Pharmaceutical Industry Research Credit Audit Technique Guide

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The taxpayer names and addresses shown in this publication are hypothetical.

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I. Overview

A. Background / History

(1) The credit for increasing research activities (research credit) available to companies can be challenging from an examination perspective due to practices unique to the pharmaceutical industry, highly technical audit issues, distinguishing between product innovation versus product development, and differentiating between product development and/or process development. This Audit Technique Guide (ATG) discusses some of the areas of focus within the pharmaceutical industry. Throughout the document the term “drug” is used to refer to chemically synthesized drugs, therapeutic biological products, combination products, and/or medical products with a drug component.

A.1. Purpose of the Pharmaceutical ATG

(1) This document provides audit technique guidelines for the IRS examiner reviewing the credit for increasing research activities reported by taxpayers in the pharmaceutical industry. These guidelines also provide helpful information to industry taxpayers. This document is not legally binding and should not be relied upon as such. This document is also not designed to remove the examiner’s discretion to vary audit techniques or procedures as appropriate for any given examination. Rather, it is designed to reduce burden for all stakeholders by: (1) providing for the examiner an overview of the drug development process in pharmaceutical companies (Overview of Drug Development Process); (2) identifying examination techniques that would be helpful to the audit (Examination Techniques); and (3) describing example activities and their relative level of risk (Risking of Activities). This ATG is not intended to address all potential research credit issues (refer to the Audit Techniques Guide: Credit for Increasing Research Activities (i.e., Research Tax Credit) IRC 41).

(2) These guidelines are not an official pronouncement of the law or the Service’s position and cannot be used, cited, or relied upon as such. Nothing in this document precludes an examiner from using alternative audit techniques or from proposing any proper adjustment, even if the adjustment arises from an activity that would not normally be audited if the examiner had applied the guidelines in this paper.

(3) Understanding the drug development process and related audit risks when analyzing the business activities and the respective business components can minimize audit burden. A thorough understanding of the taxpayer’s business and methodology used to identify and gather the Qualified Research Expenses (QREs) reported for the credit is critical in validating the amount reported. As with any taxpayer reporting the research credit, identification of the business components is imperative within the pharmaceutical industry.

A.2. Pharmaceutical Industry Overview

(1) The pharmaceutical industry consists of drug manufacturers, biotechnology companies, and the distribution and wholesale companies that handle the products/drugs and medications produced. This industry is primarily focused on chemical compounds (small-molecule drugs based on chemical synthesis) and biological compounds (large-molecule drugs based on living cell lines).

(2) The Food and Drug Administration (FDA) is the federal agency responsible for protecting the public health by ensuring the safety, efficacy, and security of products (i.e., drugs, biological products, medical devices) through control and supervision of various industries.

A.3. Overview of Drug Development Process

(1) The pharmaceutical product development process is composed of the following five stages:

- Discovery and Development: Basic laboratory research to identify potential drug candidates.
- Pre-Clinical Research: Drug candidates undergo testing in the laboratory (in vitro studies) and in animals (in vivo studies) to understand safety.
- Clinical Research: Drugs are tested on humans to assure that they are safe and effective.
- FDA Drug Review: Data collected from the pre-clinical and clinical research submitted to the FDA for marketing and sales approval in the United States.
- FDA Post-Market Drug Safety Monitoring: Once the drug is approved for marketing and sale, the FDA conducts surveillance and collects data to assure continued safety.

(2) The drug development process is often non-linear. The drug products may need further development/research after the data is reviewed. For example, a taxpayer can be in the clinical research stage with a drug product and discover an adverse reaction to the drug in the human population. The company may need to take the drug back to the pre-clinical animal models or another stage.

A.4. Drug Development Process Stages

(1) **Discovery and Development** - During the discovery and development phase, researchers identify or “discover” a specific molecule that plays a crucial role in producing therapeutic effects for a disease. Researchers test many different compounds to determine which compound(s) might stop or reverse the effects of a particular disease. The researchers may be testing many compounds with

the hope of identifying a potential drug candidate. The researchers could be generating computer models/using artificial intelligence, conducting laboratory (in vitro) experiments, and/or conducting other research to assess the viability of the compound. The results of the experiments are reviewed by various researchers who may recommend that the compound be moved forward as a potential new drug product.

