
The effects of extending intellectual property rights protection to developing countries: A case study of the Indian pharmaceutical market

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Introduction

The TRIPS agreement

- TRIPS & WTO (1995): member countries must recognize and enforce product patents in all fields of technology including pharmaceuticals
- Low-income developing countries given till 2005 to amend or introduce appropriate patent legislation to recognize patents filed after 1995
- TRIPS agreement highly contentious
- debate continues regarding flexibility governments should have to impose price controls or require compulsory licensing

Introduction...

The debate

- Poor countries claim pharmaceutical product patents will result in higher prices for essential medicines
- The idea of a better-ordered world is one in which medical discoveries will be free of patents and there will be no profiteering from life and death.”

Indira Gandhi (1982)

Introduction...

The other side

- Global research-based pharmaceutical companies claim most patented products have therapeutic substitutes, hence large price increases unlikely
- “High priced medicines after change in patent laws is a misconception.”

Organisation of Pharmaceutical Producers of India

- Patents will spur R&D on developing-country specific diseases, increase foreign investment, transfer of technology

Introduction...

What is known

- Very few empirical studies on pharmaceutical markets in poor developing economies
 - per-capita health expenditures low
 - most medical expenditures met out-of-pocket
 - burden of disease different
 - conditions of transport, storage, administration different
- Claims based on assumptions and priors, not evidence

Comparing the health sector in low-income and developed economies

	India	Pakistan	Canada	U.S.A.
Information on health expenditures				
Total health expenditures as % of GDP	4.9	4.1	9.1	13.0
Per-capita total health expenditures (US \$)	23	18	2058	4499
Public health expenditures as % of total	17.8	22.9	72.0	44.3
Private health expenditures as % of total	82.2	77.1	28.0	55.7
Out-of-pocket expenditures as % of total	82.2	77.1	15.5	15.3
Top ten leading causes of burden of disease in 1998: all ages				
India		U.S.A. and Canada		
Cause	DALYs (000)	Cause	DALYs (000)	
Acute lower respiratory infection	24,806	Ischaemic heart disease	2,955	
Perinatal conditions	23,316	Unipolar major depression	2,511	
Diarrhoeal diseases	22,005	Alcohol dependence	1,736	
Ischaemic heart disease	11,697	Road traffic injuries	1,670	
Falls	10,897	Cerebrovascular disease	1,651	
Unipolar major depression	9,679	Osteoarthritis	1,029	
Tuberculosis	7,578	Diabetes mellitus	1,017	
Congenital abnormalities	7,454	Trachea/bronchus/lung cancers	996	
Road traffic injuries	7,204	Dementias	940	
Measles	6,474	Self-inflicted injuries	858	

Source: World Health Report—2002 (WHO (2002))

Introduction...

What we do in the paper

- Use detail product-level data from India to estimate key demand and supply parameters: own and cross-price elasticities, expenditure elasticities, marginal costs
- In the period covered by our data, India did not recognize pharmaceutical product patents; hence many products available that were under patent in the U.S.
- Carry out counterfactual analyses of what prices, consumer welfare, firm profits would have been had patents been in effect

Introduction...

The basic thought experiment

- Had patents been in effect, domestic products that were in violation of patents would have to be withdrawn from the market
- Estimates of key demand and supply parameters can then be used to simulate the effects of product withdrawal on prices, consumer welfare and profits

Introduction...

Disclaimers

- Limitations of counterfactual analyses:
 - version of Lucas critique—important behavioral parameters may change under the new IPR regime
 - TRIPS applies only to products patented post-1995, most of which are still undergoing clinical trials in the U.S. and hence not in our data
- Counterfactual estimates therefore need to be interpreted with care

Introduction...

