Chapter 8:
Access to Pharmaceuticals: State-Industry-Market[152]

- S. Srinivasan and Malini Aisola[153]

At the turn of Independence in 1947, India's pharmaceutical production was worth Rs 10 crore. By 1952, the total turnover of pharmaceutical companies, foreign and Indian, was Rs 35 crore, of which 62 per cent (Rs 21 crore) was of Indian companies. This included Rs 1.16 crore in the public sector. In 1970, the situation was reversed. MNCs had 68 per cent of the pharma market. Of the leading 50 pharmaceutical companies in 1971, 33 were foreign. The total formulations market in India in 1972 was Rs 360 crore. There was very little bulk drug (or active pharmaceutical ingredient (API)) production in India by foreign pharma companies despite the Government's exhortations for self-reliance and saving foreign exchange. The goal of MNCs in India was minimum risk and maximum profit[154].

The Patents Act 1970, passed in 1972, replacing the 1911 Patents and Designs Act, changed the entire scenario. The new Act by excluding product patents for medicines, initiated a dream run for India's local pharmaceutical industry. As a result several Indian entrepreneurs and business groups started making drug intermediates and bulk drugs. By 1999-2000, most of the bulk drugs India needed were made in India[155] as also the machinery and the technology that were needed. Scientists at government institutions, the National Chemical Laboratory (NCL), Pune, and the Regional Research Laboratory (RRL, renamed Indian Institute of Chemical Technology, IICT), Hyderabad, played stellar roles in this saga of bulk drug revolution by synthesizing and discovering more efficient ways of making many of the bulk drugs[156]. The domestic formulation industry grew by leaps and bounds to Rs 18,354 crore in 2000-01 which would increase to almost Rs 90,000 crore by 2015-16.

India had an enviable spread of public sector enterprises in pharmaceuticals until about 1970. Public sector pharmaceutical plants were set up to control the "commanding heights" of the Indian economy. The Hindustan Antibiotics Limited (HAL) was set up in 1954, itself inspired by the experience of the Haffkine Institute, Bombay, and some of its leading scientists. HAL and the Indian Drugs and Pharmaceuticals Ltd (IDPL) established in 1961, would do commendable work in laying the foundations of a technological base for making APIs and formulations with the then goals of self-reliance and import substitution in mind. But after the post-Patents Act 1970 boom of the pharmaceutical industry, and the gradual whittling down of public sector undertakings by indifferent governments, IDPL stagnated and was declared a sick industry – a case under the Board of Industrial and Financial Reconstruction (BIFR). A similar fate was shared by other PSUs like HAL, Bengal Chemicals, et al[157]. Many technocrats from IDPL moved on to chart their future in private entrepreneurship[158].

By the turn of the millennium India was recognized as the "pharmacy for the third world". It started supplying many of the critical medicines for HIV/AIDs to Africa and Brazil. Between 1972 and 2005, any newly patented medicine launched in the West, would be manufactured in India within 3-4 years at a fraction of the price (say, less than 10 per cent of the innovator's price)[159].

By 1995 however this status of India had eroded for a number of reasons, chiefly because of the predatory moves of global Big Pharma in introducing new definitions, norms and rules of behavior for international trade in pharmaceuticals. Consequently, the 'reverse engineering' of Western pharmaceutical innovations being practiced in India took the flavor of a pejorative. With words like 'property' and 'rights' it even acquired connotations of theft, piracy and violation of inalienable and incontrovertible 'rights' bestowed on the original innovators[160].

Underlying the WTO/TRIPS and the product patent only regime, was/is a politics of extraordinary self-interest of Big Pharma MNCs and their governments. Big Pharma cartelized, but only to have the rug pulled from under their feet in South Africa in 2000 when Cipla cited India-made AIDs drugs prices that were a fraction of those of Western pharma cartels[161]. Under massive international pressure from civil society, the cartel of 39 pharmaceutical companies was forced to withdraw their case against the South African Government over a law to improve access to antiretrovirals. Big Pharma struck back, soon enough, however, riding on the fears and disinformation they had generated, armed now with overpriced biologicals.

The damage control, post-2005 – in the aftermath of disallowing reverse engineering through process patents – was initiated by using the flexibilities wrought and won in the final version of TRIPS, and the subsequent reaffirmation in the Doha Declaration of 2001. These flexibilities,[162] enshrined now in the 2005 amendments of the Patents Act, included, famously, Section 3(d) that seeks to prevent ever-greening and patent periods beyond 20 years, by raising the standards of patentability.

Part of global Big Pharma strategy now was to make it difficult for Indian pharmaceutical companies to enter and survive in EU and American markets. However, Indian companies have mostly overcome these entry barriers, defying sceptics, even as the attempts at delegitimizing the quality and efficacy of Indian pharmaceutical products in the post-2005 era continue.

