A Review of Therapeutic Isolation, Formulation Design, and Drug Safety Policy in the Paediatric Population

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Abstract
This present study focuses on the recent guidelines which have been framed to regulate the pediatric formulations along with their implementation with a subtle mention of change in the present scenario regarding perception of safety and acceptability of pediatric dosage form. Some recent case studies regarding pediatric formulation safety failure have been emphasized to strengthen the pediatric legislative framework in India. Based on these case studies, this study calls for coordinated efforts in the field of pediatric drug safety.
Keywords: *Pediatric drug regulation, Fixed dose combinations, CDSCO, Age appropriate formulation, Pediatric drug safety*

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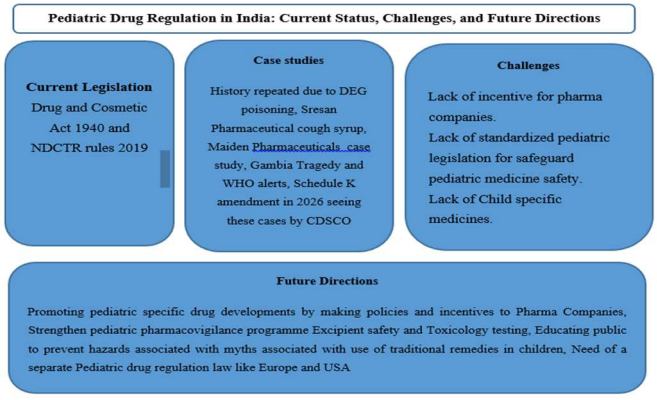

Fig 1: Graphical Abstract

1. Introduction

The medical treatment of children is a sensitive area in the pharmaceutical sciences. The scope of the present study focuses on the population ranges from the extremely low birth weight infant to the adolescent who may be physiologically equivalent to a young adult. This heterogeneity, along with the historical underrepresentation of children in clinical trials, has created a gap between medicines available and those truly suitable for paediatric use[1]. The WHO, the European Medicines Agency (EMA), and the U.S. Food and Drug Administration (FDA) have introduced guidelines over the past 20 years designed to encourage age appropriate formulations[2].

This study framed around ideas. First, it examines the scientific basis for considering children as therapeutically distinct from adults. Second, it examines the regulation of pediatrics pharmaceutical, cosmetics and neutraceuticals products in India. Third, it examines the availability of pediatric medicines in the Indian market and structural determinants affecting availability. Finally, it explores the current regulatory framework in India related to pediatric drug safety and the specific case of FDC cough and cold medicines,

including an in depth examination of the Coldrif contamination crisis of 2025[20].

It is a well-established fact that children's dosage forms lag behind those for adults. The 20th century outlined, ethical and practical obstacles in the conduct of clinical trials in children, and most medicines that have been used in children have not been formally evaluated in this group. This led to a "therapeutic isolation," where children were given medicines developed, dosed and formulated for adults; in many instances, pediatric dosing was simply based on a scaling up of the adult dose on weight and age basis without specific research[3].

This was recognized and resulted in a series of regulatory changes throughout the world. Legislative incentives and requirements since the late 1990s (such as the Best Pharmaceuticals for Children Act and Paediatric Research Equity Act in the United States) have encouraged manufacturers to undertake research in pediatric populations as part of the patent extension process or as a post marketing requirement[4]. The European Union (EU) has adopted a regulation that includes some measures including the Paediatric Investigation Plan[5]. WHO has also had a continuous interest in pediatric formulation; specifically, the campaign "Make Medicines Child Size" and the different versions of guidance on the development of pediatric medicine[6].

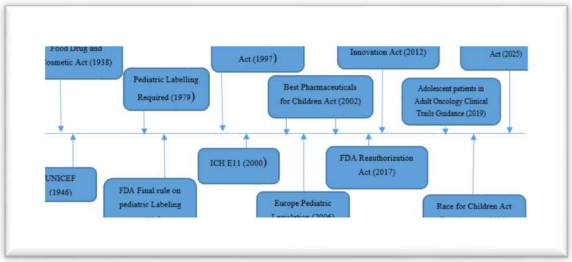

Fig 2: History of Paediatric Drug Legislation Evolution

1.2 Why India Is a Critical Case Study

India is one of the world's biggest providers of generic medicines, including a significant proportion of pediatric medicines sold within India and in export markets which including low and middle income countries; therefore, the quality and design of pediatric medicines produced in India affect not only in India but also in other countries[7]. This international dimension is reflected directly in the 2022 WHO Medical Product Alert about Indian cough syrups associated with deaths of children in West Africa[8]. Meanwhile, India has one of the largest pediatric populations in the world, so even small problems with formulation or quality of marketed products can impact a large numbers of children[9].

