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A COMPARATIVE STUDY OF ORPHAN DRUG APPROVAL PROCESS IN US, EU AND INDIA

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ABSTRACT

A medication intended to treat an uncommon medical ailment (such as Huntington's disease, myoclonus disease, Tourette syndrome, etc.) is known as an orphan drug. Pharmaceutical corporations pay little attention to them since the limited patient population makes the significant investment in drug research unjustifiable. Although the definition of rare diseases differs depending on the jurisdiction, it usually refers to the condition's occurrence, severity, and life expectancy of alternative treatments**.** The FDA initially established guidelines for orphan pharmaceuticals, which include funds for phase I/II clinical trials, tax credits for clinical research, marketing exclusivity for a predetermined amount of time, and exemption from application filing fees. Pharmaceuticals and natural items used in the diagnosis, treatment, or prevention of rare disorders are referred to as orphan medications. The European Orphan Pharmaceutical Regulation was established to promote the growth of medications to treat uncommon medical conditions and ensure that patients would have adequate access to specialized, high-quality care. A group of pharmacists enquired of the Indian authorities to enact the Orphan Drug Act in 2001 during the Indian Drugs Manufacturers Association (IDMA) convention. The population of India afflicted with uncommon diseases is reliant on orphan drugs authorised in developed countries. Developing nations also feel compelled to take

action to advance orphan medication development and manufacture. The economic development of India's pharmaceutical industries is negatively impacted by the lack of regulation surrounding orphan pharmaceuticals. A detailed study of the orphan drug approval process in the US, EU and Indiais discussed in this review article.

Keywords: Orphan Drug, FDA, IDMA, European Regulatory, Orphan Drug Act,orphan medication

1. INTRODUCTION:

The meaning of the term "orphan drug" varies according to the political, regulatory, and commercial context. Some refer to it as medications intended for children, who are known as "therapeutic orphans" since their patient base is typically too tiny to support the viability of testing pediatric dosage forms for adult-developed medications. Orphan diseases are described as medical problems having a low prevalence, and orphan medications are therapeutic compounds created to manage these conditions. However, in general, medications that are both therapeutic and commercial orphans—that is, whose patient populations are too small to make their development economically feasible—are referred to as "orphan drugs." These diverse modern meanings associated with orphan pharmaceuticals demonstrate the growing diversity of organisations involved in developing orphan drugs **[1] [2]**.

A medication developed specifically to treat an unusual medical condition known as an "orphan disease" is called an orphan medicine. It can be defined as drugs that meet the needs of public health but are not produced by the pharmaceutical industry for profit. Pharmaceutical innovators are sometimes dissuaded from creating products for incredibly small patient populations because of the high expenses and little return on investment of producing drugs under rigid guidelines **[3]**.

The US initially passed the Orphan Drug Actin 1983 to promote the creation of medications for uncommon illnesses. Drug therapy for such disorders was not commonly discovered at that time. Particular attention has been given to the OD Act of the United States and orphan drug policies of other industrialised nations, including Europe, Highlighting the necessity for India to enact legislation similar to the ODA. The laws governing orphan drugs varied between nations **[4] [5]**.