(2) **Pre-Clinical Research** - The potential new drug is tested in-vitro (somewhere outside of a living organism such as a test tube in the laboratory) and in-vivo (inside a living organism). After the researchers review the in-vitro, in-vivo studies, and associated data, the researchers make recommendations about the potential new drug. The new drug cannot be tested in humans until it successfully navigates through pre-clinical research.

(3) **Clinical Research** - After the FDA approves the Investigational New Drug (IND) application, the clinical trial research can begin in human participants.

- Phase 1 studies are conducted in small numbers (i.e., typically 20 to 100) healthy human participants (except for oncology studies and certain other conditions/diseases which may utilize human participants with those conditions/diseases even for the phase 1 testing). These studies are typically a few months in duration and many drugs move to the next phase. The main purpose of Phase 1 studies is to understand the drug's safety and safe dosage range.
- Phase 2 studies are conducted in a moderate number (i.e., typically a few dozen to about 300) of human participants with the condition/disease. These studies can last from several months to several years. Per the FDA website, approximately one third of the drugs move to the next phase. The main purpose of these clinical trials is to determine efficacy, optimal dosage, and to further evaluate safety and side effects.
- Phase 3 studies are conducted in a large number (i.e., several hundred to a few thousand) of human participants with the condition/disease. These studies can last a year to several years. There are typically more clinical trial sites in Phase 3 studies to include a broad and diverse representative study population. The main purpose of Phase 3 studies is to confirm efficacy, safety and monitor for adverse reactions. Once a Phase 3 study is completed, a pharmaceutical company can submit a New Drug Application (NDA) or Biologic License Application (BLA) to the FDA requesting FDA approval to market the drug. This application contains all the data collected throughout the clinical trial phases. Per the FDA website, approximately one third to one fourth of the drugs received FDA approval at this stage.
- Phase 4 studies are conducted in an extremely large number (i.e., several thousand) of human participants with the condition/disease. These studies are conducted after the drug has received FDA approval. In addition, these studies determine long-term safety and effectiveness of the drug

and identify any adverse effects that may not have been observed in prior clinical trials. The Phase 4 studies can continue for years, and based on the outcome, the drug manufacturer may file supplemental NDAs seeking additional indications for the drug product.

(4) **FDA Review** - The FDA reviews the data collected during the pre-clinical and clinical trial process to determine if the drug should be marketed and offered for sale in the United States. After thorough review and examination by the FDA team, the FDA decides whether to approve the drug and communicates this to the pharmaceutical company.

(5) **FDA Post-Market Safety Monitoring** - If the FDA approves the drug for marketing and sale in the United States, the pharmaceutical companies need to continue to collect data on the long-term safety and efficacy of the drug product. The post-marketing safety surveillance program is designed to detect serious and unexpected adverse events. These reported events are reviewed by the FDA on an ongoing basis and the FDA acts when warranted. The pharmaceutical company is required to submit periodic safety updates at regular intervals to the FDA.

(6) When examining the different drug development stages, examiners should ensure that the taxpayer is identifying the Qualified Research Activities (QRAs) by business component. A business component means any product, process, computer software, technique, formula, or invention. See IRC (41(d)(2)(B) and the Risking of Activities section).

A.5. FDA Application Types Used by the Pharmaceutical Industry

(1) There are five main types of drug applications that pharmaceutical companies submit to the FDA for review:

- Investigational New Drug (IND)
- New Drug Application (NDA)
- Biologic License Application (BLA)
- Abbreviated New Drug Application (ANDA)
- Over the Counter (OTC)

(2) Each drug must be approved by the FDA prior to marketing and sale within the United States.

(3) The IND is typically the initial application made by a pharmaceutical company to the FDA. The IND review verifies that the proposed research does not place human participants at unreasonable risk of harm and that there is an adequate process of informed consent for human research participants.