The regulatory framework for medicines in India has never had a dedicated, stand-alone pediatric legislation like the EU Paediatric Regulation[10]. However, pediatric drug regulations are included in general New Drug Approval requirements or in the National List of Essential Medicines. In addition Indian regulatory take action when safety signals are identified about use of drugs in children[11].

1.3 Methodology and Scope

This paper follows a narrative review format that involved aggregation of peer reviewed literature on pediatric drug safety, WHO and national regulatory guidance documents, and current news and regulatory reporting on pediatric drug safety events in India from 2022 to 2025[12]. Recent news reports were also included alongside peer reviewed literature because several regulatory developments and safety incidents were recent enough at the time of writing that they had not yet been formally published in scientific journals, yet remain important to the pediatric formulation policy discussion in India. This study examines the key regulatory flaws areas in India by examines the current pediatric dosage form legislative scenario.

1.4 Objectives of the Review

The objectives of this review are:

- To study the pharmacokinetic, physiological, and behavioral parameters which contribute for pediatric specific formulation design.
- To study the current pediatric pharmaceuticals, cosmetic and nutraceuticals products legislation in India.
- To map the regulatory landscape governing pediatric medicines in India, especially the important changes on developments between 2022 and2025.
- To critically examine recent landmark case studies of pediatric drug safety failures in India, including the FDC restriction of December 2023 and the Coldrif diethylene glycol contamination crisis of 2025.
- To identify priority areas requiring focused attention from formulation development and regulation so that safer and effective medicine can be provided to pediatrics.

2. Pediatrics are not Small Adults: The Scientific Rationale

The idea of "Children are not Small Adults" has been adopted in pediatric pharmaceutics as a slogan and is the recognition that the division of the adult dose by body weight or surface area is not always effective or even safe[13]. The physiology, pharmacokinetics and behavior of this principle are discussed below.

2.1 Developmental Pharmacokinetics

Pharmacokinetics (Absorption, Distribution, Metabolism & Excretion) differ considerably during

pediatric development[14]. Neonates have a relatively high pH in the stomach which can influence the dissolution and absorption of weakly acid and basic drugs, as well as acid labile drugs[15]. Gastric emptying time and intestinal transit are also affected, which affects the rate and extent of oral drug absorption in early infancy[16]. The capacity of the liver to metabolize drugs is still underdeveloped at birth and matures at different rates for different groups of enzymes in the first months and years of life. Neonates have reduced renal function glomerular filtration rate (GFR) normalized to body surface area which increases during infancy and reaches adult levels in early childhood[17]. Also, major differences in body composition as neonates/infants have more TBW and ECF per kg BW than adults, which impacts the volume of distribution of hydrophilic drugs[18]. Neonates have a very high surface area and skin permeability, which could have implications for topical and transdermal products such as excipient absorption through the skin[19].

2.2 Behavioral and Acceptability Considerations

In addition to pharmacokinetics, the palatability of a drug – its flavor, odor, consistency, size and convenience to take – are important because it directly influence children willing to take and able to take it and therefore therapeutic effects[20]. However active pharmaceutical ingredients (APIs) with a bitter taste need taste masking techniques like flavouring agents, sweeteners, coating techniques, complexation with cyclodextrins or ion exchange resins[21]. The dose volume for oral liquids is recommended to be limited to about 5 mL for children < 5 years and 10 mL for children > 5 years, based on practical limits of reliable swallowing and dose measurement. Another factor that influences adherence is how often the medication is to be taken; more than 2 daily doses are more difficult to adhere to, especially at school where a trained caregiver might not be around[22].

2.3 Age Classification Systems Used in Paediatric Formulation Guidance

Several international regulatory bodies have adopted ICH harmonised age classification systems to guide formulation development across the pediatric developmental spectrum. The classification used in this paper follows the categories recommended by the International Council for Harmonization (ICH) guideline E11(R1) on clinical investigation of medicinal products in the pediatric population, which aligns closely with those adopted by the EMA and FDA[23.] Table 1 summaries these categories and associated formulation considerations.

