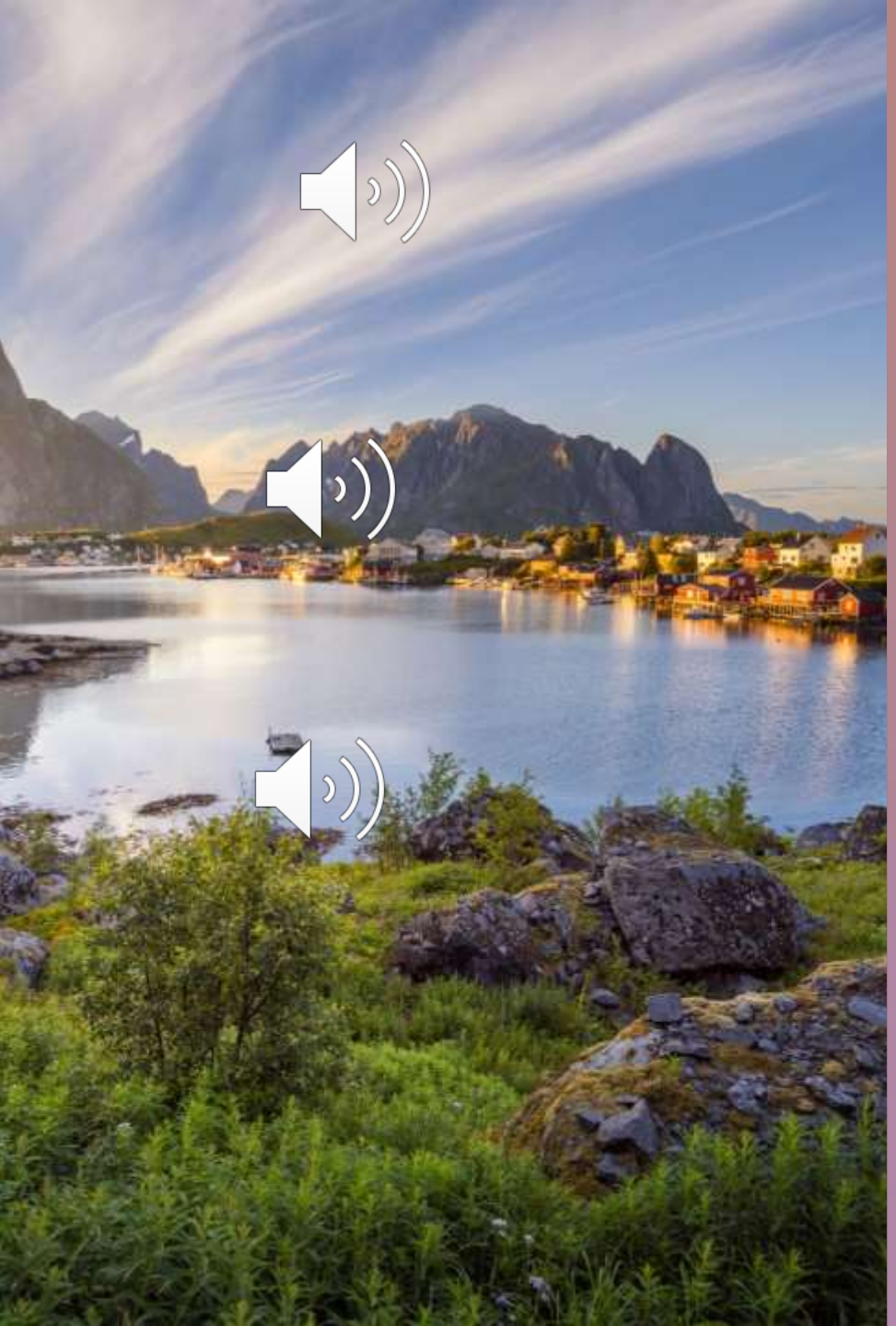


DEVELOPMENT OF NEW DRUG FROM “MAGIC DUST” FOUND IN AN UNCONTACTED TRIBE

THIS PRESENTATION IS A SMALL GUIDE ON ALL THE ASPECTS RELATED TO NEW DRUGS

DRUG DISCOVERY AND DEVELOPMENT

- **PRECLINICAL STUDIES:**

- A**) Extraction**: This essential first step involves the isolation of the active ingredient (Active Pharmaceutical Ingredient) from the magic dust using various extraction methods which include processes like maceration, percolation, Soxhlet extraction, pressing, solvent extraction.
- Let's call this extracted product from magic dust as "Element X".
- Then, the extracted product of magic dust is further sent to next following steps for Preclinical studies which involve:
- B**) Purification**: The process removes any impurities present in the "Element X".