(4) Once data is compiled from pre-clinical and clinical research, the pharmaceutical company submits either an NDA or BLA to the FDA for review

and determination if the drug is approved for marketing and sale in the United States.

(5) An NDA and a BLA are both requests to market and sell a new drug in the United States. An NDA relates to a chemically derived small molecule drug whereas a BLA, as the name implies, relates to a biologic derived from living organisms.

(6) NDA and BLA products are relatively similar in nature from the standpoint of pharmaceutical development. NDAs and BLAs differ in terms of application content, submission requirements, and approval criteria. The NDA and BLA submissions must contain data demonstrating the safety of the new drug or biologic and substantial evidence establishing the effectiveness/potency for the intended use.

(7) Generic drugs are approved using the ANDA application process. One major difference between the ANDA and an NDA/BLA submission is that the ANDA applicant must show that the generic drug has the same active ingredients (whereas the inactive ingredients do not have to be identical) and is technically equivalent to an already FDA-approved brand name drug. The FDA approval of the ANDA is effective after certain procedural requirements are complete. If successful, the generic drug is presumed safe and effective based on bioequivalence studies. Additional clinical studies to establish safety and efficacy do not need to be performed.

(8) There are two pathways to bring non-prescription drugs to market. One pathway is the drug application process which can follow either the NDA or ANDA application process. The second pathway is the Over the Counter (OTC) Drug Review (monograph process).

(9) The drug manufacturer must substantiate to the IRS examiner that the research activities performed in the development of the drug is not excluded activities under IRC 41(d)(4).

B. Relevant Terms

(1) Abbreviated New Drug Application (ANDA): The generic drug applications are abbreviated because the applicant is generally not required to perform animal experiments or conduct human clinical trials to establish safety or efficacy. The generic drug applicant must demonstrate that their drug performs the same as the equivalent branded/innovator product.

(2) Adverse Event (AE): An unexpected medical occurrence associated with the use of a drug in humans regardless of whether the occurrence was related to the drug.

(3) Bioequivalence Studies: Research comparing two or more formulations of an active ingredient contained in a drug to determine if the clinical effect is similar when administered to a human participant.

(4) Biologics License Applications (BLA): A biological product is isolated/derived from natural sources such as, but not limited to, human, animal, and microorganisms. The BLA application process is like the NDA process, but the products are fundamentally different. Also, NDAs and BLAs differ in terms of application content, submission requirements, and approval criteria.

(5) Branded/Innovator Drug: A branded, or innovator drug is originally discovered and developed by a pharmaceutical company. Currently, the term of a new patent is 20 years from the date on which the application for the patent is filed in the United States. Once the drug is approved for marketing and sale, it can be sold without any other entity violating its patent for the full duration of the patent. Generally, generic drugs may not enter the United States market until after the brand name patent expires. There are, however, some circumstances where generic drug approval can become effective before the brand name patent expires.

(6) Generic drug: A drug that is comparable to a branded/innovator drug product in dosage, form, strength, route of administration, quality, performance characteristics, and intended use. The active ingredient is the same, but the inert material making up the drug might be different.

(7) Health Economics Outcomes Research (HEOR): “Health Economics” measures the value of the drug product. “Outcomes Research” evaluates the effect of the drug on patients in a real-world setting. Health Economics and Outcomes Research measures the link between treatments and outcomes.

(8) Investigational New Drug (IND): Typically, the initial application made by pharmaceutical companies to the FDA. The IND review verifies that the proposed research does not place human participants at unreasonable risk of harm and includes an adequate process of informed consent of human participants. The FDA reviews the IND submission to assure that there are adequate protections for human participants in the clinical trials.

(9) New Drug Application (NDA): The formal submission of the collected pre-clinical and clinical trial data to the FDA for review. The data gathered from the animal models during the pre-clinical phase is submitted along with the clinical trial data to the FDA for review. The NDA application is submitted to the FDA for review of a new drug for sale and marketing in the United States.