A preview of the results

- Scenario: withdrawal of all domestic products containing four fluoroquinolone molecules
- Counterfactual estimates (US\$ millions per year):
 - Loss of consumer welfare
 - ...from reduction in product variety: 443
 - ...from upward price adjustments: 217
 - Loss of domestic firm profits 53
 - TOTAL WELFARE LOSS 713
 - Profit gains of multinational subsidiaries 57
- Sales of all systemic anti-bacterials in 2000 611

Conceptual preliminaries

- Standard analysis of patents:
 - static (short-term) pricing distortions
 - dynamic (longer-term) innovation gains
- Complications in multi-country setting:
 - country-of-origin of patent-holders
 - relative size of domestic market
 - global reference pricing
- Further complications with differentiated products such as pharmaceuticals

The setting and the data

A primer on pharmaceuticals

- Formulations: what we call medicines or drugs, pharmaceutical products that combine a therapeutically active molecule (active pharmaceutical ingredient or API) with inactive ingredients (excipients) that provide stability or ease administration of the drug
- Bulk drugs: the APIs used in formulations
- Product patents generally apply to APIs approved for particular medical indications for particular age groups
- Types of patents include patents for new chemical entities (NCE) and patents for new drug delivery systems (NDDS)

The setting and the data...

...A primer on pharmaceuticals

- Formulations usually marketed in multiple presentations (stock-keeping units or SKUs) that vary in terms of dosage form (e.g., syrup, capsule, etc.), dosage strength (e.g., 100mg capsule) and packet-size (e.g., 50 capsule bottle)
- Market research firms typically employ therapeutic classification system for categorizing formulations

Comparing the Indian pharmaceuticals market to the world market:
Shares of major therapeutic segments in retail sales

Therapeutic segment	Share of retail sales (%)			
	World: 2001		India: 2000	
	Rank	Share(%)	Rank	Share(%)
Cardiovascular system	1	19.6	4	8.0
Central nervous system (CNS)	2	16.9	6	6.7
Alimentary tract and metabolism	3	15.3	1	23.6
Respiratory system	4	9.5	3	10.4
Anti-infectives	5	9.0	2	23.0
Musculo-skeletal	6	6.1	5	7.3
Genito-urinary	7	5.7	9	3.1
Cytostatics and immunosuppressants	8	4.0	13	0.1
Dermatologicals	9	3.3	7	5.6
Blood and blood-forming agents	10	3.1	8	3.9
Sensory organs	11	2.1	10	1.6
Diagnostic agents	12	1.8	12	0.1
Systemic hormonal products	13	1.6	11	1.5
Others including parasitology	.	2.3	.	5.4

Source: World sales shares from IMS World Drug Purchases—Retail Pharmacies, IMS Drug Monitor, 2001. Indian domestic sales shares based on authors' calculations from ORG-MARG retail pharmaceutical audit.

The setting and the data...

The Indian pharmaceutical market

- Indian Patents Act (1970): excluded pharmaceutical product patents, recognized process patents for a term of 7 years
- Leftward tilt in policy during 1970s: drug price controls, restrictions on foreign equity shares, capacity expansion
- Liberalization since early 1990s
- Dramatic growth of Indian pharmaceutical industry in the last 20 years
 - Indian firms are major exporters
 - India the largest producer of formulations, by volume, and a leading bulk drug producers

The setting and the data...

The Indian pharmaceutical market

- Market structure also changed:
 - declining share of multinational subsidiaries from about 80% to 90% in 1970 to roughly 30% in 2000
 - increase in number of firms in organized sector of the industry (roughly 400 firms)
 - mushrooming of very small-scale units

The setting and the data...

Details about the data

- Data are from the retail pharmaceutical audit carried out by ORG-MARG, India's leading market research firm
- Detailed SKU-level data on price, sales, dosage form, strength and packet-size, launch date, firm, therapeutic categorization
- Data from monthly survey of several thousand retail pharmacists in nearly 350 towns and cities; estimated to cover 90% of retail pharmaceutical sales
- Monthly data for each of the four major geographical regions available from January 1999 to December 2000

The setting and the data...