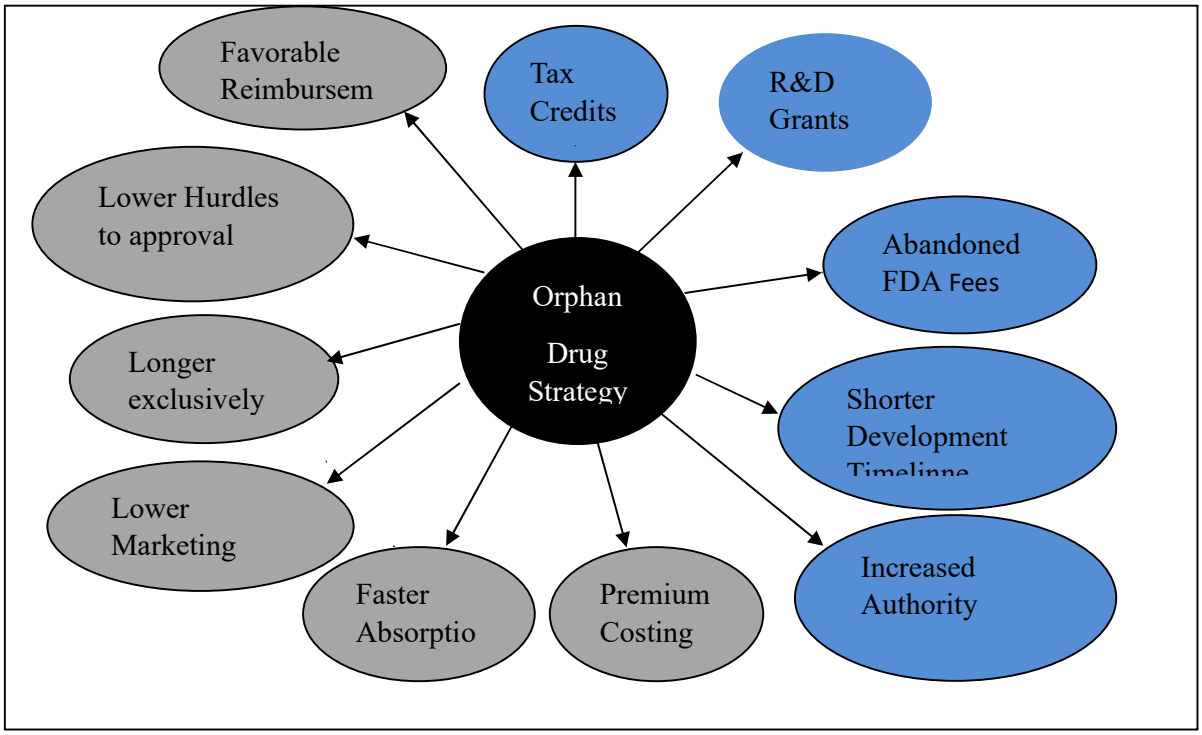

Figure 1: Orphan Drug Stratergy[6]

2. A ANALYSIS OF ORPHAN DRUG REGULATORY ACCEPTANCE PATHWAYS IN THE UNITED STATES (US), EUROPEAN UNION (EU) AND INDIA [7] [8]

Key Distinctions Among The Us, Eu, And India:

Requirement	US	EUROPE	INDIA
Organization	USFDA is one organization	Several organizations 1. Europe and the Middle East 2.CHMP 3.NationalOrganizations for Health	Single organization DCGI
Approval pathway	Single approval pathway.	Process of Multiple Approval Pathways 1.EU Community 2.Decentralised 3.Mutual Acknowledgment 4.National	Single Approval pathway.
TSE/BSE Study data	Data from TSE/BSE Studies not needed	Necessary	Necessary
Braille code	Labelling does not need to include a braille code.	Labelling requires the use of Braille code.	Labelling does not need to include a braille code.
Modifications after approval	Changes to the approved medication after approval: 1. Small adjustments 2. Calm down modifications 3. Significant modifications	Following a modification to the authorized medication. 1. StyleIA differencing 2. Style IB differencing 3 Differencing Type II	1. Modifications after approval 2. Significant alterations in quality 3. Moderate alterations in quality

Executive Condition:

Requirement	US	Europe	India
Utilization	ANDA / NDA	MAA	MAA
Disqualification categorization	Necessary	Not Necessary	Not Necessary
Count of the replicas	Three	One	One
Authorization Schedule	500-540 days	300-360 days	360-540 days
Charge	$51,520 - ANDA Application under $2 million-NDA Application	£103,059 is the national charge (including hybrid applications). Decentralized process with CMS in the UK: £99,507	50,000 INR
Exposition	eCTD & Paper	eCTD	Paper

Completed Requirements For Product Control:

Requirement	US	EUROPE	INDIA
Reasoning	ICH Q6A	ICH Q6A	ICH Q6A
Essay	90 - 100 %	95 - 105 %	90 - 110 %
Breakdown	Not Necessary	Necessary	Necessary
Recognition of Colour	Not Necessary	Necessary	Necessary
Aqua ratio	Necessary	Not Necessary	Necessary

Necessities For Production And Control:

Requirement	US	EUROPE	INDIA
Quantity of stacks	One	Three	One
Packing	At least one million section	Not Necessary	Not Mentioned
Procedure Verification	When submitting, not necessary	Necessary	Necessary
Quantity in Batch	A minimum of one lakh units or one pilot scale.	One lab batch plus twopreliminary scales, whichever is higher.	Preliminary scale group

Conditions For Stability:

Requirement	US	EUROPE	INDIA
Quantity of batches	One small-scale pilot batch or two pilot batches	(If API Stable): 2 Pilot Scale Three Main Batches (In the Event of Unstable API)	Two pilot or production scales (assuming stable API) Three Main Batches (In the Event of Unstable API)
Situation:Stability throughout the long period and stability across time	Permanent: 25°C/60%RH Mid-range: 30°C/65%RH; Quickened: 40°C/75%RH (0, 3, 6 months);	Long-term: 60%RH and 25°C Speeded up to 40°C/75%RH Mid-range: 65%RH and 30°C	Long-range:70%RH at 30°C Turbocharged: 40°C/75%RH
Minimal duration of the submission	180 days in advance and six months in duration	Six months in length, with six months of acceleration	Accelerate for six months and extend for six months.
Container orientation	Reversed and Straight	Avoid addressing	-
Section	Part 210 and 211 of 21 CFR	EU's Guidelines Regarding Pharmaceuticals, Volume 4	ICH Q1F
QP Verification	NotNecessary	Necessary	Necessary

