the product. Pivotal Clinical Trials for Drugs and Biologics are generally Phase III Clinical Trials, but in some cases approval may be based on Phase II Clinical Trials. Pivotal Clinical Trials involving investigational Devices are designed to serve as the basis for demonstrating the Device's efficacy and safety for purposes of obtaining marketing authorization.

Pivotal Clinical Trials are typically Adequate and Well-Controlled Clinical Trials. But not all Adequate and Well-Controlled Trials are pivotal. Pivotal typically denotes a trial that the applicant plans to rely on to obtain FDA approval.

Placing on the Market: the initial availability of a Device other than a Device Intended For Clinical Investigation in return for payment or free of charge, with a view to distribution and/or use on the Community market, regardless of whether it is new or fully refurbished (Art. 1 para. 2 lit. h) Directive 93/42/EEC).

Plasmid: a double-stranded genetic fragment, found in a Cell, capable of replicating independently from chromosomal DNA. Often circular and found in Bacteria, Plasmids are useful for Genetic Engineering as they can be used as Vectors to transport foreign DNA into target Cells.

PMA: acronym for Pre-Market Approval.

Points to Consider (PTC): documents issued by the FDA that are not necessarily regulations or guidelines, but represent the thinking of the FDA at a certain point in time. Points to Consider can serve to clarify FDA thinking with regard to different topics such as processes, policies and procedures.

Polygenic Disease: a genetic disease caused by the combined action of two or more Genes.

Polymer: a large Molecule composed of many smaller Molecules arranged in a repeating structure.

Post-Approval Commitment: the European Union's term for Post-Marketing Commitments, and can include follow-up measures or specific obligations.

Polymerase Chain Reaction (PCR): a technology in molecular biology used to amplify a single copy or a few copies of a portion of DNA across several orders of magnitude, generating thousands to millions of copies of a particular DNA sequence.

Post-Market Clinical Follow-Up (PMCF): according to the European Commission, a study carried out following a Device's CE Marking and intended to answer specific questions relating to a Device's clinical safety or performance when used in accordance with its approved Labeling.

Post-Marketing Commitments or Requirements (PMC/R): promises a company makes to the FDA or the EMA to provide certain additional information with respect to a company's product that has already been marketed or approved. The health authorities then use this additional information to assess and monitor the safety and efficacy of the company's product.

Post-Market Surveillance (PMS): action carried out by the Manufacturer to monitor the pharmaceutical product or Medical Device after its launch on the market to evaluate and report any Incidents and take any necessary actions.

Post-Translational Modification: the modifications that occur on a Protein after it is translated by ribosomes. These enzyme-catalyzed changes generally include the addition of a functional group to a Protein or cleaving Peptide bonds within a Protein.

Precision Medicine: a medical model focused on customizing healthcare for different patients, taking into account patient variations in Genes, environment and lifestyle. The term is often used interchangeably with Personalized Medicine, but is traditionally distinct in that Personalized Medicine may sometimes be regarded as seeking to tailor medical care uniquely for an single individual, whereas Precision Medicine focuses on the ability to classify patients into different subpopulations to better understand what ailments a particular subpopulation may be susceptible to or what treatments may be more effective for a particular subpopulation.

Pre-Clinical: see Preclinical Studies.

Pre-Emerging Biotechs: young life sciences ventures that have not yet received or are in the early stages of receiving venture funding.

Pre-IND Meeting: a meeting held between a sponsor and the FDA prior to the submission of an Investigational New Drug Application. A Pre-IND Meeting provides an opportunity to review and reach agreement on the design of animal studies needed to initiate human testing and to discuss the scope and design of clinical testing, plans for studying the product in pediatric populations and the best approach for presentation and formatting of Data in the IND.

Pre-NDA Meeting: a meeting intended to permit the exchange of information between a sponsor and the FDA about a proposed NDA. The primary purpose is to uncover any major unresolved problems, to identify studies that the sponsor is relying on as Adequate and Well-Controlled to establish a Drug's effectiveness, to identify the status of ongoing or needed studies adequate to assess pediatric safety and effectiveness, to acquaint FDA reviewers with the general information to be submitted in the application, to discuss appropriate methods for statistical analysis of the Data and to discuss the best approach to the presentation and formatting of Data in the application.

Preclinical Studies: tests or studies that are not conducted in human subjects, such as those conducted by laboratory or animal research. See Non-Clinical.

Preliminary Injunction: an equitable remedy that a patent owner may seek while a patent case is pending to prevent a party from infringing a Patent prior to the conclusion of the lawsuit. The courts apply a similar test to the eBay factors, and also will consider proof of likelihood of success on the merits.

Premarket Approval (PMA): Manufacturers of Class III Medical Devices generally must submit to the FDA a Premarket Approval (PMA) application seeking approval of the Device for commercial distribution in the United States. A PMA generally must contain:

- A complete description of the Device
- Information regarding the methods used in, and the facilities and controls used for, the manufacture, processing, packaging, storage and, as appropriate, installation of the Device
- Information regarding any applicable Performance Standards
- Data from non-clinical studies
- Data from clinical studies
- Proposed Labeling among other application components.

In making a determination whether to approve or deny a PMA application, the FDA will rely on the conditions of use included in the proposed Product Labeling as the basis for determining whether or not there is a reasonable assurance of safety and effectiveness, and for determining if the proposed Labeling is neither false nor misleading.

Prescription (Rx): a written physician's order for the preparation and administration of a particular medicine or therapy. Prescription is commonly abbreviated to Rx.

Prescription Drug User Fee Act Date (PDUFA Date): the Prescription Drug User Fee Act established time periods for the FDA to review New Drug Applications (NDA). An NDA submission to the FDA typically gets a date 10 months from submission; if the Drug has a Priority Review designation, the date is typically six months from submission. The date is a target date and not a deadline — the FDA may issue its decision before or after the date.

Pricing Approval: the approval by government health authorities of the price of a Therapeutic. Primarily applies outside the United States.

Principal Investigator: the primary individual who actually conducts a clinical investigation (*i.e.*, under whose immediate direction the product is administered or dispensed to a subject in a Clinical Trial).

Prior Authorization: in the health insurance context, a cost-reduction measure used by some health insurance companies that requires the insured (or the insured's healthcare Provider or Supplier on the insured's behalf) to obtain from the insurer a determination of Coverage for a proposed procedure or service before the insured undergoes the procedure or obtains the service. Failure to obtain Prior Authorization of the procedure or service may be grounds for denial of Coverage.

Priority: the date on which an inventor established a right to Patent an Invention — often the effective filing date of the Patent. In order for an application to provide Priority for a Patent claim, it must satisfy the Written Description and Enablement requirements for the claim.

