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Review Article

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Regulatory and Quality Compliance of Oncology Products – A Global perspective

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Abstract

The development and manufacturing of oncology products pose unique challenges in ensuring both regulatory compliance and high-quality standards. Oncology products, often complex biopharmaceuticals, play a critical role in cancer treatment, necessitating stringent oversight to safeguard patient safety and therapeutic efficacy. This abstract provides an overview of the key considerations in regulatory and quality compliance within the context of oncology product development.

Regulatory agencies worldwide, such as the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and others, have established comprehensive guidelines specific to oncology product development. These guidelines address various stages, from preclinical studies to clinical trials and market approval. Robust regulatory strategies, including well-designed clinical trial protocols and effective interactions with regulatory authorities, are essential to navigate the complex regulatory landscape.

The manufacturing of oncology products demands adherence to strict quality standards to ensure product consistency, safety, and efficacy. Good Manufacturing Practice (GMP) regulations set forth by regulatory agencies require manufacturers to implement and maintain quality systems throughout the entire production process. Quality control measures, including rigorous analytical testing, process validation, and aseptic processing, are crucial components in achieving and maintaining compliance. Oncology products often have unique safety profiles, and risk management plays a pivotal role in regulatory and quality compliance. Comprehensive risk assessments, including identification and mitigation strategies for potential risks, are integral components of regulatory submissions. Post-marketing surveillance and pharmacovigilance programs contribute to ongoing risk assessment and management.

Ensuring regulatory and quality compliance in the development and manufacturing of oncology products is essential for bringing safe and effective therapies to patients. A thorough understanding of regulatory guidelines, implementation of robust quality systems, and proactive risk management strategies are critical elements in navigating the dynamic landscape of oncology product development.

Keywords: Oncology, USFDA, EMA, GMP, Post-marketing Surveillance, Pharmacovigilance

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1. Introduction

Objective

The focus of the study undertaken was to develop the specific guidance for manufacturing of oncology drugs. There are no specific guidelines for production or bio study or bio waiver of oncology drugs. To study the guidelines of regulatory authorities like USFDA and EMA for biostudy and biowaiver for oncology drugs. Briefing out the specific points from guidelines for oncology drug manufacturing.

Oncology

The term oncology means a branch of science that deal with tumours and cancers. The word “onco” means bulk, mass, or tumour while “-logy” means study. Cancer is the name given to a collection of related diseases. In all types of cancer, some of the body’s cells begin to divide without stopping and spread into surrounding tissues. Cancer can start almost anywhere in the human body, which is made up of trillions of cells.

Cancer is a genetic disease that is, it is caused by changes to genes that control the way our cell’s function, especially how they grow and divide. Genetic changes that cause cancer can be inherited from our parents. One important difference is that cancer cells are less specialized than normal cells. That is, whereas normal cells mature into very distinct cell types with specific functions, cancer cells do not. This is one reason that, unlike normal cells, cancer cells continue to divide without stopping. There are over 100 different known cancers that affect humans. Cancers are often described by the body part that they originated in. These types include

Carcinoma, Sarcoma, Lymphoma and Leukaemia, Germ Cell tumour, Blastoma.

The global demand for cancer drugs market was valued at approximately $ 112.90 billion in 2015 and is expected to generate revenue of around $ 161.30 billion by end of 2021, growing at a CAGR of around 7.4 percent between 2016 and 2021. The market is dominated by North America, followed by Europe, Asia and rest of the world. The cancer diagnostics market in Asia is expected to grow at highest rate from 2015 to 2020. The cancer drugs market is segmented on the basis of the different therapeutic segment including immunotherapy, targeted therapy, chemotherapy, hormone therapy and others. The US is by far the leading cancer drugs market by country in North America. This growth is mainly due to the well-developed healthcare infrastructure and the increase in research and development on cancer drugs. Growth in Asia-Pacific market is expected to be driven by increasing tobacco consumption, growing population and increasing disposable income.

Global oncology trend report by IMS states that from 2012 to 2016, 49 new oncology medicines have been launched but these new options are available uniformly in all countries. The United States has access to the most, a total of 41. In Europe, Germany is on the top of the list with 38, followed by the United Kingdom with 37, then Italy (31) and France (28). Oncology drugs are also more widely available in western European countries than their counterparts in eastern Europe. Collectively they are pursuing almost 600 indications, most commonly for non-small cell lung cancer, breast, prostate, ovarian and colorectal cancers. The ten largest oncology companies measured by their current sales of existing cancer drugs collectively have 130 molecules in their late-stage pipelines. Roche's Rituxan, Avastin, and Herceptin take the lead, with $ 21 billion in sales for these three drugs alone. According to The Wire, India is the fourth largest supplier of pharma to the US, with exports worth $ 5.1 billion. The UK is the second largest market for Indian pharma exports, which stood at $ 464 million in 2016. India also exported to other developed markets in 2016, including Australia ($ 220 million), Germany ($ 161 million), France ($ 145 million), Netherlands ($ 143 million), Canada ($ 143 million) and Belgium ($ 125 million).