Of late however, many Indian pharma companies, including entities like Cipla and Natco that have been contesting the patent worthiness of several products of Western companies in Indian courts and with some success, have become inclined to partnerships, albeit unequal, with Western pharmaceutical companies. Many have become willing partners in the voluntary licence deal of Gilead for its costly Hepatitis C product Sovaldi (sofosvubir). We discuss more on this later.

Post 1972, as the "animal spirits" of private entrepreneurship were unleashed in the pharma industry, the scenario especially for the poor in India, has been a dismal case of poverty amidst plenty. There has been no consistent grand political vision of health services for all, except for the occasional rhetoric at the time of signing progressive international covenants related to health.

By the turn of the millennium, except for a few states like Tamil Nadu and Kerala, health care of the majority of the populace was left in the hands of the market. The market here meant the poorly regulated private sector consisting of private practitioners and private hospitals mainly let the bottom line drive the content and quality of their curative practice. For most State Governments and even the Central Government, health was/is not a political priority. The logic and the brouhaha of expanding horizons of pharmaceutical capital are too much of an alluring narrative for industry as well as Government. Price control of a broad range of medicines that came about in 1979 during the Janata Government has been gradually whittled down over the next 15 years.

Overpriced medicines are a fact of life in India. As we see, a number of historical factors, changing political economic climate, the state's withdrawal from the social sector, especially health, in the overarching context of the rapacity of global pharmaceutical industry have contributed to whittling down access to affordable medicines in India.

We elaborate in this chapter three of the cited factors: price regulation and the proliferation of Fixed Dose Combinations (FDCs), pricing of patented drugs and the interplay of the state, industry and market therein.

1. Price Control, Affordability, Availability and Access

State Intervention and Market Failure: The argument for price regulation/control is the persistence of market failure. The pharmaceutical market is riddled with market failure – the same medicine sells at a wide range of prices, where price has no relation to the cost of production, and the market is distorted by unethical drug promotion. Stiglitz (1989) and Akerlof (1970)[163] have identified the existence of information asymmetries as a cause of market failure.

The doctor-patient-pharmaceutical industry interface is rife with asymmetries. The patient has no power and knowledge to make a decision on what medicine s/he buys as that is decided by the prescriber who, in turn, is influenced by the 'choices' offered by the pharmaceutical industry and its unethical drug promotion. Therefore, the higher priced brands prevail. Each company claims superiority of its brand of the same medicine promoting the general notion that the higher priced brands are of better quality[164].

Competition in the classical sense (of many producers entering the field resulting in reduced price of a drug) does not usually occur in the Indian pharmaceutical market. When a generic enters the market for the first time, there is competition and lowering of prices, of the API as well as the formulation, with respect to the price of the innovator. But after some time when several producers start making the same formulation, the generic formulation is sold at a wide range of prices, positioned as it were to the varying purchasing powers of its buyers. However, because the consumer has little choice, the bulk of the market is skewed towards the higher priced brands. Therefore, the principle that "many producers will bring down the price of the product" does not work. There is competition of sorts, but it does not work in favour of consumers because they are led to believe, despite actual evidence to the contrary, that the lower the price, the lesser the efficacy of the medicine.

In India, with universal health coverage still a distant dream, electoral compulsions of market failure in medicines has resulted in the pharmaceutical market – at least some parts of it – being brought under price regulation, even if in desultory way.

Contrary Pulls of Price Control: The contentious discourse around price control of medicines in India that began in the 1960s (circa the war with China) has rolled into contemporary neo-liberal times, when the market is considered a better arbiter of prices. Today there is even a semantic hesitation to call it a price control policy – as against price regulation. The former smacks of the 'inefficient' socialist times and the latter is considered tempering wisely unbridled laissez faire in a politically sensitive arena like health care, even as we let the markets play it out.

The policy instruments for price control, the National Pharmaceutical Pricing Policy (NPPP) 2012 and the Drug Price Control Order (DPCO) 2013, have several problems. As we show below, these are at best tokenistic in their attempts at price regulation.

The actual price control, or regulation, always hovers around two factors that see a great deal of lobbying on the part of pharma companies and 'rent collection' on the part of the ruling elite: a) the range of drugs to be put under price control and therefore, the methodology for selecting these drugs and b) the actual formula to determine the ceiling price beyond which the formulation cannot be sold. As a result of successful lobbying over the years, the scope of price control had been successfully restricted to 74 drugs by 1995 from a high of 347 drugs in 1979[165].