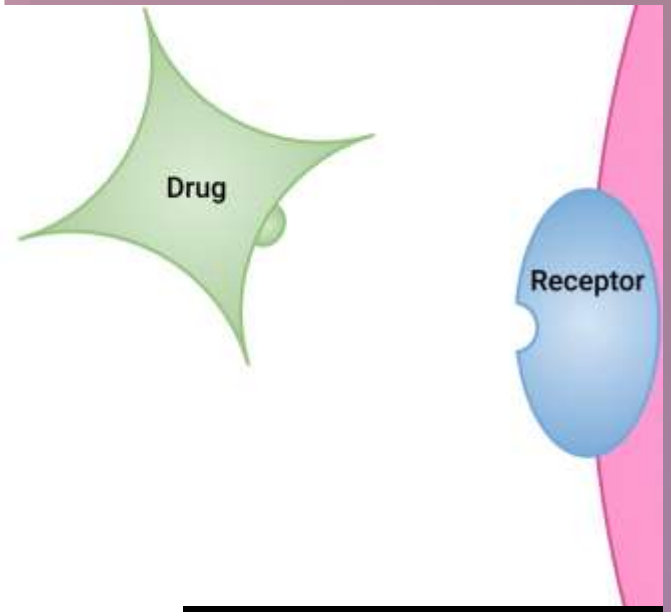
- C) **Characterization**: The Element X is then characterized using various toxicological studies and to develop the right formulation of the drug, such as the dosage, route of administration and drug delivery system.

- D) **Target Identification**: The identification of right target of Element X can help researches to develop more effective and safer drug.

- E**) Target Validation**: Target validation of the newfound element X is performed which include the processes such as Genetic manipulation, chemical inhibition, Bioinformatics and various Animal models. This validation helps us to reduce the risk of drug failure in clinical trials.

- F**) ADME studies**: These studies are conducted on the Element X and find this new API's Absorption, distribution, metabolism, excretion properties. These studies are important for ensuring that the drug is safe and effective and help in preventing drug interactions and adverse reactions.