Costs of oncology therapeutics and supportive care drugs grew to reach $ 107 billion globally in 2015, an increase of 11.5% over 2014 and up from $ 84 billion in 2010, as measure at invoice price levels. These costs are expected to reach $ 150 billion globally. The US accounts for 46% of the global total market for therapeutics, up from 39% in 2011, due in part to a strengthening US Dollar over this time period and more rapid adoption of newer therapies. The pharm emerging markets, comprising 13% of the global total in 2015, increased their medicine costs annually by 15% on average over the years.

The distribution of cancer drugs through hospitals or retail pharmacies varies widely across health systems, and is shifting due to reimbursement changes and expanded use of oral formulations, especially for targeted therapies. The mis of spending on oncology drugs between hospitals and retail channels varies widely across countries reflecting differences in healthcare practice, reimbursement and mix of formulations. In some European markets including Italy, Spain and the UK, costs have shifted to hospital channels over the past five years while in Canada, France and the US costs have increased more rapidly in retail channels.

There are many types of cancer treatment. The types of treatment that you receive will depend on the type of cancer you have and how advanced it is. Some people with cancer will only have one treatment. But most people have a combination of treatments, such as surgery with chemotherapy and/or radiation therapy. When you need treatment for cancer, you have a lot to learn and think about. It is normal to feel overwhelmed and confused. But, talking with your doctor and learning about the types of treatment you may have help you feel more in control. Types of cancer treatments include *surgery, radiation therapy, chemotherapy, immunotherapy, targeted therapy, hormone therapy, stem cell transplant, precision medicine.*

European guidelines on investigation of bioequivalence

This guideline specifies the requirements for the design, conduct, and evaluation of bioequivalence studies for immediate release dosage forms with systemic action.

USFDA guidelines on Bioavailability and Bioequivalence studies for Orally Administered Drug Products - General Considerations.

This guidance is intended to provide recommendations to sponsors and/or applicants planning to include bioavailability and bioequivalence information for orally administered drug products in investigational new drug applications (INDs), new drug applications (NDAs), abbreviated new drug applications (ANDAs), and their supplements. This guidance contains advice on how to meet the BA and BE requirements set forth in part 320 (21 CFR part 320) as they apply to dosage forms intended for oral administrations.

Classification schemes for carcinogenicity based on hazard identification have become outmoded and serve neither science nor society

Classification schemes for carcinogenicity based solely on hazard-identification such as the IARC monograph process and the UN system adopted in the EU have become outmoded. They are based on a concept developed in the 1970s that chemicals could be divided into two classes: carcinogens and non-carcinogens. Categorization in this way places into the same category chemicals and agents with widely differing potencies and modes of action. This is how eating processed meat can fall into the same category as sulphur mustard gas. Approaches based on hazard and risk characterization present an integrated and balanced picture of hazard, dose response and exposure and allow informed risk management decisions to be taken. Because a risk-based decision framework fully considers hazard in the context of dose, potency, and exposure the unintended downsides of a hazard only approach is avoided, e.g., health scares, unnecessary economic costs, loss of beneficial products,

adoption of strategies with greater health costs, and the diversion of public funds into unnecessary research. An initiative to agree upon a standardized, internationally acceptable methodology for carcinogen assessment is needed now. The approach should incorporate principles and concepts of existing international consensus-based frameworks including the WHO IPCS mode of action framework.

A pan-European comparison regarding patient access to cancer drugs.

This report examines whether patients across Europe have equal and early access to new innovative cancer drug therapies and highlights the existence of inequities.

USFDA Guidelines on Cancer Drug and Biological Products – Clinical Data in Marketing Applications.

This document provides recommendations for sponsors on data collection for cancer clinical trials submitted to FDA to support marketing claims in new drug applications (NDAs), biologics license applications (BLAs), or supplemental applications for new indications.

Proposal to waive in vivo bioequivalence requirements for WHO Model List of Essential Medicines immediate-release, solid oral dosage forms.

