RESEARCH PAPER

Occupational Exposure to Active Pharmaceutical Ingredients in Drug Manufacturing: Toxicological Risks and Regulatory Compliance Under the Occupational Safety, Health and Working Conditions Code, 2020

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ABSTRACT

The pharmaceutical manufacturing sector in India presents a singular regulatory paradox: the very substances manufactured to heal human populations are capable of causing profound occupational harm to the workers who produce them. Active Pharmaceutical Ingredients (APIs), designed to elicit specific biological responses at defined therapeutic doses, do not discriminate between the patient who receives a controlled prescription and the manufacturing worker who inhales aerosolised particles during milling, granulation, or tableting operations. The occupational absorption of APIs—without the clinical indication, informed consent, or dosing precision that governs therapeutic use—constitutes a distinct category of toxicological risk that demands a correspondingly specialised regulatory response. The enactment of the Occupational Safety, Health and Working Conditions Code, 2020 (Act No. 37 of 2020), which came into force on November 21, 2025, consolidating thirteen pre-existing labour statutes, represents the most significant reform of India's occupational health architecture since the Factories Act, 1948. Yet the critical question this paper interrogates is not whether the OSH Code, 2020 represents legislative progress—it undeniably does—but whether that progress is adequate to the specific, scientifically documented hazards confronted by India's pharmaceutical manufacturing workforce. Drawing on the established toxicological literature on API exposure, a critical analysis of the OSH Code's provisions, comparative review of the EU EMA health-based exposure limit framework and the ISPE Occupational Exposure Band system, and the constitutional jurisprudence of the Supreme Court of India, this paper argues that the OSH Code's general provisions—while necessary—are insufficient without robust sector-specific subordinate legislation establishing enforceable Occupational Exposure Limits (OELs), Highly Potent API (HPAPI) containment mandates, biological monitoring obligations, and intersectoral coordination mechanisms between DGFASLI and CDSCO. The paper concludes with a detailed reform framework grounded in comparative law, toxicological science, and constitutional obligation.

Keywords: Active Pharmaceutical Ingredients (APIs), Occupational Exposure Limits (OELs), OSH Code 2020, HPAPI, Pharmaceutical Manufacturing, Hazardous Processes, Occupational Health, India Labour Law, Constitutional Right to Health.

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1. Introduction: The Paradox of the Pharmaceutical Workplace

There is an inherent irony embedded in pharmaceutical manufacturing that legal scholarship has insufficiently examined. The pharmaceutical factory worker labours in the production of compounds designed to alleviate human suffering—yet the manufacturing process itself regularly exposes that worker to those same pharmacologically active compounds under conditions that the manufacturer would never countenance in a clinical setting. A patient receiving cyclophosphamide for cancer treatment does so under precisely monitored dosing, informed consent, regular haematological surveillance, and specialist clinical oversight. The worker who packages the cyclophosphamide API receives none of these protections as a matter of legal obligation in India today, and the chronic, cumulative absorption that results has been scientifically documented to produce chromosomal damage, mutagenic urinary profiles, and elevated cancer risk in pharmaceutical manufacturing populations (Sessink & Bos, 1999).

This paper begins from the premise that the occupational health challenge of API exposure in pharmaceutical manufacturing is qualitatively different from conventional industrial chemical hazards, and that this qualitative difference demands a regulatory architecture designed specifically around the unique intersection of toxicological science and pharmaceutical manufacturing practice. Conventional industrial chemicals—solvents, heavy metals, airborne particulates—are hazardous at concentrations many orders of magnitude higher than their therapeutic equivalents. APIs, by contrast, are engineered for biological activity at the lowest possible dose. The OEL for a typical industrial solvent like toluene is 188 mg/m³; the OEL for a representative HPAPI may be as low as 0.001

µg/m³—a differential of nine orders of magnitude. No general industrial safety standard can bridge this gap without pharmaceutical-specific content.

The regulatory backdrop is defined by the OSH Code, 2020, which came into force on November 21, 2025, consolidating India's occupational safety regime into a single statute covering establishments with ten or more workers, with specific provisions for hazardous processes. The Code's consolidation of thirteen predecessor statutes represents a structural achievement that must be credited. But the constitutional jurisprudence of the Supreme Court of India—from *Bandhua Mukti Morcha v. Union of India* (1984 SCR (2) 67) through *Consumer Education and Research Centre v. Union of India* (1995 AIR 922) to the 2024 silicosis judgment (2024 INSC 582)—establishes that the right to a safe and healthy workplace is a non-derogable facet of the fundamental right to life under Article 21, and that the adequacy of statutory protection is itself justiciable. This paper argues that the OSH Code, 2020 falls short of that constitutional standard in its application to pharmaceutical API manufacturing, and maps the specific legislative and administrative reforms required to bridge that gap.

