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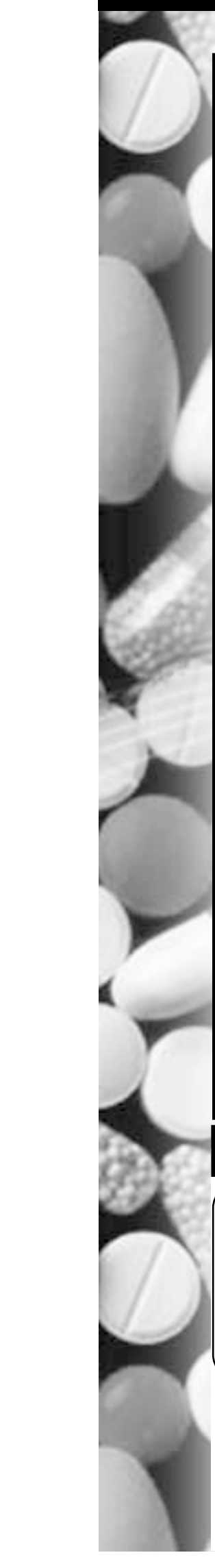

Editors Desk

Healthcare consumer activism is a rare commodity in India.There are several issues but very less action. Iam hugely surprised that many organizations have come together regarding the vexatious fixed dose combination drugs.

To ensure that healthcare community is aware of the recent developments we are publishing salient points from the case filed at Chennai high court.

Currently the issue is with Drug technical advisory board for indepth study and the judiciary. Although the commitee met and found several FDC highly illogical, the time taken to arrive for a final conclusion is too high.

The world health organization has made several observations, remarks and statements regarding FDC.Our governement , industry,medical profession and judiciary should take cognizance and follow WHO.

It is regretble in India every reform intiated by executive gets challenged in the courts and we remain in the dark ages.For example the constitution ad functioning of CDA on the lines of FDA is going nowhere.

I get mails from several international dignitaries why Pharmacy is not recognised as health profession.It seems our honourble health minister has time only for anti-tobacco campaign.There is urgent need to focus energies how to engage the services of community pharmacists in improving national health indicators.

Bill & melinda gates foundation awarded MSH a 3.8 usd million grant for building capacity in retail drug sellers in Tanzania.This is a welcome move.Investing in the most ignored but important grass root healthcare workers.

We at Pharmed Trade News invite all individuals and organizations to partner with us in building capacity in retail drug sellers.

(V. Bhava Narayana)

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LEPTOSPIROSIS

As urban sprawl spreads throughout the globe, so do poor urban ghettos and the infectious diseases that are perpetrated by unsanitary slum conditions. Weill Cornell researchers stationed in the urban slums of Salvador, Brazil, have discovered that certain unhealthy living conditions lead to transmission of leptospirosis, a life-threatening disease caused by the bacterium Leptospira. Over a half-million people are infected, killing 1 in 10, each year. The disease, which is characterized by fever, abdominal pain, and can lead to severe pulmonary bleeding, kidney damage and meningitis, is transmitted through animal contact (commonly rat urine). Dr. Albert Ko, senior author of the study and physician-scientist from the Division of International Medicine and Infectious Disease at Weill Cornell Medical College, and his research team stationed at Oswaldo Cruz Foundation/Brazilian Ministry of Health in the city of Salvador, tested a group of 3,171 slum residents for Leptospira antibodies - a marker of past infection with the bacterium.

The researchers identified several variables that raised the risk of infection within those who tested positive for past infection, including persons living at the bottom of valleys (raising flood risk), those around open sewers or near accumulated refuse, and those who saw rats or lived in the presence of chickens. The scientists also determined that socio-economic factors contributed to risk: an increase of only $1 (USD) per day in per capita household income was associated with a substantial 11 percent decrease in infection risk. The researchers believe that improving sanitation can greatly curb the rate of infection. The study is published in a recent issue of PLoS Neglected Tropical Diseases.

HAEMOGLOBIN MEASUREMENT

Masimo, the inventor of Pulse CO-Oximetry(TM) and Measure-Through Motion-and-Low-Perfusion pulse oximetry, announced it has received FDA clearance for its breakthrough noninvasive and continuous total hemoglobin monitoring technology (SpHb(TM)). The availability of Masimo SpHb technology should make hemoglobin measurement more convenient and broadly available to clinicians in both hospital and outpatient settings — helping them make earlier and better clinical decisions, improve patient safety and decrease costs. Noninvasive total hemoglobin will be offered as part of the upgradable Masimo Rainbow SET technology platform.