Priority Review: under the Prescription Drug User Fee Amendments (PDUFA), the FDA agreed to specific goals for improving the drug review time and created a two-tiered system of review times — Standard Review and Priority Review. A Priority Review designation means that the FDA's goal is to take action on an application within six months either of receipt or of the 60-day filing date, depending on the type of application (compared to 10 months under Standard Review). A Priority Review designation is intended to direct overall attention and resources to the evaluation of such applications. To be eligible for Priority Review, an application generally must be for a product intended to treat a serious condition and that, if approved, would provide a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention

of the serious condition compared to available therapies. According to the FDA, "Significant improvement may be illustrated by the following examples: (1) evidence of increased effectiveness in treatment, prevention or diagnosis of a condition; (2) elimination or substantial reduction of a treatment-limiting adverse reaction; (3) documented enhancement of patient compliance that is expected to lead to an improvement in serious outcomes; or (4) evidence of safety and effectiveness in a new subpopulation." Specific statutory provisions also provide for Priority Review for certain types of applications, including an application for a Drug that has been designated as a qualified infectious disease product, a Supplement to an application that proposes a labeling change for a Drug pursuant to a report on a pediatric study, or an application or Supplement for a Drug submitted with a Priority Review Voucher.

Priority Review Voucher: a voucher issued by the FDA to the sponsor of an approved application for (1) a product intended to treat or prevent certain tropical diseases; or (2) a product intended to treat or prevent a rare pediatric disease. The voucher entitles the holder to designate an NDA or BLA for a different product as qualifying for a Priority Review, and is transferable, including by sale. Unlike the approved application for which the voucher is issued, the application using the voucher need not be for a product for a tropical disease or a rare pediatric disease.

Private Payor: generally, private health insurers and managed care organizations.

Prodrug: inactive derivatives of active drug Molecules that must undergo an enzymatic or chemical reaction to release the active parent Drug into a body. Prodrugs are often used to improve drug delivery and targeting or reduce drug toxicity.

Product Insert / Instructions for Use: a document which must be included in the packaging of every Medical Device to inform the user in particular about the name or trade name of the Medical Device, the name and address of the Manufacturer, the product's intended purpose, performances and undesirable side effects, the proper installation, avoidance of certain risks, risks of reciprocal interference during specific investigations or treatment, as well as other specific information if necessary (cf. Annex I, Sec. 13.1 and 13.6 Directive 93/42/EEC).

Product Labeling: a term construed by the FDA to refer to all written, printed or graphic material associated with a regulated product, including the product insert. Product Labeling typically includes all promotional material about a regulated product that is not Advertising.

Product Liability: legal liability for distributing or selling a defective product.

Product Literature: those informational documents concerning a particular product, often including Promotional Materials, datasheets, safety information, operating manuals and related documentation.

Prokaryote: a single-celled organism that lacks a distinct cell nucleus and membrane-bound organelles. Bacteria are prokaryotes.

Promotional Materials: the documents and other materials used by a company to market and advertise a product, including websites, brochures, emails, fliers, and print or media advertisements.

Proof of Concept: a demonstration meant to verify that certain ideas or theories are feasible, such as a particular Invention, business model, product or service.

Prosecution: the process of applying for a Patent, including drafting and filing the application, communicating with the PTO Examiner, and, if necessary, amending the claims to establish patentability.

Prospective Payment System (PPS): a method of Reimbursement in which payment for an item or service is based on a predetermined, fixed amount. The payment amount for a particular service is derived based on the classification system for the service (for example, diagnosis-related groups for inpatient hospital services). CMS uses separate PPSs to reimburse Providers for inpatient and outpatient hospital services, home health agencies, hospice services, inpatient psychiatric services, inpatient rehabilitation services, long-term care hospital services and skilled nursing services.

Protected Health Information (PHI): under HIPAA, information (1) that is created or received by a healthcare Provider, health plan, employer or healthcare clearinghouse; (2) that relates to the past, present, or future physical or mental health or condition of an individual; the provision of healthcare to an individual; or the past, present or future payment for the provision of heath care to an individual; (3) that identifies the individual or for which there is a reasonable basis to believe can be used to identify the individual; and is (4) transmitted by or maintained in any form or medium. PHI includes PHI transmitted or maintained in electronic form, which is known as electronic PHI or ePHI.

Protecting Access to Medicare Act of 2014 (PAMA): enacted on April 1, 2014, PAMA, principally revised the payment and coverage methodologies for clinical laboratory tests paid under the Clinical Laboratory Fee Schedule (CLFS). Starting January 1, 2016, applicable laboratories are required to report Private Payor payment rates and corresponding volumes of tests. The statutorily required collection of Private Payor rates for laboratory tests from applicable laboratories will be the basis for the revised payment rates for most laboratory tests on the CLFS beginning in January 2018.

Protein: any of various complex organic Molecules composed of one or more amino acid chains and that contain carbon, hydrogen, nitrogen, oxygen and other elements. Proteins form essential parts of organisms, are coded for by Genes and play a role in a wide range of Cell processes.

Protein Engineering: the design and Development of new Enzymes and Proteins with desirable functions. Synthetic Proteins are generally created by modifying amino acid sequences.

Proteome: a term analogous to Genome, the entire set of Proteins that is or can be expressed by a Cell, tissue or organism at a particular time. A proteome varies with time and the conditions that an organism experiences.

Proteomics: the large-scale study of Proteins, their structures and their functions, or the study of Proteomes. Applications of Proteomics include improving understanding of cellular function and the identification of Proteins associated with various diseases.

Providers: generally, institutions and individuals licensed to provide healthcare services (for example, hospitals, skilled nursing facilities, physicians, dentists, pharmacists, etc.).

Under Medicare regulations, a Provider is defined by the phrase "provider of services" and means a hospital, critical access hospital, skilled nursing facility, comprehensive outpatient rehabilitation facility, home health agency, hospice program, or for certain purposes, a fund as defined in the specific provisions of the Social Security Act; any organization (including an HMO, PPO, or group medical practice) that provides healthcare services and follows a formal peer review process for purposes of furthering quality healthcare, or any other organization that, directly or through contracts, provides healthcare services. The Medicare definition does not include physicians or other practitioners, or other facilities or entities that furnish healthcare items or services. Such entities are considered Suppliers.

Under the Health Insurance Portability and Accountability Act (HIPAA), a healthcare Provider includes healthcare Providers that transmit any health information in connection with transactions for which the U.S. Department of Health and Human Services has adopted standards (such as physicians, clinics, hospitals, psychologists, pharmacies, etc.); health plans (including health insurance companies, HMOs, self-insured / employer-sponsored health plans, and healthcare clearinghouses) (*i.e.*, entities that process nonstandard health information received from another entity into a standard format, or vice versa).

PTAB: acronym for Patent Trial and Appeal Board.

Public Health Service Act (PHSA): the statute that, primarily establishes the regulatory framework for Biological Products (Biologics) and Follow-on Biologics.

Pulmonary: of, affecting or relating to the lungs.

Public vs. Private Health Insurance in Germany: health insurance, either public or private, is compulsory in Germany. Public health insurance (Gesetzliche Krankenversicherung, GKV), on the one hand, is open to anyone and fees solely depend on the income of the insured person; access

and fees do not reflect the individual´s health condition/status. Private insurance (Private Krankenversicherung, PKV), on the other hand, is not open to every person and is characterized by an individual agreement between insured and insurer taking into consideration the person's age and individual health status after a respective medical investigation. The insured can opt into certain terms he/she deems important or favorable and to a certain extent negotiate the scope and quality of medicinal supply and services. Private insurance requires an above average income (*i.e.* approx. above EUR50,000/year). It is the political will to reduce and consolidate the number of public health insurance companies; therefore a number of public health insurance companies merged in the past, *e.g.* one of the largest mergers was the merger of DAK Deutsche Angestellten Krankenkasse, one of Germany's largest public health insurance companies, with BKK Gesundheit, one of Germany's largest company health insurance funds, to DAK Gesundheit (Latham advised its client DAK in this merger).