2. The Toxicological Dimensions of API Exposure: Science, Risk, and the Limits of General Industrial Safety Standards

2.1 The Nature of the Hazard: Why APIs Demand a Special Regulatory Category

The foundational insight of pharmaceutical occupational hygiene—that API exposure constitutes a distinct category of occupational hazard—was systematically articulated by Heron and Pickering (2003) in their authoritative review published in *Occupational Medicine*. Conducting a systematic MEDLINE-based literature review, Heron and Pickering established that "APIs are designed to produce biological change in the human body, which is an unacceptable outcome in the pharmaceutical worker," and concluded that "adverse effects on health from exposure to potent agents, such as corticosteroids, sex hormones and antibiotics, can occur" unless "careful risk assessment and appropriate control measures are implemented" (Heron & Pickering, 2003, pp. 357–362). The significance of this conclusion extends beyond its clinical content: it establishes that the hazard posed by API exposure is not incidental or hypothetical, but pharmacological and inherent—constituted by the same molecular mechanism that makes the API therapeutically valuable. Regulatory frameworks that treat API exposure as equivalent to exposure to generic industrial chemicals therefore misapprehend the nature of the hazard from the outset.

This pharmacological specificity has profound implications for the methodology of hazard control. The general principle of industrial hygiene—that hazardous substances can be controlled by reducing airborne concentrations below an established threshold—applies to APIs only if the threshold is derived from the API's specific pharmacodynamic and toxicological profile, not from generalisable physical properties. Naumann et al. (1996), in the seminal paper establishing pharmaceutical OEL methodology, argued for a "performance-based" approach in which the OEL is derived from the No Observed Adverse Effect Level (NOAEL) or Lowest Observed Adverse Effect Level (LOAEL) identified in preclinical and clinical data, adjusted by a series of safety factors to account for interspecies differences, intraspecies variability, exposure duration, and severity of the pharmacological endpoint (Naumann et al., 1996, p. 33). This methodology, subsequently refined by Reddy et al. (2022) in the *Journal of Applied Toxicology* to incorporate Benchmark Dose modelling and read-across approaches for data-poor compounds, makes clear that pharmaceutical OEL derivation produces exposure limits "thousands of times lower than typical industrial chemical exposure limits" for high-potency compounds. The ISPE Occupational Exposure Band (OEB) system operationalises this approach by classifying APIs into five hazard bands—from above 1,000 µg/m³ for the lowest-hazard compounds to below 1 µg/m³ for HPAPIs—with the lowest band encompassing compounds including cytotoxic drugs, potent steroids, and targeted oncology agents that require maximum containment technology for safe manufacture.

The practical consequence is that the Indian legal framework's general provisions on dust control, ventilation, and PPE provision—whether under the Factories Act, 1948 or its successor, the OSH Code, 2020—provide no meaningful protection against API exposure unless supplemented by compound-specific OELs and containment standards. The absence of such standards in Indian law is not a minor technical gap; it is the fundamental reason why thousands of pharmaceutical manufacturing workers in India operate in conditions of unquantified, unverified API exposure daily.

2.2 The Documented Health Consequences: From Sensitisation to Malignancy

The health effects of occupational API exposure documented in the scientific literature span a spectrum from reversible sensitisation responses to irreversible systemic harm, and any serious regulatory analysis must engage with this spectrum in full, because the regulatory response required differs significantly across it.

At the sensitisation end of the spectrum, occupational exposure to beta-lactam antibiotics—penicillins and cephalosporins—produces IgE-mediated type I hypersensitivity reactions in a significant proportion of manufacturing workers, manifesting as occupational asthma, rhinitis, and urticaria (Heron & Pickering, 2003). The clinical consequence is that affected workers must be

permanently removed from beta-lactam manufacturing environments to prevent progressive and potentially fatal allergic disease. Beta-lactam sensitisation is irreversible; once a worker is sensitised, no level of engineering control can permit continued assignment to that role. The regulatory emphasis must therefore be on prevention through pre-employment screening, biological monitoring to detect early sensitisation, and strict engineering controls below the sensitisation threshold—none of which is currently mandated by Indian law.

At the severe end of the spectrum, occupational exposure to cytotoxic and antineoplastic APIs poses mutagenic, carcinogenic, and teratogenic risks that warrant comparison with the asbestos hazard that generated India's constitutional occupational health jurisprudence. Sessink and Bos (1999), in their comprehensive review in *Drug Safety*, documented biological monitoring data from pharmaceutical manufacturing workers demonstrating cyclophosphamide absorption—confirmed by urinary drug quantification—"even when protective measures were taken and safety guidelines were followed," and calculated excess cancer risk levels from the measured urinary concentrations that would be considered unacceptable by any regulatory standard (Sessink & Bos, 1999, p. 355). Chromosomal aberrations and sister chromatid exchanges—validated biomarkers of DNA damage and harbingers of potential carcinogenesis—have been consistently documented in cytotoxic drug manufacturing workers across multiple independent studies. That these findings have not prompted pharmaceutical-specific occupational health regulation in India represents a fundamental failure of regulatory precaution.

