HYDERABAD'S PHARMACEUTICAL POLLUTION CRISIS:

HEAVY METAL AND SOLVENT CONTAMINATION AT FACTORIES IN A MAJOR INDIAN DRUG MANUFACTURING HUB

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This report was published in January 2018 by Nordea and the Changing Markets Foundation.

The author of the report is the Changing Markets Foundation, with on-the-ground research by Ecostorm.

Designed by Pietro Bruni, helloo.org

Printed on recycled paper

Water sampling behind the Aurobindo plant at Borpatla

Executive Summary

This report explores the impacts of pollution from pharmaceutical production sites in the Indian city of Hyderabad, one of the world's largest "bulk drug" manufacturing hubs, which supplies tonnes of medicines to markets across the European Union and United States every year.

As part of its ongoing engagement with drug companies and their suppliers regarding pollution in the pharmaceutical supply chain, and following the publication of "*Impacts of Pharmaceutical Pollution on Communities and Environment in India*"[1] in March 2016, Nordea commissioned the Changing Markets Foundation to conduct a follow-up investigation in India, the results of which are presented here.

Based on findings from two field trips (one in April 2017, during the dry season, and one in September 2017, during the rainy season), interviews with NGO experts and people living or working in the affected areas as well as in-depth analysis of media coverage and academic studies, this report confirms the findings of the 2016 study by showing that pharmaceutical companies in Hyderabad are continuing to discharge untreated or inappropriately treated wastewater into the environment and that local and national authorities are failing to get the situation under control. It concludes that the situation in Hyderabad has not improved in the past two years – if anything, it has deteriorated. Furthermore, with plans afoot to expand the city's pharmaceutical production capacity over the coming years and the lack of credible regulation and measures to control manufacturing emissions, the future looks grim for the area's inhabitants.

The centrepiece of the report are results from the testing of water samples collected adjacent to pharma factories and some of the city's waterbodies in September 2017 which highlight the occurrence of a range of heavy metals and industrial solvents commonly used in pharmaceutical manufacturing. In some cases, these were found to be present at extremely high concentrations, orders of magnitude higher than maximum regulatory limits or safe exposure levels, which points to substantial human and ecological risk potential.

The mere presence of some of these substances is cause for alarm given their extreme toxicity. In addition, the occurrence of mixtures of chemicals shows a lack of adequate water treatment prior to discharge (or potentially no treatment whatsoever). Depending on the water flow in receiving water bodies, and the distance from the effluent source, the actual concentrations of these chemicals from the discharge source could be many magnitudes greater that the concentrations detected in samples.

These findings come amidst repeated warnings from the scientific community about the dire state of India's water resources. Numerous factors, including climate change, industrial activity and a growing population are placing unbearable pressure on the country's water, drying up rivers and lakes and precipitating a dramatic decrease in groundwater.[2] This is already causing acute social and economic distress which is only predicted to worsen over the coming years. Beyond the evident human health impacts, the corporate sector, including the pharmaceutical industry itself, also depends on a reliable supply of clean water. The effects

HYDERABAD POLLUTION HOTSPOTS

Summary of key pollution problems at pharmaceutical sites and water bodies reported in recent studies and the media

MSN | sms pharmaceuticals ltd | HETERO Research is Development | Mylan | AUROBINDO Committed to healthier life! | Dr.Reddy's

Aurobindo IA
Solvents,
Hexavalent Chromium

Borewell in Gaddapotharam village
Heavy metals, solvents
Hexavalent Chromium

Gaddapotharam Lake
Dead fish (1,000)

Circular well/tank, Gaddapotharam village
Drug resistant bacteria, antimicrobials,
heavy metals, solvents, Hexavalent Chromium

Hetero I
Heavy metals,
solvents

Borewell in Kazipally Village
Solvents

Effluent channel, Kazipally Village
Drug resistant bacteria, heavy metals,
solvents, Hexavalent Chromium

Medchal Lake
Dead fish
(up to 60,000)

Shamirpet Lake
Dead fish
(up to 60,000)

Ramky Hazardous Waste Plant
Drug resistant bacteria,
heavy metals, solvents,
Hexavalent Chromium

SMS Pharma Unit I
Solvents, heavy metals

MSN Pharmachem (Rudraram)
Resistant bacteria
antimicrobials

MSN Pharmachem (Pashamylaram)
Resistant bacteria,
antimicrobials,

Mylan VII
Heavy metals, solvents,
Hexavalent Chromium

Aurobindo III
Heavy metals,
Hexavalent Chromium

Mylan III
Heavy metals,
Hexavalent Chromium

Dharani Nagar, Kukatpally
Toxic foam

Dr Reddy's Plant II
Heavy metals,
Hexavalent Chromium

Ramakrishnapuram Lake
Toxic foam

Rampally Lake
Dead fish (up to 30,000)

Isnapur Lake
Dead fish (over 50,000)

drug resistant bacteria,
antimicrobials,
heavy metals, solvents,
Hexavalent Chromium

Highest levels of fluconazole ever found in the environment recorded here

Gandigudem Cheruvu (lake)
Dead fish (230,000)

In October 2017, almost every fish in Gandigudem lake died. The TSPCB found traces of chloromethane, an industrial solvent used by the pharmaceutical industry, in the fish. Local police registered a criminal case against Aurobindo, Mylan, SMS Pharma, Vantec and Sriram.

The TSPCB issued closure notices to 14 pharmaceutical units, including Lee Pharma, Vivin Laboratories, Kekula Pharma, Total Drugs, Rakshi Pharma and KRS Pharma.