Bioequivalencia Summary:

Requirement	US	EUROPE	INDIA
CRO	FDA evaluated	MHRA evaluated	CDSCO
Hold Sample	The sample amount needed for analysis 5 times over	Not at all necessary	-
Fasted / Fed	Must follow the advice of OGD	Not at all necessary	As advised by CDSCO
keeping of specimens	Five years from the application's filing date	Not at all necessary	Three years following the application's filing date
Research on over-the-counter medications	Contrary to US RLD everywhere. to consult the FDA website's "BE recommendations" for help.	In opposition to the EU reference product (ERP) withdifferent nation	Exception of Thailand, where BE must be finished locally against the local reference product, compared with any country

3.ORPHAN DRUG REVIEW PROCESS IN THE US: [9]

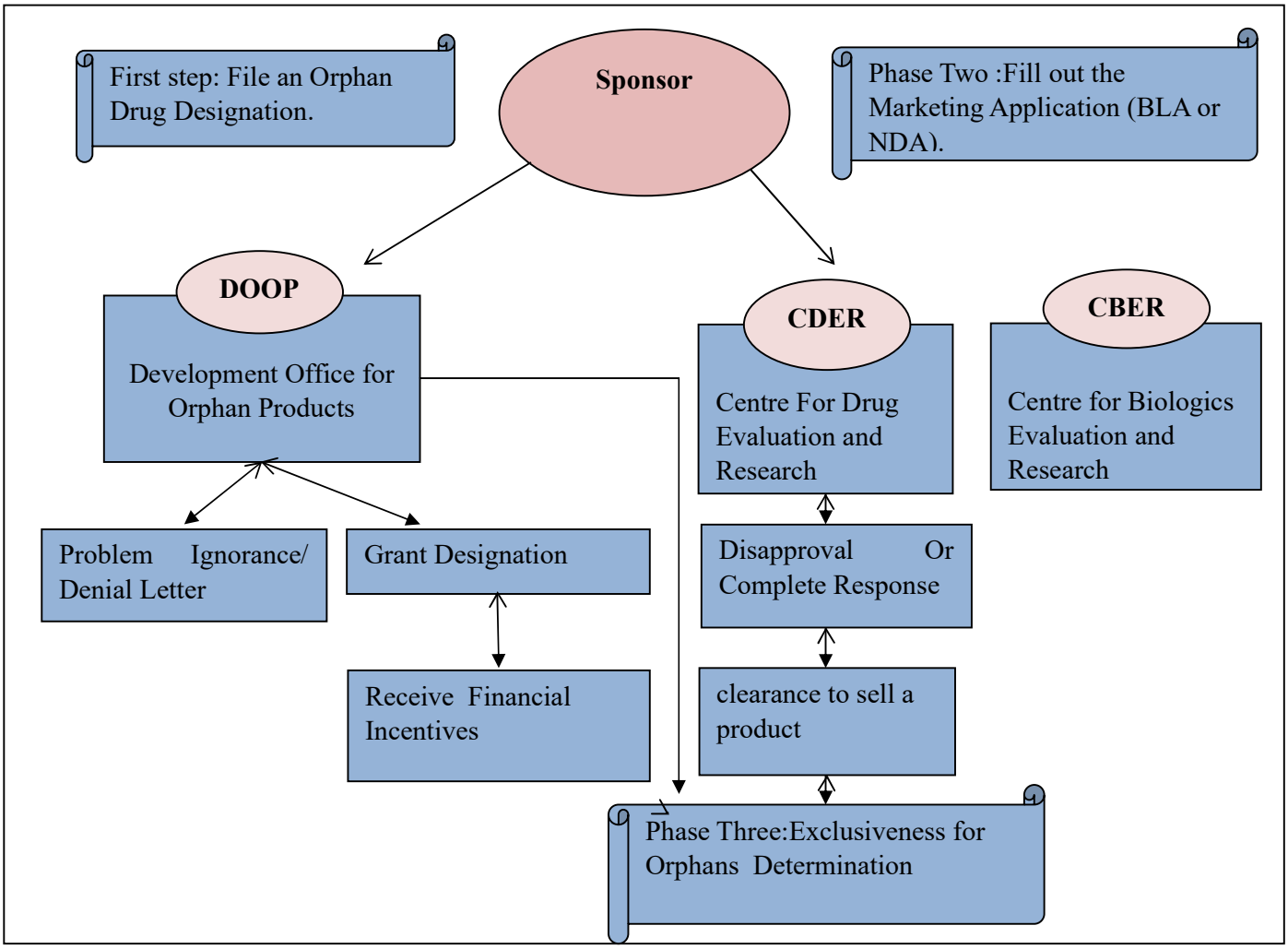

Figure 2: Orphan Drug Review Process In The Us

4. ORPHAN DRUG REVIEW PROCESS IN EUROPE: [10]

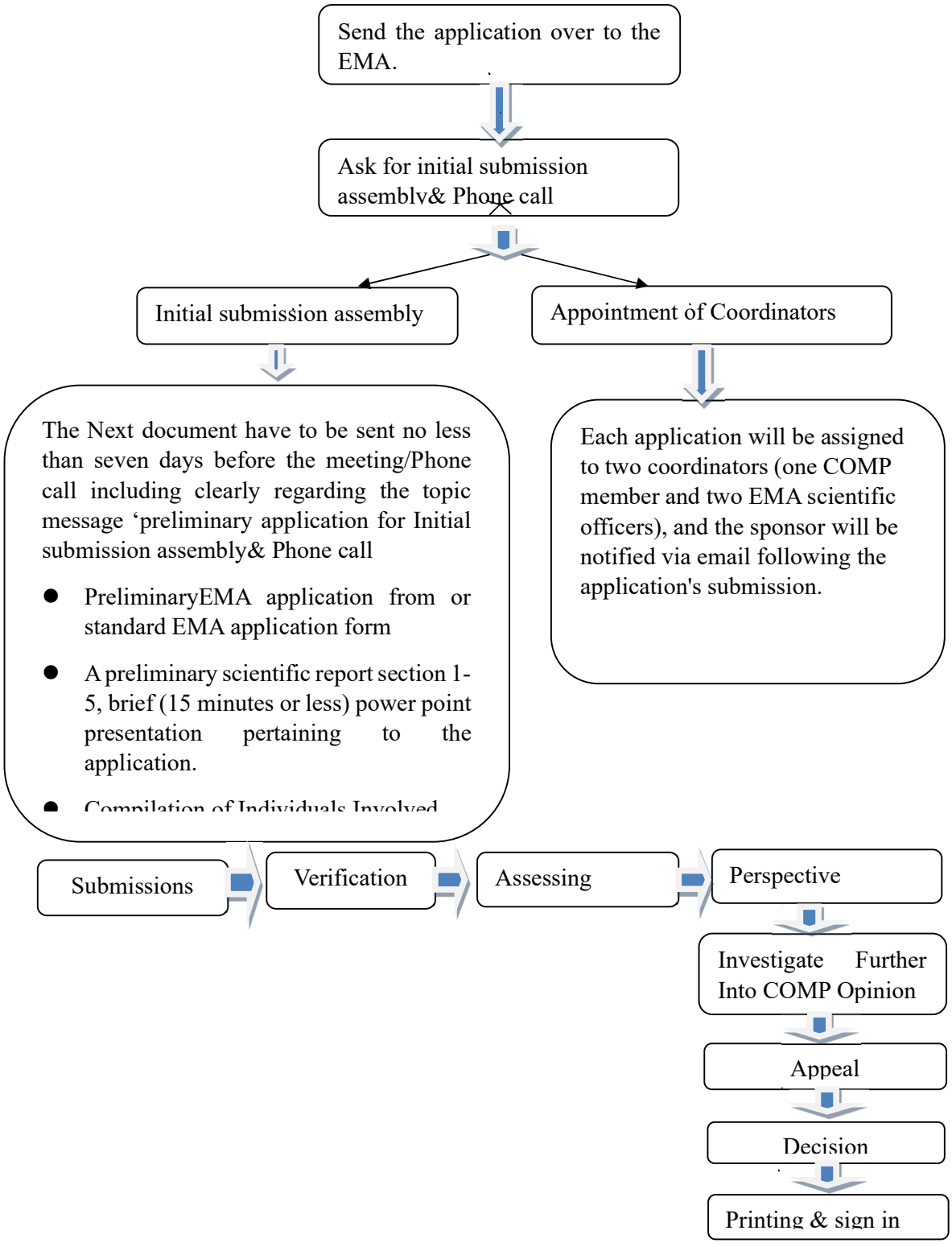

Figure 3: Orphan Drug Review Process In Europe

5.ORPHAN DRUG REVIEW PROCESS IN INDIA:[11]