The systemic anti-bacterials segment

- We focus on the systemic anti-bacterials segment of the market, and within that on the quinolones sub-segment
- Systemic anti-bacterials include all the original miracle drugs (for treatment of bacterial infections) that sparked the development of the research-based pharmaceutical industry as well as later generations of molecules
- Systemic anti-bacterials accounted for about 20% of retail pharmaceutical sales in India in 2000
- Systemic anti-bacterials segment divided into several sub-segments, each representing a family of related molecules

**All India sales share of and expenditures on various sub-segments
within the systemic anti-bacterials therapeutic segment**

2000

Therapeutic sub-segment	Share (%) of sales of systemic anti-bacterials: 2000	Sales (Rs. millions): 2000
Tetracycline, doxycycline and combinations	5.0	1,367
Chloramphenicols and combinations	1.7	460
Ampicillin, amoxycillin, cloxacillin	24.1	6,631
Cephalosporins	27.9	7,671
Trimethoprim and combinations	3.3	903
Macrolides	10.6	2,913
Penicillins	2.5	685
Other anti-biotics including aminoglycosides	4.2	1,158
Quinolones and fluoroquinolones	20.8	5,722
Total	100	27,509

The setting and the data...

...systemic anti-bacterials segment

- Within systemic anti-bacterials we focus on the quinolones sub-segment
- newer generations of quinolones (called fluoroquinolones) have a wide spectrum of activity—drug of choice for a range of bacterial infections
- Leading fluoroquinolone molecules were under patent in the U.S. during the period (roughly) covered by our data

The fluoroquinolones sub-segment

Molecule	Share (%) of sales of quinolones		Sales (Rs. millions): 2000	
	Domestic firms	Foreign subsidiaries	Domestic firms	Foreign subsidiaries
Ciprofloxacin	53.0	2.7	3,030	156
Norfloxacin	11.2	0.1	640	3
Ofloxacin	11.6	3.1	665	177
Sparfloxacin	10.8	0.1	620	4
Lomefloxacin	1.5	.	86	.
Pefloxacin	1.3	0.1	72	5
Levofloxacin	0.0	.	0	.
Nalidixic acid	1.3	.	73	.

Basic information about the four fluoroquinolone molecules

	Ciprofloxacin	Norfloxacin	Ofloxacin	Sparfloxacin
U.S. or European patent-holder	Bayer	Merck	Ortho-McNeil	Rhone-Poulenc
Year of U.S. patent expiry	2003	1998	2003	2010
Year of US-FDA approval	1987	1986	1990	1996
Year first introduced in India	1989	1988	1990	1996
No. of domestic Indian firms	75	40	17	25
No. of foreign subsidiaries	8	2	2	1
No. of products of domestic firms	90	48	21	30
No. of products of foreign subsidiaries	10	2	2	1
Sales weighted average price per-unit API of products produced by:				
Domestic Indian firms	11.23	9.04	88.73	78.11
Foreign subsidiaries	10.29	4.99	108.15	.

Analytic framework and estimation approach

A road map

- Recall basic thought experiment: get at effects of introduction of patents by simulating effects of withdrawing products that are in violation of patents
- To implement counterfactual simulations need:
 - demand parameters for calculation of virtual prices and expenditure switching effects
 - estimates of marginal costs
 - money metric of consumer welfare

