

## THE SCIENCE AND POLITICS OF NIMESULIDE: RETRACING THE 'CAREER' OF A CONTROVERSIAL DRUG

Parvathi K Iyer\*

***Abstract:** The present paper undertakes a socio-historical examination of a 'controversial' drug Nimesulide. Through a detailed documentation of the drug's entry and marketing in India and the subsequent litigation in connection with its safety and efficacy issues, the paper attempts to examine the relative power of the pharmaceutical industry in the shaping of knowledge claims and attributes related to the potency, safety and efficacy of drugs. The paper also discusses how the attributes of the drug were represented by different sets of actors, including the petitioner, print media, health activists, firms, regulatory officials and medico-scientific experts. In this connection, it also examines the 'lay-expert' divide, sought to be created by regulatory officials and the medico-scientific community, in the course of the litigation, in order to justify their assessments of the drug and its implication for the knowledge claims related to the safety and efficacy related attributes of the drug and its therapeutic career. Thus the paper deals with the social process of a knowledge claim wherein the civil society elements also play a key role.*

**Key Words:** *Nimesulide Controversy, lay-expert divide, role of regulatory bodies, role of medico-scientific community, role pharmaceutical industry, knowledge claim.*

### **Backdrop:**

The paper attempts to undertake a socio-historical examination of a 'controversial' drug Nimesulide. Through a detailed documentation of the drug's

---

\*Assistant Professor, Centre for Studies in Science, Technology and Innovation Policy, Central University of Gujarat, Gandhinagar :382030,  
Email: [parvathikiyer@gmail.com](mailto:parvathikiyer@gmail.com)

entry and marketing in India and the subsequent litigation in connection with its safety and efficacy issues, the paper attempts to examine the relative power of the pharmaceutical industry in the shaping of knowledge claims and attributes related to the potency, safety and efficacy of drugs. (The material for the case study was acquired from the legal documents in the possession of Social Jurist and discussions with two lawyers belonging to the same organization, as well as secondary sources and insights provided by health activists, regulators and other respondents. Social Jurist is the lawyers' group, which filed the public interest litigation in the Delhi High Court in 2002 in connection with the safety and efficacy of Nimesulide.)

The paper commences with an outlining of the history pertaining to the discovery of the drug in the United States and its approval in a few European countries. It then examines the broad context of its entry in the Indian market and its 'success' as a revenue generating drug among domestic manufacturers. The subsequent sections examine the trajectory of the litigation in connection with the drug, including the arguments and counter-arguments put forward by the parties in the litigation and the judgment by the Delhi High court on the drug. The paper concludes with a discussion of how the attributes of the drug were represented by different sets of actors, including the petitioner, print media, health activists, firms, regulatory officials and medico-scientific experts. It discusses the 'lay-expert' divide, sought to be created by regulatory officials and the medico-scientific community, in the course of the litigation. Of course this controversy is emergent of the attempts to justify each of the contending parties' assessments of the drug and its implication for the knowledge claims related to the safety and efficacy related attributes of the drug and its therapeutic career.

Controversies involving safety and efficacy concerns related to drugs may also be understood as scientific controversies. Scientific controversies typically

involve broad areas of uncertainty, the making of decisions in the context of limited knowledge or lack of conclusive evidence, struggle over credibility, the power of certain actors to define certain kinds of knowledge claims as more objective and acceptable, intra-institutional concerns, professional interests and even the influence of extra-scientific factors on supposedly technical decisions<sup>1</sup>. The present paper also attempts to demonstrate how all of the above factors came into play in the Nimesulide controversy.

### **History of the Drug:**

Nimesulide, an anti-inflammatory and analgesic<sup>2</sup> drug, was originally synthesized by Dr George Moore and his research team at Riker Laboratories, Minnesota in 1971. The laboratory eventually became a part of the firm, 3M Pharmaceuticals in the United States.<sup>3</sup> The drug was synthesized with the intention of providing a better therapeutic alternative in comparison to the existing class of non-steroidal anti-inflammatory drugs (NSAIDs) in terms of providing relief from inflammation and pain due to musculoskeletal disorders and also fever without the adverse effects demonstrated by these drugs in the form of gastro-intestinal injury. However, during the subsequent assessments by the United States Food and Drug Administration (USFDA), the drug reportedly failed to live up to its original promise and was therefore denied approval by the regulatory body.<sup>4</sup>

The synthesis of the drug is also linked to the discovery of an enzyme, Cox-2, at the University of Rochester in the United States, and the prevailing

---

<sup>1</sup> Abraham (2008, 2003, 2002.), Jassanoff (2004), Webster (1991)

<sup>2</sup> A drug whose primary indication is relief from inflammation and pain, but which is also used to control fever

<sup>3</sup> Helsinn Healthcare S.A. 2007. "Licencing is our core business." *European Musculoskeletal Review*.

<sup>4</sup> Gulhati, 2003. "Nimesulide: Unessential Drug: Unnecessary Risk. Unpublished report. The report was one of the documents used by Social Jurist, the organization which filed the PIL, in the preparation of the legal materials in relation to the case. However, there seems to be some dispute on this point as the Indian Medical Association claims that since no application was received by the FDA for marketing the drug, there was no question of the drug not being approved or prohibited in the United States. The Swiss firm Helsinn's reports on the drug are also vague and unclear on this point

competition among pharmaceutical firms engaged in research on Cox-2 inhibitors. The inhibition of both Cox-1 and Cox-2 enzymatic reactions is required for gastric injury. The failure to receive regulatory approval from the USFDA was on the grounds that, apart from Cox-2, Nimesulide was also inhibiting Cox-1 to some extent.<sup>5</sup>

The drug was subsequently licensed to Helsinn, a Swiss company, in 1980. Helsinn acquired from 3M, the world-wide licensing rights for the drug and proceeded to carry out tests related to the clarification of its pharmacological and clinical profile. However, the firm failed to get approval for the drug in Switzerland. The firm subsequently licensed it to another German firm, Boehringer, for introduction in the Italian market.<sup>6</sup> The drug subsequently underwent clinical trials in the country and was given approval for marketing in 1985. Later, the drug was reintroduced in Switzerland. However, permission was granted, solely for the use of the drug in tablet form and only for use by adults.<sup>7</sup> (Gulhati, 2003 & Rane, 2003).

### **Entry and Marketing of the Drug by Firms in India:**

In India, marketing approval for Nimesulide was first sought by Panacea Biotech Ltd, a Delhi-based company.<sup>8</sup> Permission was sought, both to import the drug (under Rule-122-A of the Drugs and Cosmetics Act, 1940) and to market it (under Rule 122-B) in December 1994. The drug subsequently received marketing approval in January 1995.<sup>9</sup> However, the permission pertained to the marketing of the drug only in 100mg tablet form.

---

<sup>5</sup> Rane, 2003. 'Why risk our children to Nimesulide'. *Health Action*

<sup>6</sup> The Italian regulatory environment for drugs has always been regarded as more permissive in comparison to other West European and American markets

<sup>7</sup> Till date, Switzerland does not permit the use of the drug in children

<sup>8</sup> Letter to the Drugs Controller, India, Directorate General of Health Services Ltd, dated December 1, 1994

<sup>9</sup> Letter from Drugs Controller, India to Panacea Biotech, Delhi dated January 13, 1995

Subsequently, the drug was also marketed by other domestic firms<sup>10</sup>, including companies like Ranbaxy, Dr Reddy's Laboratories, and Nicholas Piramal etc. There were eight different tablet forms and nine different fixed dose combinations of the drug with other drugs. In all there were 255 brands of the drug in the market during this period (Rane, 2003). The drug had been approved for inflammatory musculoskeletal disorders but was subsequently promoted as first line anti-pyretic therapy.<sup>11</sup> Some of the brands marketed by leading Indian firms during this period included: Dolamide (Ranbaxy), Parazolandin (Sarabhai Piramal), Nise Spas (Dr Reddy's), Nise DT (Dr Reddy's), Nimulid – MD (Panacea Biotech), Nimulid-EF (Panacea Biotech), Pronim QR (Unichem). The 255 brands of the drug included 25 mg suspension (drops), 50 mg tablets, 100 mg dispersible tablets and 150 mg tablets.<sup>12</sup> They were marketed by leading firms, in addition to medium scale and small scale firms.