Ronald Miller, MD, Professor and Chair of the Department of Anesthesia and Perioperative Care at the University of California at San Francisco (UCSF) stated, “Management of appropriate blood levels is vitally important to sustain life. Without up-to-date hemoglobin levels, patient bleeding in the operating room, recovery room, intensive care or trauma departments — where blood loss is common — can often go undetected until it poses critical short and long-term dangers to health and recovery. The ability to immediately and continuously measure hemoglobin levels will facilitate the timely administration of appropriate blood products. Conversely, during surgery, because blood is a precious and costly resource, continuously measuring hemoglobin levels noninvasively can help clinicians avoid unnecessary blood transfusions and decrease costs by more effectively titrating blood and blood replacement products.”

Joe E. Kiani, Chairman and CEO of Masimo, said, “Developing breakthrough technologies that enhance patient safety and automate patient care is a responsibility that we take seriously. With noninvasive hemoglobin as part of the upgradable Masimo Rainbow SET platform, we are proud to be revolutionizing the way clinicians can assess anemic status and make more timely decisions that affect millions of patients worldwide.”

The need for better hemoglobin monitoring to manage blood levels is reinforced by recently published controlled studies that show the safety of blood transfusions can be improved by the use of transfusion thresholds. In a 2008 study by the Cochrane Collaboration titled Transfusion Thresholds and Other Strategies for Guiding Allogeneic Red Blood Cell Transfusion, reviewers examined evidence from ten trials — reporting outcomes on a total of 1,780 patients — and found that “restrictive transfusion strategies reduced red blood cell transfusions by 42%.”

Additionally, while noting that not all of these results were statistically significant and that additional studies are required to confirm the findings, the Cochrane reviewers also reported that, “on average, mortality was 20% lower with the restrictive compared with the liberal transfusion triggers.” Similarly, five of the ten studies examined showed a reduction in hospital length of stay, while three showed a reduction in ICU length of stay. (1) Continuous, noninvasive hemoglobin monitoring with Masimo Rainbow SET SpHb may enable more restrictive transfusion triggers and help maintain optimal hemoglobin levels for critically-ill patients. In addition to facilitating better blood level management, Masimo Rainbow SET’s noninvasive hemoglobin monitoring capability should also help clinicians better manage chronic anemia, a blood disorder affecting two billion people worldwide that is one of today’s most prevalent public health problems. Masimo Rainbow SET SpHb should provide hospitals, emergency medical professionals, dialysis centers, family physicians, cardiologists, pediatricians and other care providers with a more convenient and accessible way to manage this pervasive condition.

More than 350 million invasive hemoglobin lab tests are performed each year in the U.S. alone, making it one of the most common laboratory tests. Hemoglobin lab tests are costly, time-consuming and require that clinicians use a needle to draw a patient’s blood — however, they only provide delayed and intermittent data. Masimo’s SpHb technology requires no invasive procedures and provides continuous, real-time, pain-free results. This should allow clinicians to perform fewer lab tests, better manage blood transfusions and hemodialysis procedures, speed detection of internal bleeding, and more efficiently assess chronic anemia — all of which should help improve patient outcomes and reduce the cost-of-care.

”No other technology can provide continuous, noninvasive hemoglobin measurements,” stated Michael O’Reilly, MD, Executive Vice President of Medical Affairs at Masimo. “Masimo Rainbow SET SpHb has the potential to revolutionize the management of both acute and chronic anemia, as well as the therapeutic interventions used to treat these conditions. We believe SpHb will provide a significant advancement in patient safety for clinicians worldwide.”

The Masimo Rainbow SET platform allows clinicians to noninvasively and continuously measure oxygen content (SpOC(TM)), carboxyhemoglobin (SpCO(R)), methemoglobin (SpMet(R)), PVI(TM) and total hemoglobin (SpHb(TM)), in addition to oxyhemoglobin (SpO2), perfusion index (PI), and pulse rate (PR). Masimo anticipates commercial availability for both SpHb and SpOC in Q3 2008 to select customers.

RALOXIFENE

The osteoporosis drug raloxifene increases bone mineral density and reduces the risk of vertebral fractures among postmenopausal women with mild to moderate chronic kidney disease (CKD), according to a study appearing in the July 2008 issue of the Journal of the American Society Nephrology. The findings indicate that raloxifene is safe and effective for women with CKD, a patient population often excluded from studies of osteoporosis drugs.

Because CKD may lead to metabolic abnormalities that accelerate bone loss, it is important to monitor bone mineral density levels in these patients

and to administer treatments when levels are low. However, the use of osteoporosis therapies for patients with this disease is highly controversial, given the drugs' previously unknown effectiveness and safety in these individuals.