Hussain Sagar lake
Toxic foam, drug resistant bacteria,
solvents

Edulabad Lake
Toxic foam,
dead fish (400,000)

Golnaka I&D
Drug resistant bacteria,
heavy metals

Amberpet Sewage Treatment Plant
Antimicrobials, drug-resistant bacteria

Musi River at Edulabad bridge
Toxic foam, drug resistant bacteria,
heavy metals

Muduchintalapalli
Arutla
Jinnaram
Dundigal
Peddakanjerla
SHAMIRPET
Ponnal
Devaryamjal
KOMPALLY
Thimmaipalli
PATANCHERU
KUKATPALLY
KAPRA
Bogaram
HYDERABAD
MOULA ALI
Ghatkesar
JUBILEE HILLS
BANJARA HILLS
Edulabad
Maharajpet
Chinnamangalaram
Medipally
DILSUKHNAGAR
Daira

of water stress and pollution therefore present a substantial material risk for businesses operating or using suppliers in India.

India's Environment Ministry classifies pharmaceutical manufacturing as a "red category" activity owing to the hazardous waste it produces. Successive studies have shown that air, water and soil in Telangana state (of which Hyderabad is the capital) are significantly contaminated by toxic chemicals and heavy metals such as copper, lead, mercury and arsenic. One 2001 article recommended that "Most of the soils should be removed from agricultural production" in Patancheru, the industrial area on the outskirts of Hyderabad where many of the city's pharmaceutical factories are situated.[6] A report published in the Journal of the Geological Society of India in October 2017 showed that groundwater in the Nalgonda district to the east of Hyderabad contains toxics including lead, cadmium, vanadium and arsenic "in concentrations that are thousands of times higher than the maximum levels prescribed for drinking water quality by the World Health Organisation (WHO) and Bureau of Indian Standards (BIS)."[7] The paper reported that one likely origin of the pollution is "the release of reactive pollutants into the atmosphere by industries", listing the pharmaceutical industry as one of the area's key 'anthropogenic' activities.[8]

Pharmaceutical pollution, whether from the excretion of drugs or industrial activity, carries specific dangers for human health and ecosystems ranging from the near elimination of entire species[9] to the feminisation of fish[10] and the spread of antimicrobial resistance (AMR). Furthermore, pharmaceutical manufacturing also uses large quantities of solvents – which are often highly toxic chemicals – and heavy metals, whose long-lasting impacts on human health have been proven and whose use is therefore regulated in many countries.

A 2011 report found that almost 70 percent of India's surface water resources and a growing percentage of its groundwater reserves are contaminated by biological, toxic, organic, and inorganic pollutants.[3] By 2015, this figure had risen to 75-80 percent based on official statistics.[4] Furthermore, an assessment by the country's Central Pollution Control Board (CPCB) reported that the number of rivers defined as "polluted" in India had more than doubled in the previous five years, from 121 to 275.[5]

Frothing effluent stream emptying into the Musi River near Edulabad village

Of particular relevance here, a series of studies over the past decade have linked uncontrolled manufacturing discharges from antibiotics factories in Hyderabad with the spread of AMR, a global health threat which could kill more people than cancer by 2050.[11] In its *Frontiers 2017. Emerging Issues of Environmental Concern* report, UN Environment identifies growing AMR linked to the discharge of drugs and particular chemicals into the environment as one of the most worrying health threats today[12], noting the role that heavy metals can play in "co-selecting" for drug-resistant bacteria alongside high concentrations of Active Pharmaceutical Ingredients (APIs).[13] At the report's launch, UN Environment Executive Director Erik Solheim drew particular attention to a pharmaceutical facility in Hyderabad, where testing of discharged water revealed that the concentration in the treated wastewater of ciprofloxacin, a vital broad-spectrum antibiotic, was strong enough to treat 44,000 people. [14]

Because of the globalised nature of today's pharmaceutical industry and inter-connected world where disease and drug resistance can spread rapidly, what happens in India concerns us all.

Key messages:

- Despite decades of campaigning by local and international NGOs and successful legal challenges at the highest Indian courts, the situation on the ground has not improved and pharmaceutical pollution is still rife in Hyderabad, affecting ecosystems and the human rights of local inhabitants. Given that a large share of these pharmaceuticals is manufactured for and sold to European and US health providers and pharmaceutical companies, it is clear that this is a supply chain issue that must be addressed in an appropriate way by the purchasers of these drugs.

- Pollution from antibiotics production is particularly problematic because it fuels the spread of antimicrobial resistance (AMR), which can easily travel far beyond India's borders. For instance, a 2010 study by Swedish researchers showed that seven out of eight travellers to India returned to Sweden carrying drug-resistant bacteria in their gut.[15] Many pharma manufacturers in Hyderabad produce antibiotics in addition to other generic ('bulk') drugs and irresponsible production practices could be an additional factor fuelling a major global health crisis.

- The pharmaceutical industry is not being adequately held to account by the Indian Government or regulators. In fact, recent developments indicate that regulation targeting the pharmaceutical industry is actually becoming more lax, and pollution levels are set to rise even further, as the government lifts restrictions on plant expansion[16], and weakens national pollution index (Comprehensive Environmental Pollution Index, or CEPI) indicators.[17]

- In Europe and the United States, pharmaceutical pollution, particularly in relation to the spread of AMR, is receiving increased attention and policy responses to

address the problem are under consideration. For example, in its response to the Review on Antimicrobial Resistance's final report, published in May 2016[18], the UK Government recommended the establishment of targets for maximum levels of antimicrobial API discharge associated with the manufacture of pharmaceutical products and urged pharmaceutical companies to improve monitoring of API emissions from directly-operated manufacturing facilities as well as those of third party suppliers, and support the installation of proper waste processing facilities to reduce or eliminate API discharge.[19] In another significant move, the Access to Medicine Foundation's Antimicrobial Resistance Benchmark 2018 compares company strategies and processes relating to wastewater management. The Foundation will use this data to further the discussion on the role of manufacturing in the environmental impact of antibiotic production.[20]