One of the major motivation for Indian firms to market the drug during the period in all its multifarious combinations and avatars was due to its being outside the purview of the Drug Price Control Order (DPCO), which meant that the drug could be sold for the price that the firm decided. The relatively recent entry of the drug in the Indian market also meant that it could be 'packaged' as a novel drug to physicians and pharmacists. The drug was regarded as a 'success' in the Indian market since it commanded a share of about Rs. 700 crores (Srinivasan, 2006).

The profits accruing to firms marketing the drug were considerable. Hypothetically, the break-up of the costs of manufacturing and marketing the drug

---

<sup>10</sup> Issues pertaining to the legal status and therapeutic rationality of these formulations and other alleged violations of the Drugs and Cosmetics Act, 1940 by Panacea Biotech and these firms would be taken up during the discussion of the case

<sup>11</sup> This means that the primary indication and approval was for pain management, with the alleviation of fever being only a secondary indication See Srinivasan, S. 2006. A Lay Person's Guide to Medicines. Locost, Vadodara.

<sup>12</sup> See Annexure D; C.W. No 8335 of 2002 (PIL). Social Jurist, A Lawyer's Group vs. Union of India and ORS. The dosage and route of delivery of these drugs , (as drops, injectibles etc), had allegedly not been approved by the Drug Controller

could be broken down as follows<sup>13</sup>: the raw material of the drug being available for Rs. 485 per kg during the period, the cost of 100mg of the drug came to just 4.85 paise. The cost of conversion of raw material to ready-to-sell tablets (processing, tableting, strip making, aluminum foil, printing of strips, packaging boxes etc.), was a maximum of Rs. 1.25 per strip of 10 tablets. The total production costs of a strip of 10 tablets would not exceed Rs. 1.75. Even if a hundred per cent mark up (i.e. another Rs. 1.75 was added to the price to pay for transportation, distributors' margin (8-10 percent), retailers' commission (16-20 per cent) and manufacturer's own profits, logically the maximum retail price (MRP) should not exceed Rs. 3.50 plus government taxes. Thus a strip of 10 tablets could be available to patients for about Rs. 4. However, the formulations were being sold by leading firms at a range of Rs. 26-29. (For e.g. Nise (Dr Reddy's Laboratories) and Nimulid (Panacea Biotech). These two brands commanded the largest shares in the market for Nimesulide formulations.

### **Adverse Reactions of the Drug & Consequent PIL in Delhi High Court:**

This upward swing in firms' revenues from the drug continued until 1999, when the death of two children due to adverse reactions of the drug was reported in Portugal. Subsequently, the use of the drug in children was prohibited in all European countries and Israel except Italy, where its use was permitted in children above six years.<sup>14</sup> The question of the drug being banned in the United States never arose since the drug had never received approval there.

On March 11, 2002, the death of an adult patient due to Nimesulide hepatotoxicity was reported in Finland. The Finnish government subsequently ordered the suspension of the use of the drug with effect from March 18, 2002. The report of the death had been preceded with other reports of liver damage there in

---

<sup>13</sup> See Gulhati, 2004. 'Drug Prices under Ministerial Microscope'. *MIMS India*.

<sup>14</sup> See WHO Pharmaceutical Newsletter 2000

the press. In May 2002, Spain banned the drug and recalled all existing stocks of the drug. This was followed by a similar action in Turkey. In Bangladesh, pediatric formulations of the drug were banned in October 2002 and Sri Lanka rejected the applications of local firms in the country to market the drug. The drug had already been refused permission for marketing in Canada, England, Australia, New Zealand, Denmark and Sweden.<sup>15</sup>

A relevant detail here is that a few medical journals had already pointed to the above adverse effects of the drugs in addition to other effects like heart related ailments etc. Some of the medical observations against the use of the drug, made by these studies, were as follows. Firstly, in relation to dosage, it was pointed out that as per the approved dosage (i.e. 5 m.g./ kg per day), mean serum concentration of the drug reached around 14.6mH. However, only 1.49 mH concentration was required to effectively inhibit Cox-1 activity. The increased serum concentration, it was pointed out, would lead to ulcers. This also meant that much before the anti-inflammatory and analgesic effect, claimed by the drug, occurred, the gastric mucous in the body would be adversely effected.<sup>16</sup> Similarly, the Journal of American Medical Association (JAMA) in 1999 (December 13: 17(6) had pointed out the likelihood of heart related adverse reactions due to the drug. All this meant that Nimesulide was not a ‘selective’ inhibitor of Cox-2 enzymatic reaction, as had been declared in studies submitted to the Indian regulatory authorities, but a ‘preferential’ inhibitor.

Subsequent to the above-mentioned regulatory developments around the world, there were critical reports in the print media about the drug circulating in the Indian markets and proving a money-spinner for Indian firms despite its associated adverse reactions being well documented by medical journals and international regulatory authorities. The other point of criticism raised by these

---

<sup>15</sup> As cited in the petition submitted by Social Justice vide WP © 8335/ 2002 in connection with the PIL, Social Jurist vs. Union of India and OTRS.

<sup>16</sup> See Gastroenterology, 1998: 115:1-1-9) as cited by Rane, 2003

reports pertained to the government's indifference to the potential hazards of the drug and its negative implications for public health.<sup>17</sup> More importantly, there were several cases of adverse reactions in India, which were reported predominantly by the print media, also in relation to the drug. Seven cases of adverse reactions due to Nimesulide<sup>18</sup> were reported at the Victoria Memorial Hospital in Bangalore and five other cases pertained to the death of children, who had been administered with the drug. Of these latter five cases, one case referred to Apollo Hospital, New Delhi<sup>19</sup>, one case referred to Holy Family Hospital,<sup>20</sup> two cases pertained to Chandigarh<sup>21</sup> and one case in Kerala was reported by *The Week*.<sup>22</sup>

The government subsequently took cognizance of these media reports and elicited the opinion of prominent doctors from the Indian Medical Association and the Indian Association of Pediatrics on the safety and efficacy of the drug, with particular reference to its use in children. The Drug Controller, India sought and was subsequently sent a letter in favour of the drug by Dr K.P.S. Sachdeva, President of the Indian Association of Pediatrics. The drug controller also sought an opinion regarding the drug from the doctors in the Indian Medical Association. The Indian Medical Association (IMA), subsequently conducted an opinion poll on the safety of Nimesulide.<sup>23</sup> The questionnaire, administered confidentially to its doctors, among other information, also elicited details pertaining to the years of practice, the number of the years the concerned doctor had been using the drug, the total number of patients on whom the drug had been administered with age-

---

<sup>17</sup> Kamath and D'Silva, 2002. Pain on the Side: Banned drugs still do the circuit. *Times of India*. November 19, 2002; 'Sick Medicine. *Times of India* editorial dated October 5, 2002

<sup>18</sup> WP©8335/2002 &CM 1119/03. Judgment delivered on 10.03.2004

<sup>19</sup> News article by Dr Anupam Sibal in Times of India (October 4, 2002); as cited by Gulhati 2002. MIMS India. November

<sup>20</sup> Reported on 'We-The People' in *Star News* channel on October 20, 2002 as cited by *ibid*.

<sup>21</sup> Kalpana Jain, 2002. 'Popular Fever Drug Placed Under Review' in Times of India, New Delhi edition dated 4-10-02, as cited by *ibid*.

<sup>22</sup> Letter from Dr Ajitha Gopakumar of Kerala, *The Week*, November 17, 2002 as cited by *ibid*

<sup>23</sup> Annexure K, WP© 8335/2002 &CM 1119/ 03. Copy of the form by IMA asking for the opinion of various specialists on the safety of the drug.

wise details of the patients', the indications for which the drug had been used, including pain, fever, arthritis, gynecological pain, urethritis prostatitis and cancer-related pain.