To determine whether raloxifene is a suitable treatment option for women with CKD, Dr. Areef Ishani, of the Minneapolis VA Medical Center and University of Minnesota, in Minneapolis, MN, and his colleagues analyzed data from the Multiple Outcomes of Raloxifene Evaluation (MORE), a multi-center, randomized, placebo-controlled trial of 7,705 postmenopausal women with osteoporosis. They examined the effect of raloxifene over three years on the rate of change of bone mineral density, incidence of fractures, and adverse effects in women with and without CKD.

The investigators found that irrespective of kidney function, patients taking raloxifene experienced a greater increase in spine bone mineral density and a reduction in vertebral fractures compared with patients taking a placebo. Raloxifene also increased hip bone mineral density, most prominently in women with mild to moderate CKD.

The study's results have significant clinical relevance because many postmenopausal women have unidentified CKD. The findings are reassuring in that raloxifene can safely be used in women who have decreased kidney function.

The study, entitled, "The Effect of Raloxifene Treatment in Postmenopausal Women with CKD," is available online at http://jasn.asnjournals.org/ and coincides with Osteoporosis Awareness Month in May and National Women's Health Week from May 11-17.

PHARMACISTS ROLE IN STROKE MANAGEMENT

The English Pharmacy Board of the Royal Pharmaceutical Society of Great Britain welcomes the government's emphasis on stroke treatment, as outlined in the recent announcement by the Department of Health to boost funding for stroke services.

The number of patients receiving anticoagulation therapy has increased over the last years.

Warfarin, which is used to prevent and treat the formation of harmful blood clots within the body by thinning the blood and/or dissolving clots, plays an important part in part in stroke treatment. Pharmacist management of anticoagulation is routinely offered in many hospital departments and increasingly being carried out by community pharmacists.

Paul Bennett, Chair of the English Pharmacy Board, said: "The government announcement to increase funding for stroke services will improve the support available for stroke survivors and their carers. Specialist pharmacist involvement and pharmacy-run anticoagulant clinics can effectively resolve many of the complex issues in anticoagulant therapy."

AIDCOC

The 11th annual convention of All India Drugs Control Officers Confederation (AIDCOC), which discussed the latest developments in regulatory, industry and research scenario of Indian pharmaceutical and healthcare sector, concluded in Mumbai.

In the two day convention, held on April 26 and 27, the regulatory officials paid heed to the suggestions of the industry experts, who elaborated the current trends and needs in various segments like Patent issues, stem cell research, packaging, quality management, clinical research and the regulatory harmonisation programmes.

Speaking as the chief guest in the inaugural session, Amitabh Chandra, principal secretary, Medical Education and Drugs department, Govt. of Maharashtra, asserted that the convention would help the drugs control officials to understand the overall situation in the nation and to know the needs of the industry better. He added that the confederation would be able to check counterfeit medicines, once the unity between the states is affirmed through the convention.

Dr B Suresh, president, Pharmacy Council of India (PCI), who was the guest of honour in the convention added that similar efforts from the confederation would motivate the drug regulatory officials to perform better in their jurisdiction with update information on various fields related to the job.

New therapies and innovations in pharmaceuticals like new molecules and its delivery besides disease management will bridge treatment gaps. The PCI will encourage pharmacists to equip themselves with the latest developments through continuing education programmes, added Suresh, who is also currently the president of Indian Pharmaceutical Association (IPA).

While delivering his views on the current regulatory hurdles in punishing the culprits in drug related issues, Sandeep Bishnoi, joint commissioner (Vigilance), Food & Drug Administration (FDA), Maharashtra state, said that the Drugs and Cosmetics Act should have clear norms on the details of filing First Investigation Reports (FIR) against violation of the act. He added that the rules on action against substandard drugs should be made stringent to check prevalence of low quality products in the market.

Maharashtra FDA commissioner, Dhanraj Khamatkar also appreciated the confederation for coming up with the relevant theme - Better healthcare through innovations in pharmaceuticals - which is in lines with the development in the pharma field.

Dr B Suresh gave away the Best Drugs Inspectors' Award 2008 to drug inspectors from major states. The award for 2008 were bestowed on M Amrutha Rao, Andhra Pradesh, Dr Sachidanand Prasad, Bihar, B Lal, Government of NCT, Delhi, Rupam Patel, Gujarat, Anjani Kumar, Jharkhand, Ajayaraj D Shah, Karnataka, K T More, Maharashtra, Manoj Tongra, Rajasthan, Paul Mazumdar, Tripura and Dr Sambhu Nath Dey, West Bengal.