Purple Book: a publication that lists Biological Products (Biologics), including Biosimilar and Interchangeable Biological Products licensed by the FDA. This list includes the date when the Biological Product was licensed by the FDA. It does not include a list of the Patents associated with the approved Biological Products. See Orange Book.

P-Value: a function of observed sample results used to test a hypothesis; provides a probability that can be useful in determining the significance of statistical results. A P-Value helps measure whether an outcome is due to an actual effect or chance alone.

Qualified Infectious Disease Product (QIDP): the FDA may designate as a qualified infectious disease product (QIDP) an Antibacterial or antifungal Drug for human use intended to treat serious or life-threatening infections, including those caused by an Antibacterial or antifungal resistant pathogen (including novel or emerging infectious pathogens), or qualifying pathogens listed by the FDA. Pursuant to the GAIN Act, a Drug designated as a QIDP may be eligible for an additional five years of Exclusivity on top of certain other Exclusivity periods for which the product may be eligible. In addition, an application for a Drug designated as a QIDP is eligible for Priority Review and designation as a Fast Track Product.

Qualified Person: an individual — usually an employee — who is responsible for compliance with any legal requirements in the pharmaceutical sector with regard to manufacturing, examination and release of a pharmaceutical product before placing such product on the market.

Qualified Person Responsible for Pharmacovigilance (QPPV): a person — usually an employee — appointed by a pharmaceutical company who is personally responsible by law for ensuring that the company meets

the legal requirements with regard to monitoring the safety of a medicinal product on the European market. Any company that intends to distribute a medicinal product within the EU or the EEA must have a QPPV.

Quality Agreement: an agreement between two parties, often in conjunction with a manufacture, supply or other agreement, which delineates product or project parameters and Specifications and specifies each party's responsibilities thereto.

Quality System Regulation (QSR): the FDA's current good manufacturing practice requirements for Devices, set forth at 21 C.F.R. Part 820, governing the methods used in, and the facilities and controls used for, the design, manufacture, packaging, Labeling, storage, installation and servicing of all finished Devices intended for human use.

Qui Tam: a type of legal action permitted by the FCA and certain state statutes allowing a private individual or entity, known as a whistleblower or Relator, to assist on behalf of the government or a governmental entity in the prosecution of false or fraudulent conduct. Persons filing such actions may receive a portion of any recovery by the government, usually 15-30%, plus attorney's fees.

Radiology: the branch of medicine that uses imaging techniques, such as computed tomography (CT), Magnetic Resonance Imaging (MRI), X-rays and Ultrasound techniques, to diagnose and treat diseases.

Rapporteur and Co-Rapporteur: members of the diverse committees of the EMA (CHMP, CVMP or COMP) who examine the Marketing Authorisation Applications, community referrals and requests for Orphan Drug designation.

Rare Disease: also known as an Orphan Disease, a Rare Disease is one that affects a small percentage of the population. The FDA defines such diseases as a condition that affects fewer than 200,000 people worldwide. In the United States, the 1983 Orphan Drug Act created financial incentives, including tax credits, research assistance and exclusive marketing periods for orphan-designated products with FDA approval, which resulted in the Development of a variety of Orphan Drugs. Similar legislation has been enacted in other legal jurisdictions worldwide.

Rational Drug Design: the process of discovering new Drugs based on knowledge of a Biological Target. Generally, a Molecule associated with a disease is identified and assessed, then a drug Molecule is designed to inhibit or promote certain reactions in an organism to respond to the disease.

Reagent: a substance or compound used to cause a chemical reaction. Reagents can be used to detect the presence of other substances or cause certain chemical transformations.

Recombinant DNA Advisory Committee (RAC): according to the FDA, "a panel of national experts representing various fields of science, medicine, genetics, ethics and patient perspectives that considers the current state

of knowledge and technology regarding research with recombinant or synthetic nucleic acid molecules. RAC also advises the Director of the National Institutes of Health (NIH) and the NIH Office of Biotechnology Activities (OBA), and reviews research proposals involving human gene transfer research, also referred to as Gene Therapy the FDA requires, "all human gene transfer clinical trials occurring at or sponsored by institutions receiving NIH funds for research with recombinant or synthetic nucleic acid molecules must be submitted to OBA for review by the RAC."

Reexaminations: a process by which a third party or an inventor can have a Patent reviewed by a patent examiner to verify that the subject matter it claims is patentable. To have a Patent reexamined, an interested party must submit prior art that raises a substantial new question of patentability.

Reference Listed Drug (RLD): according to the FDA, a Reference Listed Drug is "an approved drug product listed in the Orange Book to which a generic version is compared to show that the products are bioequivalent. A sponsor seeking approval to market a generic equivalent must refer to the RLD in its Abbreviated New Drug Application (ANDA)."

Reference Medicinal Product / European Reference Product (ERP): a medicinal product that has been authorized by a Member State or by the European Commission on the grounds of a complete dossier (*i.e.* submission of quality, preclinical and clinical Data) and on the basis of which the Marketing Authorisation application for a generic medicinal product is made.

Reference Product: a Biological Product (Biologic) licensed under 42 U.S.C. § 262(a). A Biosimilar Product Applicant seeking approval under 42 U.S.C. § 262(a) must specify a Reference Product and biosimilarity will be evaluated against that product.

Reference Product Sponsor: the company that owns or has the rights in the Reference Product. See Reference Product and BPCIA Exchange.

Registration Trial: see Pivotal Clinical Trial.

Regulatory Approval: see, *e.g.*, New Drug Application (NDA), Biologics License Application (BLA) and Premarket Approval (PMA).

Regulatory Approval Application: an application a pharmaceutical company makes to a health authority to investigate, License or market a new product and/or Indication.

Regulatory Authority: a governmental agency responsible for regulating Drugs, Biologics, Medical Devices, or other products, services or activities, for example the FDA in the United States or the EMA in the European Union.

Regulatory Documentation: any and all of the following:

- Submissions to a Regulatory Authority, including but not limited to applications, registrations and notifications, and including all supporting documentation such as studies, Data and other files
- Approvals, Licenses, clearances, designations, waivers, exemptions and other such authorizations or permits issued by a Regulatory Authority
- Correspondence to or from a Regulatory Authority, including but not limited to acknowledgement letters, information requests, pre-meeting briefing packages and preliminary responses, meeting minutes, Complete Response Letters and other communications with a Regulatory Authority
- Reports of adverse drug experiences, Pharmacovigilance databases and other safety filings, including all associated documentation and related records
- Warning letters, untitled letters, FDA Form 483s or other notices of inspectional observations or notices of any pending or threatened audit, investigation, claim, hearing, proceeding, arbitration, enforcement action or other action issued by a Regulatory Authority
- Manufacturing records and related documentation

Regulatory Filing: see, *e.g.*, Regulatory Documentation, New Drug Application (NDA), Biologics License Application (BLA) and Premarket Approval (PMA).

Reimbursement: the term is frequently used in reference to payment made by a Third-Party Payor (*e.g.*, an insurance company) for healthcare items or services provided to the payor's Beneficiaries and deemed eligible for payment by such payor. Reimbursement often occurs after such items or services are rendered.