Table 1. Age Classification Categories and Associated Formulation Considerations

Age Group	Age Range	Key Characteristics
Preterm Neonates	Born before 36 weeks gestational age	Immature organ systems; highly vulnerable to drug toxicity; limited protein binding capacity
Term Neonates	0 to 27 days	Rapid physiological changes; immature renal and hepatic function; higher skin permeability
Infants , Toddlers	Infants (0 to 12 months), Toddler (12 to 36 months)	Rapid growth; developing hepatic enzyme systems; oral liquid formulations preferred
Children	2 years to 11 years	Increasing metabolic capacity; solid oral dosage forms becoming feasible; first-pass metabolism active
Adolescents	12 years to 16–18 years	Near-adult pharmacokinetics; hormonal changes affect drug metabolism; growing autonomy in consent

A further dimension not captured is that child's actual age and developmental or chronological age may not always be the same[24]. For instance, premature infants, may have a chronological age of several months but physiological maturity more comparable to a much younger infant[25]. Therefore for general guidance age groups are useful but they do not always reflect a child's individual needs. Formulation guidance increasingly recognizes that age based categories serve as a starting point but for clinical judgment, healthcare professionals should consider each child's mental and physical development when selecting and prescribing medicines[26].

3. Availability of Age Appropriate Medicines for Children in India

There is a disparity in the availability of dedicated pediatric formulations in India in different therapeutic categories, although India has emerged as a leading

supplier drug globally for generic drugs[27.] This is attributed to a number of structural factors:-

3.1 Economic and Market Factors

An extra investment in the development of a pediatric formulations are required with the correct stability studies, palatability testing and packaging for accurate low volume dosing and the money may not be recovered if the market share for the molecule in the pediatric population is low compared to the adult market[28]. Consequently, a lot of generic manufacturers are still manufacturing adult dosage strength tablets for certain drug classes and the physicians and caregivers have to depend on the extemporaneous compounding or altering the formulations of adult tablets to get to the desired strength[29].

3.2 The Role of Fixed Dose Combinations (FDCs)

Fixed dose combinations, made up of combination of 2 or more APIs in one product, have been exploding in the Indian market, which also includes pediatric cough and cold products[30]. FDCs can be convenient and enhance adherence provided the combination is rational and each component has been appropriately dosed for the target population; but, the Indian market has traditionally had many FDCs that were approved at state level where the rationality of the combination was not well checked by the central authority[31]. This includes medicines with montelukast despite warning from regulators about psychotropic side effects in certain jurisdictions and medicines that combine antihistamines and decongestants which have limited evidence of effectiveness in children[32].

The proliferation use of such FDCs has been identified by both Indian and international researchers act as a contributor to irrational prescribing in pediatric cough and cold management, an area where evidence for the benefit of pharmacological intervention is limited, and where the WHO has specifically advised against the use of over the counter cough and cold medicines in children under five years of age[33].

3.3 Schedule M, Good Manufacturing Practice, and Excipient Quality

Under the Drugs and Cosmetics Act and associated Rules, cough syrups and other liquid oral formulations are regulated as drugs requiring compliance with Good Manufacturing Practice (GMP) standards set out in Schedule M, including requirements for raw material testing, in process controls, finished product testing, and documentation. For pediatric liquid formulations, the testing of pharmaceutical grade solvents and humectants for DEG and EG content is a critical control point, since these toxic contaminants can enter the supply chain through adulterated or industrial grade raw materials[35]. As discussed in Section 6, gaps in the consistent application of these controls have been directly implicated in fatal pediatric poisoning events[46].

3.4 The National List of Essential Medicines and Paediatric Coverage

India's National List of Essential Medicines (NLEM) provides a framework for prioritizing medicines considered to address the population's most important health care needs, and successive editions have included pediatric specific formulations and strengths for a range of conditions, including pediatric antibiotics, antimalarial, and oral rehydration salt[37]. However, NLEM inclusion does not, by itself, guarantee the availability of an age appropriate formulation in the private retail market, where the majority of pediatric medicine purchases in India occur, particularly for self-treating conditions such as upper respiratory tract infections[38].

3.5 Pricing, Access, and the Incentive Structure for Formulation Innovation

Under the Drug Price Control Order, price regulation has an impact on the commercial availability of developing new pediatric formulations, especially for off patent products where ceilings price could be applied which reduce margins for extra development and manufacturing costs[39]. There are important access goals served by price control, but there is a structural tension between the incentive to invest in pediatric specific formulation work and the price control[40]. In India, policy strategies such as differential pricing policies which account for the extra development and quality assurance expense incurred in the creation of dedicated pediatric formulations have not been widely used[41].