It aims to give national authorities sufficient background information on the various orally administered active pharmaceutical ingredients (APIs) on the WHO Model List of Essential Medicines (EML), also considering local usage of the API, to enable them to make an informed decision as to whether generic formulations should be subjected to in vivo bioequivalence (BE) studies or whether a biowaiver can be granted.

2. Good Manufacturing Practice requirement for various class of Product

GMP is the part of quality assurance which ensures that products are consistently produced and controlled to the quality standards appropriate to their intended use. GMP is aimed primarily at diminishing the risk inherent in any pharmaceutical production. Such risks are essentially of two types: *cross contamination* and *mix-ups*.

Under GMP

All manufacturing processes are clearly defined, systematically reviewed for associated risks in the light of scientific knowledge and experience, and shown to be capable of consistently manufacturing pharmaceutical products of the required quality that comply with their specifications. Qualification and validation are performed. All necessary resources are provided, including:

i. Sufficient and appropriately qualified and trained personnel.

ii. Adequate premises and space.

iii. Suitable equipment and services

iv. Appropriate materials, containers and labels

v. Approved procedures and instructions.

vi. Suitable storage and transport.

vii. Adequate personnel, laboratories and equipment for in-process controls;

Instructions and procedures are written in clear and unambiguous language, specifically applicable to the facilities provided. Procedure is carried out correctly and personnel are trained to do so. Records are made (manually and/or by recording instruments) during manufacture to show that all the steps required by the defined procedures and instructions have in fact been taken and that the quantity and quality of the product are as expected. (1)

Any significant deviations are fully recorded and investigated with the objective of determining the root cause and appropriate corrective and preventive actions is implemented. Records covering manufacture and distribution, which enable the complete history of a batch to be traced, are retained in a comprehensible and accessible form. The proper storage and distribution of the products minimizes any risk to their quality and takes account of good distribution practices. A system is available to recall any batch of product from sale or supply. Complaints about marketed products are examined, the causes of quality defects investigated and appropriate measures taken in respect of the defective products to prevent recurrence. (2)

Powder Drugs

If powder drugs are handled, procedures should be established and followed to appropriately manage cross-contamination risk, particularly if the powder is cytotoxic or highly sensitizing. FDA recommends the physical segregation of areas in which powder drugs are exposed to the environment. (3)

Containment

Dedicated production areas should be considered when material of an infectious nature or high pharmacological activity or toxicity is involved (e.g., certain steroids or cytotoxic anti-cancer agents) unless validated inactivation and/or cleaning procedures are established and maintained. (4,5)

3. Regulatory Requirements for Oncology Products

Bio study related specific requirements (6-8)

3.1 USFDA

Bioavailability: The rate and extent to which the active ingredient or activity moiety is absorbed from a drug product and becomes available at the site of action.

Bioequivalence: The absence of a significant difference in the rate and extent to which the active ingredient or active moiety in pharmaceutical equivalents or pharmaceutical alternatives becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study.

IND/NDA

BE documentation can be useful during the IND and NDA period to establish links between:

i. Early and late clinical trial formulations

ii. Formulations used in clinical trial and stability studies, if different

iii. Clinical trial formulation and to-be-marketed drug product; and

iv. Other comparisons, as appropriate

In each comparison, the new formulation or new method of manufacture is the test product and the prior formulation and the prior formulation or method of manufacture is the reference product. (6)

ANDA

BE studies are a critical component of ANDA submissions. The purpose of these studies is to demonstrate BE between a pharmaceutically equivalent generic drug product and the corresponding reference listed drug. Together with the determination of pharmaceutical equivalence, establishing BE allows a regulatory conclusion of therapeutic equivalence.

For immediate-release drug products, we recommend that the appropriate USP method must be submitted. If there is no USP method available, we recommend that the FDA method for the reference listed drugs be used. If the USP and/or FDA methods are not available, we recommend that the dissolution method development report described above be submitted.

For modified-release products, dissolution profiles using appropriate USP method (if available) can be submitted. If there is no USP method available, we recommend that the FDA method for the reference listed drug to be used. In addition, we recommend that profiles using at least three other dissolution media and water be submitted.