BPOS HIRING DOCTORS & NURSES

In a bid to supplement shrinking incomes from sectors like finance and banking, more and more outsourcing firms in India are looking at new areas of business. They are hiring medical professionals - doctors and nurses - to deal with medical insurance settlements of their foreign clients. For instance, Noida-based BPO Xansa has a team of doctors that looks into the insurance and legal aspect of settling medical claims. The doctors assess prognosis, underwrite and evaluate the mortality rate of customers and the risk involved. Similarly, four other outsourcing firms – Wipro BPO, TCS, Cognizant and HCL –are hiring doctors, nurses and paramedics. The average salary for these professionals could start from Rs 45,000 and go up to Rs 3 lakh per month, according to industry sources.

MAHARASTRA FDA DRIVE

Maharashtra Food and Drug Administration (FDA) has launched a campaign to assess the quality standards of cosmetics products manufactured and marketed in the state by collecting and testing the samples from the cosmetic manufacturers across the state.

The two-month campaign will be completed by the end of May and the test results are expected to reach the regulator's office by June 10, 2008 according to FDA sources. Starting from the beginning of April, the FDA officials have collected almost 125 samples from the cosmetics manufacturers from various parts of the state till the middle of May. The administration is expected to pick up another 80 samples by the end of this month.

Health Canada

The Health Canada, the federal health department of Canada, has once again advised the consumers not to use any Ayurvedic medicine without its approval, as some of the products may contain high levels of heavy metals. The reminder comes in the wake of recent reporting of high level metal content in an Ayurvedic products in British Columbia.

The authority refers to a report published in the British Columbia Medical Journal, in March 2008, about a domestic case of adverse reaction on an adult male from consumption of Pushpadhanva Rasa, manufactured by the Shri Dhanwantari Ayurvedic Pharmacy in India. The patient had been taking one tablet of this product to 'increase vigour' for over a number of years and the product was found to contain extremely high levels of lead, mercury and arsenic, according to the Health Canada report.

ZYDUS CADILA

has received four product approvals from US FDA. The group has received approvals to market Pravastatin' sodium tablets USP 10, 20, 40 and 80 mg and tentative approvals for Escitalopram Oxalate' tablets 5,10 and 20 mg, Losartan Potassium and Hydroeblorthiazide tablets 50 mgII2.5 mg and 100 mgtI5 mg and Anastrazole tablets 1mg.

DABUR PHARMA LTD

one of the country's anti-cancer drug makers, has sold off a total 73.3 per cent stake in the company to the Singapore unit of Germany's Fresenius Kabi AG for Rs 8,782 million (¸ 139 million) or at 76.5 rupees apiece. The move allows the Burmans of Dabur Pharma (who held 65.3 per cent of the equity in March 2008) to exit the pharmaceutical business and concentrate more on the bread-and-butter FMCG business under Dabur India and its new retail venture.

The new acquirer Fresenius Kabi also announced a public offer to acquire up to a further 20 per cent shareholding for a price of Rs 76.50 per share in cash. Fresenius Kabi has entered into an agreement with a third party to secure the participation of 2.4 per cent of Dabur Pharma's share capital in the public offer.

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IN THE HIGH COURT OF JUDICATURE AT MADRAS
[SPECIAL ORIGINAL JURISDICTION]
M.P. No. _____ OF 2008
IN W. P. NO 35844 OF 2007

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AFFIDAVIT OF R. DESIKAN

I, R. Desikan, S/o. Raghavachariar, Hindu, aged about 75 years, residing at No.2/228, Chinnandikuppam Road, Vettivankeni, Chennai 600 041, do hereby Solemnly affirmed and sincerely state as follows:

1. I am the 5th Petitioner in the above mentioned Petition to implead and I am well acquainted with the facts and circumstances of the case.

2. I am filing the present affidavit on my behalf and on behalf of the other 4 Petitioners.

3. The present Petition to implead is filed by All-India Drug Action Network (AIDAN) Medico Friend Circle Low Cost Standard Therapeutics Drug Action Forum-Karnataka CONCERT, (Centre for Consumer Education, Research, Teaching, Training and Testing) partly in support of the letter dated 14.08.2007 issued by the 2nd Respondent and in public interest. The said letter has been issued in the interest of public and we the Petitioners herein are concerned about the irrational and improper licensing procedures of several fixed dose combination (FDC) Drugs that are prevailing in the market.

4. The Petitioner No.1, the All India Drug Action Network (AIDAN) is an internationally well-regarded and reputed all-India network of socially concerned consumer and health action groups, medical and health professionals and academics from medical colleges. AIDAN has been active since 1982 in advocating a rational drug policy based on essential generic drugs, weeding out of harmful, irrational, wasteful and useless drugs in the market. It has brought out several publications and critiques of drug policy pronouncements of India, promoted awareness among the public and media. All the five Petitioners are part of the AIDAN as well as Medico Friend Circle and another all-India network called Jan Swasthya Abhiyan, a national and international movement advocating access to health care as a human right.