Between sensitisation and carcinogenicity lies the category of systemic pharmacological effects from hormonal API exposure. The manufacturing of hormonal contraceptives and hormone replacement therapy formulations exposes workers to compounds with potent endocrine activity at airborne concentrations achievable in inadequately controlled manufacturing environments. Heron and Pickering (2003) documented clinical case series of gynecomastia in male workers, menstrual irregularities and galactorrhoea in female workers, and adrenal suppression in corticosteroid API manufacturing personnel—effects arising not from accidents but from routine operational API exposure below concentrations that would trigger general industrial dust control measures (Heron & Pickering, 2003, p. 360). The reproductive toxicological significance of these effects—for workers of reproductive age who constitute a substantial proportion of the pharmaceutical manufacturing workforce—raises constitutional concerns under Article 39(e), which directs the State to ensure citizens are not forced to work in conditions injurious to their health or to the health of their children.

For HPAPIs, the threshold for adverse health effects is so low that wipe sampling of pharmaceutical manufacturing surfaces has demonstrated residual contamination at concentrations sufficient to produce pharmacological effects through dermal absorption during normal maintenance activities, even in the absence of active manufacturing operations. The FPS Pharma industry analysis confirms that for HPAPIs with OEL below 10 µg/m³, "risk mitigation of handling potent APIs can only be accomplished through the adoption of containment systems"—specifically isolators, downflow booths, and closed-system processing equipment validated through SMEPAC testing to achieve the required Containment Performance Target (FPS Pharma, 2022). The absence of any Indian statutory requirement for HPAPI containment equipment qualification represents a fundamental regulatory gap.

2.3 The Epidemiological Evidence Gap and Its Regulatory Implications

A recurring limitation in the toxicological literature—acknowledged by Heron and Pickering (2003) themselves—is the relative paucity of large-scale epidemiological studies demonstrating population-level mortality outcomes in pharmaceutical manufacturing workers. This arises from the relatively small workforce at individual pharmaceutical plants, the healthy worker effect, the long latency between cytotoxic drug exposure and clinical malignancy, and the absence—in India as elsewhere—of mandatory occupational disease registries.

The regulatory temptation is to treat this evidential limitation as a reason to delay sector-specific regulation—to await definitive epidemiological proof before imposing additional compliance obligations. This temptation must be firmly resisted for both scientific and legal reasons. The scientific argument is the precautionary principle: where a substance is known to be biologically active at very low concentrations and plausible mechanisms for occupational harm have been established through mechanistic toxicology and biological monitoring studies, the absence of definitive epidemiological mortality data does not constitute evidence of safety. The legal argument is equally compelling: the Supreme Court in *Consumer Education and Research Centre* (1995) did not require epidemiological proof of excess mortality among asbestos workers before issuing constitutional directions—it required only the demonstration that workers were exposed to a substance of known hazardous potential without adequate protection. The same analytical framework applies with full force to pharmaceutical manufacturing workers exposed to cytotoxic drugs and HPAPIs. Critically, the gap in epidemiological evidence is itself a

product of the absence of biological monitoring requirements and occupational disease registries—both of which must be mandated by the reformed regulatory framework.

3. Critical Analysis of the OSH Code, 2020: Advances, Ambiguities, and Analytical Gaps

3.1 The Legislative Architecture: What the Code Achieves

The OSH Code, 2020 achieves four significant structural advances that deserve recognition before its limitations are examined. First, the consolidation of thirteen statutes into a single Code eliminates the jurisdictional confusion and compliance arbitrage that the fragmented earlier regime enabled—pharmaceutical manufacturers previously operated across the intersection of the Factories Act, the Contract Labour Act, and multiple state-level rules, with the result that regulatory gaps were exploited with reasonable legal cover. The Code's unified coverage of all establishments employing ten or more workers, combined with its explicit provision that hazardous establishments are covered regardless of size, closes this gap for small and medium API manufacturers who previously fell between statutory stools.

Second, the employer duty under Section 23—requiring employers to ensure, so far as is "reasonably practicable," the health, safety, and welfare of all workers—adopts a standard that cannot, in the pharmaceutical context, be satisfied by generic ventilation and PPE measures. The "reasonably practicable" standard, properly interpreted, requires the employer to demonstrate knowledge of the specific pharmacological hazards of APIs being manufactured and implementation of controls calibrated to those specific hazards. Third, the hazardous process provisions under Section 38—requiring health records, competent person supervision, worker information, emergency planning, and periodic medical examination—establish a statutory framework for occupational health surveillance that, though incomplete, provides legal authority upon which pharmaceutical-specific subordinate regulations can be built. Fourth, the Code's digital compliance architecture—replacing multiple returns with a single electronic return and providing for digital health records—creates the infrastructure for a national pharmaceutical occupational health surveillance system.