- By failing to crack down on manufacturing emissions, Indian pharma manufacturers risk jeopardising supply contracts with companies and procurement bodies in Europe, the US and other regulated markets. For example, European NGOs have recently called for major procurement bodies including the UK's National Health Service (NHS), German health insurance companies, and French hospitals to blacklist the worst offending polluters and embed environmental criteria in all contracts with pharmaceutical suppliers.[21] Several of these organisations are now reviewing the situation. In Sweden, the country's regions have come together and introduced environmental criteria and audits in their contracts.[22]

After many decades of inaction, it is encouraging to see that the dangers linked to pollution from pharmaceutical manufacturing are beginning to receive the attention they deserve; the negative impacts of uncontrolled pharmaceutical manufacturing discharges have been clearly exposed as a supply chain problem that must be resolved between manufacturers in third countries and their clients in key export markets. However, despite recent moves by some pharmaceutical companies to start moving towards more responsible production, the industry and regulators are not moving fast enough to address a threat of such magnitude. Multinational pharmaceutical companies which outsource API production to Indian suppliers have a duty to take rapid action to put a stop to pollution in their supply chains. Governments and medical agencies must change the way drug manufacturing is currently regulated and include environmental criteria in Good Manufacturing Practices (GMP) to ensure that manufacturers address wastewater treatment.

1. Introduction

A. Background to the report

As part of its ongoing engagement with drug companies and their suppliers on pollution in the pharmaceutical supply chain and following the publication of "*Impacts of Pharmaceutical Pollution on Communities and Environment in India*"[23] in March 2016, Nordea commissioned the Changing Markets Foundation to conduct a follow-up investigation in India, the results of which are presented in this report.

The objective of the investigation was to provide an updated snapshot of the situation on the ground in Hyderabad, which is a major hub of 'bulk drug' production in India, and whose pharmaceutical manufacturers have repeatedly found themselves at the centre of pollution scandals.

Hyderabad is famous for its lakes, built over centuries to serve the city's water and irrigation needs. Once praised for their purity, they have suffered badly as a result of the city's industrial development, with data released at the end of 2016 showing that 23 out of 25 water bodies had been rendered unfit for irrigation and industrial cooling, let alone for drinking and domestic use. Local NGOs note that seepage of harmful chemicals into groundwater is another concern as toxic substances can travel several kilometres below ground contaminating borewells used to supply drinking water.[24] The Musi River, which flows through Hyderabad is India's 6th most polluted river according to the country's Central Pollution Control Board (CPCB).[25]

The pharmaceutical industry is frequently labelled the most polluting industry in Hyderabad. While a wide range of pharmaceutical Active Pharmaceutical Ingredients (APIs) and finished dose products are manufactured in Hyderabad, most of the research so far has focused on pollution from antibiotics production, which is particularly problematic because it fuels the spread of AMR. Most bulk pharma manufacturers in Hyderabad produce antibiotics and previous research conducted by Changing Markets and other organisations focused on antibiotic manufacturing units.

In October 2016, Changing Markets published a report, *Superbugs in the Supply Chain* [26], which presented findings from the testing of wastewater near pharmaceutical manufacturing plants in Hyderabad. The study exposed the occurrence of resistant bacteria at almost half of the sites tested, likely caused by pharmaceutical manufacturing discharges in the city's industrial areas. A steady flow of academic studies and media reports in the Indian and European press also indicate that the pharmaceutical pollution remains rife. In May 2017, German television channel *Das Erste* broadcast a documentary "*The invisible enemy - deadly superbugs from pharma factories*" that further raised alarm about pharmaceutical pollution in Hyderabad. In water samples taken at some sites featured in the documentary, scientists found concentrations of antibiotics several hundred to several thousand times higher than levels predicted to select for resistance. What is more, all of the samples were found to contain dangerous, multidrug-resistant pathogens.[27]

For the purposes of this report, the investigation team revisited sites featured in "*Impacts of Pharmaceutical Pollution on Communities and Environment in India*" in April and September 2017 in order to determine whether the situation has improved, obtaining photographic evidence of pollution around these sites and in rivers, lakes, and wells in their vicinity and the industrial areas they are part of. Local people living or working in the affected neighbourhoods were interviewed in order to build a comprehensive picture of current conditions in Hyderabad and its surrounding areas. In addition to this, water samples taken in September 2017 at the selected sites were tested at an independent laboratory, Specialty Analytical in Oregon, United States, for the presence of toxic substances, specifically a variety of industrial solvents and heavy metals relevant to pharmaceutical production. The research did not seek to determine concentrations of antibiotics or the prevalence of resistant bacteria in waste water as a lot of the evidence gathered recently and presented elsewhere has already addressed these aspects.

Low production costs mean that India has become one of the biggest hubs of bulk drug manufacturing in the world

B. The Indian pharma industry

India plays a key role in global pharmaceutical production, with nearly 2.5 million people employed directly or indirectly in the country's pharma sector.[28] Pharma is one of the fastest growing segments of the Indian economy and has experienced rapid and sustained expansion since the second half of the 20th century. Faced with stiff competition from China, which is flooding the market with cheap pharmaceutical APIs, a new drive to boost India's bulk drug industry was announced in 2015, with a high-level committee recommending the establishment of large manufacturing zones or "mega parks" across the country.[29]

According to India's Centre for Science and Environment (CSE), in 2007 manufacturing costs in India were 30-40% lower than those in the United States and western Europe, with labour costs one-seventh of those in the US.[30] More recently, in 2016, an article in The Washington Post sponsored by the Indian government initiative Make In India claimed that the costs of running an FDA-inspected manufacturing plant in India are 50% lower than in 'developed' countries. According to Make In India, operation and production costs run 40-70% lower (due to factors including equipment sourcing and tax incentives) and labour costs are on average 60-70% less.[31]

Many public health experts rightfully highlight the ground-breaking role India has played in terms of making affordable medicines widely accessible thanks to generics production. The availability of cheaper medicines has helped achieve significant progress in tackling global health crises such as the HIV/AIDS epidemic, particularly in developing countries. However, with inadequate rules in place to regulate the environmental impact of pharmaceutical manufacturing, it is important to acknowledge that cheap and irresponsible production has also come at the expense of the health of thousands of people in drug-producing countries, notably India and China. In the case of pollution from antibiotics factories, the risk is that it is fuelling the AMR crisis, which it is predicted will kill more people than cancer and diabetes combined by 2050.