Estimating demand

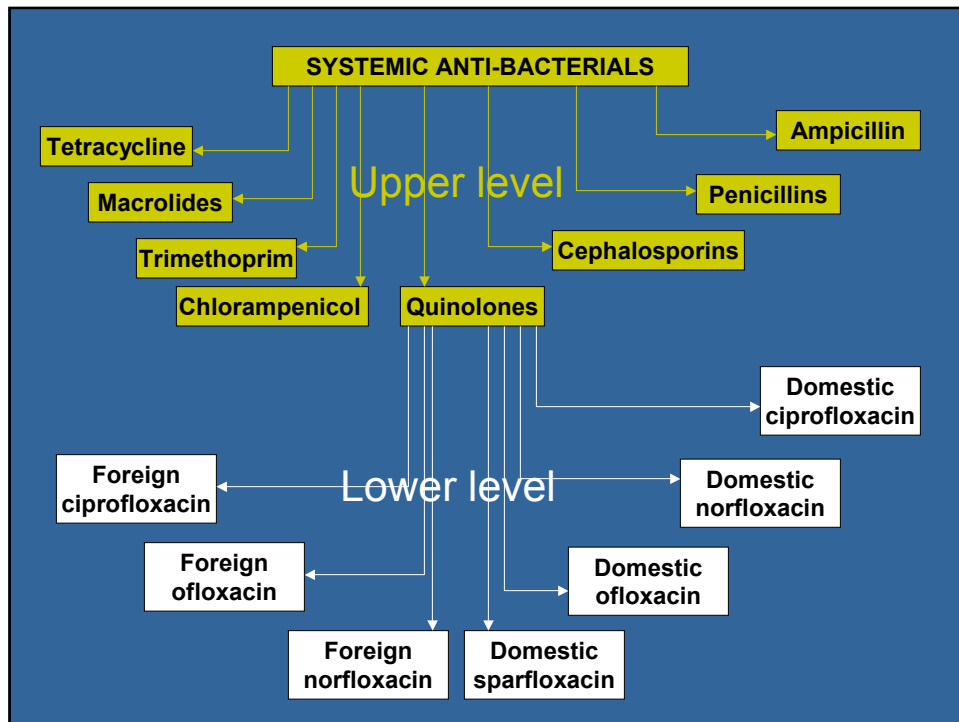
Challenges and choices

- Key challenge: multiplicity of differentiated products, limited time-series
- Discrete-choice framework
 - unit demand assumption untenable
 - physical sales data not in comparable units
 - tendency for discrete-choice approaches to overstate welfare from product variety—virtual price at which demand for a product decreases to zero is infinite
- Alternative approach: multi-stage budgeting

Estimating demand...

Multi-stage budgeting

- Exploit natural hierarchical taxonomy of therapeutic categories to estimate two-level demand system, employing AIDS specification of demand in both levels
- Aggregate products into groups: all products within a product-group contain the same molecule and are produced by firms with the same domestic status
- Upper level corresponds to allocation of expenditures to sub-segments within systemic anti-bacterials segment
- Lower level captures allocations to product-groups within the quinolones sub-segment



Estimating demand...

Pros and cons of two-level AIDS system

- Pros:
 - Flexible functional form
 - Can be applied to market-level data
 - Finite virtual prices
- Cons:
 - approximate approach—exact approach requires empirically implausible restrictions on higher-level demand system (Gorman (1959))

Estimating demand...

Econometric specification

- Upper level AIDS system:

$$\omega_{Gt} = \alpha_G + \sum_H \gamma_{GH} \ln P_{Ht} + \beta_G \ln \frac{X_t}{P_t}$$

- Lower level AIDS system (Q = quinolones):

$$\omega_{it}^Q = \alpha_i^Q + \sum_j \gamma_{ij}^Q \ln p_{jt}^Q + \beta_i^Q \ln \frac{X_{Qt}}{P_{Qt}}$$

- Impose restrictions on lower level system:
restrictions implied by theory, additional restrictions
to reduce number of parameters to be estimated

Estimating demand...