The Indian Medical Association subsequently submitted its conclusions and recommendations to the Drug Controller, India:<sup>24</sup> The report mentioned that fifty doctors had responded to the opinion poll and the total number of patients, whose data was submitted by them, pertained to 5,29,792 patients. Of these, 170917 patients belonged to the age group 0-1 years, 1,58,528 patients belonged to the age group 1-5 years, 109589 patients belonged to the age group 5-12 years, 31,149 patients belonged to the age group 12-30 years, 34,089 patients belonged to the age group 30-60 years and 25,520 patients belonged to the age group above sixty years. The report mentioned that the conclusions and recommendations were based on a 'scientific analysis' of the data as well as the opinions expressed by experts at the special plenary session organized by the Association.

These conclusions and recommendations were:<sup>25</sup>

Nimesulide is a safe drug for use in India. Nimesulide is safe even in the pediatric age group. Nimesulide is as safe as or even better than other NSAIDs. A post marketing survey of all drugs in India should be conducted regularly. A causal relationship between drug and the side effect must be definitely established before any steps for restricted use or banning the drug are even thought of. It is noticed that all drugs have some or the other side effects and medically it is established that the risk-benefit ratio has to be weighed before a drug is prescribed. The IMA strongly recommends that stray cases being reported by lay media without any scientific data and establishment of causal relationship should never be given any importance by drug regulatory authorities. It has been noticed by the majority of the doctors that most of the side effects seen with nimesulide are

---

<sup>24</sup> *Ibid.*

<sup>25</sup> WP© 8335/2002 &CM 1119/ 03. Copy of the conclusions and recommendations submitted by IMA to Drug Controller, India. 'National Recommendations on Nimesulide Safety.' Date not mentioned in the document obtained from Social Jurist.

common with other NSAIDS; both in pediatric and adult age groups, and that the benefits far outweigh the side effects.

The Indian Medical Association clearly labeled Nimesulide as a safe drug, even for use in children, despite the reports of its adverse reactions in a few medical journals, mentioned earlier in the chapter. It gave a clean chit to the drug and expressed its disdain of the media reports, claiming that these allegations had been made without ‘scientific’ proof and clear establishment of causal relationship pertaining to the adverse effects of the drug.

The report also contained the details of the statistical analysis and extrapolation carried out by the IMA on 4,00,000 practicing doctors on the basis of the information derived from fifty doctors on the safety of the drug.<sup>26</sup> The petition submitted by Social Jurist indicates that the Review Committee of the drug was constituted sometime in October 2002. Subsequent to the IMA report details being made public, the print media carried reports of the regulatory body bowing to pressure from pharmaceutical firms and called for strict scientific evaluation of the controversial drug. A news item in the *Times of India* quoted the then Drug Controller General, India, Ashwini Kumar<sup>27</sup> as stating that the government had decided to give a clean chit to the drug. The item also quoted the drug controller as mentioning that Israel had decided to withdraw the ban on the drug and that Bangladesh’s decision to ban the use of the drug may not have been a scientific decision. However, the drug controller conceded to the deficiencies in drug adverse reaction monitoring systems in the country and mentioned about the need for short-term studies on the drug at three or four centers, according to the news report.<sup>28</sup>

This clearly indicates that though the government had given a clean chit to the drug, they were still unsure of its safety profile. Subsequently, a petition was

---

<sup>26</sup> Annexure L. WPC© 8335/2002 &CM 1119/ 03. The report and statistical analysis does not have any mention of details regarding its date of submission to the Drug Controller, India

<sup>27</sup> In 2002.

<sup>28</sup> Jain 2002. ‘Clean Chit for Drug Minus Monitoring.’ *Times of India* article dated December 17, 2002.

filed by Social Jurist in the high court of Delhi on December 17, 2002. The respondents named in the petition were the Union of India, the government of National Capital Territory of Delhi, the Drug Controller of India, Panacea Biotech Ltd., Dr Reddy's Laboratories Ltd. and Ranbaxy India Ltd.<sup>29</sup> The petition named these respondents,

... in the matter of failure on the part of the respondents to protect the health of the citizens of their own country by providing them with safe and rational medicines and drugs and in the matter of failure on the part of the respondents to protect the tender age of the children and the kids of the country and in the matter of violation of fundamental right under article 21 and article 45 of the constitution, as the respondents failed to protect the life of the people by not imposing a ban on the drugs which are injurious to their health and in the matter of violation of the Drugs and Cosmetics Act 1940 and Rules framed there under: Schedule 'H', Rule 65, Rule 97; Schedule-'Y' Rule no 1.2 (Para 4) Rule 122-E, Drug Policy 1986 (Rule 8,9,10), Drug Policy 1994 (Rule 12, 13, 14 & 15), Drug Price Control Order 1995 and in the matter of 1. Constitution of India, 2. Drugs and Cosmetics Act, 3. Drug Policy 1986, 4. New Drug Policy 1994 and Drug Price Control Order 1995. (*ibid*)

### **Arguments made by the Petitioner :**

The counsel for the petitioner raised several arguments and points in the submissions to the court during the period of the litigation. One of these arguments pertained to the origin of the drug and the fact that the drug had failed to receive the approval of the FDA in its country of origin, the United States, despite the millions of dollars spent in its research and discovery. The implication here was that the USFDA had very strict standards of assessment and that by itself was proof enough of the questionable nature of the drug's safety profile (Petitioner's submission-1)

A related argument here pertained to the Cox-2 Selectivity claim of the drug. It was stated that the approval and marketing of Nimesulide had been

---

<sup>29</sup> Civil Writ Petition No 8335 Of 2002. In the matter of Social Jurist vs. Union of India and ORS.

instituted with the claims that the drug was a selective inhibitor of Cox-2 enzymatic reaction and hence did not have any adverse impact on the gastro-intestinal system. The counsel, however, pointed out that these claims had been made on the basis of studies conducted by Adis International Ltd. in New Zealand, a company, which had close links with the pharmaceutical industry. The counsel further referred to independent studies, published in reputed academic journals, which had amply demonstrated that the drug was not a “selective” but “preferential” inhibitor of Cox-2 and therefore was harmful to the gastro-intestinal system (*ibid*). The counsel’s submission also elaborated on the banning of the drug in several European countries and even countries like Bangladesh.<sup>30</sup> Another important argument pertained to the violation of rules related to the import of drugs under the Drugs and Cosmetics Act, 1940. It was pointed out that as per Rule 30-B of the Drugs and Cosmetics Act,

...no drug, the manufacture, sale and distribution of which is prohibited in the country of origin, shall be imported under the same name or under any other name except for the purpose of examination, test or analysis.

The argument here was that the use of the word “prohibited” signified “not permitted.” Also, the ‘country of origin’ with reference to Nimesulide meant the United States rather than the country from which the drug was being purchased and that the intention of the legislature was to ensure that no drug which had been refused permission in its country of origin should be allowed to be imported into India. This being the case, the permission granted by the Drugs Controller, India to import the drug was in violation of this rule, according to the petition. With respect to the marketing approval of the drug, it was argued that studies in reputed journals had already established that the drug did not offer any novel therapeutic benefits over existing drugs in the market. It was enquired as to why

---

<sup>30</sup> These details have already been elaborated upon in the previous section.

greater leniency had been shown to the drug in terms of permitting firms to market it, particularly when it had been demonstrated that the drug was not an essential one.