4. Regulation of pediatric Pharmaceuticals, Cosmetics, Neutraceuticals products in India

4.1 Paediatric Pharmaceuticals Regulation

India's drug regulatory framework is primarily governed by the Drugs and Cosmetics Act 1940, and its subsidiary legislation. The New Drugs and Clinical Trials Rules 2019, notified under the DCA, represent the most significant recent reform in India's drug regulatory framework[42]. The NDCTr 2019 substantially revised the provisions for clinical trials, including pediatric clinical trials, and introduced several new requirements aligned with international regulatory standards and ICH guidelines. In India there is no separate legislation to regulate the safety and efficacy of pediatric dosage forms[42-33].

4.2 Pediatric Cosmetic Regulations

Table 2:- Paediatric Cosmetic Regulation Evolution

Legislation	**Which it Covers for Baby Cosmetics**
Drug and Cosmetic Act 1940 (Amended 2008)	Primary legislation defining cosmetics , prohibiting

	manufacture/import without license
Cosmetic Rules 2020	Registration process, application forms (COS-1 TO COS-10), labelling, prohibited ingredients, GMP norms [43]
BIS Standards IS 4011:2015	Safety requirements for baby soaps and toiletries[44.]
BIS Standards IS 6608	Baby powder (talc free and talc based) safety norms[45.]
Cosmetics (Amendments) Rules 2023	Updated list of prohibited/restricted ingredients; aligns with EU Cosmetics Regulation for baby products [46.]
Schedule M (Part XV) – Cosmetics	GMP norms for cosmetics manufacturing facilities in India[46.]
Legal Metrology (Packaged Commodities) Rules 2011	Mandatory labelling- MRP , net weight, batch number, manufacturing date, expiry[47]
Consumer Protection Act 2019	Liability for misleading claims on baby cosmetics products[48]

4.3 Pediatric Nutraceutical Regulation in India

Food Safety and Standards Regulations, 2011[51].
Letter Regarding Licensing of Infant Food Other than those Specified in Food Safety and Standards (Food Products Standards and Food Additives) Regulations, 2011 and their compliance. According to this notification the FSSAI has clearly mentioned that the infant milk substitutes, Feeding Bottles and Infant Foods (Regulation of Production, Supply and Distribution Act, 1992) stipulates that any such infant food products which do not have standards under FSS Act, 2006 are need to seek prior approval of the Central Government of India. the FSS (Prohibition and Restriction on Sales) Regulations, 2011 also clarifies that 'No person shall manufacture, sell, store or exhibit for sale, an infant milk food, infant formula and milk cereal-based weaning food, processed cereal-based weaning food and follow up formula except under Bureau of Indian Standards Certification Mark'[52]. Testing of these infant food products is similar to that of any other food product. During testing, microbial and chemical contamination must be considered. The labelling of nutrients and their contents must be checked to ensure they are in compliance to the regulations. Labels must be checked to make sure that they are according to the requirements of the country[53].

5. Recent Regulatory Developments and Case Studies in India (2022 2025)

The main regulatory developments around the safety of pediatric drugs in India, in the last 4 years (2022–25) are reviewed as follows: Restriction of a very common cough and cold combination dosage forms; Large scale quality surveillance of cough syrups (2024)[34]. Contamination crisis of cough syrup with diethylene glycol in 2025. Their importance for regulation is summarized in Table 3.

5.1 The CPM Phenylephrine FDC Restriction (December 2023)

The CDSCO also directed manufacturers to non-use of a widely marketed fixed dose combination (FDC) of chlorpheniramine maleate (2 mg) and phenylephrine hydrochloride (5 mg) in children under four years of age and reflected this in the labelling and package inserts of the product in December 2023[54]. This order came after the Subject Expert Committee (SEC) recommended it in June 2023 amidst reports of a minimum of 141 child deaths linked to cough syrups globally[49].

The restriction was based on two considerations coming together, first the need to re-evaluate the therapeutic benefit of such FDC in young children and second the quality of excipients used while making cough syrup[50]. Other cough and cold FDCs, which were mentioned in the same reports, were also being reviewed, and a study in 2023 showed that several FDCs containing montelukast have been marketed without proper regulations; some of these products were sold as OTC[51].