3.2 The Analytical Gaps: Where the Code Fails Pharmaceutical Workers

The advances described above are real but insufficient, and their insufficiency is analytically demonstrable rather than merely asserted. The central argument of this paper is that the OSH Code, 2020 fails pharmaceutical manufacturing workers in four interconnected ways: the absence of substance-specific OELs; the absence of technology-specific containment requirements for HPAPIs; the absence of biological monitoring obligations; and the absence of intersectoral regulatory coordination with CDSCO. Each failure is analytically distinct, but they interact to produce a regulatory regime in which a pharmaceutical manufacturer handling cytotoxic HPAPIs in open-process operations can be in full technical compliance with the OSH Code while exposing workers to API absorption levels that would be considered unacceptable under any scientifically defensible occupational health standard.

The absence of pharmaceutical OELs is the most fundamental gap. The Code establishes the duty to maintain a safe working environment, but provides no quantitative standard against which to assess compliance. Without an OEL, neither the employer, Safety Officer, inspector, nor court can determine whether the airborne API concentration in a manufacturing environment is acceptable. The employer cannot know whether engineering controls are adequate without a compliance target; the Safety Officer cannot conduct meaningful environmental monitoring without reference values; the inspector cannot determine whether a violation has occurred without an enforceable exposure limit; and the court cannot adjudicate a compensation claim without an objective measure of excessive exposure. The entire edifice of occupational health regulation for pharmaceutical manufacturing rests on a foundation that does not exist in Indian law.

The HPAPI containment gap compounds the OEL gap in a particularly dangerous way. Even if OELs were established, they would be operationally meaningless without requirements for the engineering controls necessary to achieve compliance for compounds with OELs in the nanogram-per-cubic-metre range. For OEB 5 compounds with OELs below 1 $\mu g/m^3$, standard ventilation systems and even powered air-purifying respirators cannot reliably maintain worker exposure below the OEL. The only technically viable approach is closed-system isolator processing with validated containment performance. The OSH Code's general requirement for a safe working environment under Section 23 does not—and cannot, without pharmaceutical-specific technical standards—mandate isolator technology or require SMEPAC qualification testing. A manufacturer of a potent cytotoxic HPAPI can satisfy the literal requirements of Section 23 by providing standard industrial PPE while exposing workers to HPAPI concentrations orders of magnitude above any scientifically defensible OEL. This is not theoretical; it is the operating reality of a significant segment of India's API manufacturing sector.

The absence of biological monitoring obligations creates a third analytical gap that is perhaps the most practically consequential. Sessink and Bos (1999) established that biological monitoring of pharmaceutical manufacturing workers using

urinary drug quantification can detect systemic absorption even in the presence of formally compliant engineering controls, revealing exposure through dermal absorption and inadvertent ingestion pathways that airborne monitoring misses. The OSH Code's Section 38 provides authority for periodic medical examinations in hazardous processes, but this provision has never been implemented to require pharmaceutical-specific biological monitoring. The result is a regulatory system in which systemic API absorption in pharmaceutical manufacturing workers goes not merely unregulated but unmeasured—making the fundamental occupational health risk invisible to both regulators and workers.

Finally, the regulatory silo between DGFASLI and CDSCO means that a pharmaceutical manufacturer may receive a clean GMP certificate from CDSCO while simultaneously operating API manufacturing facilities with inadequate occupational exposure controls that violate the OSH Code. Conversely, a labour inspection may identify general workplace deficiencies without the technical pharmaceutical expertise to assess API-specific containment adequacy. This regulatory arbitrage is structural, and closing it requires not merely administrative coordination but legislative mandate.

3.3 The Problem of Subordinate Legislation: Structure Without Substance

The OSH Code is an enabling statute: its general provisions acquire operational content through subordinate rules made by Central and State Governments. The Code's effectiveness in protecting pharmaceutical workers therefore depends critically on pharmaceutical-specific subordinate rules. The available evidence on their status is not encouraging. As of early 2026, full implementation depends on final central and state rules, with many states still operating on drafts and implementation "progressing" without certainty (Complinity, 2026). The Code's general provisions are in force, but the sector-specific technical content that would give those provisions operational meaning for pharmaceutical API manufacturing—OELs, HPAPI containment requirements, biological monitoring protocols—does not yet exist in any enacted form.

The Gujarat precedent—where the state government has finalised pharmaceutical-specific OSH rules for chemical and pharma clusters including mandatory digital audit trails for chemical handling, emergency plans, and periodic mock drills—represents a template that the Central Government must systematically evaluate for national replication (Complinity, 2026). State-level variation in pharmaceutical OSH standards is itself a problem in a sector where many manufacturers operate across multiple jurisdictions, creating competitive distortions and worker protection gaps that only central rules can eliminate.

4. Constitutional Foundations and Judicial Mandate for Pharmaceutical Worker Protection

4.1 The Article 21 Right to Health and Its Occupational Dimension

The constitutional architecture of worker protection in India rests on a foundation far more robust than the statutory provisions that directly address occupational safety. The Supreme Court of India's interpretation of Article 21—guaranteeing the right to life and personal liberty—as encompassing the right to health, the right to a dignified working environment, and the right to protection from known occupational hazards, provides a constitutional standard against which the adequacy of the OSH Code, 2020 must be assessed. This standard is not merely aspirational; it is judicially enforceable through writ jurisdiction and generates specific, mandatory obligations on both the State and private employers.