Another related issue highlighted by the petition here pertained to the legal procedure in connection with the launching of Nimesulide and its fixed dose combinations. According to them, the procedure should have included the marketing approval from the Drug Controller, India under Rule 122 (E) and Schedule Y.<sup>31</sup> Under certain conditions, particularly in public interest, the drug controller could waive off the requirement of clinical trials, particularly when adequate data in the form of published studies was available from other countries. The counsel argued that in the case of Nimesulide, no such public interest was involved since it had been established that it was not an essential drug. It was also argued that the ‘studies’ submitted to the Drug Controller, with respect to Nimesulide were the studies conducted by Adis International, instead of those in peer-reviewed or independent journals. The central point made here was that since Adis drew its entire income from the pharmaceutical industry, there was a clear ‘conflict of interest’, lack of adequate scientific credibility and bias, which made its publications unacceptable in the matter of regulatory approval of the concerned drug. The petition also alleged that other details pertaining to the drug’s approval status or adverse reactions or withdrawal in other countries, permission for clinical trials on human subjects, other laboratory, animal and human studies and procuring of test license had not been complied with and that the drug had been approved in violation of these rules. Other allegations made by the petition in this context pertained to the violation of Drugs and Cosmetic rules by firms like Reddy’s Labs, Ranbaxy and others, with respect to the lack of legal approvals for the marketing of single-dose and fixed dose combinations by these firms.

---

<sup>31</sup> Schedule Y relates to the mandatory laboratory, animal and human clinical tests carried out in India with respect to new drugs. These include 1) Animal toxicology, reproductive tests and carcinogenicity studies, among other tests; 2) Bioavailability studies of the drug; 3) Dissolution studies in comparison with other drugs; 4) Stability studies and 5) Clinical studies on patients in India.

Another argument made here was with respect to the dosage and route of administration of the drug. Since the approval letter of the Drug Controller had permitted Panacea Biotech to market only 100mg plain Nimesulide tablet, all other formulations needed prior approval. It was argued that Panacea Biotech had marketed several illegal formulations of the drug. These formulations were:

1. *Nimulid (DS)*: (Nimesulide 200 mg tablet)
2. *Nimlid Kid Tablet*: (Nimesulide 50 mg tablet)<sup>32</sup>
3. *Nimulid-MD Tablet*: (Nimesulide 100 mg as dispersible tablet)
4. *Nimulid-EF Tablet*: (Nimesulide 100 mg as effervescent tablet)

The petition also enquired as to the grounds on which these formulations were being allowed to be marketed. The argument was also that the indications for which the drug had been approved were,

...Inflammatory conditions, including joint disorders such as rheumatoid arthritis, post-traumatic and post-operative painful condition and fever.<sup>33</sup>

This meant that the approval of the drug was for inflammatory condition accompanied by pain and fever and there was no approval for fever or pain not associated with inflammatory condition. Further, it was argued that fever or pain were symptoms that needed to be diagnosed and only when these were associated with an inflammatory condition, could the drug be used. Yet the drug was being marketed as a first-line remedy for fever and pain. In the above context, it was further stated that no prior permission had been acquired for the marketing of drug in the form of suspensions and drops and also that, as per the provisions of the

---

<sup>32</sup> The Drug Controller, India had refused permission to the firm to market the formulation vide letter dated May 17, 1996 (as cited in Annexure D, Petitioner's Submission, Civil Writ Petition No 8335 Of 2002. In the matter of Social Jurist vs. Union of India and ORS )

<sup>33</sup> Vide letter dated 13-01-1995 by the Drug Controller, India as cited in Annexure E, Petitioner's submission, *ibid*.

approval, Nimesulide had to be treated as a new drug and therefore these formulations required prior approval. It was alleged that dozens of such formulations had been marketed without such approval.

### SOME FORMULATIONS MARKETED BY LEADING FIRMS

1. Nimesulide 50mg/ 50 ml suspension formulations: *Auronim* (Aurobindo Pharma), *Nimegesic* (Alembic),  
*Nimfast* (Cadila Pharmaceuticals), *Nimuflex* (Sarabhai), *Novogesic* (Glenmark), *Orthobid* (Nicholas Piramal),  
*Pronim* (Unichem Pharma) and *Zega* (Sun Pharmaceuticals)
2. Fixed-dose combinations of Nimesulide: These included:
  - a) Nimesulide + Paracetamol combinations: *Dolamide* (Ranbaxy), *Nimica Plus* (Ipca Laboratories), *Parazolandin* (Sarabhai Piramal),
  - b) Nimesulide + Dicyclomine combinations: *Nise Spas-DS* (Dr Reddy's Laboratories)
  - c) Nimesulide + Tizanidine combinations: *Nimulid MR* (Panacea)
  - d) Nimesulide + Serratiopeptidase combinations: *Nimulid SP* (Panacea)
  - e) Nimesulide+ P-Piperidinoethoxy-O-Carbomethoxybenz ophenone combinations: *Novigan-N* (Dr Reddy's)

(Source: Petitioner's Submission, Annexure G)

The therapeutic rationality of these fixed dose combinations, mentioned above, also came into question. The allegations here pertained to the combining of these different active ingredients with Nimesulide, (a) without assessing their 'combined therapeutic rationality' and (b) without taking into account the different dosing intervals for these active ingredients. The argument was that combinations could be allowed only under exceptional and specific circumstances and that the overlooking of these 'established scientific facts' by the firms would prove to be potentially hazardous for the consumers of these formulations. It was also argued that the drug was not marketed for children in any other country in world except Brazil

(children over three years) and Italy (children over six years), whereas in India, the drug was being marketed for new-born babes.

The opinion poll conducted by the Indian Medical Association also came in for criticism on various counts. These included the ‘statistically microscopic’ size of the sample, which represented the opinions of only fifty doctors out of a total population of four lakhs of doctors, the ‘rudimentary, inappropriate and deficient’ nature of the form filled in by the doctors included in the sample, the discrepancies in the data as revealed in the extrapolation results and the Indian Medical Association’s financial ties with the pharmaceutical industry. In this regard the petition scathingly stated that,

The entire exercise was based on the memory of fifty doctors, dating back to past ten years, when Nimesulide was not in use. Nimesulide came to the market after January 13, 1995. The ‘opinion poll’ was conducted in the end of 2002. Thus the drug was in use for less than eight years and yet the doctors were asked to scratch their heads for memory and answer if they were using Nimesulide more than ten years ago. (Petitioner’s submission: 10)

And further added that:

An analysis and extrapolation done on all doctors on the basis of “data” conducted shows that Nimesulide is administered to a minimum of 108 crores children and 18.75 crores adults every year. If so, Nimesulide should have a sale of Rs 2,042 crores each year, while the total actual sale (as per ORG-MARG figures) is around Rs 200 crores. (*ibid*)

With regard to the IMA’s ties with the industry, reference was made to a similar case involving the drug *Cisapride*, where the association had given a clean chit to it in spite of a ban on it by the USFDA and that the fact that the IMA did not engage in routine monitoring of the adverse drug reactions but only intervened when the drug was in danger of being withdrawn. The petition also alluded to the

IMA's corrupt practices, which had been highlighted in the media.<sup>34</sup>

### Arguments by the Ministry of Chemicals and Fertilizers and the Petitioner's Response:

Following the submission of the petition in the High Court of Delhi, the petition came up for motion hearing on December 20, 2002. Subsequently, the High Court served notice on the respondents to appear before the court and show cause against the admission of the petition on January 8, 2003.<sup>35</sup> In a separate order, the petitioner was also permitted to implicate the Ministry of Chemicals and Fertilizers as one of the respondents<sup>36</sup>. The issue here related to the banning of two drugs, *Terfinadine* and *Astemizole*. The counsel for the petitioner had argued that in the case of these two drugs, a ban had been instituted by the Expert Committee of the central regulatory body in spite of no local data on adverse reactions and the availability of the drug in countries like UK, Australia, Finland, Germany etc. The petition questioned the exception made in the case of Nimesulide and also its status as a drug outside price control.

The Ministry of Chemicals and Fertilizers in its counter-affidavit<sup>37</sup> stated that the drug was not eligible for price control since it did not cross the minimum annual turnover limit. The submission alluded to the Drug Price Control Policy 1994, which states that even when a drug is not placed under price control,

... a strict watch would be kept on the movement of prices as it is expected that their prices would be kept in check by the forces of market competition. The government may determine the ceiling levels beyond which increases in prices would not be permissible.