Reimbursement Support Services: can include a variety of activities such as providing information regarding or assessing Coverage for particular Drugs, Devices or procedures using such Devices, providing assistance with Prior Authorizations, verifying Coverage, assisting with appeals of denials of Coverage, working with Patient Assistance Programs or charities to assist in Coverage of a product or service and similar activities. Some companies specialize in providing outsourced Reimbursement Support Services to pharmacies and other clients.

Reissues: a patent application filed after a Patent has already been granted in order to correct an error in an issued Patent that would otherwise render the Patent wholly or partially invalid.

Relator: the private citizen or whistleblower who files suit under the False Claims Act on behalf of the government to assist in the prosecution of false or fraudulent conduct. After an investigatory period, the government then has the choice to either take over and prosecute the suit (typically called

intervening) or to decline intervention in the case. Relators may receive a part of any recovery by the government, usually between 15-30%, plus attorney's fees. If the government declines intervention, the relator can proceed alone as plaintiff on behalf of the government.

Remuneration: the transfer of anything of value, directly or indirectly, overtly or covertly, in cash or in kind, including for example: gifts, Discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests, and any item or service at an amount inconsistent with Fair Market Value.

Representations and Warranties: the written statements a party makes with respect to the information contained in a contract, attesting that the other party can rely on the information as true and correct.

Reverse Payment: a type of settlement in a generic pharmaceutical litigation in which the Branded Company will pay the generic company to settle the case. The Supreme Court ruled in *Federal Trade Comm'n v. Actavis, Inc.* that antitrust challenges to such payments should be reviewed under the rule of reason. Also sometimes referred to as pay for delay agreements.

Rheumatology: a branch of internal medicine and Pediatrics that studies the diagnosis and therapy of certain musculoskeletal diseases and autoimmune conditions known as rheumatic diseases. Such diseases include rheumatoid arthritis and lupus.

Ribonucleic Acid (RNA): a polymeric Molecule composed of the Molecules adenine, cytosine, guanine and uracile. RNA codes, decodes, expresses and regulates Genes. RNA is generally found in nature as a single-strand, unlike DNA, which generally appears as paired double-strands. RNA is synthesized from DNA through a Transcription process wherein an Enzyme known as RNA polymerase forms a RNA sequence complementary to an originating DNA template.

Right of First Negotiation: the right to engage in Good Faith Negotiations to enter into a particular transaction with the other party, prior to the other party negotiating with other parties.

Right of First Offer: the right to make the first offer to a party before that party entertains offers from other parties to enter into a particular transaction.

Right of First Refusal (ROFR): when a party that owns an item of property or a right agrees with a counterparty that it will not sell the property or right to a third party without first giving the counterparty a right to match the third party's offer. If the counterparty meets the offering price, the first party will be obligated to sell the property or right to the counterparty. A Right of First Refusal is generally the strongest form of counterparty right and is distinguished from, in order of increasing strength, a Right of First Negotiation and Right of First Offer.

Right of Reference: the right of one party to access and cross-reference another party's Regulatory Approvals and related documentation and Data with respect to a certain product (including Drug Master Files) for use in obtaining the first party's own approvals for the products. In the United States, Right of Reference is a term of art defined at 21 C.F.R. 314.3(b).

Risikoklassen Medizinprodukte (Classification of Medical Devices)

(Germany): the classification of Medical Devices based on risks involved in their usage. According to Annex IX of the European Medical Device Directive 93/42/EEC, Medical Devices are to be classified in one of four available risk classes. Each of these four risk classes sets forth certain entry requirements in order to be marketed in the EU (based inter alia on criteria such as duration and invasiveness of its application and usage).

Risk Evaluation & Mitigation Strategy (REMS): a requirement that the FDA may impose as part of the approval of a new product, or for an approved product if new safety information arises, when the FDA determines that a REMS is necessary to ensure that the benefits of a particular Drug outweigh its risks. A REMS may include the Development and distribution of a medication guide and patient package insert, implementation of a communication plan, including letters to healthcare Providers and/or other methods of disseminating information, and Elements to Assure Safe Use of the Drug due to its inherent toxicity or potential harmfulness. A REMS may also include training, experience and/or certification requirements for prescribers; certification requirements for pharmacies; requirements that the Drug be dispensed only in certain settings or only to patients with certain documentation; monitoring requirements; and/or a requirement for a Patient Registry. For example, if a Drug carries the risk of severe birth defects, a REMS may require a negative pregnancy test from the patient prior to the dispensing of each Prescription.

Rolling Forecast: a forecast, which may be binding or non-binding, predicting the amount of product a party anticipates requiring to be supplied by the other party, which is periodically updated so that the forecast rolls forward and extends a certain amount of time into the future. Often the more distant forecast will be non-binding, and, will become binding at a certain more proximate point in time.

Royalty: a payment obligation (typically for developing Intellectual Property) found in many Licenses that is tied to sales or Net Sales of certain products Covered by such Intellectual Property. Generally, a Royalty will obligate a Licensee to pay a Licensor an amount designated as a percentage of Net Sales of Licensed Products. A Royalty can be fixed (*e.g.* 3% of Net Sales) or tiered based on sales volumes or sales amounts in any given time period (*e.g.* 1% for Net Sales below US$1 million in a given year, 3% for Net Sales in between US$1-3 million in a given year, and 5% for Net Sales in excess of US$3 million in a given year). For royalty arrangements with healthcare professionals, royalty

payments typically exclude those derived from products purchased by the healthcare professional or any facility affiliated with the individual to ensure that medical decisions by physicians are based on the best interests of patients and in compliance with applicable state and federal fraud and abuse laws.

RNA: abbreviation for Ribonucleic Acid.

RNA Interference: also known as RNAi, refers to interference of Gene Expression by short sequences of double-stranded RNA.

Safe Harbor: in the particular context of the AKS, regulatory provisions established by the OIG that set forth various business practices and financial arrangements that, although they potentially implicate the AKS, will not be prosecuted as violations of the law, provided the practice or arrangement adheres to the criteria of the applicable safe harbor. Compliance with an AKS Safe Harbor is not mandatory and noncompliance with a safe harbor does not necessarily result in the violation of the AKS.

Sarcoma: a rare cancer, Sarcoma tumors occur in connective tissues. There are two main types of Sarcoma, soft tissue Sarcoma and bone Sarcoma.

Scientific Advice: applicants can request Scientific Advice and protocol assistance of the EMA at any stage of the Development of a medicine, regardless of the relevant authorisation procedure. The Committee for Medicinal Products for Human Use (CHMP) is in charge of the Scientific Advice and protocol assistance for human medicines on the recommendation of the Scientific Advice Working Party (SAWP).

Scientific Advice Working Party (SAWP): a standing working party established by the Committee for Medicinal Products for Human Use (CHMP) with the sole purpose of providing Scientific Advice and protocol assistance. The EMA defines the SAWP as "a multidisciplinary group, which comprises a chairperson, 28 members including three members of the Committee for Orphan Medicinal Products (COMP), one member of the Paediatric Committee (PDCO) and one member of the Committee for Advanced Therapies (CAT)."