5.2 Mandatory Batch Testing and the 2024 Quality Surveillance Findings

In response to the 2022 Medical Product Alert by WHO regarding Indian manufactured cough syrup linked to the deaths of children in West Africa, the CDSCO had issued guidelines on mandatory testing of batches of cough syrup before export. There was also sudden increase of quality monitoring surveillance activity in India[53].

From the 7,087 batches of cough syrups tested, around 353 were identified as Not of Standard Quality (NSQ) for various reasons such as the detection of DEG/EG in excess amount, failure of assay tests, microbial contamination, and variations in pH and fill volume. The overall NSQ rate at around 5% may seem relatively low, but several hundred of the substandard batches is still a significant quantity of potentially

unsafe medicine that enters the supply chain. NSQ findings were most often assay failures and pH/volume deviations, although DEG/EG contamination, although smaller in number, but had more serious clinical consequences since they were associated with fatal nephrotoxicity[53].

5.3 The Coldrif Diethylene Glycol Contamination Crisis (2025)

The most serious pediatric event during the period under review was the occurrence of acute kidney injury among infants and young children, mostly below five years of age, in the Chhindwara district and adjoining areas of Madhya Pradesh, India, due to the use of a cough syrup called Coldrif that was manufactured by Sresan Pharmaceuticals in Tamil Nadu, India[56].

Affected children initially presented with mild respiratory symptoms consistent with the common cold, for which the syrup had been administered, but rapidly progressed to severe dehydration, persistent vomiting, abdominal pain, difficulty urinating, and ultimately acute kidney injury and renal failure. Laboratory testing by the Madhya Pradesh government confirmed DEG contamination in Coldrif syrup, leading to a state ban on the product on 2 October 2025. By mid October 2025, the death toll associated with Coldrif poisoning had risen to at least 24 children, the majority under five years of age, with additional children hospitalized.

The Coldrif crisis closely mirrors earlier DEG contamination incidents associated with Indian manufactured cough syrups in other countries, highlight that the underlying quality control failure, inadequate testing of propylene glycol or glycerin raw material for DEG/EG contamination had not been fully resolved by the testing mandates introduced in 2023 for export bound products[63]. In addition, monitoring of medicines sold within India did not prevented from reaching Indian consumers[57].

5.4 Broader FDC Rationalization (April 2025)

In April 2025, the CDSCO directed all State Drug Controllers to stop the manufacture, sale, and distribution of 35 unapproved fixed dose combinations covering multiple therapeutic categories, including several cough and cold and analgesic products. The directive reiterated that approval by a State Licensing Authority does not means approval for the central new drug or FDC approval required under the Drugs and Cosmetics Act, addressing a long standing regulatory loophole that had allowed numerous FDCs, including pediatric formulations, to enter the market without central level rationality review[65].

.5 Summary of Regulatory Timeline and Significance

Table 3. Summary of Major Regulatory Actions Affecting Paediatric Cough/Cold Formulations in India, 2022 2025

Year	Regulatory Action / Event	Significance for Paediatric Formulation Policy
2022	WHO Medical Product Alert: Indian manufactured cough syrups linked to child deaths in West Africa	Triggered international scrutiny of Indian paediatric liquid formulation quality systems
Dec 2023	CDSCO directed CPM (2 mg) + phenylephrine (5 mg) FDC not to be used in children below 4 years; mandatory label warnings	First formal age based restriction on widely sold pediatric cough/cold FDC
2024	CDSCO mandated batch wise testing of cough syrups prior to export	Strengthened quality assurance pipeline; first step that latter helped to create a larger system foe checking medicine quality across India
2024	CDSCO surveillance: ~353 of 7,087 cough syrup batches classified NSQ, including DEG/EG contamination	Quantified scale of quality failures; case strengthen check for excipient grade controls
2025	Coldrif syrup (Sresan Pharmaceuticals) contaminated with DEG; linked to >20 child deaths in Madhya Pradesh	Most severe recent pediatric drug safety crisis in India; intensified calls for FDC rationalization and stricter excipient controls
April 2025	CDSCO directed State Drug Controllers to stop manufacture/sale	Reinforced that state licensing authority approval does not means approval from

	of 35 unapproved FDCs across therapeutic categories	central new drug/FDC approval

6. Areas Requiring Special Consideration for Paediatric Drug Safety in India

The case studies reviewed pointouts toward several areas where focused attention of formulation scientists, manufacturers, regulators, and health systems is required to improve pediatric drug safety in India[66].