The foundational authority is *Consumer Education and Research Centre & Ors. v. Union of India & Ors.* (1995 AIR 922; 1995 SCC (3) 42), in which the Supreme Court, adjudicating a PIL concerning asbestos workers, held that "the right to health and medical care is a fundamental right under Article 21" and that workers' right to health is "an integral facet of the meaningful right to life". The Court's detailed directions—requiring hygienic working conditions, periodic comprehensive medical examinations, maintenance of health records throughout employment and thereafter, insurance coverage for occupational disease, and prohibition on dismissal during treatment—established the constitutional minimum of employer obligation in hazardous industries. Crucially, the Court did not condition its directions on proof of actual mass morbidity among asbestos workers; it acted on the basis of the known, scientifically documented hazardous potential of asbestos and the demonstrable absence of adequate legal protections for exposed workers. The analytical parallel to pharmaceutical manufacturing workers exposed to cytotoxic HPAPIs is precise: the scientific documentation of harm potential is at least as strong, the demonstrable inadequacy of legal protections is equivalent, and the constitutional obligation is therefore equally engaged.

The Court further held that the occupational right to health "must be read with Articles 38, 39(e), 41, 42, 43, and 48A" of the Constitution, embedding it within the Directive Principles requiring the State to ensure just and humane conditions of work and to protect workers from conditions injurious to their health. Article 39(e)—which directs the State to ensure citizens are not compelled to work in conditions injurious to their health—generates a specific constitutional obligation to ensure that workers are not forced, by the economic realities of a competitive generic pharmaceutical labour market, to accept employment in HPAPI manufacturing environments without adequate legal protection.

4.2 Absolute Liability and the Constitutional Accountability of Pharmaceutical Manufacturers

The doctrine of absolute liability, established in *M.C. Mehta v. Union of India* (1987 SCR (1) 819), provides an additional and analytically powerful basis for the constitutional accountability of pharmaceutical manufacturers who fail to protect workers from API exposure. In *M.C. Mehta*, the Supreme Court departed from the English rule in *Rylands v. Fletcher* and established that enterprises engaged in inherently hazardous activities are subject to absolute liability—without the traditional defences of act of God or consent—for any harm caused by their hazardous activities to workers and the surrounding community. Manufacturing HPAPIs—compounds engineered for pharmacological activity at sub-microgram concentrations—constitutes an inherently hazardous activity for purposes of the *M.C. Mehta* doctrine. The "escape" that triggers liability need not be a dramatic industrial accident; it encompasses the chronic, low-level absorption of cytotoxic HPAPIs by manufacturing workers through inhalation and dermal contact in circumstances where the employer failed to implement the containment controls necessary to prevent that absorption. On this analysis, a pharmaceutical manufacturer who operates HPAPI manufacturing in open-process conditions without isolator containment or compound-specific OEL-based controls would be absolutely liable for any occupational malignancy, reproductive injury, or systemic pharmacological harm suffered by workers—and the absence of statutory OELs in Indian law does not displace this constitutional liability; it merely means that constitutional accountability operates independently of statutory compliance.

4.3 The 2024 Silicosis Judgment as Precedent and Analytical Template

The Supreme Court's 2024 judgment in *Writ Petition (C) No. 110 of 2006* (2024 INSC 582) provides the most recent and analytically closest precedent for pharmaceutical manufacturing worker protection. The Court characterised "the pervasive and unchecked prevalence of silicosis among workers in various industries" as a violation of Article 21, and issued systematic directions encompassing mandatory dust suppression, respirator provision, periodic biological monitoring (spirometric and radiological), occupational disease registration, and compensation mechanisms for affected workers and their families (Supreme Court of India, 2024). The analytical framework of this judgment—that chronic occupational disease arising from particulate inhalation in conditions of inadequate regulatory enforcement constitutes a continuing Article 21 violation requiring systemic judicial remedy—transfers directly to pharmaceutical API manufacturing. Both involve chronic inhalation exposure to respirable particulates; both involve the failure of general industrial safety standards to address substance-specific biological hazards; both involve employers who possess knowledge of the hazard yet implement inadequate controls; and both produce disease outcomes with long latency periods that obscure the causal link and delay legal redress.

The silicosis judgment's emphasis on mandatory biological monitoring as the cornerstone of the protective regime is particularly instructive. The Court recognised that the adequacy of engineering controls cannot be verified without independent measurement of the biological effect on workers, and that monitoring systems dependent solely on employer-reported environmental measurements are insufficient where employers have financial incentives to underreport exposure. Applied to pharmaceutical manufacturing, this reasoning compels the argument that biological monitoring of pharmaceutical manufacturing workers—measuring API absorption rather than merely airborne concentrations—must be a mandatory element of any constitutionally adequate occupational health framework.