5. Dr Mira Shiva, M.D (Internal Medicine), currently co-convener of All-India Drug Action Network (AIDAN), and Director for Initiatives in Health and Equity, and formerly Director of Women, Health and Development and Rational Drug Policy (formerly Public Policy Division) of the Voluntary Health Association of India (VHAI), has been active over 30 years in the advocacy of a pro-people drug and health policy. She is the first recipient of the Dr. Olle Hansson Award for showing moral courage and her contribution to rational use nationally and globally. She was part of the Government of India Committees on Price Control Review and Pharmaceutical Research and Development as well as the National Working Group on Patent Laws, Health Action International, Action for Rational Drugs Asia (ARDA), and Women and Health (WAH!) network. She was the National Focal Point for the National Profile on Women, Health and Development – a WHO initiative with VHAI, later published as a report she helped co edit. She has edited Rational Selection of Drugs (1986), Rational Drug Policy (1986), Investigation of IV Fluid Contamination – a report, Banned and Bannable Drugs (1996), She is one of the founder members of People's Health Movement. Dr Mira Shiva is also the Chairperson HAI- AP, Chairperson Task Force on Consumer Education; Task Force on Safety of Food & Medicine (MOHFW); Member Expert Committee on Safety of Medicines & Medical Devices (National Human Rights Commission), Coordinator Initiative for Health, Equity & Society; co-editor Towards Comprehensive Women's Health Policy & Programme published by SAHAJ Baroda/WAH! Pune, 2002.

6. Petitioner No.2, Medico Friends Circle (MFC), registered as a public trust at Pune. MFC is an all-India network active since 1975 of socially concerned health action individuals, medical and health professionals and health researchers and academics from all over India. MFC members have been active in the Drugs issue, campaign against hazardous contraceptives, the Bhopal Gas Tragedy and follow-up in terms of epidemiological research, reaching relief to the affected and legal follow-up, some of which in the Hon'ble Supreme Court.

7. Dr Anant Phadke, MBBS, is a well-regarded senior member of the Medico Friend Circle, and currently Co-ordinator of SATHI-CEHAT, the action center of Anusandhan Trust, evolved from CEHAT. SATHI-CEHAT has been a leading element in the Jan Swasthya Abhiyan, largest the nationwide network of health activists in India. Dr Phadke has been an active player in the the Health and Science Movement in India for the last 30 years and more. He is well-known for his contributions through. Medico-Friend Circle, All India Drug Action Network (AIDAN), Lok Vignyan Sanghatana, LOCOST, etc. He has been involved in training of Village Health Workers and Primary Health Care issues since 1978. Dr Phadke has co-authored training manuals for Community Health Workers and has contributed about 75 and 150 articles respectively in English and Marathi, to various health magazines and lay-press on different topics related to the People's Science and Health movement, especially on the Drug Policy in India. Dr Phadke has also authored/co-authored books and papers on pharmaceutical and health policy issues including the classic study on drug availability in Satara District,

"Drug Supply and Use: Towards a Rational Policy in India", Sage, New Delhi, 1998.

8. Petitioner No.3, Low Cost Standard Therapeutics (LOCOST), is a nationally reputed public trust and NGO based at Baroda, Gujarat. LOCOST has since 1983 been consistently and ethically promoting the idea of rational essential drugs by actually manufacturing and supplying them to those working with the poor all over India on a not for profit basis. LOCOST has been active in drug policy and pricing issues and has been an important and authentic source of the actual costs of making good quality essential drugs stressing on demystifying technology for the cause of the poor. LOCOST's publications in English and Gujarati include A Lay Person's Guide to Medicine (2006).

9. S. Srinivasan, Managing Trustee of LOCOST has been active in the field of health care, low cost drugs, transfer of pharmaceutical technology to LDCs, issues of disadvantaged children and human rights, and relief in disaster situations. . He is an active member of the PUCL, Baroda, SAHAJ (Society for Health Alternatives), Medico Friends Circle and AIDAN. Srinivasan has also been active in health care management issues and was the coordinator of Health Care Administration Education at VHAI, New Delhi as well as has been the editor of the periodical "Health for the Millions" (VHAI). He has authored, coauthored/or and edited Management Process in Health Care (1982), The Banyan Tree –A Guide to Holistic Health Practitioners, Vol 1-3 (1989-91), A Guide to Stress Management (1999) and A Lay Person's Guide to Medicine (2000) as well as several articles on drug policy, pricing and related issues in the Economic and Political Weekly. Srinivasan is a graduate and postgraduate of IIT Kharagpur and IIM Bangalore.