The Ministry also accepted that data pertaining to the compilation of drugs for price control had not been updated after March 31, 1990. The response of the petitioner to

---

<sup>34</sup> Petitioner's submission: Annexure M.

<sup>35</sup> Vide notice issued to respondents by Administrative Officer (Writs) for Registrar General on December 31, 2002, CW-8335/02.

<sup>36</sup> Order dated February 4, 2003.

<sup>37</sup> Vide February 1, 2003.

the Ministry's submission was that Nimesulide was eligible for price control since it had a minimum annual turnover of Rs four lakhs and the view that the market forces would check the unnatural spiraling of prices had been proved wrong in the case of the drug. The petitioner mentioned that the cost price of ten tablets of Nimesulide was less than Rs 1.80<sup>38</sup> and that if the drug had been placed under price control, then even after a 100% mark-up, the price would not go above Rs 4.00. The petitioner quoted the retail prices of ten tablets of some of the brands in this context. These included: *Nise* (Dr Reddy's Labs): Rs 25.00, *Nicip* (Cipla): Rs 25.74 and *Nimulid* (Panacea Biotech): Rs 29.00.

The petitioner also argued that the failure of the ministry in updating data relating to the compilation of the list of drugs under price control had led to a large number of drugs being placed outside the price control mechanism and indiscriminate rise in the prices of these drugs.

### **Arguments by the Drug Controller, India and the Petitioner's Response :**

With reference to the original approval to the drug for marketing purpose<sup>39</sup>, the Drug Controller's submission mentioned that since Nimesulide was listed in the European pharmacopoeia, it had wide acceptability. The petitioner's response to this was that the drug had also been listed in the British pharmacopoeia but had not been given approval in the United Kingdom.<sup>40</sup> Further, it was argued that the purpose of a pharmacopoeia was to provide chemical information and method to test the purity of the drug and that it did not provide any information on the uses of the drug, dosage, adverse effects or any other clinical uses. The point put forward here by the petitioner was that the listing of the drug in a pharmacopoeia did not automatically exclude it from being banned.<sup>41</sup>

---

<sup>38</sup> The break up of the costs of manufacturing and marketing of the drug has been explained earlier in the previous section

<sup>39</sup> Mentioned earlier on in the chapter in the previous section

<sup>40</sup> Petitioner's submission: 10

<sup>41</sup> *ibid*

The Drug Controller's submission also stated that Nimesulide had acceptability since it had been mentioned in the Standard Treatment Guidelines, 2002. The petitioner's argument here was that the book had been published before the adverse effects of the drug, which had been reported abroad, were known in India. In addition, the Drug Controller mentioned that, in 1996, prior to the approval of Nimesulide suspension for pediatric use<sup>42</sup>, it had engaged in consultations with renowned pediatricians. The petitioner, however, argued that details pertaining to the names of these experts, the method of their selection and details regarding their conflicts of interests, if any, had not been provided by the Drug Controller. Moreover, at the time of seeking such an opinion, Nimesulide was not being used in India in pediatric patients, which meant that the concerned pediatricians could not have had clinical experience with the drug. A related point made here was that during the period, there were no scientifically acceptable journal articles on the use of Nimesulide in children.

The drug controller also pointed out that, other than media reports, there had been no conclusive evidence of adverse reactions in the case of the drug and therefore there was no need for withdrawal or banning of the drug from the market. It was argued that Nimesulide was still being used in a number of countries like Brazil and Italy and therefore it could be safely used in India. The petitioner's response here was that there was no established and reliable mechanism and infrastructure for monitoring adverse reactions in the country and that in the absence of these and isolated adverse events that had occurred abroad and in India, it was better to suspend if not ban the drug, until further studies to establish its safety and efficacy had been conducted. In this context the petitioner stated that:

When it comes to children, when it comes to unessential drugs like Nimesulide, when it comes to situations where a large number of safer, well tried and tested alternatives are available, the prudent course of action in

---

<sup>42</sup> Vide letter NO. 12-32/94-DC dated June 17, 1996 issued by the then Drugs Controller General, India, Dr P. Dasgupta to Ms. Panacea Biotech

the interest of the health of patients is to immediately suspend the use and then review, as it has been done in Finland, Spain, Turkey, Bangladesh etc. If United States, Britain, Canada and over 140 countries can live without Nimesulide, so can India. Nimesulide has no India-specific use. (Petitioner's submission: 11)

Interestingly enough, the Drug Controller's submission conceded that in general, formulations, which were unapproved by India's central regulatory agencies and which had not been evaluated for their effectiveness, were being prescribed and sold in the country. The blame was, however, squarely laid on state regulatory officials, for the indiscriminate issuing of manufacturing licenses for drugs, which had not been approved by the central health ministry. In the interim period, firms like Dr Reddy's Labs and Nicholas Piramal, withdrew some of their Nimesulide related brands from the market. Dr Reddy's withdrew its fixed dose combinations of Nimesulide such as *Nise Spas*, *Nise Spas DS*, *Novigan N*, *Niap* and *Nise MR*, while Nicholas Piramal withdrew its Nimesulide tablets for adults.<sup>43</sup>

### **Arguments by Ranbaxy<sup>44</sup> the Pharmaceutical firm :**

The arguments in favour of the validity of the marketing approvals issued and the safety and efficacy of Nimesulide was made by Ranbaxy, one of the respondents in the case. The firm, in its response, contended that the PIL was not maintainable. Its response included extracts from articles published in several medical journals, which had conclusively documented that Nimesulide was an effective anti-pyretic and had demonstrated efficacy in "soft tissue pain, post operative pain and inflammation"<sup>45</sup> and was safer than paracetamol in one safety evaluation study

---

<sup>43</sup> Dr Reddy's Nise brand, the leader in the NSAIDS anti-inflammatory segment, is still available in the market.

<sup>44</sup> Documents pertaining to the submissions made by other firms were not available with Social Jurist and could not be obtained from the concerned firms or other sources. From the discussions with Mr Agarwal, Social Jurist, it was revealed that their submissions to the court were along the same lines as had been made by Ranbaxy with respect to the drug.

<sup>45</sup> Para 3, Counter-affidavit on behalf of respondent no 6, in the matter of CW 8335/02, filed through Khaitan & Khaitan, advocates for the said respondent. (The document, obtained from Social Jurist, does not have the date of filing of the affidavit)

related to intolerance to non-steroidal anti-inflammatory drugs. Incidentally, most of these articles were based on the studies conducted by the New Zealand firm, Adis International. The counter-affidavit also mentioned another journal article<sup>46</sup> in relation to the principle adverse events from Nimesulide, with particular reference to hepatic injury. The article mentioned that up to 1997, about twenty five such cases had been reported, where in fourteen of them, factors such as co-prescription with other NSAIDS, anti-cancer agents or pre-existent liver disease had contributed to the adverse reactions. A causal relationship with Nimesulide was established in seventeen of these cases. The article also mentioned that in nineteen of these cases, the affected patients were elderly women, with an average age of sixty one years. Nineteen of these patients recovered and there was one case of death, where the patient had been concomitantly prescribed with hormonal drugs.

The respondent further submitted the drug had a good safety profile and that in other clinical studies, adverse events associated with Nimesulide had been established as occurring in relation to disturbances associated with the gastric or nervous system and to a lesser extent with skin or the body as a whole.<sup>47</sup> The respondent also alluded to another post-marketing survey conducted on 22,938 patients with osteoarthritis in Italy, who had been administered with short-term (1-3 weeks) Nimesulide therapy, which had conclusively demonstrated the good “tolerability profile” of the drug. Mild forms of gastro-intestinal disturbances, skin reactions and dizziness, somnolence and headache were the most commonly reported adverse reactions in 1887 of these cases. The respondent further asserted that no serious gastro-intestinal complications had been observed in the study, which had involved a significantly large number of respondents.<sup>48</sup> The point sought to be made through the references to the above-mentioned and other studies was that adverse reactions with Nimesulide had mostly occurred only in cases of

---

<sup>46</sup> Rainsford, KD. 1999. ‘Relationship of Nimesulide safety to its pharmacokinetics: Assessment of adverse reactions.’ *Rheumatology*, 38 (suppl. 1):4:10.