Any 'formula' or 'methodology' based on market considerations (like market share, number of producers and therefore, presence/absence of competition) generally results in an unsatisfactory, if not absurd, list of drugs to be put under price control. Such was the case with the DPCO 1995 and the draft Pharmaceutical Pricing Policy of 2002. The latter was stayed by the Karnataka High Court and the Supreme Court. The DPCO

1995 had only 74 drugs under price control, half of which were drugs rarely in use, an eventuality resulting from the criteria adopted for selecting these drugs.

Likewise, the formula adopted for deciding ceiling prices is important. The usual norm till the onset of DPCO 2013 was cost-based pricing, that is, cost of ingredients, plus conversion costs plus margin (in the case of DPCO 1995, the margin called Maximum Allowable Post-manufacturing Expenditure (MAPE) was 100 per cent). The DPCO 2013 relied on the simple average, of price to retailer of brands with 1 percent market share, plus retailer's commission of 16 percent, as the ceiling price. The choice of the simple average formula defies logic and has been critiqued by several commentators including the authors[166]. For instance, among statistical indices that measure spread, why simple average and not mode or median, or weighted average of the lowest 3 prices?

The current policy, NPPP 2012 and DPCO 2013, were announced hastily after the judicial reprimand in the decade old and still ongoing PIL (AIDAN and Ors Vs Union of India and Ors in WP (Civil) 423/2003). The run up to DPCO 2013 saw tremendous lobbying and resulted in modifications amounting to a 'balancing act' in the policy with the following features laden with escape hatches:

- All 348 drugs in National List of Essential Medicines (NLEM) 2011, in the specified strengths and presentations, were put under price control. (At the time of going to press, a revised NLEM (hereafter NLEM-2015) comprising around 380 medicines has been announced in December 2015.) NLEM-2015 will be the new basket of medicines for price control. In the new list, 70 medicines from the older list have been deleted and replaced with 106 other medicines. Our comments below and elsewhere in the chapter are applicable to both NLEM lists unless indicated otherwise.)
- The ceiling price is the simple average price of price to retailer of brands with more than 1 per cent market share plus 16 per cent retailer's trade commission.
- Only 348 drugs in their specified strengths and presentations (totaling about 620) are under price control as specified in the NLEM-2011. This means the following categories are excluded from price control:
    - Strengths, dosage forms and presentations of the 348 essential drugs not mentioned in the NLEM-2011 (e.g. Paracetamol 650 mg and 1000 mg were excluded from price control as only paracetamol 500 mg tab was specified in the NLEM-2011. Paracetamol 650 mg tab is included in the recently announced NLEM-2015. In a few cases, NLEM-2015 mentions a continuous range of strengths, for example, for migraine, Acetylsalicylic acid, 300 to 500 mg.)
    - Chemical analogues of medicines listed in the NLEM-2011 are generally excluded. For example, only Atorvastatin is under price control because it is the only statin mentioned in the NLEM-2011 but all other statins, like Rosuvastatin, Simvastatin, etc. are excluded.
    - All existing combinations, of NLEM plus NLEM, NLEM plus non-NLEM, and non-NLEM plus non-NLEM medicines, are excluded.

NLEM-2015 perpetuates, with respect to price control, the problems of NLEM-2011: it leaves out all isomers, derivatives, chemical analogs, limits to specific dosages, etc. This problem arises because the NLEMs, neither 2011 nor 2015, were drafted with price control as the major focus. In fact there needs to be a separate expanded list of essential and lifesaving drugs that remedies the problems of relying on an NLEM for price control.

Many useful drugs for asthma – for example, Monteleukast – are excluded from price control. For diabetes, only Glibenclamide, Metformin and Insulin (of a certain kind only) were under price control as only these were mentioned in NLEM-2011. In the NLEM-2015 however Glibenclamide has been replaced by the more useful Glimepiride but other overpriced and useful diabetics like say

Acarbose or Gliptins continue to be excluded[167]. Further, highly expensive drugs like Meropenem, Imipenem, Cilastatin, Tigecycline, Colistin, Abciximab, Tirofiban, and Eptifibatide are out of the NLEM-2015 and hence out of price regulation.

According to Government's affidavit filed in the Supreme Court during November 2013, only 18 per cent (Rs 13,097 crore) of the then domestic market of Rs 71,246 crore was under price control (using IMS TSA December 2012 MAT data). This means that a major chunk, of the pharma market, viz., 82 per cent, has slipped out of the DPCO-2013 purview.