10.Petitioner No.4, Drug Action Forum – Karnataka is a registered, independent NGO campaigning for rational drugs and rational policy. Its members are drawn from diverse back ground including doctors, lawyers, trade union workers etc. the main objective of Drug Action Forum – Karnataka is to empower the consumer with emphasis on policies of the government with regard to medicines and health and to promote the Essential Medicine concept. Some of its publications include "Hepatitis – B vaccination: Misleading Policy and Promotion".

11.Dr Gopal Dabade is a qualified ENT surgeon and has been involved in the consumer awareness programmes for over two decades. He also worked, for a period of three and half years with Civil Society in European Parliament on the issue of Patents and Access to Medicine as part of a German NGO "BUKO Pharma – Kampagne". He is one of the coauthor for "A Study on Drugs for Treating Anaemia".

12.Petitioner No.5, CONCERT was registered as a trust in the year 1997, in Chennai, India. The main objective of the trust was to establish an Asian Centre in Southern India for Consumer Education, Consumer Products Research and Testing of International Quality. This Centre will also provide

education and training in all consumer related subjects and activities catering to the needs of the entire Asian community.

13.Mr R. Desikan has rendered yeoman service on consumer related issues over 30 years and is one of the leading consumer activists of the country.

14.The filing of the present Petition is for the reason that the Drug Controller of India (DCGI) has directed all States Drug Controllers to take necessary action with respect to FDCs', mentioned in the list that are permitted by the State Drug Controllers, on the ground that the FDCs licensed by State Authorities are not permitted by the Office of the 2nd Respondent. The action to be initiated on several fixed dose combination (FDC) drugs (more than 300 in number) stating that they are irrational and/or for not following proper licensing procedures or for lack of adequate supportive data.

15.The Petitioners state with regard to the definition, Combination products also known as Fixed Dose Combinations (FDC's) are combination of two or more active drugs present in a dosage form. FDC's infact have certain advantages in certain situations.

16.The Petitioners herein appreciate this move by the DCGI's order inter alia for the following reasons:

1. FDCs specified by the DCGI for weeding out (Annexure 1) are unscientific. The safety of these FDC's (as also FDC's in general) is not studied. FDC's in general increase the chances of adverse drug reactions and drug-drug interactions.

2. There are only a handful of FDC's which are recommended by standard medical authorities like reputed pharmaceutical textbooks or the World Health Organisation (WHO). In the WHO's 14th list of 312 Essential Medicines, only 18 are FDC's. In the latest list of March 2007, there are 347 essential drugs that include only 26 FDCs (for a list see further below). All FDC's in the market which are not recommended by standard medical authorities are irrational and need to be weeded out for a number are reasons:

a) FDC's are an economic waste when only a single ingredient drug can do. Unaware patients tend to get exploited as FDCs are marketed as superior to single ingredient drugs.

b) Pharmacopeias in general specify only quality test procedures and standards for single ingredient drugs. Quality procedures for the FDCs are dependent on the manufacturer's word in the absence of scientific third-party validation. In addition, this overloads the already stretched and strained quality labs as well as the limited number of drug inspectors (about 1000) in this country.

c) Such a large presence of FDC's, in different dosages, and brand names, creates confusion for the prescriber and increases chances of medication errors that are harmful, and sometimes even fatal, for the patient.

d) FDC's apart from confusing patients and scientifically inclined doctors, pose a problem in price regulation. It is easier to fix ceiling prices for single ingredient drugs and the NPPA (National Pharmaceutical Pricing Authority) has limited resources to deal with the issue of appropriate pricing of FDC's.

17.The applicant's appreciates the move by the DCGI for the above reasons and totally support any move to ensure the implementation of the DCGI's order, which has been unfortunately challenged by Drug Industry representatives.

18. However the Petitioners contend that the order barely touches the essence of the problem of irrational FDC's in India and tends to give the impression of being arbitrary, superficial, and at best, a tokenistic exercise for the following reasons:

a) The DCGI has not enumerated comprehensive, fundamental principles of describing drugs and their fixed dose combinations as irrational.

b) India's market is full of irrational fixed dose combinations (FDC's). The Applicant states that, recognizing the magnitude of problem of irrational/unscientific FDC's in India, the present action merely touches a small part of the problem even as it gives, wrongly, the impression of clearing the therapeutic chaos in the Indian market.

c) The Indian market is also full of inessential and hazardous drugs which should not have been approved in the first place at all. These need to be removed within a specified time limit by the DCGI.

d) An analysis of the top-selling 300 drugs as per ORG-Marg/Nielsen retail audit shows that more than 60 % of them are irrational.