<sup>47</sup> Para V, counter-affidavit submitted by respondent

<sup>48</sup> Para vi, *ibid*

the drug being prescribed with other kinds of medication and that the drug was a highly selective indicator of Cox-2 enzymatic reaction, with no adverse impact on the gastro-intestinal system. The respondent also quoted a media report on the IMA study,<sup>49</sup> which stated that:

Nimesulide has minimal side effects. The benefits of taking the drug outweigh its side effects...The data clearly showed that the side-effects of the drug were nothing more than common gastro-intestinal problems such as nausea and vomiting...The only note of caution is that people who are suffering from liver disorders should be prescribed the drug after a proper check-up. The drug is alright even for people who have had liver-related problems in the past, said Dr Sanjiv Malik, honorary General Secretary of the IMA...Most countries, like Israel, have now withdrawn the ban, said Dr Malik.

The argument was also that Nimesulide was safer than any other class of non-steroidal anti-inflammatory drugs being sold in the country and therefore there was no case for its ban while other NSAIDS were freely available in the market. The respondent also pleaded with the court to order the Indian Medical Association or the Drugs Controller to produce the report, which had declared the drug as safe. Ranbaxy also informed the court that it was manufacturing the brand '*Dolamide*' with a valid license dated 19-2-2001<sup>50</sup>, which had been issued by the Drugs Controller. With reference to *Dolamide*, Ranbaxy further stated that the formulation was a combination of the bulk drugs *Nimesulide* and *Paracetamol*, for treatment of painful inflammatory conditions. The product insert of the drug indicated its use,

...for the symptomatic relief of painful inflammatory conditions viz osteoarthritis, rheumatoid arthritis, ...and otitis. It is also an effective anti-pyretic.

The firm added that, in the same literature, certain precautions had also been

---

<sup>49</sup> Kumar & Parthanobis 2003. "IMA ends debate: Nimesulide is safe. Article in "*Hindustan Times*" dated January 13, 2003

<sup>50</sup> Vide letter No.AP/Ranbaxy/2001/rd issued by Drug Controller's office

prescribed, which specifically stated that caution should be exercised when *Dolamide* is administered to patients with renal and hepatic impairment and that it should not be given to patients with moderate to severe hepatic impairment. It was also emphasized that the product insert specifically mentioned that,

... the efficacy and safety of Nimesulide and Paracetamol are well established in children, however, in view of the dosages of the two ingredients in the formulation, *Dolamide* is not recommended for the use of children.

Further, Ranbaxy also pointed that the adverse effects of the drug including minor effects like nausea, vomiting etc. had been described in the product insert and that from all of the above, it was amply clear that the respondent had elaborately explained the effects of the drug and its dosages.<sup>51</sup> The respondent also informed the court that no adverse drug reaction had been reported with respect to *Dolamide*, which proved that the drug was safe and effective for treatment.

Similarly in its para-wise reply to the petition filed by *Social Jurist*, Ranbaxy denied any illegal complicity with the drug control authorities, since the brand was being produced and marketed with a valid license. The firm also denied giving incomplete or misleading information about the drug and referred to its product insert as evidence for the same. With reference to the adverse deaths reported abroad and in India, Ranbaxy stated that there was no conclusive proof of the same and interestingly enough, added,

The suspension of the drug in the countries mentioned, and the petitioner is put to strict proof of the same, appears to be a measure of abundant precaution rather than any conclusive finding against Nimesulide. If there had been any conclusive evidence, the drug would have been permanently prohibited rather than temporarily suspended. Furthermore, if as per the information of MIMS, on which the petitioner has relied, the drug has been referred to a scientific advisory body of the European Council, the Committee for Proprietary

---

<sup>51</sup> Para iii, iv, v. Respondent's counter-affidavit.

Medicinal Products (CPMP), the petitioner may be directed to provide the report of the said committee.

The implication here was that the withdrawal of the drug in countries abroad and the call for its banning in India was a ‘precautionary’ move, with no basis in the form of medical evidence<sup>52</sup>. Further, Ranbaxy stated that Nimesulide,

... like any other form of medicine, has certain side-effects, which may manifest themselves in certain persons....It may be pointed out herein that the petitioner contradicts himself when he states that the USFDA has never been approached by drug manufacturers for a license to manufacture Nimesulide, whereas in the previous paragraph, the petitioner had alleged that Nimesulide had been positively banned in the United States. ...it is respectfully submitted therefore that the allegations made by the petitioner are reckless perjuries and the only intention of the present petition is to prejudice this honourable court against the manufacturers of Nimesulide and its formulation.<sup>53</sup>

The above statements implied that due to genetic variability in the population, the occurrence of side effects in some individuals, administered with the drug, was common. Moreover, Ranbaxy, in turn, alleged that there were certain inconsistencies in the statements made in the petition, in the context of the drug’s regulatory status in the United States and that the intention of the petition was to prejudice the court against the manufacturers of the drug. In addition, the firm criticized the use of the words ‘misbranded’, ‘adulterated’ etc mentioned in the petition, claiming that since *Dolamide* was being manufactured and sold with a valid license and its product literature had not made any false claims pertaining to the indications for use of the brand or its efficacy, the interpretations implied by the petitioner in the above context were not applicable. The respondent further alleged that:

... It is worth noting, however, that the petitioner chooses to place

---

<sup>52</sup> Para-wise reply of the respondent to the petition, Para 4 & 5, Petitioner’s submission.

<sup>53</sup> *Ibid* Para 6, Petitioner’s submission

greater reliance on baseless and unsubstantiated media reports authored by lay persons instead of believing the report of the expert review committee consisting of eminent scientists and doctors, which have admittedly given a clean chit to the drug, Nimesulide. It is denied that there is no effective mechanism for the monitoring of adverse drug reactions (ADRs) in India. It is submitted that there are five recognized pharmacovigilance centers and these centers report the cases of ADRs directly to the World Health Organization. It is respectfully submitted that this court is being deliberately misled by the petitioner through concealment of material evidence.<sup>54</sup>

The point sought to be established by the firm was that any adverse reactions pertaining to the use of its brand could have been effectively reported by the existing five ADR monitoring centers and that the petition had chosen to ignore the expert opinions on the drug made by the review committee of the central regulatory body and instead had chosen to highlight media reports, which had not provided any substantial ‘scientific’ proof.

### **Arguments on the DTAB’s Assessment of the Drug :**

Having heard the arguments of all the parties to the litigation, the Delhi High Court subsequently ordered the Drugs Technical Advisory Board (DTAB) of the central regulatory body to examine the safety related aspects of the drug and its single dose and fixed dose combinations available in the market, both for use by adults and children<sup>55</sup>. The court also ordered the DTAB to submit its report within three months of the date of issue of the said order. The petitioner was also provided the liberty to submit the material/representation on the subject matter to the DTAB. The petitioner pleaded with the court to be provided with a copy of the Central regulatory body’s expert committee assessment of the safety related aspects of Nimesulide<sup>56</sup> and also to be informed about the date and details of the DTAB

---

<sup>54</sup> Ibid Para 20-21, Petitioner’s submission

<sup>55</sup> Order dated 20-02-2003, CWP No 8335/02.

<sup>56</sup> Report of the sub-committee meeting held on October 9, 2002 submitted by the Drugs Controller, India to the high court of Delhi.

meeting, in order to be able to participate in its deliberations<sup>57</sup>. The request was granted by the High Court.