Hyderabad is a major hub of bulk drug production and the pharmaceutical industry provides thousands of jobs in Telangana. However, it is also one of the state's biggest polluters. This year Telangana was among the top 5 Indian states in terms of environmental violations; according to local environmentalist Capt. J. Rama Rao, most of these cases involve polluting pharmaceutical industries, which make the air and water "unfit for residents."[32]

While big pharma companies such as Aurobindo and MSN Pharmaceuticals were at the centre of pollution

scandals reported over 2016 and 2017, another noteworthy trend has been observed in the area. Already in 2007, CSE stated that "[c]ost-cutting on pollution control is an important factor behind [India's] competitive advantage" and in the same way that industrialised countries in Europe and North America outsource production to India to cut costs, "big Indian companies sub-contract many, including the most polluting, processes to small-scale firms, which are notorious for lack of pollution control." What is more, "bigger companies have already started running small units to meet in-house requirements under different names."[33] More recent intelligence from the ground suggests that the subcontracting of production continues to be common practice in Hyderabad. In June 2016, for example, investigators operating on behalf of Changing Markets were informed by a local contact that most of the big plants based in Hyderabad receive part of their supply from smaller, often unlicensed plants, which blatantly flout pollution regulations.[34]

Facts about the Indian pharmaceutical industry

- The Indian pharmaceutical market is expected to grow to US$100 billion by 2025.
- India is one of the world's leading suppliers of generic drugs, with generic drug revenues of US$15 billion in 2014.
- Over half of India's pharmaceutical exports are to highly regulated markets such as the US and the EU. Pharma exports from India are expected to reach US$30 billion by 2020.
- Anti-infectives, which include antibiotics, antivirals and antifungals, are the largest segment on the domestic market, accounting for one-quarter of total turnover.
- India's Environment Ministry classifies pharmaceutical manufacturing as a "red category" activity owing to the hazardous waste it produces.

Sources:

Impacts of pharmaceutical pollution on Communities and environment in India, 2016

The Hindu, 30.11.2017, Developing on the pharma success story

Villager points out illegal effluent streams coming from Shri Kartikeya Pharma factory in Polepally, Hyderabad

2. The situation in Hyderabad

A. A city blighted by pollution with inadequate monitoring and enforcement

Despite decades of campaigning by local and international NGOs, and successful legal challenges at the highest Indian courts, the pollution situation on the ground in Hyderabad has not improved since the last report published by Nordea in 2016. In the two years since then, a string of pollution incidents related to pharmaceutical manufacturing have taken place. Some of these have been extremely serious, resulting in the launch of criminal proceedings against the companies involved.[35] Every new case places an additional burden on the local populace who are rapidly losing patience with the situation.

Every week the local and national media brings fresh news of pollution misery – from foaming lakes giving off a toxic stench to choking air pollution; from soil erosion to the shrinking and drying up of Hyderabad's vital water sources.

Critical water pollution

Once known as the 'city of lakes', the ecological plight of Hyderabad's numerous water bodies has been well-documented in Indian media reports. An article in the Times of India, published in June 2017, reported that of the city's 3,000-odd lakes which existed in the 1970s, less than half remain intact today; the rest have either dried up, disappeared, or are shrinking.[36] Reasons behind this decline include developers illegally draining lakes to make way for real estate projects, household garbage and waste being dumped into water bodies – and a seemingly unstoppable tide of industrial pollution entering the waterways.

The disappearance of vital water sources has many obvious, and some not so obvious, impacts on the people of Hyderabad. The loss of standing water sources is compounding the shortage of water already felt in some areas of India through drought and lower precipitation levels – national news outlet The Hindu reported in July 2017 that, if no action is taken, India could be on course for a fivefold reduction in available water by 2050.[37] During May and June 2017, Hyderabad experienced average daily highs of 43 degrees Celsius, the highest temperature recorded there in a decade.[38] Climate change experts from the Indian Institute of Science predict that this will become the norm in years to come, due to rising pollution and continued deforestation, further exacerbating water shortages.[39]

Meanwhile, pollution in the city's remaining 1,500 lakes has reached critical levels. A number of news reports in April 2017 outlined the impacts of industrial pollution on Edulabad Lake, located 5-6km east of Hyderabad's Outer Ring Road (ORR), which are making residents' lives a misery.[40] As recently as two decades ago, the 800-900-acre lake was used by villagers for swimming and fishing. "Today, it is a stinking cesspool that

froths due to toxic chemicals released by Hyderabad's various pharmaceutical industries."[41]

One visible sign of heightened industrial pollution in Hyderabad water bodies is foam or froth appearing on the lakes. Edulabad Lake itself has reportedly been frothing for two decades; in June 2017, Ramakrishnapuram (R K Puram) Lake to the city's southeast was also reported to be foaming with toxic effluents, causing alarm among residents using nearby borewells for their water supply.[42] In July, the continued presence of foam on R K Puram Lake forced residents to purchase their water from alternative sources, placing them under financial strain and further exacerbating water stress on the city.[43] After disappearing for one month, the foam reappeared in the lake in August.[44]

At the end of August 2017, foaming effluent from the Dharani Nagar in Kukatpally reportedly covered 50

The Musi River, seen here covered in toxic foam, flows through the centre of Hyderabad

houses in the neighbourhood with toxic foam, triggering an evacuation of residents. Locals said this was the third time the canal had begun foaming this year.[45] By September, Hyderabad's rainy season, toxic foam was reported at five lakes across the city.[46] In October, there were reports of manholes bursting across the city, spilling toxic froth and forcing people to stay inside their homes.[47]