(10) Over the Counter (OTC): Medicines sold directly to a consumer without the requirement for a prescription from a health care professional.

(11) OTC Monograph: Defines the active substance, and related conditions (dosage, directions of use, labeling and testing for non-prescription drug products) in a therapeutic area that is recognized as safe and effective under section 505G of the Federal Food, Drug and Cosmetic Act. FDA has authority to change the conditions required for a drug to be recognized as safe and effective. Non-prescription drugs conforming to an OTC monograph are not required to be individually reviewed and approved by the FDA before U.S. marketing.

(12) Pharmacokinetics (PK): The drug's journey throughout a living organism. Absorption is how the drug moves from the administration site to the site of action. Distribution is how the drug moves throughout the bloodstream to various parts of the living organism. Metabolism is the process of breaking down the drug. Excretion is how the drug is removed from the living organism.

(13) Serious Adverse Event (SAE): An adverse event associated with the use of a drug in a patient that meets the serious criteria and must be reported to the FDA. Per the FDA, the serious criteria include death, life-threatening, initial, or prolonged hospitalization, disability or permanent damage, congenital anomaly, or birth defect, required intervention to prevent permanent impairment or damage (devices) or other serious important medical events.

C. Law / Authority

(1) For a deeper understanding of the law related to the IRC 41 research credit, refer to the Audit Techniques Guide: Credit for Increasing Research Activities (i.e., Research Tax Credit) IRC 41.

(2) IRC 41(d)(2)(B) defines a business component as any product, process, computer software, technique, formula, or invention which is to be held for sale, lease, or license, or used by the taxpayer in a trade of business of the taxpayer.

(3) IRC 41(d)(4)(A) provides that any research conducted after the beginning of commercial production of the business component is not qualified research under IRC 41(d)(1).

(4) IRC 41(d)(4)(C) states that any research related to the reproduction of an existing business component (in whole or in part) from a physical examination of the business component itself or from plans, blueprints, detailed specifications, or publicly available information with respect to such business component is not considered qualified research for purposes of IRC 41(d)(1).

(5) IRC 41(d)(4)(F) defines foreign research as any research conducted outside the United States, the Commonwealth of Puerto Rico, or any possession of the United States.

(6) IRC 41(d)(4)(H) & Treas. Reg. § 1.41-4(c)(9) with cross reference to § 1.41-4A(d) defines funded research as any research to the extent funded by any grant, contract, or otherwise by another person or governmental entity.

(7) Treas. Reg.1.41-4(c)(2)(iv) provides a special rule for clinical testing. Clinical testing of a pharmaceutical product prior to its commercial production in the United States is not treated as occurring after the beginning of commercial production even if the product is commercially available in other countries. Additional clinical testing of a pharmaceutical product after a product has been approved for a specific therapeutic use by the Food and Drug Administration and is ready for commercial production and sale is not treated as occurring after the beginning of commercial production if such clinical testing is undertaken to establish new functional uses, characteristics, indications, combinations,

dosages, or delivery forms for the product. A functional use, characteristic, indication, combination, dosage, or delivery form shall be considered new only if such functional use, characteristic, indication, combination, dosage, or delivery form must be approved by the Food and Drug Administration.

(8) In the pharmaceutical area, expenditures for quality control, ordinary testing or inspection of materials or products for quality control should not be included in either the IRC 174 expenditures or the IRC 41 credit computation. Although the costs of obtaining a patent are considered research and experimental expenditures under IRC 174, these costs should not be included in the IRC 41 credit computation because these activities do not meet the requirements of qualified research.

D. Examination Techniques

(1) Initial Planning Activities

- Determine if the pharmaceutical company is a manufacturer of branded/innovator products, generic products, and/or OTC products by reviewing the taxpayer's website, Form 10-K, annual reports, or other public sources.
- Obtain an overview and understanding of the company's worldwide research organization.
- Gain an understanding of taxpayer's mergers, acquisitions, and dispositions for the audit period.
- Identify the legal entities that performed research activities.