As per the submission by the Drugs Controller to the Delhi High Court, the sub-committee meeting of the DTAB, held on October 9, 2002, had reportedly considered the available literature on the drug, the opinion of All India Institute for Medical Sciences (AIIMS), information available from the ADR monitoring centre at New Delhi and Lucknow etc. about any serious events reported at these centers. The submission mentioned that no report indicating causal relationship of any adverse event on the use of the drug had been received by the regulatory body.<sup>58</sup>

In addition, the submission mentioned that it had decided to obtain feed back on the use of the drug from leading orthopedic surgeons, gastroenterologists and rheumatologists. The Indian Academy of Pediatrics (IAP) and the Indian Medical Association (IMA) had also been approached to elicit information from their members in the use of the drug. Causal relationship with serious liver toxicity or Reye's Syndrome, as alleged in media reports on the use of the drug, were not reported by any of these experts. The ADR centre at Victoria Hospital, Bangalore, which had documented nearly 200 ADRs due to various drugs since 2001 had reported only seven cases pertaining to Nimesulide and these had been mostly skin-related reactions.<sup>59</sup>

Further, the Drug Controller's submission also informed the court that the feed-back from these experts had been examined in its subsequent meeting held on December 10, 2002. With respect to the reports appearing in the press, the submission stated that the consensus view of the committee was that, on the basis of available evidence, there was no indication of any causal relationship with the

---

<sup>57</sup> *Ibid*, request submitted to the high court of Delhi dated 12-03-03.

<sup>58</sup> As mentioned in the judgment delivered by the high court of Delhi at New Delhi on October 3, 2004, WP © 8335/02 on 'Safety of Nimesulide Drug'.

<sup>59</sup> *Ibid*.

drug in the reports of the above-mentioned adverse reactions. The submission also referred to the Delhi Society for the Promotion of Rational Use of Drugs (DSPRUD), which had in its publication entitled '*Standard Treatment Guidelines 2002*', recommended the use of Nimesulide along with other drugs like ibuprofen and paracetamol for controlling fever in adults as well as children.<sup>60</sup>

The Drug Controller also informed the court that, in relation to the use of the drug in children, the Indian Association of Pediatrics, in addition to their opinions, had also elicited the opinion of leading pediatricians in an Indo-UK Symposium, held from February 1-3, 2003 at New Delhi. In this regard, the Drug Controller stated that though most of the experts had opined that on the basis of their experience with the drug, there was no justification to ban the use of the drug in children, they had nevertheless advocated caution in regard to its use in any hepatotoxic condition and its co-administration with other drugs for hepatotoxicity. In addition, the Drug Controller informed that some experts had suggested dilution in the dose of suspension drops for children. However, Dr S.K. Gupta, Head of the Department, Pharmacology, at AIIMS had advised against it, stating that any arbitrary change in the strength of the dosage would necessitate a further clinical study, the drug controller's submission added.<sup>61</sup> With reference to the rationality of the fixed dose combinations of the drug, namely its combination with paracetamol (marketed by Ranbaxy) and other muscle relaxants, the submission added that these combinations had been in use for a long period of time and had been well accepted, with no reports of adverse reactions and therefore their use for short-term relief from pain and inflammation could be continued.

In this context, it is also worth going into the expert opinions expressed by different members of the sub-committee. The IMA honorary Secretary General,

---

<sup>60</sup> The arguments made by the petitioner about the acceptability of the drug based on its recommendation in the Standard Treatment Guidelines has already been dealt with earlier in the chapter.

<sup>61</sup> As mentioned in the judgment delivered by the high court of Delhi at New Delhi on October 3, 2004, WP © 8335/02 on '*Safety of Nimesulide Drug*'.

Sanjiv Malik stated that:

The material furnished by the petitioners appears one-sided and the facts have, in many instances, been projected in a distorted manner rather than on a very scientific footing. The regulatory authorities of UK or USA never received the application for marketing the drug, so there is no question of the drug being prohibited or not approved in these countries. There are similar drugs like Analgin, which have been used in many countries including India, but never used in the United States, United Kingdom etc. Due to various reasons and commercial viability etc, drugs marketed in one country may not be marketed in other countries. The use of Nimesulide was suspended only in 3 countries, though it is in use in about 50 countries. Israel has again permitted its use, after evaluating its overall safety data. No country has in the strict sense of the term banned the drug. The survey conducted by the Indian Medical Association was an extensive one and revealed that the drug is very useful and well accepted in the medical community. Even the Indian Academy of Pediatrics has also endorsed the continued use of the drug in children. There is no overall evidence to suggest that its use should be prohibited..To paint all these expert and professional bodies as having vested interest or lacking sound knowledge just because they have not taken the stand taken by the petitioner is rather unfortunate.

The remarks made by the IMA honorary Secretary General implied that the petitioner's accusations were 'unscientific' and 'prejudiced' against the experts of the sub-committee merely on the grounds that they had a different opinion about the drug and that the assessment made by the sub-committee had greater validity since it was grounded in scientific evidence and had been made by individuals with proven professional expertise in the field. The expert's facts about the regulatory status of the drug in US and UK were also different from those mentioned by the petitioner. The use of the drug in India in contrast to its absence in drug markets of United States and United Kingdom was attributed to commercial rather than scientific reasons and was justified on the grounds of lack of adequate evidence with

respect to adverse reactions.

Other experts advocated its use in adults as well as in children on grounds that an extensive benefit-risk assessment had been undertaken on scientific norms. The reference was obviously to the IMA study. However, the two pharmacologists in the committee advocated the use of the drug in infants as drops only after further review and examination by the Drugs Controller. The DTAB members, in reference to the above assessments made by the sub-committee, added that the drug could be incorporated in Schedule H since it had not been given a schedule.<sup>62</sup> The DTAB also recommended that state licensing authorities order firms marketing Nimesulide suspension drops to discontinue selling of these formulations with immediate effect, until further studies were carried out. The body also took serious note of the bypassing of Drug Controller, India's approval in the case of granting of licenses by the state regulatory authorities for 'new drugs' and warned the state authorities to desist from doing so in future.

### **Petitioner's Counter-arguments :**

The petitioner's submission to the high court of Delhi alleged that there had been ethical and legal shortcomings in the composition and functioning of the sub-committee of the DTAB. It was argued that the membership of the expert committee was not in conformity with the requirements of Section 45 & 46 of the Indian Evidence Act. The petitioner's submission stated that:

...Even otherwise, many members are not 'experts' in the field of monitoring ADRs, (such as Dr Sanjiv Malik, Honorary Secretary General of the Indian Medical Association. One member (Dr B.N.A. Narayanan) from a drug manufacturing company is not totally free from bias because of obvious reasons. Three official members have themselves approved either Nimesulide or Nimesulide FDCs and hence are not free from bias. They

---

<sup>62</sup> This was another of the points raised by the petitioner in their preliminary submission to the court. The petitioner had observed that to merely state that the drug was to be sold on prescriptions of registered medical practitioners without giving it a schedule did not give it a legal basis as chemists selling it without prescription could not be prosecuted since the drug had not been formally categorized as falling under Schedule H. (Schedule H consists of prescription only drugs under the Drugs and Cosmetics Act, 1940).

cannot be involved in deciding the fate of a drug, which they themselves have approved, not to mention the fact that the two State Drug Controllers, who are members of the Committee, have been involved in approving irrational Nimesulide FDCs without the authority of law, and ‘indiscriminately’ as claimed by the DCI himself in his affidavit to the Delhi High Court. The Committee has 10 members, out of which 4 members are from national bodies (ICMR, IMA, DCI, IPA), 5 from institutions in Delhi and only one from outside Delhi, that too a person (FDA commissioner from Gujarat), who is not free from bias. A national level expert committee should not have 5 members from Delhi and none from other states while deciding the fate of a controversial drug that affects the entire country. The nominee of the Indian Medical Association, both in his official capacity as well as individual capacity, has a conflict of interest with the subject matter. He should not have been permitted to be on the committee. IMA gets funds for its activities from the drug industry while its nominee publishes promotional publications on drugs including “sponsored articles” from the drug industry. As per the minutes of the meeting, there is no mention of any discussion on the conflict of interest aspect dual commitments, competing interests or competing loyalties.