The reasons behind the foaming lakes continue to be fiercely debated. The Telangana State Pollution Control Board (TSPCB) published a report in October stating that the froth is a result of detergents being used by residents and sewage disposal.[48] However, local people vehemently deny that detergent could be responsible for the reported "pungent smell", "rashes on [their] skin" and "fever and disease" that they suffer during each foam outbreak[49]; they believe instead that industries are discharging effluents into the lakes.[50]

Between May and June 2017, thousands of dead fish washed ashore at Rampally, Shamirpet and Medchal lakes – as many as 30,000 were found at Rampally Lake, while up to 60,000 were washed ashore at Shamirpet and Medchal lakes.[51] According to government officials, the crisis was due to the heat; as previously mentioned, Hyderabad was experiencing a heatwave with daily average temperatures of 43 degrees Celsius. However, according to the Indian news channel NDTV, environmentalists were not surprised by the incident – "after decades of being abused with a steady inflow of untreated sewage, industrial and agricultural chemicals, lakes are in oxygen distress," they claimed.[52]

There are also frequent reports of "fish kill" as a result of toxic contamination at Edulabad Lake. In October 2017, thousands of dead fish washed ashore as a result of toxic contamination.[53] With still no action to remove the dead fish several days after the incident, locals were alarmed about the potential impacts on the health of children attending a school next to the lake shore. Hundreds of families in the villages of Edulabad and Dammaiguda which are dependent on fishing as their sole source of livelihood were also worried about how they would sustain themselves over the coming year. P. Krishna, general secretary of the Edulabad Gangaputra Sangham, told the Deccan Chronicle that the fishermen had "been rendered jobless for at least a year-and-a-half."[54]

In April 2017, the investigation team were told by Mr Shankar, the Sarpanch of Edulabad that children attending the village school suffer from skin and eye conditions. He had organised for a mobile medical camp and an eye camp to visit the village and produced some statistics – out of 200 school children aged 6-15 years old attending, 70 presented with eyesight problems (often watering eyes), and 120 with problematic skin conditions. In this quite small village population, he says that there are 20-25 children who suffer from epilepsy. The investigators also visited a farm in Edulabad and spoke to the family there. They discussed their medical problems with the team; the elderly farmer's wife said that whenever she works in the paddy fields she develops a rash on her hands, arms and legs, where the skin roughens and eventually breaks and blood comes to the surface. It takes several weeks to heal after she stops the work. She said this began ten years ago, before that she had never had skin problems and indeed they all used to drink the river water. The family also showed the limbs of their two children, one of 14 and one of 4. Both had faint but observable rashes and small white spots all the way up their legs, and the younger of the two had developed a sore around one of the spots of about 5cm diameter. They explained that the "English medicine" didn't work (the informant said this referred to antibiotic cream) and so they had turned to an Ayurvedic hospital and had been using a

In October 2017, hundreds of thousands of dead fish were washed ashore from Gandigudem Lake, close to Bollaram and Kazipally Industrial Areas (credit- The News Minute)

turmeric and oil paste treatment which they found to be helpful provided they kept out of the water (this is quite difficult given that they live on a paddy farm and need to work in the water). The informant said that a local doctor had told him there was widespread antibiotic resistance in the local community, hence antibiotic creams were not effective in treating these problems. The farmer said that one of his cows had miscarried a 3-4-month-old foetus 15 days ago, this was the second of his cows that had miscarried in the last 1-2 years. Ten years ago such an event was unheard of.

Also in October 2017, the discovery of **over 200,000 dead fish in Gandigudem Cheruvu**, a lake just north of Bollaram and west of the Kazipally Industrial Development Area resulted in a criminal complaint by the Fisherman Cooperative Society against several pharmaceutical companies: Hetero Pharma, Aurobindo, Mylan, SMS Pharma, Vantec and Sriram.[55] Local people cited industrial pollution as the cause of the mass death and a local official confirmed that "Preliminary findings suggest toxic chemicals from Kazipally Industrial area as cause of fishkill."[56] So serious was the incident that the deputy director of the Telangana fisheries department issued the following advice: "Fish from tanks with mass mortality shall not be consumed. In polluted tanks, there could be heavy metals in the fish and when they are consumed, it automatically affects humans."[57] Samples collected by the TSPCB showed traces of chloromethane, a solvent used by the pharmaceutical industry which triggers neurological and reproductive ill-effects in humans, in the water and the dead fish.[58] Chloromethane was also found in a number of the water samples taken by the investigation team for this report (see chapter 3).

Soil and air pollution

It is not just Hyderabad's water that is being impacted by pharmaceutical pollution. A study referred to in the New Indian Express in March 2017 showed that industrial pollution is also having a severe impact on soil quality. The study collected soil samples from four areas close to pharmaceutical industries in Medchal, Maisammaguda (near Kompally), Bachupally and Dundigal; 13 samples fell into the 'poor' category of the Soil Quality Index (SQI), while 3 fell into the 'average' category.[59] Another study published in 2016 by a faculty member at Malla Reddy Engineering College (MREC) also highlighted the issue of soil pollution in Hyderabad, showing that pharma pollution had affected soils by reducing organic matter and fertility. Soil samples from 53 locations surrounding pharma industries were tested, of which 43 samples fell into the SQI's 'poor' category.[60]

Air pollution from pharmaceutical production is also a persistent problem for the people of Hyderabad, with doctors reporting a steep rise in respiratory problems in residents living close to pharmaceutical factories in recent years.[61] In July 2017 the Air Quality Index by the TSPCB showed that there are 13 areas of the city where the air pollution levels have crossed the threshold limit, causing breathing discomfort to residents with lung and heart ailments. However, as the Times of India reports, while residents have lodged complaints with the TSPCB, little has been done to improve the situation: "Many people in the colony have begun to develop skin problems and a persistent cough. The pollution in the air is evident, as we can literally see the pollutants float in the air. We have tried speaking to the pollution control board and other concerned civic authorities but all our efforts have been in vain," one resident told the media outlet in July 2017.[62] Lack of action taken by the TSPCB and other authorities is a common thread running through media reports of pollution in Hyderabad.