(2) Execution – Requesting Information/Initial Review

- Request the accounting, financial, policy manuals or other documents describing the company's procedures or methodologies used to identify research business components and expenses.
- Determine if the taxpayer has any collaboration agreements, licensing agreements, cost sharing agreements, relationships with universities/academic research centers, and/or partnerships, etc. Request copies of applicable agreements.
- Determine qualified research business components for purposes of reporting the IRC 41 research tax credit and to capture the associated research expenses as they attach to each business component claimed by the taxpayer.
- Solicit an explanation of the process by which the taxpayer tracks research and development business components, how they are identified, and how budgets are approved.
- Review taxpayer-provided research credit studies or relevant research credit workpapers and support, such as engagement letters,

contracts/purchase orders, business component data, and any other public sources. Although a well-prepared research credit study may offer some probative value, it is highly unlikely that a research credit study alone will substantiate a claimed research credit.

- Determine the locations of the patients in clinical trials to exclude the expenses connected to patients located outside of the United States, the Commonwealth of Puerto Rico, or any possession the United States. See IRC 41(d)(4)(F) for a definition of foreign research, which is not considered qualified research.
- Identify and review each business component and understand the research being conducted.
- Request a list of applicable patents and/or pending patent applications for the years under examination. Review listing provided as it relates to business components identified and reported for the credit.
- For business components in the clinical research stage, determine if the business component is for a branded/innovator, generic, or OTC drug product. Both generic and OTC drugs are higher risk if they utilize an ANDA application for submission to the FDA.
- Identify the third-party R&E service providers, funding entities, and the parties that own the risk and rights to the results of any qualified research.
- Request a walkthrough of taxpayer's underlying support, such as workpapers and methodology, to understand amounts reported on the research credit line of the tax return.
- See Audit Techniques Guide: Credit for Increasing Research Activities (i.e., Research Tax Credit) IRC 41 for further details about the funded research exclusion and audit steps.

(3) Execution of Issue-Specific Examination – Business Components Established

- Examine expenses associated with each business component and determine if the activities reported satisfy both the requirements for qualified research activities (QRAs) under 41(d) and Treas. Reg. 1.41-4 and the qualified research expense (QRE) requirements of 41(b) and Treas. Reg. 1.41-2.
- Review the wages contained within each business component and determine what activities the employees performed for the years under examination. Employee titles, departments, resumes, and job descriptions are informative, but the activities need to be assessed to determine if the employee is performing qualified research. Full year employee wages should not be duplicated for employees changing positions during the year.

- Conduct interviews to understand the research activities that the company performed during the tax years under examination.
- Request a tour of the various facilities and/or a physical layout of the relevant R&E departments/buildings. This can help the examiner generally understand where the research is being performed, who is doing the research, who is supervising the research, and which researchers work in and around the laboratories.
- Determine if the taxpayer is reporting research credit on Form 6765 along with the Orphan Drug Credit (See Audit Techniques Guide: Credit for Increasing Research Activities (i.e., Research Tax Credit) IRC 41 for details on the Orphan Drug Credit) on Form 8820. Review the QREs to ensure that the taxpayer did not double count expenses by also reporting current qualified clinical testing expenses.
- Closely review QREs from activities supporting FDA submission activities or post marketing activities. These activities do not involve qualified research and do not directly support qualified research unless they meet Treas. Reg. 1.41-4(c)(2)(iv) requirements.
- Review the QREs to ensure that the FDA application user fees (i.e., Prescription Drug User Fee Act (PDUFA), Medical Drug User Fee Amendment (MDUFA), etc.) are not included since they are not qualified expenses.
- Generic drug activities and expenses require additional review by the examiner to validate that the activities undertaken qualify for the research credit as opposed to the products approved through the NDA/BLA applications.