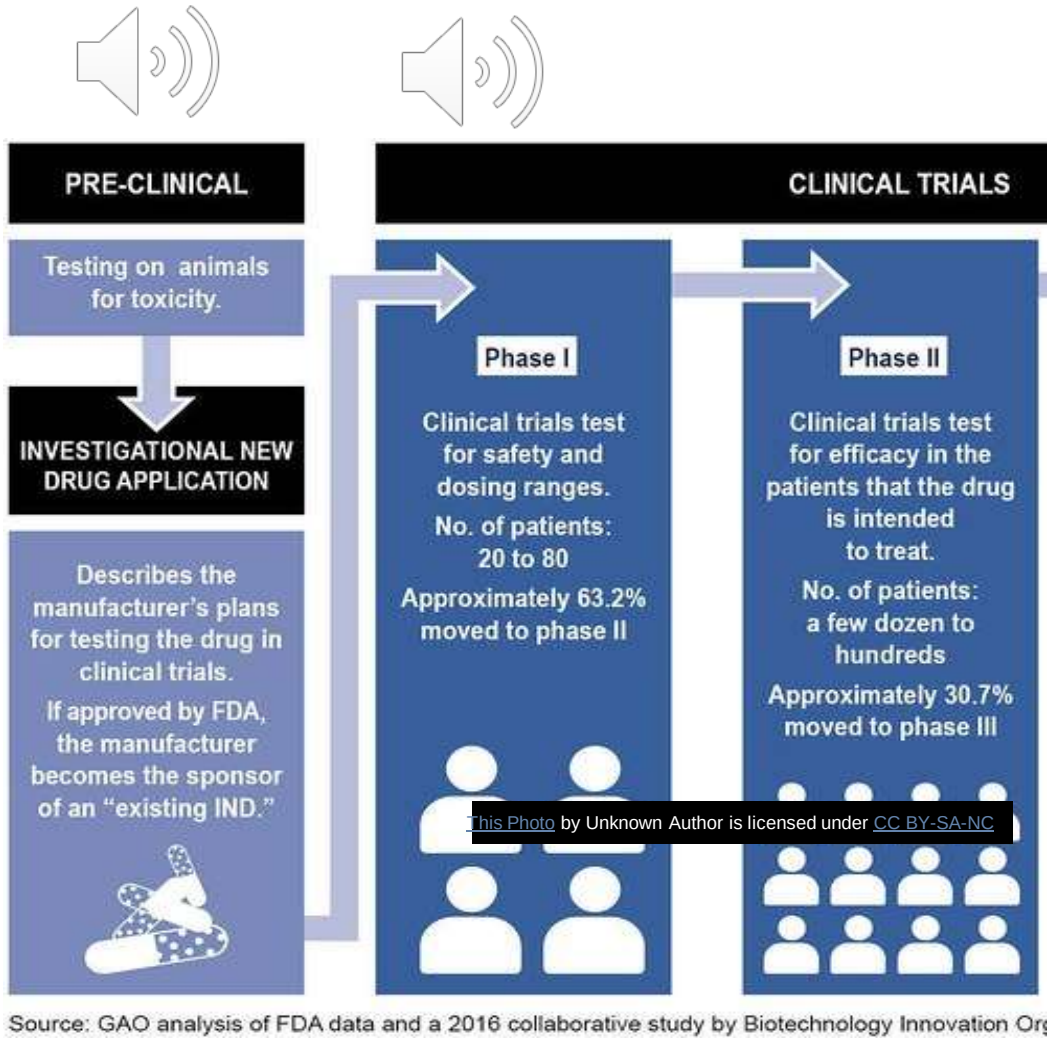
- G**) Pharmacodynamics**: These studies on Element X are conducted to study the way it interacts with the target molecule and Mechanism of action is known.
- H) **Target product profile**: This is a form of document in which it outlines the desired characteristics of Element X. Then this is used as a guide to the development of products from this API.
  - SAR (Structure Activity Relationship): Both qualitative SAR and quantitative SARs are performed on Element X to determine the structural features that are associated with a particular biological activity. The predicament of SAR involves drug screening, optimization, avoiding toxicity, predicting drug metabolism, Understanding the drug action.
- This isolation and refinement of magic dust is important because it is possible to study all the properties of the magic dust in detail to determine each magic dust's optimal dose and dosing regimen, which can hel reduce the risk of side effects and help to improve the chances of the drug being effective.
- Moreover, indications for use can help to ensure that the drug is used only for which it is effective and help to prevent the drug from being used for off-label purposes, which can turn out to be dangerous. Furthermore, by understanding the indications for Element X, it is possible to design new drugs that are safer and more effective than the original refined magic dust.



IND APPLICATION

The next step for our Element X is to pass is through the process of IND Application:

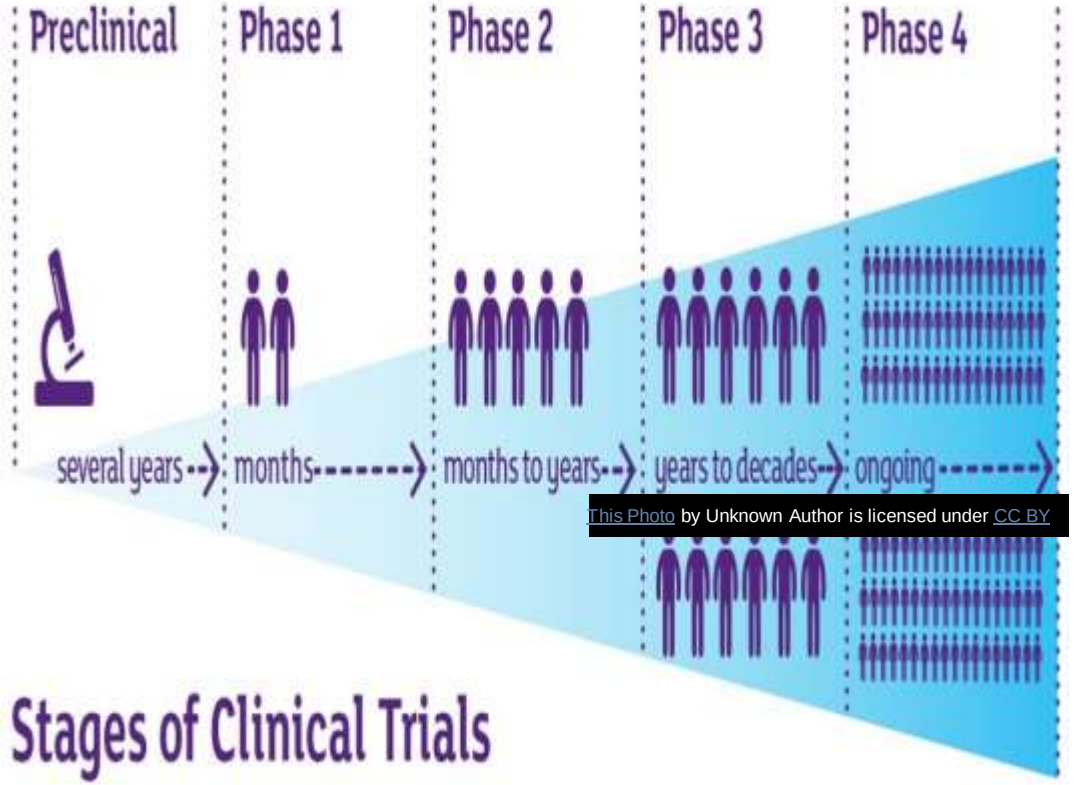
- To be transported or supplied over state borders, a medicine must first be the subject of an approved marketing application, according to current Federal law. A sponsor must apply for an exception from that legal requirement because it is likely that it will want to transport the experimental medicine to clinical investigators in numerous states. Only through IND the sponsor technically obtains this exemption from FDA.
- There are three types of IND's:
- a) Investigator IND:
- This IND is submitted by a physician who begins the inquiry, conducts it, and is directly responsible for the administration or dispensing of the investigational medicine. In order to examine an unapproved treatment, an approved product, or both for a new indication or in a new patient group, a doctor may file a research IND.
- b) Emergency use IND:
- This IND allows the utilization of an experimental drug in an emergency situation. It is also utilized for patients who don't fit the requirements of an established study protocol or when none is available.
- c) Treatment IND:
- The treatment INDs are filed for drugs which are showing promising results in clinical testing for life-threatening conditions. However, the final clinical work is conducted and then FDA review occurs.



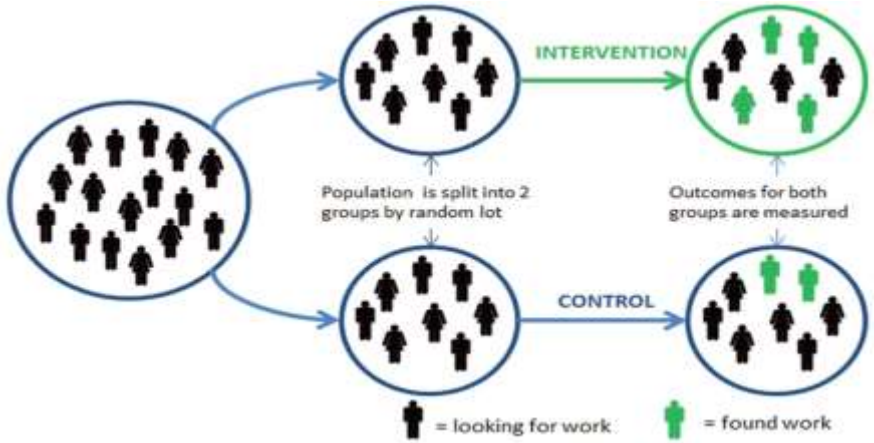
- The IND application must contain information in three broad areas which are:
- Animal Pharmacology and Toxicology studies, Manufacturing information, Clinical protocols and Investigator Information.
- So, according to the above three types of IND's, our magic dust (Element X) falls in category of "Treatment IND" and I choose the application of Treatment IND for submission for the new drug to the FDA for approval.
- Once, the IND is submitted there is a waiting period of 30 calendar days before initiation clinical trials. During this time, the FDA has the opportunity to review the IND for safety to assure that research subjects will not be subjected to any risk.
- After the IND is filed and approved by the FDA, the process of clinical trials beg
- The risk vs benefit profile associated with utilization of the Element X (magic dust) for clinical purposes can be established by conducting:
- After the IND is filed and approved by the FDA, the process of clinical trials begins.
- A) Preclinical studies b) clinical trails c) Postmarking surveillance