5. International Regulatory Frameworks: A Comparative Critical Analysis

5.1 The EU EMA Framework: Health-Based Limits as Regulatory Standard

The most analytically rigorous framework for pharmaceutical worker protection currently in operation internationally is the EU system centred on the EMA Guideline (EMA/CHMP/CVMP/SWP/169430/2012). The guideline requires derivation of an Acceptable Daily Exposure (ADE) for all APIs—defined as the dose level below which, based on all available pharmacological and toxicological data, there is no pharmacological or adverse effect in any individual who receives that dose daily for a lifetime. The ADE methodology—comprehensively analysed by Moody et al. (2016) in *Regulatory Toxicology and Pharmacology*—uses a systematic factor-based approach in which the NOAEL from the most sensitive pharmacological or toxicological endpoint is divided by adjustment factors for route extrapolation, interindividual variation, and occupational exposure duration (Moody et al., 2016, p. 39). The resulting ADE can then be converted to an OEL using parameters for worker breathing rate and body weight, providing an enforceable airborne exposure limit directly derived from the API's biological activity profile.

The analytical strength of the ADE/OEL methodology lies precisely in its substance-specificity. Unlike the general threshold approach of industrial chemical regulation, the pharmaceutical OEL methodology treats each API as an individual hazard requiring individual assessment—a scientific necessity given that two corticosteroids may have HPA-axis suppression potencies that diverge by a

factor of 100, or two cytotoxic drugs may require OELs at opposite ends of the HPAPI spectrum. The EU requirement that pharmaceutical manufacturers derive an ADE for every API before production commences therefore serves not merely as a worker health protection—it forces pharmaceutical manufacturers to understand and document the biological risks they are asking their workers to bear. India's complete absence of an equivalent requirement means that the world's third-largest pharmaceutical producer operates its manufacturing sector without the basic occupational health infrastructure that has been mandatory in the EU for over a decade.

Moody et al. (2016) also identified the challenge of data-poor substances for which sufficient pharmacological and toxicological data does not support full ADE derivation, and proposed workable solutions—read-across approaches, conservative default safety factors, and the Threshold of Toxicological Concern (TTC) methodology. The existence of these solutions undermines any argument that the complexity of pharmaceutical OEL derivation justifies regulatory inaction in India.

5.2 The ISPE OEB Framework and Its Translational Value

The ISPE OEB system provides a practically important complement to the ADE/OEL methodology by offering a classification tool usable before formal OEL derivation is complete. By assigning APIs to five hazard bands based on pharmacological potency and linking each band to a specific containment strategy, the OEB system allows manufacturers to implement appropriate engineering controls even for compounds for which a full ADE has not yet been derived (ISPE, 2010). An Indian pharmaceutical manufacturing rule that adopted OEB classification as a mandatory first step—requiring manufacturers to classify each API before production commences and to implement the corresponding containment strategy—would provide meaningful worker protection immediately, without waiting for the development of comprehensive pharmaceutical OELs.

The SMEPAC testing framework, which provides a validated method for verifying that containment equipment achieves its specified Containment Performance Target using lactose monohydrate as a surrogate, allows pharmaceutical manufacturers to verify containment performance before committing workers to HPAPI manufacturing operations (FPS Pharma, 2022). The availability of this validated methodology makes any argument that HPAPI containment requirements would be technically unverifiable entirely untenable.

5.3 Comparative Synthesis: The Reform Gap

A critical comparative synthesis reveals a consistent and analytically significant pattern: India's pharmaceutical occupational health regulation lags the international scientific and regulatory consensus by approximately two decades, and the lag is not attributable to resource constraints but to the absence of regulatory will and the failure to translate scientific knowledge into domestic regulatory requirements. Indian pharmaceutical manufacturers exporting to the EU or the US are already required—by the regulatory conditions of those export markets—to derive ADEs, implement OEB-compliant containment systems, and maintain biological monitoring programmes for their workers. These same manufacturers, operating facilities that produce exclusively for the domestic market, face no equivalent requirements under Indian law. The regulatory consequence is a two-tier occupational health standard: workers in export-oriented plants benefit from internationally benchmarked protections while workers in domestically-oriented plants are governed by the OSH Code's inadequate general provisions.

This regulatory arbitrage is unconstitutional. The right to a safe working environment under Article 21 does not admit of market-destination-based differentiation. The constitutional right of a pharmaceutical worker in a domestic-market API facility to protection from cytotoxic HPAPI exposure is identical to the right of a worker in an export-oriented facility; both are protected by *Consumer Education and Research Centre* (1995) and both benefit from the absolute liability doctrine of *M.C. Mehta* (1987). Closing this regulatory arbitrage gap—by legislating into Indian law the pharmaceutical occupational health standards that Indian manufacturers already apply in their internationally regulated operations—is both the practical objective and the constitutional imperative of the reform agenda proposed below.