Further details

- Instrumental variables estimation to deal with possible aggregation bias
- Economic endogeneity of prices not an issue—
prices only infrequently adjusted
- Instruments: prices of five largest SKUs within each product group, within-product-group Herfindahl indices
- Bootstrapped standard errors

Modelling the supply side

Estimating marginal costs

- Modify standard approach in empirical IO
- Assume Bertrand competition with differentiated products, subject to price controls
- For products containing molecules subject to price controls:

$$MC_i = \bar{p}_i [1 - \text{allowed markup}]$$

- For products NOT subject to price controls:

$$MC_i = \bar{p}_i \left[1 + \frac{1}{\varepsilon_{ii}(\bar{p}_i, \bar{p}_{-i})} \right]$$

Counterfactual analysis

Obtaining the estimates

- Compute **virtual prices** for domestic products **withdrawn** from market by setting demand to zero
- **Simultaneously** compute profit-maximizing prices and associated market shares for product groups remaining in the market
- Calculate consumer welfare loss using **compensating variation** measure

$$\begin{aligned} CV &= E(U^0, P^1) - E(U^0, P^0) \\ &= E(U^0, p_{Q,F}^1, p_{Q,D}^1, P_{-Q}^0) - E(U^0, p_{Q,F}^0, p_{Q,D}^0, P_{-Q}^0) \end{aligned}$$

Results

The structure of demand

- Upper-level AIDS estimates indicate demand for quinolones quite sensitive to composite price of quinolones
- Lower level AIDS estimates indicate that within the quinolones sub-segment, demand for the various product groups is highly elastic
- Cross-price elasticities indicate that domestic products, even when they contain different molecules are close substitutes

Implied unconditional price and expenditure elasticities
within the quinolones sub-segment

Product group	Elasticity with respect to:							Overall quinolones expenditure
	Prices of foreign product groups			Prices of domestic product groups				
	Cipro	Norflo	Oflo	Cipro	Norflo	Oflo	Sparflo	
Foreign ciprofloxacin	-4.813* (1.527)	0.016 (0.063)	0.042 (0.061)	4.192* (1.831)	0.159 (0.100)	0.069 (0.062)	0.020 (0.057)	0.378 (0.381)
Foreign norfloxacin	0.610 (2.521)	1.631 (1.755)	0.622 (2.500)	1.986 (2.499)	-9.146 (5.897)	1.786 (2.216)	1.768 (2.195)	0.767 (0.792)
Foreign ofloxacin	0.016 (0.058)	0.015 (0.058)	-1.343* (0.349)	-0.055 (0.119)	0.023 (0.060)	0.177 (0.333)	0.047 (0.052)	1.109* (0.113)
Domestic ciprofloxacin	0.174* (0.075)	0.002 (0.003)	-0.005 (0.003)	-1.631* (0.103)	0.071* (0.012)	0.096* (0.012)	0.109* (0.014)	1.167* (0.027)
Domestic norfloxacin	0.011 (0.013)	-0.051 (0.032)	0.005 (0.013)	0.356* (0.072)	-2.361* (0.163)	0.453* (0.054)	0.462* (0.055)	1.113* (0.063)
Domestic ofloxacin	0.010 (0.017)	0.013 (0.016)	0.070 (0.105)	0.895* (0.113)	0.673* (0.072)	-2.919* (0.219)	0.603* (0.064)	0.688* (0.086)
Domestic sparfloxacin	0.005 (0.019)	0.012 (0.014)	0.038* (0.015)	1.107* (0.118)	0.661* (0.070)	0.570* (0.061)	-2.703* (0.187)	0.373* (0.080)

Notes: Standard errors in parentheses. Elasticities calculated at average revenue shares. Asterisk denotes significance at 5% confidence level.

Results...

...the structure of demand

- That domestic products appear to be close substitutes is a genuine empirical finding, not an artifact of the specification
- Most likely explanation has to do with the structure of distribution networks: the retail coverage of domestic firms (as a group) is much more comprehensive than that of multinational subsidiaries
- Quite possible therefore that local pharmacies more likely to have in stock domestic products containing different molecules than they are domestic and foreign versions of the same molecule

Results...