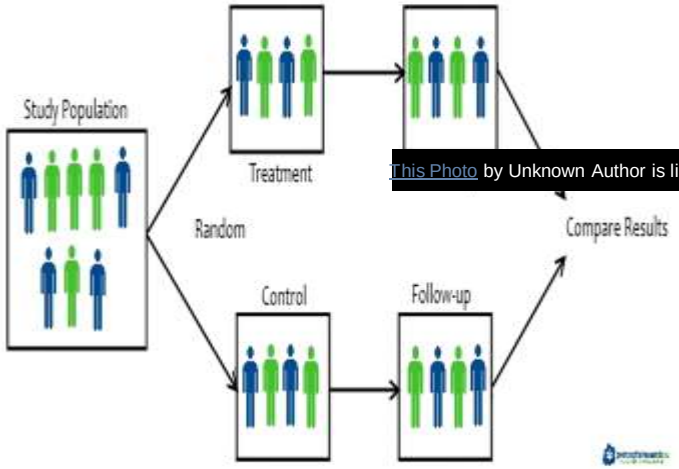
CLINICAL TRIALS

- Clinical trials for Element X are conducted to determine effectiveness, to test safety and identify side effects. The FDA requires phase 1,2,3 trials to be conducted to determine if the drug can be approved for the further use.
- Each phase has a different purpose.
- a) PHASE I: This tests the extracted Element X on a small group of healthy volunteers (20-80) for determining the safety, side-effects to find out if there are any side effects. This process may take up to several months.
- b) PHASE II: This phase involves the testing of Element X in a large number of volunteers (100-300) with the disease or condition which the Element X is anticipated to treat and by this we can assess its safety and efficacy. This process can take from several months to 2 years.
- c) PHASE III: This phase involves the gathering of information from several hundred to a few thousand people about safety and effectiveness of Element X. This process can take from 1 to 4 years.
- d) PHASE IV: This phase of clinical trials involves the post-marketing studies that are conducted after the approval use of Element X incorporated drugs to collect additional data on safety and efficacy. This is an on-going process and there is no set time limit.



TYPES OF CLINICAL TRIALS





- There are different types of clinical trials conducted which may include:

- A**) RCT (Randomized Controlled Trials):**
- These RCT's are relied upon to assess the safety, efficacy and appropriate dosage of drugs for diseases. RCT's involve two arm studies.
- These traditional RCT studies rely on the principles of "Frequentist statistics" which establishes parameters at the beginning of the trail and held them constant throughout the trials. This has less flexibility in leveraging data that came in during the course of the trial as the trial results are extremely linked to interpretation of then trial results.

"As we have 12 different types of magic dusts and 12 different Element X's extracted from the respective dust's we perform Adaptive Randomization trials also known as Bayesian statistics."

- B) **Adaptive Randomization:**
- This process estimates the probability of treatment effects based on data as it is accumulated.
- The adaptive trial feature has the ability to continuously add, drop or graduate the treatment arms throughout the life of the trial.
- The researchers could add a treatment arm to an existing platform in order to study the effects of the particular drug.