6. Towards a Comprehensive Reform Framework: Bridging the Gap Between Constitutional Obligation and Regulatory Reality

6.1 Establishing a Pharmaceutical OEL System Under the OSH Code

The most urgent and foundational reform required is the establishment of a pharmaceutical-specific OEL system under the subordinate rules of the OSH Code, 2020. This system should be developed through a consultative process involving the Ministry of Labour and Employment, CDSCO, DGFASLI, the Indian Pharmaceutical Alliance (IPA), the Bulk Drug Manufacturers Association (BDMA), and independent toxicological experts, adopting the ADE/OEL methodology established by Naumann et al. (1996) and refined by Reddy et al. (2022) as its scientific foundation. For APIs with comprehensive data packages—those for which an ADE has already been derived by pharmaceutical companies for EU or US regulatory purposes—derivation of an Indian OEL could be substantially completed within two years of commencing the consultative process. For data-poor compounds,

OEB classification based on pharmacological class and structural analogy should serve as the operative regulatory standard, with OEB-linked containment requirements mandatory from the point of OEB classification.

The OEL system should be maintained in a publicly accessible database, updated as new pharmacological and toxicological data becomes available, and linked to the CDSCO drug approval database to ensure that OELs are derived for all new APIs entering Indian manufacturing before production commences. A mandatory OEL review cycle—at minimum every five years, or upon availability of significant new toxicological data—should be established in the rules.

6.2 HPAPI Containment Mandates, Intersectoral Coordination, and Safety Officer Reform

Concurrent with OEL development, the OSH Code's subordinate rules should establish mandatory containment requirements for HPAPI manufacturing that are technologically specific and verifiable. For OEB 4 compounds, the rules should require engineering controls validated through mandatory air monitoring. For OEB 5 compounds, the rules must mandate closed-system isolator processing with SMEPAC-verified Containment Performance Targets, pre-commissioning qualification testing, periodic requalification, and biological monitoring for all workers in OEB 5 manufacturing. The Safety Officer threshold for pharmaceutical establishments handling OEB 3-5 compounds should be reduced from the Code's general threshold of 500 workers to 50 workers, reflecting the elevated compound-specific hazard. Safety Officer qualifications for pharmaceutical establishments should include demonstrated competency in pharmaceutical occupational hygiene, OEB classification, OEL interpretation, and biological monitoring design.

The structural prerequisite for these requirements to be effectively enforced is mandatory intersectoral coordination between DGFASLI and CDSCO. Joint inspection protocols under which CDSCO's GMP inspection team includes occupational hygiene competence—and DGFASLI's pharmaceutical inspectors receive training in API hazard classification and containment technology assessment—would eliminate the current regulatory arbitrage. Unified licensing conditions encompassing both GMP and occupational health requirements should be the standard for pharmaceutical manufacturing facility approval. The Gujarat model of finalised pharmaceutical-specific OSH rules with digital audit trails, chemical handling accountability, and mandatory emergency mock drills should be evaluated for immediate national replication under central subordinate rules.

6.3 Biological Monitoring, Reproductive Hazard Provisions, and Occupational Disease Surveillance

Biological monitoring reforms require both legislative and administrative action. The OSH Code's Section 38 should be supplemented by pharmaceutical-specific subordinate rules mandating biological monitoring—with compound-specific analytical methods, action levels, and medical review protocols—for all workers in OEB 3-5 manufacturing. The biological monitoring action level should be set at a fraction of the OEL to allow early detection of systematic control failures before adverse health effects manifest. Workers whose results exceed the action level must be entitled to immediate temporary reassignment to lower-hazard work without loss of pay—explicitly mandated to prevent the economic disincentives that currently discourage workers from disclosing occupational health concerns. The Central Government should establish a national pharmaceutical occupational health surveillance database under DGFASLI, aggregating anonymised biological monitoring data, occupational disease notifications, and incident reports to enable epidemiological analysis—directly addressing the evidence gap identified by Heron and Pickering (2003).

Reproductive hazard provisions require specific legislative attention. Workers of reproductive capacity engaged in the manufacture of reproductive toxins—including hormonal APIs and cytotoxic drugs—should receive specific written risk communication prior to assignment. Pregnant workers and workers planning pregnancy should have a statutory right to temporary transfer to equivalent employment without exposure to reproductive toxins, with transfer costs borne by the employer. These provisions, which have EU analogues in Directive 92/85/EEC, can be implemented under Section 23 of the OSH Code through pharmaceutical-specific subordinate rules without primary legislative amendment, removing any practical obstacle to timely introduction.