According to a recent estimate (co-author Malini Aisola with Thomas Zacharias, August 2015, unpublished), about 86.6 per cent (Rs 72,730 crore) of the market is out of price control (PharmaTrac MAT January 2015 data). The therapeutic category breakdown is as follows: anti-diabetes (93 per cent), antimalarials (75 per cent), anti-infectives (69 per cent), anti-neoplastics (80 per cent), blood-related (86 per cent), cardiac (80 per cent), derma (95 per cent), gastro intestinal (90 per cent), hormones (65 per cent), neuro/CNS (89 per cent), ophthal/otologicals (95 per cent), pain/analgesics (93 per cent), respiratory (96 per cent), sex stimulants/rejuvenators (100 per cent), stomatologicals (100 per cent), urology (96 per cent), vaccines (71 per cent), vitamins/minerals/nutrients (99 per cent), others (99 per cent). Of the formulations excluded from price control, combinations account for more than 48 per cent (around Rs 35,413 crore). This corresponds to roughly 42 per cent of the total pharmaceutical market sales (Rs. 84,017 crore), (MAT January 2015).

How can a policy that results in more than 86 per cent of the market falling outside price control basket be considered a policy controlling drug prices? Although it apparently meets the directives of the Supreme Court to formulate a price control policy for essential and life saving drugs, it does not comply with the Supreme Court order[168] stating that the formula for bringing medicines under price control should not be changed. It is a policy that disproportionately reflects prices of brands with a perceived and inflated brand value rather than the actual cost of production. It is a policy which, as we see from Tables 8.1-8.3, legitimizes super profits to the tune of 2000-4000 per cent even after price control. These high profits are used in turn to fuel, and are fuelled by, questionable marketing practices in the name of brand promotion.

We present some tabular data below to illustrate some of the averments on overpricing we have made previously. Table 8.1 shows the range of prices used in calculating ceiling prices. The lower prices are closer to the cost of production. If anything, it shows the irrelevance of the cost of the production in calculating the ceiling price. This fact more clearly shown in Table 8.2 comparing col.7 and col. 9.

Table 8.1: Range of Prices to Retailer (PTR) Used for Calculating Simple Average Price (in INR)

Name of drug	Lowest price with 1 per cent market share	Highest price with 1 per cent market share	Simple average price (Without 16 per cent retailer markup)*
Acyclovir 200 mg tabs per 10	32.70	148.10	62.90
Atenolol 100 mg tabs per 10	3.00	42.30	32.10
Atorvastatin 5 mg tabs per 10	13.50	52.50	32.90
Azithromycin 500 mg tabs per 10	41.6	393.3	171.2
Losartan 50 mg tabs per 10	9.20	56	37.10

Source: NPPA Working Sheets (2013). * Ceiling price is the simple average of price to retailer of brands with 1 per cent market share plus retailer's commission of 16 per cent (NPPA Working Sheets 2013).

Table 8.2: Conversion or Manufacturing Costs as Per cent of Cost Price; and Cost Price Compared to DPCO-2013 Ceiling Price

1	2	3	4	5	6	7	8	9
Name	**Raw Material price per kg**	**No of tablets per kg of raw material**	**Cost of API per 10 tabs**	**Total raw material cost per 101 tabs**	**Con-version or Mfg costs per 10 tabs**	**Total cost per 10 tabs**	**Conv. or Mfg cost as per cent of total cost**	**DPCO-2013 ceiling price as of Aug 2015, per 10**
Albendazole tabs 400 mg	1,337	2,500	5.35	5.99	2.91	**8.90**	33	**103**
Atorvastatin tabs 10 mg	16,887	89,000	1.90	2.07	1.22	**3.29**	37	**67.40**
Atenolol 50 mg tabs	1,231	20,000	0.62	0.72	0.82	**1.54**	53	**22.80**
Amlodipine 5 mg	3,136	140, 000	0.22	0.36	0.59	**0.95**	62	**31.30**
Cetrizine tablets 10 mg	3,499	100,000	0.35	0.45	0.70	**1.15**	61	**19.90**

Source: Authors. Based on data sourced from the in-house records of LOCOST (Low Cost Standard Th erapeutics) with which S. Srinivasan is associated.

Note: Costs and Prices in INR.

Table 8.3: Comparison of DPCO-2013 and RMSC Rates (Price in INR)

1	2	3	4	5	6	7
No.	**Name of drug, strength and use**	**Indication**	**Simple avg ceiling price as per DPCO- 2013 (valid as of August 2015)**	**RMSC 2015 procurement rates**	**DPCO-2013 ceiling price/ RMSC rate**	**DPCO-2013 ceiling price per cent greater than RMSC rate**
1.	Imatinib tab - 400 mg, 10 tabs	Anti-cancer	2,962.7	29.0	102.2	10,116
2.	Amlodipine tab - 5 mg, 10 tabs	Antihyperten-sive	31.3	1.0	32.5	3,150
3.	Enalapril maleate tab - 5 mg, 10 tabs	Antihyperten-sive	32.7	1.2	28.4	2,739
4.	Atorvastatin tab - 10 mg, 10 tabs	Blood choles-terol lowering agent	67.4	2.5	27.0	2,596
5.	Cetrizine tab - 10 mg, 10 tabs	Antiallergic	19.9	0.8	26.2	2,522
6.	Alprazolam tab - 0.5 mg, 10 tabs	Sedative, sleep inducer	22.2	0.9	25.3	2,428