Consumer welfare impacts

- Loss of consumer welfare from reduction in product variety mitigated by cross-segment expenditure switching but magnified by upward price adjustments
- Impact of expenditure switching on consumer welfare small relative to other effects
 - initial loss from reduction in variety: Rs. 21.2 bn (71%)
 - gain from expenditure switching: Rs. -1.3 bn (-5%)
 - further loss from price increases: Rs. 9.8 bn (34%)
 - TOTAL: Rs. 29.7 bn
- Patent-expired therapeutic substitutes therefore need to be available within fairly narrow segments

Counterfactual estimates of consumer welfare losses
from product withdrawals due to the introduction of pharmaceutical patents
Total compensating variation (Rs. billion per year)

Counterfactual scenarios: withdrawal of one or more domestic product groups	Reduction in variety and...		
	Reduction in variety	Cross-segment expenditure switching	Within-segment price-adjustment and cross-segment expenditure switching
Only ciprofloxacin	5.814* (0.720)	5.742* (0.703)	8.192* (0.787)
Only norfloxacin	0.748* (0.088)	0.748* (0.088)	0.955* (0.085)
Only ofloxacin	0.316* (0.065)	0.316* (0.065)	0.514* (0.071)
Only sparfloxacin	0.085 (0.059)	0.086 (0.058)	0.313* (0.063)
Ciprofloxacin, norfloxacin and ofloxacin	9.698* (1.492)	9.500* (1.434)	15.086* (1.751)
Ciprofloxacin, norfloxacin and sparfloxacin	8.665* (1.503)	8.479* (1.449)	13.971* (1.787)
Ciprofloxacin, ofloxacin and sparfloxacin	6.759* (1.162)	6.625* (1.129)	11.448* (1.408)
Norfloxacin, ofloxacin and sparfloxacin	0.343 [†] (0.203)	0.343 [†] (0.200)	1.316* (0.255)
Ciprofloxacin, norfloxacin, ofloxacin and sparfloxacin	21.265* (8.010)	19.927* (8.184)	29.717* (6.367)

Notes: Bootstrapped standard errors in parentheses; * denotes significant at 5% confidence level; [†] denotes significant at 10% confidence level.

Results...

...consumer welfare impacts

- Substantial loss of consumer welfare from reduction in product variety—more than 50% of overall losses under most scenarios
- Suggests possible role for compulsory licensing
- if the value of product variety derives from coverage of distribution networks and associated ease of access, this component of consumer welfare loss may be transitory
 - with India recognizing patents, MNC subsidiaries may invest in expanding distribution networks

Results...

...consumer welfare impacts

- Evidence of multiplier effects:
 - estimated consumer welfare loss from simultaneous withdrawal of all four domestic product groups more than 3 times the sum of the estimated losses under the 4 scenarios where only one of the domestic product groups is withdrawn

Results...

Predicted price increases

- Predicted price increases larger when more domestic product groups withdrawn from the market
- Under scenario involving withdrawal of all four domestic product groups, predicted price increases for foreign product groups between 200%(ofloxacin) and 750%(ciprofloxacin)—matches prices reported for Pakistan
- Estimated virtual prices for domestic products withdrawn from market between 2 to 10 times observed prices under most scenarios

Results...

Foregone profits of domestic firms

- Under some scenarios total profits of domestic firms go up because withdrawal of some domestic products reduces competition for remaining domestic products
- Magnitude of domestic profit losses small relative to loss of consumer welfare

Counterfactual estimates of foregone profits of domestic producers from product withdrawals due to the introduction of pharmaceutical patents (millions of rupees per year)