Scientific Advisory Board (SAB): distinct from a company's board of directors, biotechnology companies often have a separate scientific advisory board populated by academic, industry or medical experts that provides advice and guidance pertaining to certain scientific questions and aspects of product Development.

Scientific Advisory Board (SAB) Member: individuals who serve on advisory boards that allow companies to obtain information or advice on such topics as the marketplace, products, therapeutic areas and the needs of patients. Companies use this advice to inform their efforts to ensure that the therapies they produce and market are meeting the needs of patients.

Scientific Exchange: the exchange of information about an investigational Drug or Device by the product developer that is not considered by the FDA to be promotion due to the independent scientific or medical circumstances of the exchange. Generally speaking, information shared in the context of Scientific Exchange must be non-promotional, shared by science professionals and in a forum meant for scientific discussion. The FDA has been criticized, however, for its failure to provide specific guidance on what constitutes Scientific Exchange.

Secondary Considerations: objective evidence tending to show that an Invention was not obvious over the asserted prior art, and to guard against the use of improper hindsight in the Obviousness analysis. Secondary Considerations may include, for example, Commercial Success, industry recognition, long-felt but unsolved need, unexpected results and copying by competitors.

Secondary Payor: a health insurance plan, policy or program for which the obligation to pay on a claim for Reimbursement of healthcare items and services arises only to the extent the primary payor did not cover the full cost of the item or service. Depending on the circumstances and nature of the claim for Reimbursement, Medicare, Medicaid or another insurer may be a Secondary Payor.

Section (k): Section (k) of the BPCIA establishes the process for licensing a Biosimilar Product. It describes the requirements of the Biosimilar application, sets forth the standard for FDA approval, and establishes a period of market Exclusivity for Reference Products and for early Biosimilar Product Applicants whose products are determined to be interchangeable with the Reference Product. An applicant that applies to License a Biosimilar Product is referred to as a section (k) applicant in the BPCIA.

Self-Disclosure Protocol (SDP): a process by which Providers and Suppliers may voluntarily disclose self-discovered evidence of potentially fraudulent activities — including violations of the AKS and employment of excluded individuals — to the OIG and seek to resolve any associated liability without the costs and disruptions associated with a government-directed investigation and litigation. Providers and Suppliers seeking to resolve such violations under the Self-Disclosure Protocol may also receive reduced settlement demands and avoid mandatory compliance obligations under a CIA. CMS has also implemented a Self-Disclosure Protocol for violations of the Stark Law.

Sensitive Personal Data: under the Directive and the GDPR in the EU, Sensitive Personal Data that relates to racial or ethnic origin, political opinions, religious or philosophical beliefs, trade or labor union membership, physical or mental health (including genetic and biometric data), sexual life, or criminal offenses. In the EU, Sensitive Personal Data is subject to heightened protection and more severe limitations on its use and disclosure.

In the US, Sensitive Personal Data is Personal Data which may be subject to state Data Breach notification laws. While these laws vary by state, typically this is Data that could be used for identity theft purposes, such as a natural person's name in combination with (1) social security number; (2) driver's license or state identification number; (3) date of birth; or (4) bank or financial account number, or credit or debit card number in combination with any required security code, access code, or password that would permit access to an individual's financial account. Many states also consider identifiable health information to be Sensitive Personal Data. This information is also typically PHI which is subject to HIPAA.

Sequestration: automatic, across the board budget cuts in the amount of US$1.2 trillion over nine years enacted as part of the Budget Control Act of 2011 that took effect in 2013 when Congress could not agree on a plan to reduce the deficit. Sequestration included aggregate reductions of Medicare payments to Providers at 2% per fiscal year.

Serious Adverse Drug Experience: in the United States, the FDA defines a serious adverse drug experience as any "untoward medical occurrence associated with the postmarket use of a drug in humans, whether or not considered drug related, occurring at any dose, that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, or results in a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the aforementioned outcomes." Under 21 C.F.R. § 314.80, each adverse drug experience that is both serious and unexpected, whether foreign or domestic, must be reported to the FDA no later than 15 calendar days from initial receipt of the information.

Serious Adverse Event (SAE): in the United States, the FDA defines a Serious Adverse Event as "any untoward medical occurrence associated with the investigational use of a product in humans, whether or not considered product related, that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disruption of the ability to conduct normal life functions, or results in a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the aforementioned outcomes." Under 21 C.F.R. § 312.32, any suspected Adverse Event that is both serious and unexpected must be reported to the FDA.

In the EU the Clinical Trials Regulation defines a Serious Adverse Event as "any untoward medical occurrence that at any dose requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, results in a congenital anomaly or birth defect, is life-threatening, or results in death." Reference: Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on Clinical Trials on medicinal products for human use, and repealing Directive 2001/20/EC.

Serious Adverse Reaction (SAR): see Serious Adverse Event (SAE).

Service Mark: similar to a Trademark but used for distinguishing and identifying services rather than goods.

Sherman Antitrust Act: enacted by Congress in 1890, a statute prohibiting any unreasonable interference (by reason of conspiracy, contract, or combination) with the usual, ordinary and freely competitive pricing or distribution system of the open market in interstate trade (resulting in restraint of trade, monopolies or attempts to monopolize).

Short Interfering RNAs: also known as siRNAs, are short sequences of double-stranded RNA, which cause degradation of mRNA of the same sequence, and thus reduction of the expression of the particular Gene.

Sicherheitsbe-auftragter (Safety Officer) (Germany): a person that Manufacturers nominate who examines known risks associated with medical products. The examiner must evaluate risks and is responsible for appropriate corrective actions if applicable.

Similar Active Substance: Article 3(3) of Regulation (EC) No. 847/2000 defines a Similar Active Substance as an identical active substance, or an active substance with the same principal molecular structural features (but not necessarily all of the same molecular features) and which acts via the same mechanism. Commission Regulation (EC) No 847/2000 of 27 April 2000 laid down the provisions for implementation of the criteria for designating a medicinal product as an Orphan Medicinal Product and definitions of the concepts Similar Medicinal Product and clinical superiority.

Similar Medicinal Product: Article 3(3) of Regulation (EC) No. 847/2000* defines a Similar Medicinal Product as a medicinal product containing a Similar Active Substance or substances as contained in a currently authorized Orphan Medicinal Product, and which is intended for the same therapeutic Indication.

Reference Commission Regulation (EC) No 847/2000 of 27 April 2000 which laid down the provisions for implementation of the criteria for designating a medicinal product as an Orphan Medicinal Product and definitions of the concepts Similar Medicinal Product and clinical superiority.

Single Ascending Dose (SAD): refers to single ascending dose studies that take place during a Phase I Clinical Trial. In a SAD study, an experimental Drug is dosed to a small group of participants who are monitored for side effects. If there are no adverse side effects, another group receives a slightly higher dose of the Drug and is monitored. The process is repeated until either certain pre-calculated safety levels are reached or a dose is reached where intolerable side effects start appearing, which is the maximum tolerated dose. See Multiple Ascending Dose (MAD).

Single Nucleotide Polymorphism (SNP): pronounced "snip", a SNP is a Genetic Variation wherein a single nucleotide is substituted for another in DNA or RNA. SNPs occur normally throughout DNA. SNPs can be identified to locate Genes associated with disease, predict responses to Drugs, susceptibility to disease and the inheritance of disease Genes. While many SNPs do not cause problems, a single SNP or a group of SNPs can cause disease.