1	2	3	4	5	6	7
No.	**Name of drug, strength and use**	**Indication**	**Simple avg ceiling price as per DPCO- 2013 (valid as of August 2015)**	**RMSC 2015 procurement rates**	**DPCO-2013 ceiling price/ RMSC rate**	**DPCO-2013 ceiling price per cent greater than RMSC rate**
7.	Domperidone tab - 10 mg, 10 tabs	Antivomiting agent	24.9	1.1	22.7	2,174
8.	Diclofenac Sodium tab - 50 mg, 10 tabs	Painkiller	21.5	1.2	18.3	1,730
9.	Atenolol 50 mg for 14 tabs	Antihyperten-sive	31.92	1.7	19.2	1,817
10.	Olanzapine tab - 5 mg, 10 tabs	Antipsychotic	32	1.9	16.8	1,580

Source: Prices available at: http://rmsc.health.rajasthan.gov.in/content/raj/medical/rajasthan-medical-services-corporation-ltd-/en/home.html# and http://www.nppaindia.nic.in/. Accessed on November 2017. Data analysis by Aisola and Zacharias (2015).

Table 8.2 shows that in the case of relatively low priced material, the cost of conversion is almost as much as the cost of the raw material. In the case of amlodipine, the raw material cost is less than the conversion cost. A comparison of the cost price (Col. 7) and DPCO-2013 ceiling price (Col. 9), columns shown in bold, shows that the ceiling price methodology legitimizes high margins, making price control an eyewash.

Table 8.3 compares the tender procurement rates of the Rajasthan Medical Services Corporation (RMSC) with the DPCO 2013 ceiling prices. A comparison with that of the Tamil Nadu Medical Services Corporation (TNMSC) reveals similar results of margins of 1000-3000 per cent and in the case of Imatinib (Table 8.3, Sr No 1), generic equivalent of Novartis' Glivec, it is 10,116 per cent! This is not to argue that medicines be sold in the retail market at the prices of the TNMSC/RMSC. Instead, based on the evidence there is room for advocating reasonable cost-based pricing plus sufficient margins so that the prices reflect the cost of production. The tender prices are merely a base and an index of comparative overpricing of the retail market prices of medicines.

To use a minimal list like NLEM for price control is a flawed idea. The basic purpose of minimalistic lists like NLEM is that Essential Medicines included in it should be available at all times in various public health care facilities. Any essential list is a guide for use mainly for procurement in government health services - if the Government restricts its purchases and prescriptions to a limited essential drug list like the NLEM - which are available to about 20 per cent of the population. Even here, as studies and reports have shown the availability of essential medicines is poor[169]. In rational medical practice, many medicines beyond the NLEM are used. For example, chemical analogues and therapeutic equivalents and life saving drugs depending on special needs for a patient are also used. If treatment were confined to only the drugs mentioned in the NLEMs 2011/2015, cure and management of chronic life-threatening problems like diabetes and asthma would become impossible for many patients.

The National Pharmaceutical Pricing Policy (NPPP) 2012 is a minimalistic interpretation by policy makers of the Supreme Court order to put all essential and life-saving drugs under price control. The DPCO 2013, in turn, has therefore, limited impact. Nevertheless if justice is to be done to the poorer sections of the population, a separate list for price control, larger than the NLEMs 2011/2015 needs to be formulated, supported by a free universal public health care system that matches the United Kingdom or Canada or the Scandinavian countries.

2. Fixed Dose Combinations and Access to Medicine

The large availability of irrational medicines – mostly in the form of Fixed Dose Combinations (FDCs) – comes in the way of patients receiving adequate and appropriate treatment. Initially not many in number, FDCs today are in several thousands, a large proportion having no therapeutic rationale.

What kind of FDCs should be approved? The WHO recommended guidelines for acceptability of FDCs are summarized here:

- Clinical documentation justifies the concomitant use of more than one drug.
- Therapeutic effect is greater than the sum of the effect of each.
- The cost of the combination product is less than the sum of individual products.
- Compliance is improved (that is, when two or more medicines are to be taken separately, as in the case of TB, the user tends to avoid one or two medicines after sometime. This can be avoided if all three medicines are combined into one).
- Sufficient drug ratios are provided to allow dosage adjustments satisfactory for the majority of the population.

FDCs that do not satisfy these guidelines should be considered irrational.

Proliferation of FDCs: Why has India's pharmaceutical industry been manufacturing and marketing FDCs – many of them irrational and harmful – for the last five decades? How, in the first place, did it get licenses for marketing and/or manufacturing these?