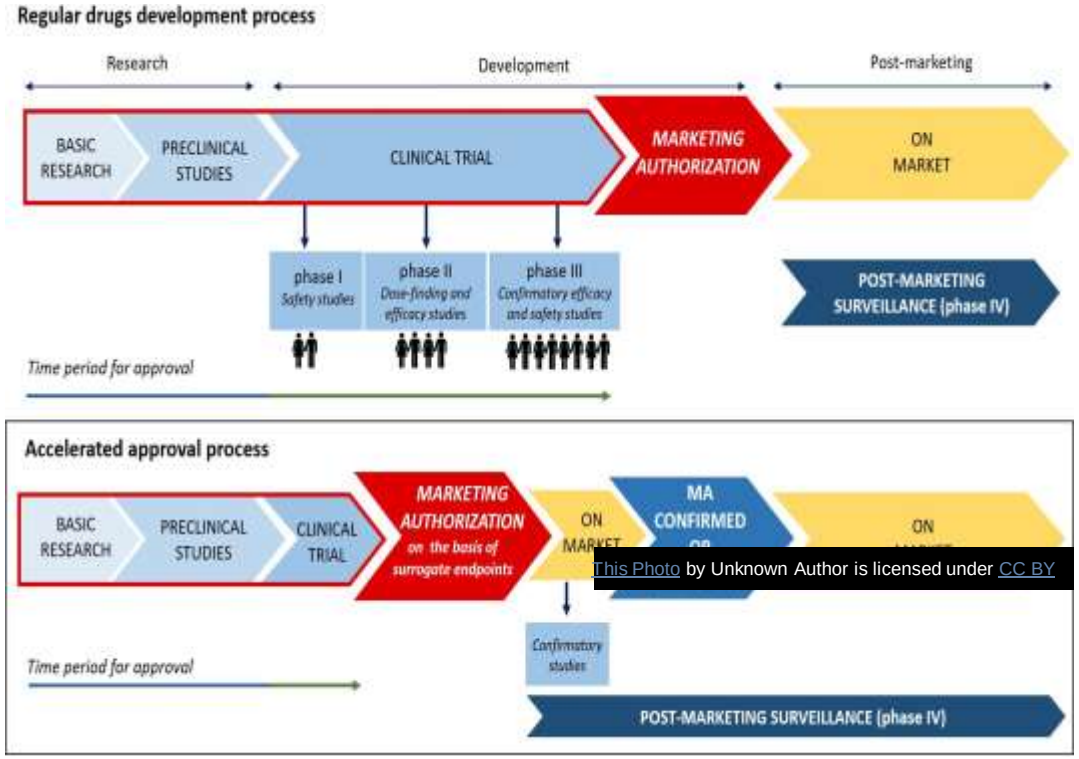
NDA APPLICATION

- A New Drug Application covers all the topics of the new drug, which in our case is the Element X of magic dust, the NDA's purpose is to demonstrate that a drug is safe and effective for its intended use.

- To file an NDA for Element X, we have included data beginning from preclinical data to phase 3 clinical trials, which should include studies, all the gathered information and analyses along with clinical results:

- The purpose of the NDA is to provide enough information to permit FDA review to make better decisions of the following:

  - Whether the medication is risk-free and efficient for the intended use(s) and whether the advantages of the medication exceed the disadvantages.
  - To what extent and with what information the drug's proposed labeling (package insert) is appropriate.
  - Whether the processes used to make the medicine and the measures taken to ensure its quality are sufficient to retain the drug's identity, strength, quality, and purity.
- The documentation of the NDA is required to inform about the results of the animal studies, how the drug behaves in the body and how it is manufactured, processed and packaged.



FDA REVIEW AND APPROVAL

- Once FDA receives an NDA, the review team is in the charge of deciding if the NDA application is complete. If the NDA application is not complete and the review team is not satisfied the team can refuse to file, the NDA. If the application complete, the review team has about 6-10 months to make a decision to approve our drug or not. The process of review involves:
  - Each member of the review team thoroughly examines the area of the application that pertains to him or her. For instance, a pharmacologist evaluates the data from animal studies while the medical officer and statistician review the clinical data. Additionally, there is a supervisory review for each technical specialty that is represented on the team.
  - Each member of the review team thoroughly examines the area of the application that pertains to him or her. For instance, a pharmacologist evaluates the data from animal studies while the medical officer and statistician review the clinical data. Additionally, there is a supervisory review for each technical specialty that is represented on the team.
  - The project manager compiles all of the individual reviews and additional paperwork, including the inspection report, into an "action package." The FDA will use this paper as the official record. A top FDA official decides based on the review team's recommendation.
- **FDA APPROVAL:**
- If the FDA finds that our new drug Element X is safe and effective for its intended use, the FDA works with the applicants to develop and refine prescribing information (also called Labelling).
- Labelling describes the basis of approval and how to use the drug at its best.
- Post- Market Drug Safety Monitoring:
- Though the drug is proven for its safety and efficacy, it is not possible to have complete information about the safety of drug at the time of approval. The real essence of a product's safety matures over a period of time which may take months and even years that make up a product's lifetime the marketplace. The FDA can add cautions to the dosage or use gar information as well as other measures for more serious issues in case if the FDA review reports any problem with the product.