In September 2017, The Hindu revealed that the TSPCB and Environment Protection Training and Research Institute (EPTRI) had found high levels of volatile organic compounds (VOC) in the industrial areas of Bollaram, Kazipally and Jeedimetla where numerous pharmaceutical factories are located. An official noted that: "The levels were high and lapses identified in the industry include leaks, storage places with uncovered solvents that cause these volatile chemicals to evaporate." The study was reportedly submitted to the government for communicating corrective measures to the industry, with a "detailed volatile organic compounds study" planned for the end of 2017.[63]

During the same month, a report published by the Energy Policy Institute at the University of Chicago showed that Hyderabadis are losing 2.3 years of life expectancy, because the government-set levels of acceptable air pollution are higher than those recommended by the World Health Organization (WHO).[64]

An effluent disposal truck in Patancheru. Recent months have seen a spate of incidents involving the illegal dumping of hazardous waste in and around Hyderabad

Illegal waste dumping

Recent months have seen a spate of incidents involving the illegal dumping of hazardous waste in and around Hyderabad. In April 2017, the TSPCB identified 27 drums of hazardous waste dumped in Jinnaram village; a news article in Telangana Today reported that three men had been identified as the culprits and taken into custody – although it does not describe what the waste contained, or where it is likely to have originated.[65]

In late April 2017, the Minister for Municipal Administration & Urban Development in Telangana, KT Rama Rao, conducted a surprise inspection of the Jeedimetla industrial area, which is home to numerous pharmaceutical factories, following complaints from residents.[66] Following this inspection, a pollution task force was set up in Hyderabad, comprising officers from the TSPCB, the Telangana State Infrastructure Corporation (TSIC) and revenue and police departments.[67]

CCTV cameras were installed in seven locations, with the feed provided to Board officials and the Greater Hyderabad Municipal Corporation (GHMC). According to the news articles outlining these plans, officials hoped the CCTV would act as a deterrent. However, the industries found ways around these, as illustrated by an incident in May, when a tanker camouflaged as a transport lorry was caught releasing effluent into the Musi River.[68] During the same month, TSPCB officials and the police also intercepted a tanker that was illegally dumping chemical waste and releasing toxic air into the atmosphere on the premises of an abandoned construction site.[69]

An article in The Hindu in November 2017 noted that illegal dumping of effluent remains common practice in the pharmaceutical industry and also highlighted cost as a motivating factor.[70] While companies claiming to have "zero liquid discharge" should in theory be sending their effluents to common treatment plants such as the Patancheru Effluent Treatment Plant (PETL),[71] in reality they "don't always toe the line."[72]

Isnapur Lake receives waste flowing through open channels from the Patancheru Industrial Area

With this in mind, it is troubling that the authorities seem to be putting their faith in the industry to monitor illegal dumping itself, with Telangana Today writing in May 2017 that the TSPCB had met with industry representatives and directed that they "take up self-regulation to control pollution from their units."[73] However, based on the evidence presented in this report, it seems unlikely that the introduction of industry self-regulation will change anything in Hyderabad.

Pollution Index watered down

When the Indian government introduced a national pollution index in 2009 to identify critically polluted industrial areas across India (Comprehensive Environmental Pollution Index or CEPI), it was hoped that this would force industries to curb their polluting activities. However, according to environmental publication Down to Earth, in the eight years since the index was introduced, no significant improvement has been seen.[74]

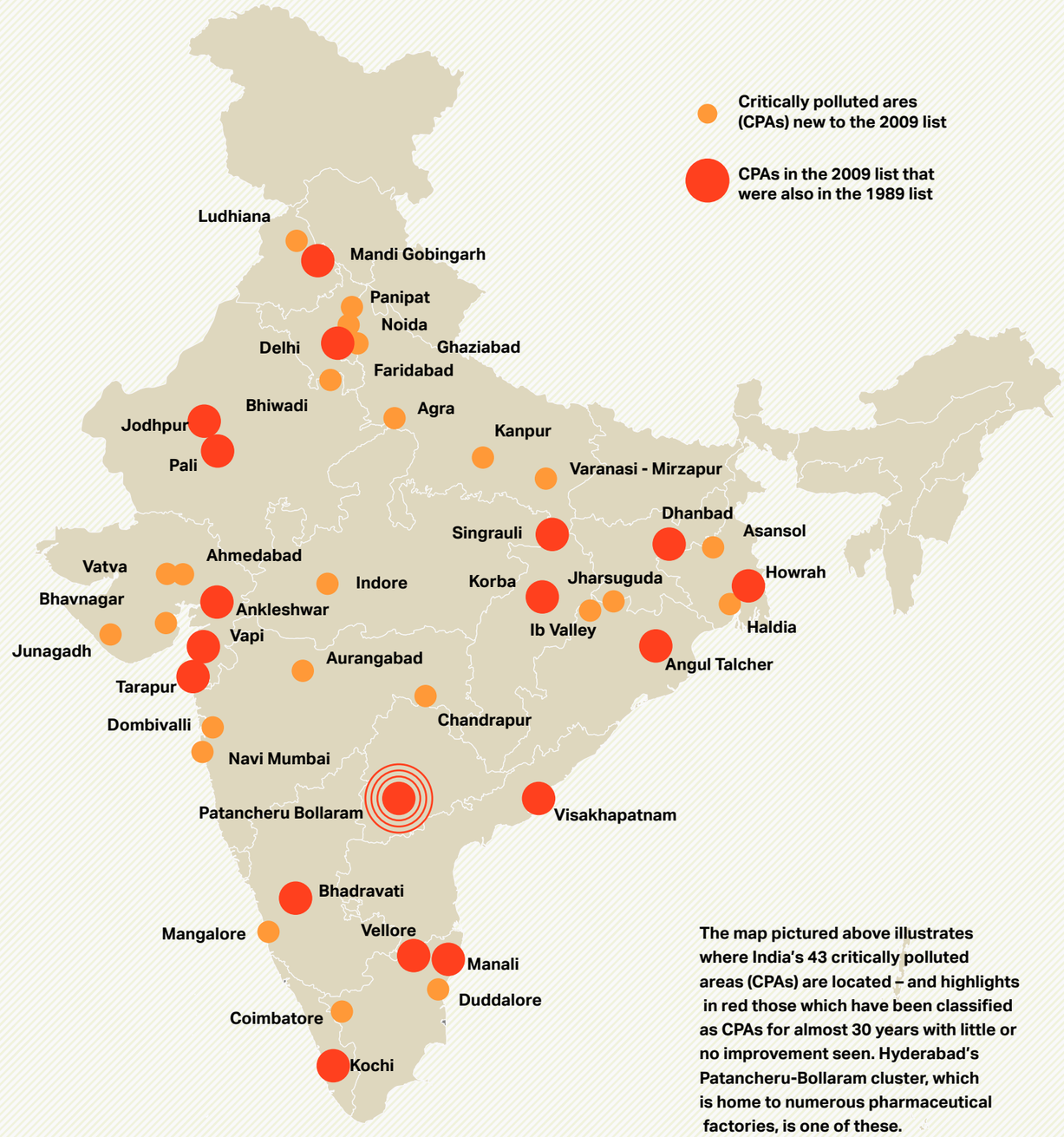
This is clearly the case in Hyderabad where, despite the classification of the city's Patancheru-Bollaram industrial cluster as being 'critically polluted'[75], the situation has progressively deteriorated. In fact, a Senior Advocate of the Indian Supreme Court recently described the cluster's common effluent treatment plant (CETP) itself as "*a major source of pollution*", noting that "*if the Government of Telangana does not wake up to the stark reality of large-scale environmental degradation in Patancheru-Bollaram Industrial Estates, it could turn out to be a Bhopal tragedy [in] slow motion.*"[76]