Part of the reason for the uncontrolled growth of FDCs is the pressure of competition and new products. Marketing heads of pharmaceutical companies in collaboration with their medical directors, invent combinations of two or more drugs, often launching them without a critical, scientific assessment of their therapeutic benefits and rationale. Moreover, before 1988 the Drugs and Cosmetics Act did not contain the legal provisions relating to FDCs[170]. Between January 1961 and November 2014, the number of FDCs approved by the CDSCO/DCGI was 1193[171], not all of them rational.

Before September 1988, it was a free for all, and manufacturing and marketing of FDCs was not limited to just the list of FDCs approved by the DCGI since 1961. As per these provisions introduced in 1988, FDCs were included in the definition of new drugs (per Rule 122-E), under which they remain new drugs up to four years after the date of its first approval. Notwithstanding the new provisions, there was considerable murkiness with regard to the role of state and central authorities that clarified only in 2002 when Rule 69 (6) and 75 (6) were added to the Drugs and Cosmetics Rules. These rules inserted on May 1, 2002 stated that all new drugs including FDCs that qualified as *new drugs* were to have prior approval of the DCGI after which a license for manufacture may be sought from the state licensing authorities (SLAs). In the absence of this clarificatory rule, a large number of FDCs have been licensed for manufacture by SLAs without being approved for marketing by the DCGI at the centre. Approval by DCGI involved, after 1988, production of proof of safety and efficacy. Part of the problem was also that during Indian pharma boom during 1998-2002, neither the centre nor the states strictly enforced the laws on that had been passed for FDCs.

FDCs are, of course, necessary in some select circumstances. These are few in number and cover FDCs for AIDS, TB, malaria, ORS, iron plus folic acid for anemia, trimethoprim + sulphamethoxazole, etc. In the National List of Essential Medicines 2011, out of 348 medicines, only 18 (5.2 per cent) are FDCs. An editorial in *MIMS India* (August 2012) mentions that in an analysis of 1,811 commonly sold products, 43 per cent (that is 773 products) were combinations. Other estimates of number of FDCs vary between 40 to 60 per cent of the number of formulations in the Indian domestic market; the latter number is

estimated around 50,000 (*PharmaTrac* Jan 2015).

An analysis, done by one of the authors (Aisola with Zacharias 2015) of the 50,000 plus branded medicines in *PharmaTrac* (MAT June 2015), shows about 43 percent of the market are combinations and more than 50 per cent of which are likely to be irrational. In another study by the authors, in August 2015, of the top selling 300 formulations accounting for Rs 58,452 crore (which is 69.6 per cent of the total domestic market of Rs 84,017 crore (PharmaTrac, 12 months ending Jan 2015)), FDCs assessed to be outright irrational and unscientific accounted for Rs 12,757 crore (21.8 per cent) of Rs 58,452 crore. This comprised 72 items of the top selling 300 drugs. Extrapolating the percentage of the irrational and unscientific FDCs to the total market of Rs 84,000 crore, irrational FDCs would account for approximately Rs 18,500 crore.

Yet, this is likely to be a gross underestimate. A large proportion of these irrational FDCs contain at least one NLEM medicine. But none of these are under price control. There are numerous similar examples as shown in Table 8.4 In most cases FDCs of an essential drug form 50 to 80 per cent (see Col.6) of the total market involving the essential drug. Almost all these FDCs are likely to be irrational.

Table 8.4 Market for NLEM-2011 Drugs and Combinations

Name of NLEM drug	Therapeutic category	Total annual sales (MAT Jan 2015, Rs. cr)	Sales of formulations coming under price control (Rs. cr)	Sales of formulations excluded from price control (Rs. cr)	
				Non-NLEM additional strengths and dosage forms	Non-NLEM formulations (combinations, isomers & others)
Ceftriaxone	Anti-Infectives	1,129.9	535	132	462.9
Ofloxacin	Anti-Infectives	1,477.3	151.8	283.3	1,042.2
Domperidone	Gastro Intestinal	1,532.8	33.5	14.9	1,484.4
Pantoprazole	Gastro Intestinal	1,328.8	167.6	460.3	700.9
Paracetamol	Pain/Analgesics	3,285.5	181.6	437.5	2,666.5
Chlorpheniramine	Pain/Analgesics	1,547	0.2	12.5	1,534.2
Amlodipine	Cardiac	1,809.7	299.1	31.5	1,479.1

Source: Data analysis by Aisola and Zacharia (2015).

Note: New formulations involving essential drugs would come under price control on a brand-by-brand basis post-implementation of DPCO 2013. These formulations are not expected to have significant market sales during the time period considered for the analysis.