There are Adverse Event reports that are to be submitted to FDA, these reports can be submitted by manufacturers, consumers, or healthcare professionals, these reports can be voluntarily submitted, or they are made mandatory. The main source for signal detection of safety events of medical products is done through the FAERS (FDA Adverse Event Reporting system)

INTELLECTUAL PROPERTY

- Intellectual property is the branch of law that protects and, indeed, encourages the creation of certain products of the mind or intellect.
- The protection of pharmaceutical businesses' investments in research and development (R&D) is one reason why intellectual property (IP) is crucial in the creation of new drugs.
- The issues that should be addressed regarding Intellectual property:
- A) **Patentability**: The patentability of new drugs is subject to laws of each country. The patents are granted to new chemical entities, new uses for existing drugs and new methods of manufacturing drugs.
- Patents are a legal mechanism by which a government body gives the exclusive right to the patent filer and excludes others from using their invention or commercially exploiting it.
- Patents are a type of intellectual property in which a patent confers a right to exclude others from practicing a patented invention.
- Patents are generally considered the strongest form of protection available for intellectual property.
- There are three different types of patents:
- a) Plant patent b) Design patent c) Utility patent
- **Patent Obtaining**:
- In US to obtain a patent, the inventor must file a patent application describing the invention.
- The claimed invention must have utility and be both new and nonobvious.

- **Patent Specification**:
- This part of patent process in which the inventor should describe the invention in detail.
- The specification must meet these requirements:
- a) Providing a written description
- b) Providing sufficient detail to teach persons of ordinary skill how to make and use invention.
- c) Reveal the best mode of making and using the invention known by the inventor at the time the application is filed.
- d) Provide at least one claim covering the applicant’s invention.

Procedure For Obtain Patents:

In order to obtain a patent in the US, an ex parte procedure must be completed between the inventor or the inventor's assignee and the PTO. The application and the PTO undertake their negotiations in writing.

- Up until the date the application publishes or the date the patent issues, whichever occurs first, the proceedings themselves and the written record of the proceedings, also referred to as the file or prosecution history, are conducted and preserved in confidence.
- Currently, pending utility patent applications are published 18 months after their priority date unless the applicant requests otherwise at the time of filing and certifies that the application has not been filed and will not be filed in any foreign country that permits publication.
- The confidentiality of the proceeding expires and the whole written record is available to the public if and when the application is published, or the patent actually issues.

B**) Copyright**: Scientific articles, clinical trial data, and marketing materials are all protected by copyright laws. They aid in keeping certain resources from being copied without permission.

C**) Trademarks**: The brand names and emblems of pharmaceutical items are protected by trademarks. They assist in setting one company's products apart from those of its rivals.

D**) Designs**: Pharmaceutical products' decorative elements are protected by designs. They can be utilized to safeguard the appearance of a drug product's package, dosage forms, and other aspects.

E) **Data Exclusivity**: Data exclusivity is a form of intellectual property that gives pharmaceutical companies exclusive rights to the data they generate via clinical trials. This helps to protect the investment that companies make in clinical trials and to ensure that they can recoup their investment from the sale of their products.

F) **Licensing**: licensing is a legal mechanism that allows governments to authorize the production of a patented product without the consent of the patent holder.

G**) Use of traditional Knowledge**: Traditional knowledge is knowledge that is held by indigenous peoples and local communities. This knowledge can be used in the development of new drugs.