The order by the DCGI does not touch these FDC's, which account for more than 90 percent of the total retail sales of drugs in India.

e) The DCGI also says the list of drugs specified by him do not have proper approval saying the approvals given by the State Licensing Authorities (SLAs) are illegal. So most likely these will be approved if they follow a new procedure specified by him. As a result the irrational drugs will find their way in the Indian market again. Unfortunately the State Licensing Authorities (SLA's) have been lax and have not followed the DCGI's guidelines in the matter.

f) The words "illegal", "irrational" and "FDCs" are used interchangeably by the DCGI (as reported in the press). The Petitioners submit while most FDC's are irrational (that is they are unscientific and do not have any mention in standard textbooks nor sanction of experts), they are deemed illegal in the instant case because of improper procedures (including lack of stability studies) followed in licensing according to the DCGI. Many more otherwise legally licensed FDC drugs that are currently being sold in the Indian market, would not pass the rationality criteria anyway. So why are they not attracting the attention of the DCGI?

g) A single ingredient drug can be also irrational if it does not meet scientific criteria of rationality of safety and efficacy. Any COMBINATION OF AN IRRATIONAL DRUG IS ALSO IRRATIONAL. Also combination of rational drugs is not in general warranted except for some 26 FDCs mentioned above.

h) A comprehensive move to weed out irrational single ingredient/fixed dose combination drugs, not merely "illegally" or "improperly licensed" drugs, will consider inter alia the following sources of irrationality:

i) Unscientific drug with no proven efficacy (or at best doubtful) efficacy in any controlled trial: e.g. Serratiopeptidase, iron polymaltose complexes (IPC), etc.

ii) Unscientific combinations which may increase adverse effects: e.g., Ibuprofen + Paracetamol; Paracetamol + diclofenac; Diazepam + Magaldrate + Oxyphenonium.

iii) Hazardous drug (side-effects of which far outweigh the benefits), e.g., Nimesulide, Analgin; and/or drugs/drug combinations, which have shown, increased mortality. e.g. Liv 52 in alcoholic cirrhosis, antioxidants (See for instance: S. Verma, P. Thuluvath. Complementary and Alternative Medicine in Hepatology: Review of the Evidence of Efficacy. Clinical Gastroenterology and Hepatology, Volume 5, Issue 4, Pages 408-416.)

iv) Combinations with suboptimal doses: e.g. many multivitamin preparations. Combinations with overdoses of drugs, e.g., some paediatric anti-TB preparations, many multivitamin preparations especially those containing Vitamin B12; many so-called iron tonics with subtherapeutic doses of iron when iron deficiency anemia is a most common deficiency. (See for instance, A Study on Drugs for Treating Anaemia, DAF-K, Dharwar, 2006.)

v) Drug not licensed for a particular use but used for unethical trials on human beings, mostly poor and illiterate. (Example: Letrozole).

19. The Petitioners states and submits that according to the WHO Expert Committee [See Use of Essential Drugs: Model List (Eleventh List). World Health Organization, Geneva, 1999] combination drugs should not be used unless there are no alternative single drugs available for treatment or no alternative single drug was cost-effective for the purpose. Experts recommend that patients be individually evaluated and those patients requiring more than one drug should be prescribed separately. Combination drugs "increase the risk of side-effects and may also needlessly increase cost while encouraging irrational 'miss and hit' therapy." [Beardshaw, V. Prescription for Change. Penang: IOCU/HAI, 1983. pp.19.] When a combination drug is used it is diffi-cult to identify which of the constituent drugs is the cause of a drug reaction. Combi-nation drugs are irrational also because their stability is doubtful, reducing the efficacy in many preparations. Moreover, drug companies frequently change the ingredients making it difficult to keep track of the changes. [Every issue of MIMS India gives a list of irrational combinations. For a more wide-ranging lists, the same can be seen: Mira Shiva and Wishvas Rane. Banned and Bannable Drugs. VHAI, New Delhi, 2004.]

20. The Petitioners herein reproduce below some relevant extracts from WHO publications that have commented on the necessity and relevance of FDCS; notably the periodically issued Reports of the WHO Expert Committees on the Use of Essential Drugs:

> "Most essential drugs should be formulated as single compounds. Fixed-ratio combination products are acceptable only when the dosage of each ingredient meets the requirements of a defined population group and when the combination has a proven advantage over single compounds administered separately in therapeutic effect, safety or compliance."

[Source: The Use of Essential Drugs: Ninth Report of the WHO Expert Committee (WHO/EDM, 2000). Also in: World Health Organization (1997). The Use of Essential Drugs. Seventh Report of the WHO Expert. TRS 867.]