Paradoxically, there is also evidence that, in the face of worsening pollution, regulation is actually becoming more lax. In 2015, the government removed certain criteria relating to health and environment from the index, purportedly to simplify the system. However, the change drew criticism from NGOs and environmental campaigners, and was even described as an "industry friendly move" by the Indian Economic Times.[77] A blanket ban on industrial expansion in all critically polluted areas, including Patancheru Bollaram, was introduced in 2010, but overturned just one year later.[78]

In 2014, the government implemented two digital monitoring systems, the Continuous Emission Monitoring Systems (CEMS) and Continuous Effluent Quality Monitoring Systems (CEQMS). Enabling real-time pollution monitoring and reporting for 17 highly polluting industries, including the pharmaceutical industry, activists hoped that accurate and credible data would enable immediate action against polluters. However, three years on, a study by CSE recently revealed that most of the equipment used for monitoring was faulty, incomplete or non-operational.[79]

India's critically polluted areas

Hyderabad's Patancheru-Bollaram cluster, home to numerous pharmaceutical factories, has been critically polluted for decades



The map pictured above illustrates where India's 43 critically polluted areas (CPAs) are located – and highlights in red those which have been classified as CPAs for almost 30 years with little or no improvement seen. Hyderabad's Patancheru-Bollaram cluster, which is home to numerous pharmaceutical factories, is one of these.

Source: Down to Earth, July 2017

Completing the bleak picture, Down To Earth claims that the governmental response is having little or no impact. When data shows high levels of pollution from an industrial plant, the Central Pollution Control Board (CPCB) and the relevant State Pollution Control Board (SPCB) will send messages to the implicated company. However, according to Down To Earth, "in most cases, these messages remain unread by the industry and no follow-up action is taken by the authorities."[80]

Pharmaceutical pollution as a driver of AMR

Pollution from antibiotics manufacturing has long been an issue of concern in Hyderabad. An academic study published in September 2016 showed that concentrations of antibiotics detected in the Hyderabad area and Musi River, which flows through the city centre, are 1,000 times higher than the usual concentrations found in rivers in developed countries, because of improper disposal of industrial effluent.[81] This is particularly problematic, as these high concentrations of antibiotics in the environment are contributing to the development of drug resistance in bacteria, as demonstrated by two reports published in the last year, further described below.

'Superbugs in the Supply Chain' Report

In October 2016, the Changing Markets Foundation published a report entitled *Superbugs in the Supply Chain: How pollution from antibiotics factories in India and China is fuelling the global rise of drug-resistant infections*.[82] The report revealed high levels of drug-resistant bacteria in areas surrounding pharmaceutical factories in Hyderabad and Visakhapatnam, where a substantial share of the world's antibiotics are manufactured, as well as in New Delhi and Chennai.

In total, out of 34 sites tested, 16 were found to be harbouring bacteria resistant to antibiotics. At four of the sites, resistance to three major classes of antibiotics (cephalosporins, carbapenems and fluoroquinolones) was detected. Resistance to one or two of these classes of antibiotics was found at a further 12 sites.

Of the antibiotics manufacturing plants tested, three factories respectively belonging to Aurobindo Pharma, Orchid Chemicals, and Asiatic Drugs and Pharmaceuticals, all of which supply export markets either directly or indirectly, were found to be resistance hotspots.

Tests by the University of Leipzig found high levels of drug-resistant bacteria in 95% of the water samples they took in Hyderabad

Photo credit: Norddeutscher Rundfunk

German researchers find "highest concentration of any drug ever measured in the environment"

In May 2017, Infection journal[83] published a study by German academics, which found "excessively high" concentrations of clinically relevant antibiotics and antifungal agents in water samples taken at sites in Hyderabad. For one substance, fluconazole, the scientists found what they believe to be "the highest concentration of any drug ever measured in the environment."