Small Molecule Compound: an organic compound often with molecular weight less than 1 kilodalton, comprised of at least two elements and in which the atoms share electrons through covalent bonds. Examples of small molecule compounds include Lipids, monosaccharides and metabolites. Drugs made from a Small Molecule Compound (Small Molecule Drugs) are often produced by chemical synthesis and more stable than Large Molecule Drugs like Biologics and biopharmaceutical Drugs.

Somatic Cell: any Cell of the body other than reproductive Cells.

Spanish Agency for Medicines and Health Products or Agencia Española de Medicamentos y Productos Sanitarios (AEMPS): the Spanish Agency for Medicine and Health Products (Agencia Española de Medicamentos y Productos Sanitarios or AEMPS) is the regulatory agency that oversees the quality, safety and efficacy of Pharmaceuticals and Medical Devices in Spain. The AEMPS is part of the Ministry of Health and Social Policy. The agency authorizes medicines for human and veterinary use; authorizes Clinical Trials; monitors and controls compliance with applicable laws and regulations which apply to cosmetics, Medical Devices, and hygiene products commercialized or used in Spain. Apart from overseeing public health in Spain, the AEMPS is the certifying authority for Medical Devices in Spain.

Special Advisory Bulletin (HHS OIG): an OIG publication intended to provide guidance to the healthcare industry to prevent Fraud and Abuse and promote high standards of ethical and lawful conduct. Each Special Advisory Bulletin addresses an industry practice or arrangement that potentially implicates fraud and abuse authorities enforced by the OIG. Although the practices or arrangements described in Special Advisory Bulletins are not always fraudulent or illegal, the characteristics and circumstances of the described practice or arrangement increase the risk of abuse of the Medicare and Medicaid program. Special Advisory Bulletins are published on the OIG's website and in the Federal Register.

Special Fraud Alert (HHS OIG): an OIG publication identifying a specific national trend in healthcare fraud or a certain abusive practice of an industry-wide character, and providing general guidance to healthcare industry participants on violations of federal law, including the AKS. Special Fraud Alerts provide notice to the healthcare industry and the general public that the OIG is aware of the described fraudulent or abusive practice, which may result in increased investigatory and enforcement activity, as well as criminal, civil and administrative actions, as appropriate. The publications also serve as a tool to encourage compliance with the law by giving industry participants an opportunity to examine their own practices, and provide guidance to assist Medicare and Medicaid fraud control units and contractors identify healthcare fraud schemes. Special Fraud Alerts are published on the OIG's website and in the Federal Register.

Special Protocol Assessment (SPA): the FDA's SPA process is designed to facilitate the FDA's review and approval of Drugs by allowing the FDA to evaluate the proposed design and size of Carcinogenicity protocols, stability protocols or protocols for Phase III Clinical Trials that are intended to form the primary basis for determining a drug product's efficacy. Upon specific request by a clinical trial sponsor, the FDA will evaluate the protocol and respond to a sponsor's questions regarding, among other things, primary efficacy endpoints, trial conduct and Data analysis, within 45 days of receipt of the request. If an agreement with the FDA is reached on design, execution and analyses, and if the results of the trial conducted under the protocol substantiate the hypothesis of the protocol, the FDA agrees that the Data from the protocol may form the primary basis of an efficacy claim in a New Drug Application, Biologics License Application or efficacy Supplements to approved NDAs or BLAs.

Specialty Pharma (SPEC Pharma): also known as specialty Drugs or Specialty Pharmaceuticals, a recent designation of Pharmaceuticals that are particularly expensive and complex to manufacture.

Specialty Pharmaceuticals: specialty, high-cost Drugs used in the treatment of complex conditions such as cancer, multiple sclerosis, hemophilia, infertility, rheumatoid arthritis, chronic forms of hepatitis and other diseases. Specialty Pharmaceuticals often require sensitive handling, storage and monitoring, and may be physician administered.

Specialty Pharmacy: a pharmacy service or entity that manages utilization of Specialty Pharmaceuticals, including services beyond dispensing and distribution, such as patient education services, case management, insurance Reimbursement, and drug administration and adherence counseling.

Specifications: a detailed description of the characteristics and properties of a given therapeutic product, which may also include requirements for production of the product.

Standard Review: under the Prescription Drug User Fee Amendments (PDUFA), the FDA agreed to specific goals for improving the drug review time and created a two-tiered system of review times — Standard Review and Priority Review. A Standard Review designation means the FDA's goal is to take action on an application within 10 months either of receipt or of the 60-day filing date, depending on the type of application (compared to six months for a Priority Review application).

Stark Law: a law, also referred to as the physician self-referral law, that prohibits physicians from making referrals for Designated Health Services payable by Medicare to an entity with which the physician or an immediate family member of the physician has a financial relationship (*i.e.*, ownership, investment or compensation), unless a statutory or regulatory exception applies, and prohibits the entity from presenting or causing to be presented claims to Medicare (or billing another individual, entity or Third-Party Payor) for those referred services. Violations of the law result in an Overpayment to the entity submitting the prohibited claim, and may result in other civil and administrative liability under the Civil Monetary Penalty Law and the FCA. The Stark Law is applicable to the Medicaid program by statute; however, CMS has not issued implementing regulations and the application of the law in the Medicaid context remains ambiguous.

Stem Cells: an unspecialized Cell that can create more copies of itself as well as different types of specialized Cells through cellular differentiation.

Step Edits: requirements established by Third-Party Payors, typically for newer Drugs or other treatments, that require the patient to first try other, typically less expensive, Drugs or treatments before the subject Drugs will be covered. Step Edits are sometimes also referred to as step therapy.

Subcontractor (HIPAA): individuals or entities operating as subcontractors of a Business Associate, who create, receive, maintain or transmit a Covered Entity's PHI. Such individuals and entities are considered Business Associates and are directly subject to HIPAA.

Subdermal: located under the skin.

Sublicense: a subordinate License, granting certain rights held by a Licensee which it obtained pursuant to a License.

Sublicense Revenue: payments received by a Licensor from a Licensee in consideration for the grant of Sublicense rights. Often subject to payment obligations to the Licensor.

Sublicensee: the person or entity receiving rights granted under a Sublicense.

Sublicensor: the person or entity granting rights it has previously been granted from a Licensor or a Sublicensee of a Licensor.

Subpoena: a court-sanctioned command requesting the production of documents or requesting that a named individual appear before a duly

authorized body at a fixed time to provide testimony. If a person receives a Subpoena but does not comply with its terms, that person may be subject to civil or criminal penalties.

Substrate: 1. in biochemistry, a substance acted on by an Enzyme. 2. in biology, the surface or material on which an organism grows or lives.

Summary of Product Characteristics (SmPC): describes a medicinal product's properties and the conditions attached to its use. This includes: name, composition, pharmaceutical form and strength, therapeutic Indication(s), adverse reactions, contraindications, shelf-life, storage conditions and marketing authorisation holder. It also contains all information a prescriber or Supplier needs for the medicinal or veterinary product's proper use. The SmPC must be approved by the Competent Authority (EMA or EU Member State) granting the Marketing Authorisation. The promotion of medicinal products, when allowed, must be consistent with the Summary of Product Characteristics.