Methods to document BA and BE

Several in vivo and in vitro methods can be used to measure product quality BA and to establish BE. These include pharmacokinetic, pharmacodynamics, clinical, and in vivo studies. Product quality BA and BE frequently rely on pharmacodynamic measures such as AUC and Cmax that are reflective of systemic exposure. (7)

3.2 Europe

Design, conduct and evaluation of bioequivalence studies

The number of studies and study design depend on the Physico-chemical characteristics of the substance, its pharmacokinetic properties and proportionality in composition, and should be justified accordingly. In particular it may be necessary to address the linearity of pharmacokinetics, the need for studies both in fed and fasting state, the need for enantioselective analysis and the possibility of waiver for additional strengths. Full study reports should be provided for all studies, expect pilot studies for which study report synopses are sufficient. Full study reports for pilot studies should be available upon request. Study report synopses for bioequivalence or comparative bioavailability studies conducted during formulation development should also be included.

The study should be designed in such a way that the formulation effect can be distinguished from other effects. If two formulations are compared, a randomized, two-period, two-sequence single dose crossover design is recommended. The treatment periods should be separated by a wash out period sufficient to ensure that drug concentrations are below the lower limit of bio analytical quantification in all subjects at the beginning of the second period. Normally at least 5 elimination half-lives are necessary to achieve this.

The product used as reference product in the bioequivalence study should be part of the global marketing authorization of the reference medicinal product. Test products in an application for a generic or hybrid product or an extension of a generic/hybrid product are normally compared with the corresponding dosage form of a reference medicinal product, if available on the market. The selection of the reference product used in a bioequivalence study should be based on assay content and dissolution data and is the responsibility of the Applicant. Unless otherwise justified, the assayed content of the batch used as test product should not differ more than 5% from that of the batch used as reference product determined with the test procedure proposed for routine quality testing of the test product. The Applicant should document how a representative batch of the reference product with regards to dissolution and assay content has been selected. It is advisable to investigate more than one single batch of the reference product when selecting reference product batch for the bioequivalence study.

The inclusion/exclusion criteria should be clearly stated in the protocol. Subjects should be 18 years of age or older and preferably have a Body Mass Index between 18.5 and 30 kg/m2. The subjects should be screened for suitability by means of clinical laboratory tests, a medical history, and a physical examination. Depending on the drug's therapeutic class and safety profile, special medical investigations and precautions may have to be carried out before, during and after the completion of the study. Subjects could belong to either sex; however, the risk to women of childbearing potential should be considered. Subjects should preferably be non-smokers and without a history of alcohol or drug abuse. Phenotyping and/or genotyping of subjects may be considered for safety or pharmacokinetic reasons.

In parallel design studies, the treatment groups should be comparable in all known variables that may affect the pharmacokinetics of the active substance (e.g. age, body weight, sex, ethnic origin, smoking status, extensive/poor metabolic status). This is an essential pre-requisite to give validity to the results from such studies. If the investigated active substance is known to have adverse effects, and the pharmacological effects or risks are considered unacceptable for healthy volunteers, it may be necessary to include patients instead, under suitable precautions and supervision. (8)

Invitro dissolution tests complementary to bioequivalence studies:

The results of in vitro dissolution tests at three different buffers (normally pH 1.2, 4.5 and 6.8) and the media intended for drug product release (QC media), obtained with the batches of test and reference products that were used in the bioequivalence study should be

reported. Particular dosage forms like ODT (oral dispersible tablets) may require investigations using different experimental conditions. The results should be reported as profiles of percent of labelled amount dissolved versus time displaying mean values and summary statistics. Unless otherwise justified, the specifications for the in vitro dissolution to be used for quality control of the product should be derived from the dissolution profile of the test product batch that was found to be bioequivalent to the reference product. (9)

Generally, biowaiver are based on two types:

Biopharmaceutical classification system:

In this, Drugs solubility and permeability is seen and based on BCS classification the bio-waiver is given. Generally, class 1 and class 3 drugs are waived.

Class 1: High Solubility – High Permeability

Class 2: Low Solubility – High Permeability

Class 3: High Solubility – Low Permeability

Class 4: Low Solubility – Low Permeability

Based on dose strength: In this, if the In-vitro bioequivalence study of higher dose strength is done. So there is no need for in-vivo bioequivalence study for other low strength doses. The dissolution profile is seen at different physiological pH and depending on F1 and F2 values the study on lowest strength can be waived. (10)

4. BCS-based Biowaiver requirements

For class-I drug

BCS-based bio-waiver are applicable for an immediate release drug product if the drug substance has been proven to exhibit high solubility and complete absorption (BCS class I). Either very rapid (> 85 % within 15 min) or similarly rapid (85 % within 30 min) in vitro dissolution characteristics of the test and reference product has been demonstrated considering specific requirements. Excipients that might affect bioavailability are qualitatively and quantitatively the same. In general, the use of the same excipients in similar amounts is preferred.