E. Documentation that Might Be Helpful

(1) Following is a list of suggested documentation that the exam team may request:

- Tax Workpapers – Request the tax workpapers and other supporting documentation used to calculate the credit. This information should be requested in electronic format with formulas as this will expedite the review and analysis.
- Qualified Wages – Request a reconciled listing of all employees' wages included in the research credit. The listing should include the employee's full name, job title, the cost center/department, and business component to which the employee was assigned.
- Qualified Supplies – Request a reconciled summary of the supplies included in the research credit. This reconciliation should identify the business component(s) to which the supplies were allocable.

- Contract Research – Request a reconciled summary of the contract research expenses included in the credit. The summary should identify the contractors, the payments to each contractor, the type of research performed, the objective of the research, and the business component(s) to which the contract research expenses were allocable.
- Organizational Chart – Request an organizational chart for the R&E department employees with wages included in the calculation of the research credit calculation to get an understanding of the reporting hierarchy.
- Job Titles, Grade Levels and Position Descriptions – Request a summary of the company's job titles, position descriptions, and grade levels within the R&E departments for each employee with wages included in the research credit calculation. This information is not the deciding factor in determining who is performing research or who is supervising the research. However, it will provide the examiner with a basic understanding of how the company is organized from a managerial and reporting structure standpoint and will help eliminate those employees that likely qualify for the credit and focus the audit to those employees that may require further examination.
- Location of participants in clinical trials – Request a patient enrollment report by country for each clinical trial. Request information on how the wages, supplies, and contract research expenses were allocated between research expenses incurred both inside and outside of the United States.

F. Risking of Activities

(1) The intention in providing examples of low, medium, and high-risk activities in the pharmaceutical drug development industry is to aid in risk analysis and to help focus audit resources. The assigned risk level of the activities does not guarantee qualification or disqualification.

- Low risk means it is likely that the activities are qualified research under IRC 41(d)(1) or qualified services under IRC 41(b). However, there may be other substantive issues to consider, such as the inclusion of high-level manager wages in qualified services and exclusions under IRC 41(d)(4); Treas. Reg. 1.41-4(c).
- Medium risk means it is likely that the activities include some activities that may be qualified research under IRC 41(d)(1) or qualified services under IRC 41(b). Therefore, it is necessary to understand the activities that were conducted and identify the supplies and wages that attach to each business component.
- High risk means it is unlikely that the activities performed are qualified research activities under IRC 41(d)(1), and/or that the associated wages are not qualified services, as defined in IRC 41(b).

(2) The activities are further divided into the five general stages of the drug development process; however, the activity can occur at other stages. This is not an all-inclusive list. As drug development procedures can differ between companies, a taxpayer may perform activities not listed in this guide. The examiner may investigate any of the reported research activities and risk them accordingly.

F.1. Low Risk Activities

(1) Discovery and Development

- Identify and screen new compounds in the laboratory, use of computer simulations, or other methods of compound identification.
- Modify and restructure compounds.
- Model the toxicology and safety data in compounds prior to testing them in animal models.

(2) Pre-Clinical Research

- Develop the formulation of compounds for animal studies.
- Test the new compound in experiments using animal models.
- Determine preliminary drug product safety.
- Determine the new compound's absorption, distribution, metabolism, and elimination (ADME) rates in the animal models or other laboratory methods.
- Develop analytical methods to confirm that the dosages of the compound are consistent.
- Scientific analysis of the animal model data.
- Establish the compound's purity, stability, and shelf life.

(3) Clinical Research

- Develop Phase 1 and Phase 2 human clinical trial protocols.
- Determine safety, tolerance, and pharmacokinetics for Phase 1 clinical trials.
- Develop manufacturing steps of the drug products after the initial data is reviewed at the laboratory scale.
- Evaluate effectiveness, dosage, and safety of compound in Phase 2 clinical trials.
- Scientific analysis of the clinical Phase 1 and Phase 2 trial data.

- Maintain the testing specifications for the drug being developed.

F.2. Medium Risk Activities

(1) Discovery and Development

- Develop and implement information technology programs for the purpose of enhancing research capabilities.