The submission alleged bias in the composition of members in the committee, competing loyalties and conflict of interests among the members and inadequate representation of experts outside Delhi, especially from the states. Further, the petitioner also alleged that the assessment was based on the information provided by the Drugs Controller and only included data favourable to the drug.

The meeting held on 10-12-2002 that took decision on Nimesulide was attended by five members, out of whom two were government nominees (not free from bias since they had approved Nimesulide and Nimesulide FDCs, one was an employee of a drug company, though representing IPA<sup>63</sup> and two pharmacologists. Thus in effect the committee consisted of just two independent experts, i.e. two pharmacologists. Since other members did not attend the meeting, for all practical purposes, the report was endorsed by two experts only. The members of the Committee did not have any material on record from outside independent sources and were dependant on

---

<sup>63</sup> Indian Pharmaceutical Alliance, one of the representative bodies of the pharmaceutical industry in India.

information provided by the Drugs Controller, India. As per the minutes of the meeting, they were provided exclusively with 'favourable-to-Nimesulide' information. Unfavourable information was not provided.

### **The Delhi High Court's Judgment:**

The Delhi High Court in its judgment preferred to deal with the legal aspects of the case as compared to the technical aspects. In reference to the technical aspects, the court declared that it was not a competent authority to deliberate on matters related to medical expertise such as safety of drugs.

It is not for this court to sit as an expert body and to render an opinion on such specialized fields such as safety of drugs. In view of the report submitted by DTAB, the use of the drug in question in the form of drops be reviewed and permitted only after its examination and approval by the office of the Drugs Controller, India. Suffice it to say that, in view of what the expert body (DTAB), after examining the matter, has stated in the report, we find that the allegations are not worth hearing further.

In addition, the court expressed its satisfaction with the review and assessment conducted by the DTAB on safety issues related to the drug. It concurred with the recommendation of the DTAB with respect to review of Nimesulide in the form of suspension drops. The court declared that the licenses produced by the manufacturers seemed valid and this was again a matter to be referred to the Central regulatory body. The court disposed off the petition in favour of the respondents and in addition, endorsed the technical decisions made by the regulatory authorities.

The above controversy provides us with an interesting glimpse into the processes and mechanisms shaping the qualification of drugs outside the realm of the firm. It provides us with an understanding of how, outside the realm of the firm, the drug mediates with other agencies, which then seek to control its

therapeutic career. The ‘Nimesulide’ controversy reveals how the terrain of drug regulation is a contested terrain, involving a ‘hybrid group’<sup>64</sup> consisting of a heterogeneous groups of actors like firms, regulatory bodies, health activists, scientists, physicians, consumers etc, involved in claims and counter-claims about the risks and benefits of drugs and in shaping knowledge claims related to their ‘attributes.’ Thus the civil society elements have proved to be playing an active role in this process.

The episode typically demonstrated all the facets of a scientific controversy. Different actors including the petitioner on one hand and the regulatory body and the medico-scientific community, on the other hand, presented different versions of the drug’s regulatory status in countries like US and UK and its legal status in India, in addition to invoking different sets of ‘medical’ facts and ‘scientific’ evidence pertaining to the drug’s efficacy and safety profile. The submissions by these actors to the court are also reflective of the struggles over credibility by these actors. Each group resorted to endorsements by opinion makers. The petition had the support and endorsement of prominent health activists of the All India Drug Action Network. The respondents sought the endorsements of prominent physicians in the Indian Association of Pediatrics, the Indian Medical Association and other medico-scientific professionals. The submissions by the petitioner alleged collusion between the firms, the regulatory body and the medical practitioners in the promotion of the drug. The petition also alleged that commercial rather than therapeutic interests had dictated the continued presence of the drug in the market despite adverse reactions. The respondents on the other hand, invoked norms of professional expertise and scientific evidence to assert the safety of the drug for use in adults and children. Each group alleged bias, the petitioner alleged conflict of financial and professional interests, and the respondents alleged prejudice and ‘over dramatic

---

<sup>64</sup> See Callon 2006.

representations’ by the media and health activists without corroborating evidence.

The attributes of Nimesulide and the resulting controversy were represented in different ways by different groups of actors during the course of the litigation. For the petitioner, Nimesulide was clearly an ‘unsafe’ drug, reinvented as therapeutically beneficial by the demands of the market and the ‘machinations’ of the firms and their collusion with regulatory bodies and physicians. The print media and activists largely represented the Nimesulide episode in the broader context of an over liberal and inefficient regulatory regime, which had allowed the Indian market to be flooded with scores of therapeutically irrational and potentially hazardous formulations. The experts involved in the assessment of the drug believed that the drug was largely ‘safe’ and ‘efficacious’ in the absence of evidence to the contrary and also saw the episode as the ‘over-dramatic’ and ‘unscientific’ representation of stray adverse drug reactions by media and health activists. The firms involved in the litigation also represented the drug as safe and therapeutically beneficial and represented the controversy as needless slander by the media and the petitioner of their legitimate economic pursuits. The central regulatory body, though it admitted to some lapses on the part of state regulators in the issuing of licenses, generally represented the controversy as a needless challenge to its ‘expertise’ and ‘scientific’ judgment.

Finally, the Nimesulide controversy hints at the ‘invisible’ hand of firms in the shaping of knowledge claims related to drugs. It tells us, how firms, in collusion with regulatory bodies and medical practitioners, may have relative power to ‘qualify’ drugs as ‘safe’ and ‘effacious’ and shape its therapeutic attributes in comparison with other actors.

## References :

- Abraham, John. 1994, Distributing the Benefit of the Doubt: Scientists, Regulators, and Drug Safety. *Science, Technology & Human Values*, 19(4), pp.493-522.
- . 1994, Bias in Science and Medical Knowledge: The Open Controversy, *Sociology* 28 (3), pp.717-36.
- . 1997, The Science and Politics of Medicines Regulation, Pp. 153–82 in M.A. Elston (ed.) *Sociology of Health & Illness Special Monograph Issue on the Sociology of Medical Science and Technology*. Oxford: Blackwell.
- . 2002a, Regulatory Science as Culture: Contested Two-Dimensional Values at the USFDA, *Science as Culture*, 11(3), pp.309-35.
- . 2002b, Drug Safety and the Safety of Patients: The Challenge to Medicine and Health from Permissive Expert Risk Assessments of Triazolam (Halcion), *Health, Risk & Society* 4 (1), pp.19-29.
- . 2002c, A Social Science Framework for the Analysis of Health Technology Regulation: the Risks and Benefits of Innovative Pharmaceuticals in a Comparative Context, *Health, Risk & Society* 4 (3), pp.305-324.
- . 2003, The Science & Politics of Medicines Control, *Drug Safety*, 26, pp.135-43.
- . 2007, Building on Sociological Understandings of the Pharmaceutical Industry or Re-Inventing the Wheel? Response to Busfield's "Pills, Power, People, *Sociology*, 41(4), pp.727–36.
- . 2008, Sociology of Pharmaceuticals Development and Regulation: a Realist Empirical Research Programme, *Sociology of Health & Illness*, 30 (6), pp. 869-85.
- Avorn, Jerry. 2007, The Marketplace Can't Give Us the Drug Safety Data We Need, *Medscape General Medicine*, 9 (1), pp. 29.
- Bryman, Alan and Robert G. Burgess. 1994, *Analyzing Qualitative Data*, London: Routledge.
- Busfield, Joan. 2006, Pills, Power, People: Sociological Understandings of the Pharmaceutical Industry, *Sociology*, 40 (2), pp.297–314.

- IDMA Bulletin, 2004, The Truth About Drug Companies in U.S.A. *IDMA Bulletin*, 35 (34), pp.10-11.
- Jones, Kathryn. 2008, In Whose Interest? Relationships between Health Consumer Groups and the Pharmaceutical Industry in the UK, *Sociology of Health & Illness*, 30 (6), pp. 929-43.
- Srinivasan, R. 2001, *Regulating Medicine and Ethics*, From the Detail Report of The Independent Commission on Health in India. New Delhi: Voluntary Health Association of India.