"It was noted that fixed-dose combinations offer certain advantages; they facilitate adherence to treatment regimens and they can delay the emergence of antimicrobial resistance. It was also noted that many illogical and ad hoc combinations of various medicines are currently being marketed in a number of countries. Any proposal to include fixed-dose combinations in the Model List should be backed by adequate proof of pharmaceutical compatibility and bioavailability. In light of these comments, the Committee recognized that its selection criteria with regard to fixed-dose combination products were in need of review and recommended that they be modified as follows:

"Most essential medicines should be formulated as single compounds. Fixed-dose combination products should be selected only when the combination has a proven advantage in therapeutic effect, safety, adherence or in decreasing the emergence of drug resistance in malaria, tuberculosis and HIV/AIDS."

[Source: WHO Expert Committee on the Selection and Use of Essential Medicines (12th: 2002: Geneva, Switzerland). The selection and use of essential medicines: report of the WHO Expert Committee, 2002: (including the 12th model list of essential medicines). (WHO technical report series; 914). Also in: WHO Expert Committee on the Selection and Use of Essential Medicines (14th: 2005: Geneva, Switzerland). The selection and use of essential medicines: report of the WHO Expert Committee, 2005: (including the 14th model list of essential medicines). (WHO technical report series; 933), page 57.]

21. A WHO manual for drug regulatory authorities has the following to state about FDC's:

"New fixed-ratio combination products are regarded as new drugs in their own right. They are acceptable only when (a) the dosage of each ingredient meets the requirements of a defined population group, and (b) the combination has a proven advantage over single compounds administered separately in terms of therapeutic effect, safety or compliance. They should not be treated as generic versions.

[World Health Organization. Marketing Authorization of Pharmaceutical Products with Special Reference to Multisource (generic) Products: A Manual for a Drug Regulatory Authority. WHO/DMP/RGS/98.5 (1998)].

22. Elsewhere a WHO publication states circumstances when FDCS are disadvantageous:

- "FDCs discourage separate titration of each active ingredient. This is a particular problem when both of the active ingredients require dose titration. Indeed, it can be argued that the very existence of an FDC discourages adjustment of doses to the patient's needs (if that is appropriate for the combination in question).
- When the active ingredients in question have different pharmacokinetics and/or pharmacodynamics, an FDC may not be appropriate.
- Unless both of the active ingredients are available as separate entities, FDCs encourage polypharmacy irrespective of whether it is appropriate for a particular patient. "

[Source: Regulation of fixed-dose combination products, WHO Drug Information, Vol 17, No. 3, 2003] (Emphasis petitioners')

23. The Applicant states that the guidelines as per the WHO recommendations for acceptability of Fixed Dose Combinations are:

a) Clinical documentation justifies the concomitant use of more than one drug.

b) Therapeutic effect is greater than the sum of the effect of each.

c) The cost of combination product is less than the sum of individual products.

d) Compliance is improved (that is when two or more medicines are to be taken separately, as in the case of TB, the user tends to avoid one or two medicines after sometime. This can be avoided if all three medicines are combined into one).

e) Sufficient drug ratios are provided to allow dosage adjustments satisfactory for the majority of the population.

24. The Petitioners vehemently states that any fixed dose combination, which does not satisfy the above-mentioned guidelines, should be considered irrational.

25. The petitioners are aware of the necessity of FDCs in some select circumstances. Indeed out of the total number of 347 essential drugs mentioned in the latest list of essential medicines by WHO (March 2007), only 26 (7.5 %) are acceptable fixed dose combinations. These cover FDCs for AIDS, TB, malaria, ORS, Iron plus folic acid for anemia, trimethoprim + sulphamethoxazole (Brand names: Bactrim/Septran), etc. The list of rational, acceptable FDC's is given below for easy reference:

26. Thus drug combinations in some cases are not only rational but are some-times even necessary. To paraphrase the WHO criteria mentioned above, FDCs are rational only when:

a) It allows synergistic action, i.e., it facilitates each other's pharmacological action, thereby producing greater effects, e.g., combined contraceptive pill, ORS, Calcium with Vitamin D.

b) It allows enhanced efficacy without disturbing each other's pharmaco-chemical actions: e.g., when the combination lignocaine with adrenaline increases the range and duration of action.

c) Combined doses are given in cases of general under-nourishment or simultaneous deficiency of all vitamins in famine conditions, e.g., Vitamin B complex, multivitamin, ferrous sulfate + folic acid, Vitamin A + Vitamin D.

d) It is necessary to reduce side-effects or toxicity, e.g., isonex + Vitamin B6 (Vitamin B_6 prevents peripheral neuritis caused by prolonged use of isonex).

e) When two or more medicines are needed in invariable proportion - e.g. iron-folic acid or when two or more medicines are always required to be given together- for example – isonex plus rifampicin to reduce the chances of development of drug resistance.