(2) Clinical Research

- Development of Phase 3 human clinical trial protocols.
- Verify dosage, effectiveness for targeted indications, and understand safety and adverse events in Phase 3 clinical trials.
- Determine the shelf life of the drug product.
- Scientific analysis of the Phase 3 clinical trial data.
- Customer complaint investigation, resolution, and corrective action for drug products from participants in clinical trials.
- Develop a commercially available drug for a new functional use, characteristic, indication, combination, dosage, or delivery form that must be approved by the FDA.

(3) FDA Review

- Develop a manufacturing process from the laboratory scale to a scale that is commercially feasible.

F.3. High Risk Activities

(1) Discovery and Development

- Quality control and/or inspection of raw materials in the clinical laboratory.
- Participate in scientific review committees.
- Provide technical guidance, strategic product development, and determine the need for future clinical trials/research.
- Preventative maintenance, calibration, and inspection of laboratory equipment.
- Equipment qualification (Installation Qualification (IQ), Operational Qualification (OQ), and Performance Qualification (PQ))
- Facility costs for environmental health and safety.

(2) Pre-Clinical Research

- Stability testing of the drug to determine shelf life and storage conditions of drug products.
- Quality control/inspection of drug for use in animal testing.
- Continuous process improvements and maintenance.

(3) Clinical Research

- Quality control and/or inspection of drug for use in human clinical trials.
- Development of Phase 4, Post Marketing Observational Studies (PMOS) human clinical trial protocols.
- Package, label, assemble, and shipment of the clinical drugs.
- Scientific analysis of data for Phase 4, PMOS human clinical trials.
- Scientific literature searches, competitive market data analysis, and/or general scientific research.
- Develop, maintain, and train employees on standard operating procedures.
- Conduct audits of clinical trial sites to assure compliance with regulatory authorities.
- Negotiate contracts with vendors/supplies.
- Collaboration agreements, strategic alliances, licensing agreements, cost sharing agreements, etc., with another party.
- Funded research (i.e., research that is funded by a grant, contract, another party, or government entity).
- Payment of upfront fees, technology access fees, milestone payments, and royalties.
- Research conducted outside of the United States, the Commonwealth of Puerto Rico, or any possession of the United States.

(4) FDA Review

- Review and compile forms/documents for submission to the FDA.
- Test of scaled-up formulations of drug transferred to a commercial production facility and tested at commercial scale.
- Design/retool or construction of a production facility to manufacture commercial drug product.
- Draft, review, and compile Clinical Study Reports (CSRs) for submission to the FDA.
- Liaison between the pharmaceutical company and the regulatory authorities.

- Provide guidance on new regulatory procedures such as FDA guidance documents or other regulatory guidance.
- Develop regulatory strategies.
- FDA application user fees (i.e., PDUFA, MDUFA, etc.)

(5) FDA Post-market Safety Monitoring (commercially available drug products)

- Quality control/inspection of commercial drug for distribution.
- Research studying patient quality of life, marketing related activities, marketing claims, and/or cost effectiveness of a drug to treat a particular condition.
- Commercial scale manufacturing of a drug product.
- Author of manuscripts, publications, etc.
- Library purchases and maintenance costs.
- Monitor and report serious adverse events (SAEs) to the FDA through routine medical safety surveillance.
- Advertisements, marketing materials, consumer surveys, and/or promotional activities.
- Interact with leaders and academics in various scientific fields and therapeutic areas to identify key opinion leaders.
- Customer compliant investigation from the public taking commercially available drug product, resolution, and corrective action.
- Gather scientific data and communicate with external and internal teams through standard response documents, presentations, and publications.
- Answer health care providers (HCPs) questions about clinical trial data and drug information.
- Facilitate practical and lawful communication between pharmaceutical companies and HCPs (i.e., off-label usage of a drug product, information on publications, safety, real-world application, etc.).
- Quality of life patient assessments/Patient Reported Outcomes (PROs)
- Market access, pricing, reimbursement from payers, policy, patient advocacy, and/or real-world evidence.

G. Additional Information Resources

(1) Research Credit Internal Revenue Service (irs.gov)