6.1 Excipient Grade Quality Assurance

The recurrence of DEG contamination incidents, despite increased regulatory attention since 2022, indicates that current controls on excipient sourcing and testing are insufficiently robust. Mandatory testing of every incoming batch of propylene glycol, glycerin, sorbitol, and similar solvents for DEG and EG using validated analytical methods such as gas chromatography, prior to release for use in manufacture, represents a non-negotiable minimum standard for any liquid oral pediatric formulation[59].

Table 4. Difference in the safe limit of excipients in pediatric and adult formulation

Excipient	Pediatric Limit	Adult Limit	Key concern
Propylene Glycol	50 mg/kg/day in children under 5 years; as low as 1 mg/kg/day in preterm/term neonates	Up to ~500 mg/kg/day generally considered safe	CNS depression, hyperosmolarity, seizures
Ethanol	EMA tolerance limit cited as low as ~6 mg/kg/day in youngest infants	Higher tolerance (varies by body weight, no fixed low ADI)	Neurotoxicity, cardiovascular effects
Benzyl Alcohol	ADI ~5 mg/kg/day; avoided entirely in neonates	Generally regarded as safe at higher doses in adults	"Gasping syndrome" in neonates
Methylparaben	Concern at levels as low as 1.2 mg/kg (bilirubin displacement risk)	ADI ~10 mg/kg/day (JECFA, adult general population)	Bilirubin albumin displacement, hyperbilirubinea
Propylparaben	Restricted in neonates similarly to methylparaben (limited data)	ADI ~10 mg/kg/day (combined parabens, JECFA)	ADI~10 mg/kg/day (combined parabens, JECFA)
Polysorbate 80	Caution in preterm neonates (linked to E-Ferol syndrome historically)	Widely used, high tolerance in adults	Hepatic/renal toxicity in low-birth-weight infants
Sorbitol	Limited data; caution in infants due to osmotic diarrhea	No fixed ADI; used commonly (osmotic laxative effect at high doses)	GI disturbance, osmotic diarrhea

6.2 Rationalization of Pediatric FDCs

The continued presence of FDCs in the pediatric cough and cold treatment, that combine ingredients with limited evidence of benefit, or that include components subject to safety warnings in other countries, suggests that the rationalization process requires periodic review of approved pediatric FDCs against current evidence is recommended[65].

6.3 Expansion of Age Appropriate Solid Dosage Forms

Greater domestic manufacturing capacity for minitablets, orally dispersible tablets, and multiparticulate systems would reduce reliance on liquid formulations for certain therapeutic categories, thereby reducing exposure to the solvent related risks associated with syrups. Given India's substantial generic manufacturing base, technology transfer and

capacity building initiatives targeting these dosage forms represent a feasible medium term intervention[61].

6.4 Post Marketing Surveillance and Pharmacovigilance

The Coldrif crisis was identified through clinical observation of a cluster of acute kidney injury cases rather than through routine batch surveillance alone, highlighting the importance of clinician level pharmacovigilance reporting and rapid signal detection systems[70]. Linking unusual pediatric clinical presentations to potential medicine related causes is an essential function of a mature pharmacovigilance system[69].

6.5 Caregiver Education and Health System Communication

The precautionary measures adopted by individual hospitals and state governments in 2025 demonstrate that health system actors can respond rapidly to safety signals, but also indicate fragmentation in response. Clear, consistent national guidance regarding the appropriate use, or nonuse, of over the counter cough and cold preparations in young children, communicated to both prescribers and caregivers, would support more uniform practice and may reduce unnecessary exposure in the first instance[67].

6.6 Off label and Unlicensed use of drugs in pediatrics

The use of medications outside of the approved indications as listed in the Summary of Product Characteristics with regard to dosage (including frequency of administration), route of administration, age group, or disease/symptom is known as off-label prescribing. The regulatory body in charge of approving new medications in India is the Drug Controller General of India (DCGI), but there are no precise guidelines regarding the off-label usage of medications. Prescription medications for indications for which they have not been licensed are now prohibited by Indian law. Two years ago, the Indian Medical Council Act was amended to make off-label prescription unlawful. The Drug and Magic Remedies (objectionable advertisement) act of 1954 makes off-label marketing by pharmaceutical businesses illegal in India[71.]