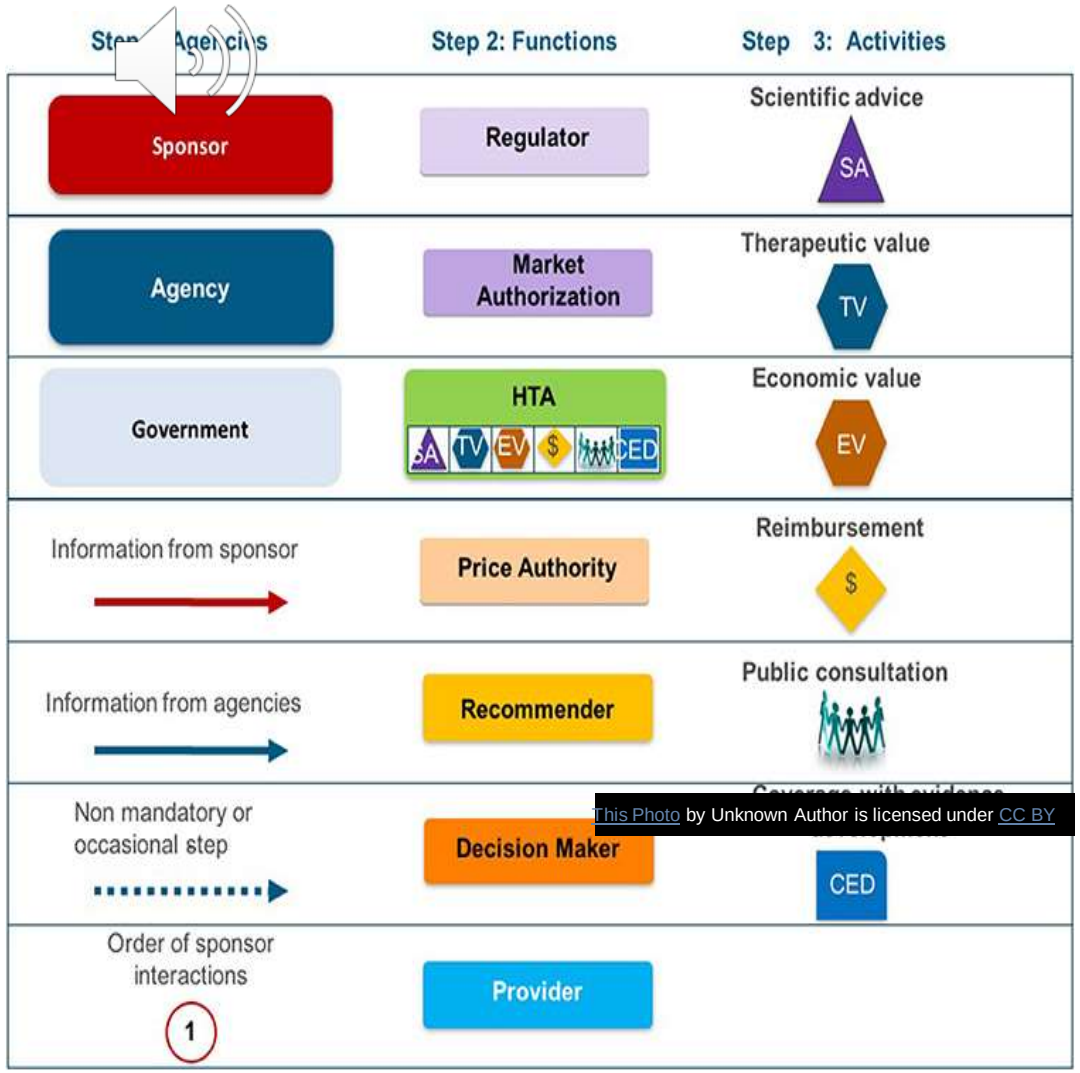
In our case of drug development, we are using the traditional knowledge of unconnected tribes as then precursor for drug development. If there is no incentives, share or royalty not given to the people of the tribe , I consider it as an ethical and legal offense. So, there is a necessity for us to obtain the consent of the traditional knowledge holders and there is a definite need to ensure that they are fairly compensated for the use of their knowledge.

PRICING AND REIMBURSEMENT

- The factors for pricing and reimbursement for our new drug in the US:

1. Clinical Benefits Of The Drug: Clinical trials should demonstrate the medication's efficacy and safety. The higher the price that may be justified, the greater the clinical benefits of the medicine.
2. The Patient Population: The patient population that the drug is meant to treat must also be considered when determining its price. Typically, medications for rare diseases cost more than those for common disorders.
3. The Payer Mix: The many types of health insurance policies that will cover the medication are referred to as the payer mix. Drugs covered by public health insurance plans, like Medicare and Medicaid, are often less expensive than those covered by private health insurance plans.
4. The Regulatory Environment: The regulatory landscape in the US is intricate and dynamic. When estimating prices and paying for new medications, pharmaceutical businesses must be informed of the most recent rules.

- The Drug's Status: Our new drug if approved by FDA may not be immediately covered by all payers. Payers may require the drug to be on the market for a certain amount of time before they cover it.
- Private Insurance: Private insurers typically have their own rules about which drugs are covered. Some insurers may cover new drugs immediately after they are approved by the FDA, while others may require the drug to be on the market for a longer period of time.



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THANK YOU

REGARDS,

REVANTH KUMAR KANNEGANTI