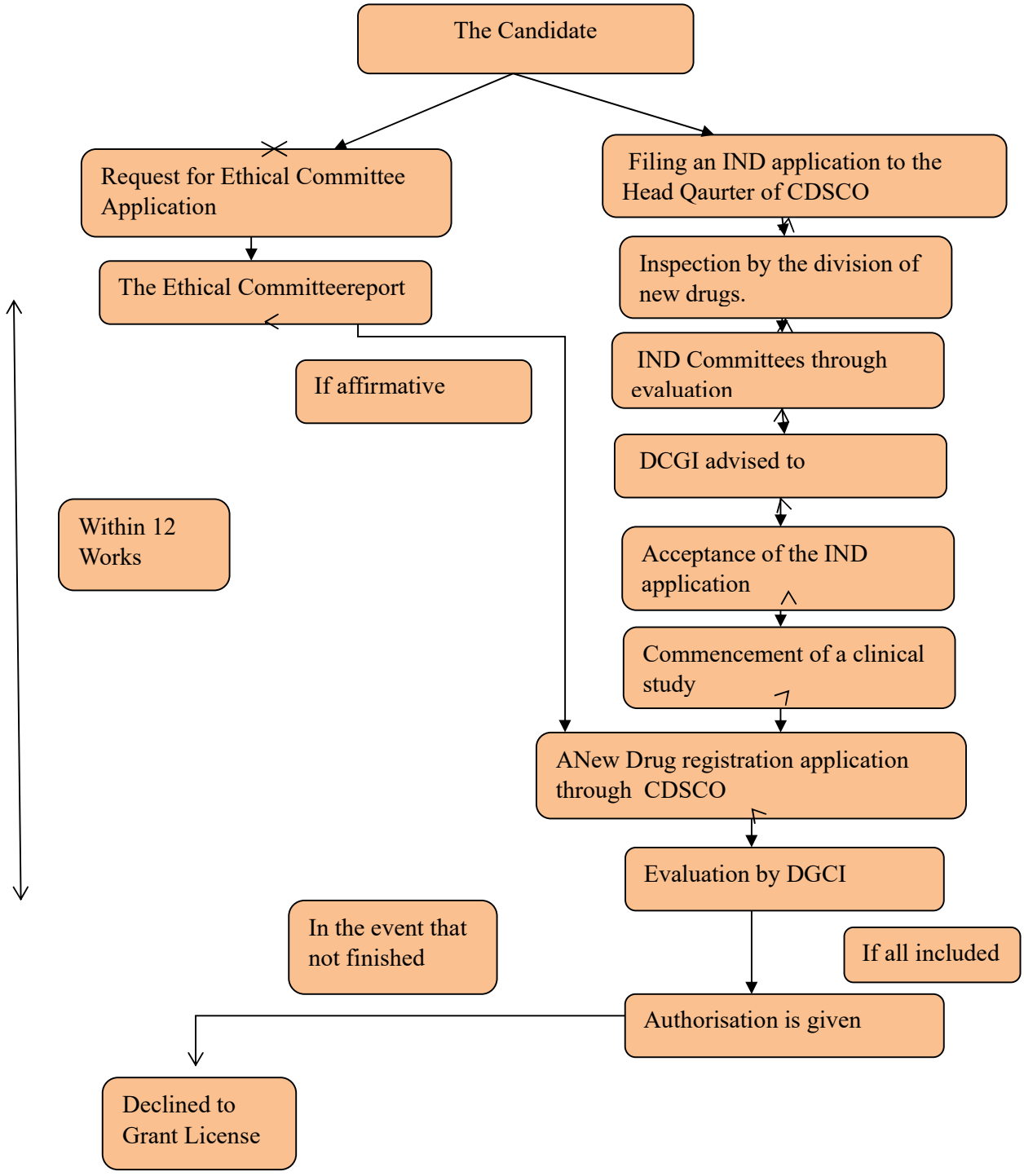

Figure 4: Orphan Drug Review Process In India

CONCLUSION:

The approval process for orphan drugs differs greatly throughout key jurisdictions in Europe, India, and the USA. The development of orphan drugs is dependent on several variables, such as the particular drug, the regulatory landscape, and the available funding. Although every location provides incentives and accelerated routes, careful evaluation is necessary before obtaining permission due to variations in definition, data needs, and regulatory structure. Even while every region takes a different approach, there is a clear trend toward giving orphan drug research priority. To guarantee fair access to life-saving therapies for patients with rare diseases, international cooperation is necessary as long as differences in regulatory frameworks and resource availability persist.

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