Supplement: an addition to the original application submitted to the FDA for drug approval that asks the FDA to approve changes to a product already approved. These changes can include new Indications, new strengths, new manufacturing, etc.

Supplemental Medicare Plan: Medicare gap or wraparound insurance that provides Coverage for some services not included in conventional Medicare Coverage, and pays or reimburses Beneficiaries for Deductibles and Copayments due for Medicare-covered services. The Coverage is designed to give Medicare beneficiaries an opportunity to fill the gaps in basic Medicare Coverage.

Suppliers: generally, individuals or entities that furnish healthcare items or services other than institutions or individuals licensed to provide healthcare services; for example, medical device and pharmaceutical Manufacturers, durable medical equipment Suppliers.

Under Medicare regulations, the term Supplier includes: a physician or other practitioner, a facility or other entity that furnishes items or services, except for entities satisfying the definition of provider of services under the Social Security Act (see Providers); any individual or entity, other than a Provider, who furnishes, whether directly or indirectly, or provides access to, healthcare services, supplies, items, or ancillary services (including, but not limited to, durable medical equipment Suppliers, Manufacturers of healthcare items, pharmaceutical Suppliers and Manufacturers, health record services [such as medical, dental and patient records], health Data Suppliers, and billing and transportation service Suppliers); any individual or entity under contract to provide such supplies, items or ancillary services; health plans as defined in National Practitioner Data Bank regulations (including employers that are self-insured), or health insurance producers (including, but not limited to agents, brokers, solicitors, consultants and reinsurance intermediaries).

Suspected Unexpected Serious Adverse Reaction (SUSAR): see Unexpected Serious Adverse Reaction (USAR).

Sustainable Growth Rate (SGR) Formula: a formula previously used to calculate a target rate for aggregate Medicare expenditures for physicians' services that was intended to control growth in such expenditures. On April 16, 2015, President Obama signed the Medicare Access and CHIP Reauthorization Act of 2015 (MACRA), which repealed and replaced the SGR formula with new methods to calculate Medicare Reimbursement for physician services.

Suture: 1.a stitch used to hold tissues together; when used as a verb, refers to the act of stitching with a suture. 2.in anatomy, a rigid joint between two or more bones.

Synthetic Biology: building of Cells or organisms from the ground up to perform certain tasks. All of the building blocks are synthesized and assembled from scratch, as opposed to being engineered and Cloned from a parent. The first artificial Cell was made in 2016 by Craig Venter and his group from synthesizing a Genome with 473 Genes.

Synthetic DNA: artificial, lab-created DNA.

Systems Biology: using Bioinformatics to look at how networks of Genes and Proteins, in groups of hundreds to thousands or more, work together instead of individually.

T-Cell: a type of lymphocyte (a subtype of white blood Cells) that matures in the thymus and performs various important functions in the immune system. There are several types of T-Cells, including killer T-Cells designed to kill Viruses and helper T-Cells that help recognize foreign Antigens and stimulate other white blood Cells to initiate various immune responses. See Chimeric Antigen Receptor (CAR), CAR T-Cell, Immuno-oncology, TCR or T-Cell Receptor.

Tmax: a Pharmacokinetic term denoting the time post-drug administration at which serum concentration of such Drug has reached peak levels. At T-max, the rate at which the Drug is absorbed equals the rate at which the Drug is eliminated. The time at which Cmax is observed.

Target: anything in an organism to which a Drug, Ligand or other chemical is directed, and, upon binding, undergoes a specific reaction, resulting in a change in its behavior or function.

Target Validation: in a Clinical Trial, the process of demonstrating that engaging a molecular Target provides a statistically meaningful therapeutic benefit at acceptable safety levels for a given Indication.

TCR or T-Cell Receptor: an adhesion Molecule on the surface of T-lymphocytes (T-Cells) that recognizes and binds to small Protein fragments (Peptides) of Antigens bound to the Major Histocompatibility Complex. See Chimeric Antigen Receptor (CAR), CART-Cell, Immuno-oncology, T-Cell.

Teaching Away: one of the Secondary Considerations of non-obviousness addressing evidence tending to show that the prior art suggests that the patented subject matter will not work and/or that criticizes, discredits or discourages the Patent's approach to solving a problem, which can be used to show non-obviousness.

Technology Transfer: the process of transferring technologies, methods, skills, knowledge and other fruits of scientific research from one party to another party.

Telomerase: also known as terminal transferase (TT), is a reverse transcriptase Enzyme that adds Nucleotides to the end of Telomeres, thus offsetting the reduction in telomere repeats that occurs during Cell division.

Telomeres: repeating nucleotide sequences at the ends of Chromosomes, which protect the Chromosomes. Over time, with Cell division and Chromosome replication, the number of telomere repeats is reduced.

Territory: in contracts, the geographical region or regions to which the rights granted under the contract apply.

Therapeutic: 1. of or relating to the branch of medicine concerned with the treatment of disease. 2. of or relating to the treatment of disease 3. (noun) something that has a therapeutic effect, such as a drug, a treatment or an exercise.

Therapeutic Goods Administration (TGA): the Australian equivalent to the U.S. FDA.

ThirdParty Administrator (TPA): a person or organization which processes claims and provides other administrative services, such as premium collection and enrollment, on behalf of a self-insured employee benefit plan or insurance company. Use of a TPA could be viewed as outsourcing claims processing responsibilities.

Third-Party Payor: any organization or entity that pays for, or otherwise insures, health or medical expenses on behalf of individuals, typically referred to as beneficiaries or recipients. Examples of Third-Party Payors include Medicare, Medicaid, TRICARE, and commercial insurance companies.

Toxicology: the study of the adverse effects of chemicals on living organisms, particularly the detection, observation and treatment of poisons in humans.

Trade Secret: any information that is not widely known or easily ascertainable, conveys a competitive economic advantage to a business and is subject to efforts by that business to maintain the secrecy of such information. Trade Secrets are a form of Intellectual Property. They cannot be registered, but instead must be protected by maintaining their secrecy and relying on contracts such as Non Competes and Non-Disclosure Agreements.

Trademark: one or more words, symbols or combination thereof used to identify the source of goods and distinguish the same from other sources. Trademarks are considered a form of Intellectual Property and are associated with certain exclusive rights. Depending on jurisdiction, Trademark rights can arise from registration and/or use.

Transcription: the process by which information in a strand of DNA is copied into a complementary strand of Messenger RNA (mRNA). Transcription is carried out by an RNA polymerase Enzyme and certain accessory Proteins known as transcription factors.

Transdermal: relating to applying a medicine or Drug through the skin into the bloodstream. A nicotine patch is an example of product that uses transdermal drug delivery.

Transfer RNA (tRNA): encompasses several forms of RNA of low molecular weight that transport specific Amino Acids to ribosomes for protein synthesis.

Translation: process where a sequence of an amino acid sequence (a polypeptide, which folds into a Protein) is synthesized from information contained in a Molecule of Messenger RNA (mRNA). The sequence of mRNA translates to the corresponding amino acid sequence it encodes.

Translational Research: the process of applying findings from basic science into medical practice to generate meaningful health outcomes.

Transparenzkodex Freiwillige Selbstkontrolle für die Arzneimittelindustrie e. V. (FSA) (Germany): codex which sets out rules governing the voluntary self-control for pharmaceutical companies.