Counterfactual scenarios: withdrawal of one or more domestic product groups	Reduction in variety and...		
	Reduction in variety	Cross-segment expenditure switching	Within-segment price-adjustment and cross-segment expenditure switching
Only ciprofloxacin	1039.700* (98.595)	1192.324* (72.265)	580.504* (112.878)
Only norfloxacin	-7.161 (21.203)	13.980 (23.442)	-131.634* (21.082)
Only ofloxacin	-51.218* (12.138)	-53.680* (14.218)	-140.422* (15.609)
Only sparfloxacin	-48.991* (14.665)	-64.062* (16.862)	-162.761* (13.880)
Ciprofloxacin, norfloxacin and ofloxacin	1235.615* (125.857)	1457.821* (68.902)	694.400* (117.348)
Ciprofloxacin, norfloxacin and sparfloxacin	1343.305* (132.197)	1522.861* (79.370)	704.810* (129.365)
Ciprofloxacin, ofloxacin and sparfloxacin	1165.991* (151.633)	1329.050* (106.079)	692.196* (168.213)
Norfloxacin, ofloxacin and sparfloxacin	-339.157* (42.546)	-340.213* (45.242)	-552.083* (48.899)
Ciprofloxacin, norfloxacin, ofloxacin and sparfloxacin	2379.083* (169.680)	2379.083* (169.680)	2379.083* (169.680)

Results...

Counterfactual estimates of total welfare loss

- Upper bound estimate of annualized loss:
 - Rs. 32.1 billion = U.S.\$713 million
- ...of which:
 - loss of consumer welfare = Rs. 29.7 billion (93%)
 - foregone domestic profits = Rs. 2.8 billion (7%)
- Middle range estimate assuming strict price controls:
 - Rs. 22.3 billion = U.S.\$495 million
- Lower bound estimate assuming reduction in product variety only a transitory phenomenon:
 - Rs. 9.8 billion = U.S.\$217 million

Counterfactual estimates of total welfare losses
from product withdrawals due to the introduction of pharmaceutical patents:
(billions of rupees per year)

Counterfactual scenarios: withdrawal of one or more domestic product groups	Reduction in variety and...		
	Reduction in variety	Cross-segment expenditure switching	Within-segment price-adjustment and cross-segment expenditure switching
Only ciprofloxacin	6.854* (0.653)	6.934* (0.666)	8.773* (0.727)
Only norfloxacin	0.741* (0.098)	0.762* (0.103)	0.824* (0.095)
Only ofloxacin	0.265* (0.072)	0.263* (0.075)	0.374* (0.080)
Only sparfloxacin	0.036 (0.069)	0.022 (0.071)	0.150* (0.072)
Ciprofloxacin, norfloxacin and ofloxacin	10.933* (1.393)	10.958* (1.400)	15.780* (1.768)
Ciprofloxacin, norfloxacin and sparfloxacin	10.008* (1.399)	10.002* (1.403)	14.676* (1.753)
Ciprofloxacin, ofloxacin and sparfloxacin	7.925* (1.049)	7.954* (1.065)	12.140* (1.324)
Norfloxacin, ofloxacin and sparfloxacin	0.004 (0.211)	0.003 (0.220)	0.764* (0.264)
Ciprofloxacin, norfloxacin, ofloxacin and sparfloxacin	23.644* (8.010)	22.306* (8.184)	32.096* (6.367)

Results...

Estimated profit gains of MNC subsidiaries

- Estimate only moderate profit gains for MNC subsidiaries:
 - Rs. 2.6 billion = U.S.\$57 million per year
- Quite small compared to:
 - U.S.\$1.6 billion, annual sales of Cipro, Bayer's patented ciprofloxacin drug
 - U.S.\$800 million, rough estimate of how much it costs to develop a new drug (Mednews (2001))

Concluding comments

- Concerns about adverse welfare consequences of TRIPS may be warranted
- Potential for substantial consumer welfare losses even if MNC subsidiaries respond to change in IPR regime by investing in distribution networks
- Use of price controls to mitigate welfare losses may backfire if this reduces incentives to expand retail coverage and access
- Compulsory licensing needs to be considered more carefully as a policy alternative
- Patents alone probably not sufficient to spur R&D—publicly funded efforts likely to remain important