The pervasive prevalence of unnecessary combinations hits the patient in multiple ways: the patient is burdened with unnecessary extra medication and mostly irrational ones, that cost more (as most of them are out of price control and the patient has to pay for unnecessary extra ingredients) and the patient is put at the risk of avoidable side effects and adverse drug reactions.

Government Response to the Problem of Unscientific FDCs: The Government of India, through the Central Drugs Standard Control Organization (CDSCO) and its successive Drug Controller Generals (DCGIs), has been intermittently trying to solve the problem of the FDCs, rational, irrational, legal and illegal, etc., over much of the 2000s.

We will not here elaborate on the chequered history of the relationship and the encounters between the FDC manufacturers and the Government since the early 2000s. This includes stay orders by three State High Courts on the attempts by the Government to resolve the

problem. These stay orders, initiated by affected pharma companies, have still not been lifted, in the absence of moves by the Government to challenge the stays.

The current state of these efforts was initiated with a letter on January 15, 2013, from the DCGI again requesting SLAs to instruct manufacturers to send to the DCGI within 18 months, data on safety and efficacy of FDCs permitted by SLCs but not approved by DCGI before October 1, 2012. In response, the DCGI received approximately 7000 applications. A Committee under the Chairmanship of C. K. Kokate was constituted to examine approximately 6320 applications in a timely manner. In March 2016, on the basis of the committee's recommendations the Government of India banned 344 FDCs totaling about 1080 applications as several brands had the same FDC. Some well known top selling brands like Corex, Phensedyl, Vicks Action 500, etc., were recommended for ban. Almost immediately several manufacturers of the banned products approached the Courts, especially the Delhi High Court that issued stay on the ban order even as the court heard the case over the next two months[172]. On December 1, 2016, the Delhi High Court gave an order quashing the ban. The reason given was that the Drug Technical Advisory Board (DTAB) was not consulted in the process leading up to the ban. The order is likely to be appealed by the Government in the Supreme Court. Surprisingly realizing the weakness of the order quashing the ban, the affected pharma companies are talking of negotiating with the Government![173]

The Kokate Committee also set aside 944 FDCs (corresponding to 1730 applications) for further deliberation, declared 1493 FDCs (corresponding to 2650 applications) as rational and asked manufacturers of 126 FDCs (corresponding to 390 applications) to furnish further data.

While these attempts by the DCGI are to be welcomed, it must be kept in mind that the Kokate Committee examined FDCs licensed for manufacture by the SLCs without prior approval for safety and efficacy by the Central Government. The Government has the more onerous task of weeding out all other remaining irrational FDCs in the market that do not necessarily meet this criteria, of irrational FDCs approved wrongly by the Central Government. Till such an eventuality, all FDCs in the market that contain one or more of the m-saving medicines marketed in India should be brought under price control. This will at the least minimize the economic burden on patients.

Concluding Note

India's pharmaceutical industry has come a long way from 1947, and from 1972. But, access issues remain, along with the challenges of affordability, availability and rationality of products. Allowing the market to regulate itself will not work. Proactive state intervention is necessary in pricing and provision of medicines and health care services to deal with the extraordinary crisis of public health in India. But for a few of state governments like that of Tamil Nadu, Rajasthan and Kerala, the availability of medicines in the public health system is erratic and uncertain[174].

The dilution of key flexibilities in India's patent laws, at the behest of Big Pharma lobbies, will put the clock back. Nor is such dilution necessary as India is fully TRIPS compliant. Efforts at opening up India to international trade must build on, not undo, the enormous strides made in the domestic pharma sector over the last 40 years.

152. Excerpts from S. Srinivasan and Malini Aisola; Access to Pharmaceuticals: role of state, industry and market, published in Equity and Access: Health Care Studies; Edited by Purnendra Prasad and Amar Jesani; Oxford University Press; 2018. Reproduced with permission from authors

153. Co-convenors, All India Drug Action Network (AIDAN)

154. For more detailed history, see Chapter 2 in: Sudip Chaudhuri.

155. As of writing, India is dependent for 60 per cent of its APIs on imports, mostly from China. The Government of India appointed Katoch Committee whose recommendations are available at http://pharmaceuticals.gov.in/document/salient-features-recommendations-katoch-committee-report-apis-0 (accessed March 3, 2016), has targeted API self-sufficiency of India on par with India's formulations industry.