Treble Damages: a term appearing in certain statutes, including the FCA, permitting a court to award triple the amount of actual damages to the prevailing plaintiff (*e.g.*, the United States in an FCA case). Patent infringement cases also allow for Treble Damages, and a recent Supreme Court case will likely increase their award. In *Halo Electronics, Inc. v. Pulse Electronics, Inc.*, No. 14-1513 (S. Ct. June 13, 2016), the Supreme Court overturned a three-part test that courts previously used to determine whether to award Treble Damages. Instead, the Court explained that judges must be given discretion when deciding whether to award Treble Damages, but also cautioned that "such punishment should generally be reserved for egregious cases typified by willful misconduct." Id.

TRICARE Retail Pharmacy Program: a comprehensive pharmacy benefit for eligible uniformed services beneficiaries. TRICARE beneficiaries may have Prescriptions filled at military treatment facilities, through a TRICARE mail order pharmacy, at a TRICARE retail network pharmacy or at non-network pharmacies. TRICARE's program utilizes a three-tier Formulary, updated quarterly, and requires Prescriptions to be filled with a generic Pharmaceutical if one is available.

TrOOP Costs: acronym for True Out-of-Pocket Costs.

True Out-of-Pocket Costs: the payments that count toward a Beneficiary's Medicare drug plan out-of-pocket threshold, which determine when the Beneficiary's catastrophic Coverage begins. Payments included in TrOOP Costs include the amount a person pays for covered Prescriptions before his or her drug plan begins to pay; the amount a person pays for each covered Prescription after his or her drug plan begins to pay; and any payments a person makes for a covered Prescription Drug during his or her plan's coverage gap, if the plan has a coverage gap.

Type A Meeting: one of three types of meetings that may occur between sponsors or applicants and FDA staff regarding the Development and review of Investigational New Drugs and Biologics and related marketing applications. A Type A Meeting is a meeting necessary to help an otherwise stalled product development program proceed.

Type B Meeting: one of three types of meetings that may occur between sponsors or applicants and FDA staff regarding the Development and review of Investigational New Drugs and Biologics and related marketing applications. Type B Meetings include Pre-IND Meetings, certain End-of-Phase I meetings, End-of-Phase II / pre-phase III meetings and Pre-NDA or Pre-BLA Meetings.

Type C Meeting: one of three types of meetings that may occur between sponsors or applicants and FDA staff regarding the Development and review of Investigational New Drugs and Biologics and related marketing applications. Type C meetings include any such meetings other than Type A or Type B Meetings.

Ultrasound: 1. a method of viewing internal body images for diagnostic or therapeutic purposes through the use of high frequency sound waves. 2. an image made by using an ultrasound.

Unexpected Serious Adverse Reaction (USAR): is defined by the Clinical Trials Regulation as any untoward medical occurrence in a subject to whom a medicinal product is administered and which does not necessarily have a causal relationship with this treatment. Reference: Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on Clinical Trials on medicinal products for human use, and repealing Directive 2001/20/EC.

United States Patent and Trademark Office (USPTO): the entity which grants US Patents and registers Trademarks.

Unsolicited Request for Off-Label Information: a request made to the Manufacturer or distributor of a Drug or Device for information regarding off-label use of that product initiated by persons or entities that are completely independent of the Manufacturer or distributor. Requests that a Manufacturer or its representative prompts in any

way are not unsolicited requests. FDA guidance provides a Safe Harbor from Off-Label Promotion enforcement in certain cases when the Manufacturer or distributor is providing off-label information in response to an unsolicited request.

Upcoding: a type of fraud that occurs when a Provider submits codes for Reimbursement for services that are more serious and more expensive than the services the Provider actually performed.

Upstream Processing: in cell manufacturing, a process starting from isolating a desired Cell to cultivating its growth to cell culture expansion through to the collection of the cell culture.

Urology: the branch of medicine that studies the urinary tract and urogenital system.

U.S. Food and Drug Administration (FDA): the US governmental agency responsible for protecting the public health by assuring the safety, effectiveness, quality and security of human and veterinary Drugs, Medical Devices, Vaccines and other Biological Products (Biologics). The FDA also regulates tobacco products and is responsible for the safety and security of most of the US food supply, all cosmetics, dietary supplements and products that give off radiation.

Use of Proceeds: how a party intends to utilize the money obtained from investors and business activities. Potential investors will want to know how their funds will be allocated before investing.

Vaccine: a substance used to confer immunity to a particular disease by stimulating production of the body's own Antibodies or defenses against such disease. Often Vaccines contain dead or weakened portions of the agent causing the disease.

Vaccine Technology: using Synthetic DNA as a code for a pathogen instead of weakened or killed Viruses which have traditionally been used in Vaccines. DNA Vaccines can be made much more quickly, cheaply, and hopefully safely than by conventional methods.

Valid Claim: in reference to a Patent, a pending, issued or unexpired claim that has not been irrevocably abandoned or declared invalid in an unappealable decision. When used as a defined term in an agreement, the specific definition of Valid Claim may define a maximum time period during which pending claims count as a Valid Claim.

Vascular: relating to vessels of the body that carry bodily fluids, particularly blood vessels such as the veins and arteries.

Vector: a vehicle, such as a Plasmid or a Virus, capable of delivering foreign genetic material into another Cell, where such genetic material can be replicated and expressed.

Virology: the study of Viruses.

Virus: an infectious agent capable of replication only within a living host Cell, essentially comprised of a nucleic acid in a protein coat.

Voluntary Disclosure: healthcare Providers, Suppliers or other individuals or entities potentially subject to civil penalties may voluntarily disclose self-discovered evidence of potential fraud to the Office of Inspector General (OIG). Entities may similarly disclose self-discovered potential violations of the physician self-referral statute — the Stark Law — to CMS. Self-disclosure can enable Providers to avoid the costs and disturbances typically associated with a government investigation. Providers who do elect to voluntarily disclose potential fraud to the OIG must follow the Provider Self-Disclosure Protocol — OIG's official process for healthcare Providers to voluntarily identify, disclose and resolve instances of potential fraud. Providers voluntarily disclosing information related to actual or potential violations of the Stark Law must follow CMS's Self-Referral Disclosure Protocol.

Wholesale Distributor: anyone engaged in wholesale distribution of Prescription Drugs or Devices, including, but not limited to, Manufacturers; repackers; own-label distributors; private-label distributors; jobbers; brokers; warehouses, including Manufacturers' and distributors' warehouses, chain drug warehouses, and wholesale drug warehouses; independent wholesale drug traders; and retail pharmacies that conduct wholesale distributions.

Working Cell Bank: derived from Cells from a Master Cell Bank, a culture of Cells intended for use in preparing production cell cultures.

Written Description: a requirement for patentability. To satisfy Written Description, a Patent specification must describe the claimed Invention in sufficient detail to show one skilled in the art that the inventor possessed the claimed Invention. 35 U.S.C. § 112(a).

Yates Memo: named after author Deputy Attorney General Sally Yates, the memo formally titled "Individual Accountability for Corporate Wrongdoing" emphasized the Department of Justice's focus on holding individual corporate executives accountable for corporate wrongdoing. The memo set forth six steps to reinforce the Department of Justice's pursuit of individual wrongdoing.

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