For Class-II Drug

The drug substance has been proven to exhibit high solubility and limited absorption (BCS class III). Very rapid (> 85 % within 15 min) in vitro dissolution of the test and reference product has been demonstrated considering specific requirements. Excipients that might affect bioavailability are qualitatively and quantitatively the same and other excipients are qualitatively the same and quantitatively very similar. (10)

4.1 According to Europe guidelines, General Bio Waiver Criteria

The following general requirements must be met where a waiver for additional strength(s) is claimed:

a) The pharmaceutical products are manufactured by the same manufacturing process,

b) The qualitative composition of the different strengths is the same,

c) The composition of the strengths is quantitatively proportional, i.e. the ratio between the amount of each excipient to the amount of active substance(s) is the same for all strengths (for immediate release products coating components, capsule shell, colour agents and flavours are not required to follow this rule).

If there is some deviation from quantitatively proportional composition, condition c is still considered fulfilled if condition i) and ii) or i) and iii) below apply to the strength used in the bioequivalence study and the strength(s) for which a waiver is considered. The amount of the active substance(s) is less than 5 % of the tablet core weight, the weight of the capsule content. The amounts of the different core excipients or capsule content are the same for the concerned strengths and only the amount of active substance is changed. The amount of filler is changed to account for the change in amount of active substance. The amounts of other core excipients or capsule content should be the same for the concerned strengths. Appropriate in vitro dissolution data should confirm the adequacy of waiving additional in vivo bioequivalence testing.

In-vivo dissolution tests in support of biowaiver of strengths:

In vitro dissolution should confirm the adequacy of waiving additional in vivo bioequivalence testing. Accordingly, dissolution should be investigated at different pH values as outlined in the previous section (normally pH 1.2, 4.5 and 6.8) unless otherwise justified. Similarity of in vitro dissolution should be demonstrated at all conditions within the applied product series, i.e. between additional strengths and the strength(s) (i.e. batch(es)) used for bioequivalence testing. At pH values where sink conditions may not be achievable for all strengths in vitro dissolution may differ between different strengths. However, the comparison with the respective strength of the reference medicinal product should then confirm that this finding is drug substance rather than formulation related. In addition, the applicant could show similar profiles at the same dose (e.g. as a possibility two tablets of 5 mg versus one tablet of 10 mg could be compared). (10)

4.2 According to USFDA, Biowaivers based on BCS (10):

USFDA guideline is applicable for BA/BE waivers (bio waivers) based on BCS, for BCS class 1 and class 3 IR solid oral dosage forms. For BCS class 1 drug products, the following should be demonstrated:

- The drug substance is highly soluble
- The drug substance is highly permeable
- The drug product (test and reference) is rapidly dissolving, and
- The product does not contain any excipients that will affect the rate or extent of absorption of the drug

For BCS class 3 products, the following should be demonstrated:

- The drug substance is highly soluble
- The drug product (test and reference) is very rapidly dissolving
- The test product formulation is qualitatively the same and quantitatively very similar

Solubility

The solubility class boundary is based on the highest strength of an IR product that is the subject of a bio waiver request. A drug substance is considered highly soluble when the highest strength is soluble in 250 mL or less of aqueous media within the pH range of 1 - 6.8 at 37 ± 1°C. The volume estimate of 250 mL is derived from typical BE study protocols that prescribe administration of a drug product to fasting human volunteers with an 8 fluid ounce glass of water.

Permeability

The permeability class boundary is based indirectly on the extent of absorption (fraction of dose absorbed, not systemic BA) of a drug substance in humans, and directly on measurements of the rate of mass transfer across human intestinal membrane. Alternatively, other systems capable of predicting the extent of drug absorption in humans can be used (e.g., in situ animal, in vitro epithelial cell culture methods). A drug substance is considered to be highly permeable when the systemic BA or the extent of absorption in humans is determined to be 85 percent or more of an administered dose based on a mass balance determination (along with evidence showing stability of the drug in the GI tract) or in comparison to an intravenous reference dose.