7. Conclusion

This paper has argued that the occupational exposure of pharmaceutical manufacturing workers to Active Pharmaceutical Ingredients represents a legally and constitutionally significant hazard that the OSH Code, 2020—despite its structural achievements—fails to adequately address. The argument has proceeded through three analytical registers: the scientific, establishing that API exposure produces documented harm of a character and severity that demands substance-specific regulatory responses (Heron & Pickering, 2003; Sessink & Bos, 1999); the statutory, demonstrating that the OSH Code's general provisions cannot, without pharmaceutical-specific subordinate legislation, provide the OELs, containment requirements, and biological monitoring obligations that adequate pharmaceutical worker protection requires; and the constitutional, establishing that the Supreme Court's jurisprudence from *Consumer Education and*

Research Centre (1995) through the silicosis judgment (2024 INSC 582) generates mandatory obligations that current regulatory arrangements do not satisfy.

The reform framework proposed in Part VI is not aspirational; it is constitutionally compelled. The right to health under Article 21, as interpreted by the Supreme Court, requires the State to establish and enforce a regulatory framework adequate to the known hazards of the workplace. The absolute liability doctrine of *M.C. Mehta* requires pharmaceutical manufacturers operating HPAPI manufacturing without adequate containment to bear the full cost of the occupational harm that results. The failure to establish pharmaceutical OELs, mandate HPAPI containment, require biological monitoring, and coordinate DGFASLI-CDSCO oversight is not merely a policy gap—it is a continuing constitutional violation, measured against the standard that India's own Supreme Court has repeatedly and clearly articulated.

India's status as the pharmacy of the world is built on the labour of workers whose health the law has not adequately protected. The OSH Code, 2020 provides the legislative vehicle for that protection; what is required now is the political will and regulatory competence to build upon it the pharmaceutical-specific framework that the Constitution demands, the science requires, and the workers of India's pharmaceutical industry have earned.

References

Bandhua Mukti Morcha v. Union of India (1984). SCR (2) 67. Supreme Court of India.

Consumer Education and Research Centre & Ors. v. Union of India & Ors. (1995). AIR 922; SCC (3) 42. Supreme Court of India.

Complinity. (2026, April 3). *OSH Code 2020 vs old labour laws in India*. https://complinity.com/blog/compliance/how-does-osh-code2020-compare-with-old-labor-laws/

European Medicines Agency. (2014). *Guideline on setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities* (EMA/CHMP/CVMP/SWP/169430/2012) . EMA.

FPS Pharma. (2022). *What is an HPAPI and why is containment necessary?* https://www.fps-pharma.com/what-is-an-hpapi-and-why-is-containment-necessary/

Heron, R. J. L., & Pickering, F. C. (2003). Health effects of exposure to active pharmaceutical ingredients (APIs). *Occupational Medicine*, *53*(6), 357–362. https://doi.org/10.1093/occmed/kqg115

International Council for Harmonisation (ICH). (2000). *Q7: Good manufacturing practice guidance for active pharmaceutical ingredients*. ICH Harmonised Tripartite Guideline.

ISPE. (2010). *Risk-based manufacture of pharmaceutical products: A guide to managing risks associated with cross-contamination (Risk-MaPP)*. International Society for Pharmaceutical Engineering.

M.C. Mehta v. Union of India (1987). SCR (1) 819. Supreme Court of India.

Ministry of Labour and Employment, Government of India. (2020). *The Occupational Safety, Health and Working Conditions Code, 2020* (Act No. 37 of 2020). Gazette of India, Extraordinary, Part II, Section 1.

Moody, C. M., Macher, J. M., & Swenberg, J. A. (2016). A harmonization effort for acceptable daily exposure application to occupational and pharmaceutical settings. *Regulatory Toxicology and Pharmacology*, *79*, 39–49. https://doi.org/10.1016/j.yrtph.2016.03.015

Naumann, B. D., Sargent, E. V., Starkman, B. S., Fraser, W. J., Becker, G. T., & Kirk, G. D. (1996). Performance-based exposure control limits for pharmaceutical active ingredients. *American Industrial Hygiene Association Journal*, *57*(1), 33–42. https://doi.org/10.1080/15428119691014882

Reddy, M. B., Morrissey, K. M., Morales-Rosado, J. A., Bae, S., & Bhuvana, S. (2022). Approaches for setting occupational exposure limits in the pharmaceutical industry. *Journal of Applied Toxicology*, *42*(1), 1–14. https://doi.org/10.1002/jat.4218

Sargent, E. V., & Kirk, G. D. (1988). Establishing airborne exposure control limits in the pharmaceutical industry. *American Industrial Hygiene Association Journal*, *49*(6), 309–313. https://doi.org/10.1080/15428119691014882

Sessink, P. J. M., & Bos, R. P. (1999). Drugs hazardous to healthcare workers: Evaluation of methods for monitoring occupational exposure to cytostatic drugs. *Drug Safety*, *20*(4), 347–359. https://doi.org/10.2165/00002018-199920040-00004

Supreme Court of India. (2024). *Writ Petition (C) No. 110 of 2006* (2024 INSC 582). Supreme Court of India.

World Health Organization. (2004). *Occupational health: A manual for primary health care workers* (WHO-EM/OCH/85/E). WHO Eastern Mediterranean Regional Office.