6.7 Strengthening the Central State Regulatory Interface

A recurring pattern across this case studies is the interface between central regulatory authority exercised by the CDSCO and the Drugs Controller General of India and state level licensing authorities[78]. The April 2025 directive concerning 35 unapproved FDCs explicitly addressed the principle that state level approval does not substitute for central authority approval [76]. A systematic analysis of currently marketed pediatric FDCs against central approval records, within a defined timeline for either obtaining central approval or withdrawal from the market, would represent a concrete step toward closing this gap[72].

7. Paediatric Regulation Measures in June 2026

Due to safety concerns over children's medications, the government added two significant
restrictions in addition to FDC ban, even if pediatric variations aren't on it:

OTC Syrup Ban: The Ministry outlawed the sale of any therapeutic syrup over-the-counter (OTC). Due to their removal from Schedule K exemptions, syrups which are mostly used for pediatric care now absolutely need a prescription from a qualified medical professional in order to be purchased. Under-4 Cold Medicine Restrictions: Due to safety concerns, rigorous regulations were strengthened to limit the sale and distribution of common FDC cold syrups containing phenylephrine hydrochloride and chlorpheniramine maleate for children under the age of four[69].

7.1 The Drugs (Fifth Amendment) Rules, 2026 modify the Drugs Rules, 1945

With effect from June 2026, the Drugs (Fifth Amendment) Rules eliminate Schedule K exemptions and require a doctor's prescription for all therapeutic liquid syrups. Furthermore, as of July 2026, the Health Ministry has issued guidelines that forbid the prescription or distribution of any cold and cough medication to children younger than two. By excluding "syrups" from the Schedule K exemptions, the Drugs (Fifth Amendment) Rules, 2026 modify the Drugs Rules, 1945. This change mandates that licensed pharmacies only sell cough and syrup-based medications with a legitimate prescription from a licensed physician[70-].

8. Research Priorities

Along with regulatory and manufacturing recommendations, this study draw attention to several research priorities. First, there is a need for India specific pharmacoepidemiological data characterizing patterns of use of cough and cold preparations in children. Second, highlights the need of a single standalone pediatric dosage form regulation law and their effective implementation to priorities the pediatric health and safety. Third, long term pharmacovigilance research examining program whether the regulatory actions documented in Section 5 have measurably reduced adverse event reporting related to pediatric cough and cold preparations which would provide an evidence base for evaluating regulatory effectiveness .

9. Conclusion

In India, recent regulatory developments between 2022 and 2025 including the restriction of a widely used cough and cold FDC for children under four years, large scale batch quality surveillance

identifying hundreds of substandard cough syrup batches, and the 2025 Coldrif DEG contamination crisis resulting in over 20 child deaths illustrate both the urgency and the complexity of pediatric drug safety. Due to lack of child specific formulations, healthcare providers prescribe the adult medicines based on age and weight basis to children. The availability of pediatric medicine is governed by two ways, firstly its inclusion in National Essential Medicine List and then comparing it to the WHO Essential Medicine List and Indian Pharmaceutical Essential List. Scarcity of child specific medicine indicates in India there is an urgent need of making policy or incentive procedures to encourage pharmaceutical companies to develop Paediatric specific formulations. Companies advertising baby products like cosmetics and neutraceuticals using false and misleading claims are controlled by implementing guidelines for approval for advertising portfolios. In India educating public is an important aspect to prevent hazards associated with the myths related to use of traditional remedies or products in children and safeguard the use of pediatric products in children.

10. Abbreviations

EMA- European Medical Agency
WHO- World Health Organization
CDSCO- Central Drug Standard Control Organization
FDC- Fixed Dose Combination
FDA- Food and Drug Administration
EU- European Union
NLEM- National List of Essential Medicines
ICH- International Conference of Harmonization
NDCTr- New Drug and Clinical Trials Rules
BIS- Bureau of International Standards
OTC- Over the counter
ADI- Acceptable Daily Intake
DCGI- Drug Controller General of India
FSSAI- Food Safety and standard Authority of India

11. Consent for publication

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12. Funding

Nil

13. Conflict Of Interest

The authors declare that there are no conflicts of interest.

14. Author contribution

Tannu gathered all the information needed for this work. Along with discussing and validating the facts Vikas Budhwar and Manjusha Choudhary provided the essential inputs for framing the article. All authors contributed to the compilation of the final manuscript.

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