Dissolution

An IR drug product is considered rapidly dissolving when a mean of 85 percent or more of the labelled amount of the drug substance dissolves within 30 minutes, using United States Pharmacopeia (USP) Apparatus 1 at 100 rpm or Apparatus 2 at 50 rpm (or at 75 rpm when appropriately justified (see section III.C.) in a volume of 500 mL or less (or 900 mL when appropriately justified) in each of the following media: (1) 0.1 N HCl or Simulated Gastric Fluid USP without enzymes; (2) a pH 4.5 buffer; and (3) a pH 6.8 buffer or Simulated Intestinal Fluid USP without enzymes. An IR product is considered very rapidly dissolving when a mean of 85 percent or more of the labelled amount of the drug substance dissolves within 15 minutes, using the above-mentioned conditions.

5. Regulatory applications of the BCS-based bio-waivers

INDs/NDAs

A specific objective of such BA information is to establish in vivo performance of the dosage form used in the clinical studies that provided primary evidence of efficacy and safety. Sponsors/applicants may wish to determine the relative BA of an IR solid oral dosage form by comparison with an oral solution, suspension, or intravenous injection

BCS-based bio waivers are applicable to the to-be-marketed formulation when changes in components, composition, and/or method of manufacture occur to the clinical trial formulation, as long as the dosage forms exhibit either rapid or very rapid dissolution (as appropriate), have similar in vitro dissolution profiles (see sections II and III), and for a BCS class 3 IR drug product, it meets the criteria for allowable differences in composition described previously

This approach is useful only when the drug substance belongs to BCS class 1 or 3, and the formulations pre- and post-change are pharmaceutical equivalents BCS-based bio waivers are intended only for subsequent in vivo BA or BE studies. They do not apply to food effect BA studies or other PK studies. BCS-based bio waivers may be applicable for pharmaceutical alternatives including other oral dosage forms.

ANDA

BCS-based bio waivers are appropriate for IR generic drug products that meet the criteria for BCS class 1 or 3. The proposed drug product (i.e., test product) should exhibit similar dissolution profiles to the reference listed drug product. The choice of dissolution apparatus (USP Apparatus 1 or 2) should be the same as that established for the reference listed drug product.

Data to Support a Biowaiver Request

The drug product for which a bio waiver is being requested should include a drug substance that is highly soluble (BCS class 1 and BCS class 3) and highly permeable (BCS class 1), and the drug product should be rapidly dissolving (BCS class 1) or very rapidly dissolving (BCS class 3). Sponsors/applicants requesting bio waivers based on the BCS should submit the following information to the Agency for review

Data Supporting High Permeability

Data supporting high solubility of the test drug substance should be developed. The following information should be included in the application:

- A description of test methods, including information on analytical method(s) and composition of the buffer solutions.
- Information on chemical structure, molecular weight, nature of the drug substance (acid, base, amphoteric, or neutral), and dissociation constants (pKa(s)).
- Test results (mean, standard deviation, and coefficient of variation) summarized in a table under solution pH, drug solubility (e.g., mg/mL), and volume of media required to dissolve the highest strength.
- A graphic representation of mean pH-solubility profile.

Data Supporting High Permeability

Data supporting high permeability of the test drug substance should be developed. Thee following information and data should be included in the application:

- A description of test methods, including information on analytical method(s) and composition of the buffer solutions.
- A rationale for the dose or drug concentrations used in studies.
- For human PK studies, information on study design and methods used along with the PK data.
- For direct permeability methods, information supporting the suitability of a selected method that encompasses a description of the study method, criteria for selection of human subjects, animals, or epithelial cell line, drug concentrations in the donor fluid, description of the analytical method, method used to calculate extent of absorption or permeability, and where appropriate, information on efflux potential (10)

Waivers of In vivo BE Studies (Biowaivers):

NDAs/ANDAs

Tablets – For lower Strength, for modified-release tablets, when the drug product is in the same dosage form but in a different strength, when it is proportionally similar in its active and inactive ingredients, and when it has the same drug release mechanism, an in vivo BE determination of one or more lower strengths can be waived based on dissolution profile comparisons, with an in vivo study only on the highest strength. USFDA recommend that the drug products exhibit similar dissolution profiles between the highest strength and the lower strengths based on the f2 test in at least three dissolution media (e.g., pH 1.2, 4.5 and 6.8). USFDA recommend that the dissolution profile be generated on the test and reference products of all strengths. (10)

6. Conclusion

Till date compilation according to regulatory aspects of oncology product is not done. Due to this reason, this project is unique. This project focuses on specific regulations for oncology products like market analysis, good manufacturing practice specific to oncology, bio-study, and regulatory submission pathway for specific oncology drug and bio waivers due to expensive manufacturing of oncology drug. There are no specific guidelines for manufacturing of oncology drugs. So due to this reason, this compilation of work is a startup for specific oncology guidance.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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