156. Interview with Yusuf Hamied, interviewed by Tarun Khanna, Bombay, India, April 29, 2013, Creating Emerging Markets Oral History Collection, Baker Library Historical Collections, Harvard Business School. Accessed Sep 27, 2015 at http://www.hbs.edu/businesshistory/Documents/emerging-markets-transcripts/Hamied_Yusuf_Web per cent20Transcript.pdf.
"Indian Pharma Industry: Decades of Struggle" byY.K.Hamied on the occasion of AV Rama Rao's 70th birthday, April 2, 2005. Accessed Sep 26, 2015 at http://www.arvindguptatoys.com/arvindgupta/avra-hamied.pdf

157. For details see, http://pharmaceuticals.gov.in/cpses. Accessed September 30, 2015.

158. For a first person account of these transitions, see: Reddy.(2015).

159. See Table 1, in Chapter 6 of this book, "Globalization, Intellectual Property Rights and Pharmaceuticals" by Amit Sengupta.

160. For the politics in the run up to WTO/TRIPS, see Bhagwati (2004.) pp.182 ff. The author, a leading economist and international trade theorist, has been adviser to the WTO, and GATT.

161. See Lofgren (2013), Chapter 3, p.55ff.

162. These flexibilities include:

- Section 3 (d) of the Patents Act was amended to exclude patentability of new forms (including derivatives of old drugs or combinations of old drugs) of known substances unless there is significant enhancement of efficacy;
- New use of an old drug, is not to be considered an invention and hence not patentable;
- Pre-grant opposition to patents applications was retained;
- Post-grant opposition to granted patents was introduced.
- In addition, definitions related to patentability criteria were modified by the 2005 amendments, especially definitions of 'invention', 'inventive step'. Other safeguards against patent abuse were introduced/modified through the 2005 amendments as well as earlier amendments of the 1970s law: Compulsory license, Bolar exception (preparation for generic launch, i.e. production for marketing approval, and marketing approval) and parallel importation. See also Chapter XX in this book on IPR.

163. Akerlof, George A. (1970). "The Market for 'Lemons': Quality Uncertainty and the Market Mechanism". Quarterly Journal of Economics (The MIT Press) 84 (3): 488–500.
Joseph E. Stiglitz (1989). "Markets, Market Failures, and Development". The American Economic Review.Vol. 79, No. 2.

164. On Pharmaceutical Market Failure, see Public-Private Roles in the Pharmaceutical Sector - Implications for Equitable Access and Rational Drug Use. Health Economics and Drugs Series, No. 005, (WHO, 1997; 115 pages).

165. For a more complete history of price control since 1962, see Chapter 8 in Chaudhuri, op.cit. Also: LOCOST/JSS (2004). Impoverishing the Poor: Pharmaceuticals and Drug Pricing in India (Vadodara/Bilaspur: LOCOST/JSS).

166. See: Srinivasan et al (2013) and Srinivasan et al (2014).

167. We should add that some anti-diabetics not mentioned in NLEM-2011 - like glimepiride, gliclazide, migitol, repaglinide, pioglitazone, sitagliptin, voglibose and acarbose - were sought to be brought under price control on July 10, 2014, by the NPPA by special notification under Para 19 of DPCO-2013 but many leading manufacturers have not complied with it and have taken the Government to court on the issue.

168. In the order passed on October 3, 2012, in WP(Civil) No. 423 of 2003, AIDAN and Ors. Versus UOI and Ors., the Supreme Court ruled: : "While adjourning the case, we make it clear that the Government should not alter the price structure of the drugs as notified vide Notification dated 13.07.1999 and similar notifications which may have been issued thereafter." An order completely ignored in the formulation of DPCO 2013.

169. Anita Kotwani. "Where are we now: assessing the price, availability and affordability of essential medicines in Delhi as India plans free medicine for all." BMC Health Services Research 2013, 13:285.

170. Specifically, Rules 122 A, B, D and E and Schedule Y in Part X-A related to requirements and guidelines for import and manufacture of new drugs including FDCs. Appendix VI of Schedule Y gives requirements for approval of various categories of FDCs.

171. Source: http://www.cdsco.nic.in/writereaddata/Aprroved per cent20FDC per cent20list per cent20till per cent20november per cent202014.pdf. Accessed January 18, 2015.

172. For a backgrounder on the context of the case filed by pharma companies on the ban of the 344 FDCs, see: Srinivasan et al 2016.

173. See http://timesofindia.indiatimes.com/india/Delhi-high-court-sets-aside-Centres-decision-to-ban-344-fixed-dose-combination-medicines/articleshow/55719568.cms, Accessed January 14, 2017.

174. At the time of going to the press, a free drugs initiative (http://nrhm.gov.in/images/pdf/in-focus/Shimla/Guidelines/Free_Drugs_Service_Intitiative.pdf) has been initiated to provide support to the states to initiate delivery mechanisms like the Tamil Nadu and Rajasthan Medical Service Corporations. The details of financial support to the states are not clear. The Jan Aushadhi scheme (http://janaushadhi.gov.in/) for availability of affordable essential drugs at the retail level has also been streamlined and 3000 outlets are to be opened.