The study, conducted by microbiologists from the University of Leipzig, tested for levels of drugs in water samples, as well as antibiotic and antifungal resistance (i.e. presence of drug-resistant microorganisms). They found high levels of drug-resistant bacteria in more than 95% of samples, and noted that "[their] findings confirm those of previous studies that have demonstrated a strong association between environmentally stable anti-infective residue pollution and the presence of MDR (Multi-Drug Resistant) bacteria."

The findings, also reported in a documentary broadcast [84] by the German channel Das Erste in May 2017[85], underline the urgency of bringing pollution at pharmaceutical manufacturing sites under control.

Access to Medicine Foundation's AMR Benchmark 2018

In recognition of the role manufacturing emissions play in contributing to the spread of AMR, the Access to Medicine Foundation's AMR Benchmark 2018 compares company strategies for limiting the impact of antibiotic manufacturing on the development of drug-resistant bacteria. In addition to other indicators including (but not limited to) appropriate access, stewardship and R&D, it assesses how companies take antibiotic discharge into account in their manufacturing and environmental risk management strategies. Crucially, it ranks companies on what information they disclose, highlighting the importance of transparency in securing lasting change and more responsible practices across the industry.[86] Industry initiatives set up to address the need for better practices in pharmaceutical manufacturing are discussed in the following section.

B. The industry response

While the environmental cost of pharmaceutical manufacturing has long been ignored by the industry, a series of initiatives over the past two years show that some companies are beginning to acknowledge the problem. The "Davos Declaration" of January 2016 and the B20 statement in May 2017 announcing the formation of an AMR industry alliance [87], suggest that the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) is starting to take AMR more seriously.

While the Davos "*Declaration on Combating Antimicrobial Resistance*" signed by over 100 companies only briefly mentioned that its signatories would "support measures to reduce environmental pollution from antibiotics" [88], this was followed in September 2016 by the publication by a smaller group of companies including AstraZeneca, GSK and Pfizer, as well as major Indian players Wockhardt and Cipla of an *Industry Roadmap for Progress on Combating Antimicrobial Resistance*, which listed measures to reduce the environmental impact from the production of antibiotics as its first priority (see Box). However, some of the worst offender companies are absent from the voluntary initiatives. The CEO of one of the signatories to the Roadmap, DSM Sinochem Pharmaceuticals, subsequently called for the industry to go further by committing to buy APIs only from manufacturers that do not pollute the environment and to introduce more transparency in the supply chain.[89]

Industry Roadmap for Progress on Combating Antimicrobial Resistance

We support measures to reduce environmental impact from production of antibiotics, and will:

1. Review our own manufacturing and supply chains to assess good practice in controlling releases of antibiotics into the environment.
2. Establish a common framework for managing antibiotic discharge, building on existing work such as the Pharmaceutical Supply Chain Initiative (PSCI), and start to apply it across our own manufacturing and supply chain by 2018.
3. Work with stakeholders to develop a practical mechanism to transparently demonstrate that our supply chains meet the standards in the framework.
4. Work with independent technical experts to establish science-driven, risk-based targets for discharge concentrations for antibiotics and good practice methods to reduce environmental impact of manufacturing discharges, by 2020.

Signatory companies:

Allergan	**AstraZeneca**
Cipla	**DSM Sinochem Pharmaceuticals**
F. Hoffman-La Roche Ltd., Switzerland	**GSK**
Johnson & Johnson	**Merck & Co., Inc., Kenilworth, New Jersey, U.S.A.**
Novartis	**Pfizer**
Sanofi	**Shionogi & Co., Ltd.**
Wockhardt	

Source: Industry Roadmap for Progress on Combating Antimicrobial Resistance, September 2016

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Has the facility developed and implemented waste and wastewater management practices?

Yes No

Do the practices cover:

Characterization of all wastes generated at the facility, including returned products, with regard to regulatory classification (e.g. hazardous waste, special waste, infectious waste, non-regulated solid waste, low-level radioactive waste) and hazardous properties (e.g. flammability, corrosivity, toxicity)?

Yes No

Are wastes that contain Active Pharmaceutical Ingredients (APIs) managed in such a way that the API is destroyed via that waste management method?

Yes No

Are there procedures in place to ensure that API, drug product, and branded materials are not diverted from the appropriate/authorized waste treatment/disposal method/facility?

Yes No

Does the facility have a system for collecting water from fire fighting?

Yes No

Does the facility evaluate the discharge of wastewater to surface waters, onsite treatment works or offsite treatment to determine potential Active Pharmaceutical Ingredient (API) / environmental impact?

(Evaluation may include: treatability, bioaccumulation potential, bio-toxicity potential, and the capacity of on-site treatment works, off-site treatment works, or Publicly Owned Treatment Works (POTWs) receiving the wastewater discharges to effectively perform treatment)

Yes No

Are APIs in wastewater subject to treatment, capture, and containment practices to reduce API concentrations to predicted no effect concentration (PNEC) levels?

Yes No

Extract from PSCI auditor Template to illustrate the type of questions it contains

The Pharmaceutical Supply Chain Initiative (PSCI), an association of pharmaceutical and healthcare companies who "share a vision of better social, environmental and economic outcomes in the communities where we buy"[90] and whose membership comprises 25 of the world's largest pharmaceutical brands, is also taking steps to address the environmental impacts of pharmaceutical production.

In the wake of the numerous pollution scandals which have come to light in the pharmaceutical supply chain, a PSCI team visited India in February 2017 to train suppliers and auditors in addressing environmental risks from manufacturing *inter alia*. An auditor training workshop was held in Hyderabad, with a dedicated session on pharmaceuticals in the environment and guidance on using the PSCI's audit template[91], which offers a robust basis for auditing suppliers, but which unfortunately remains voluntary.

A leadership roundtable with 40 CEOs and senior executives of Indian pharma manufacturers was also held in Visakhapatnam, a pharma manufacturing hub on the coast of Andhra Pradesh. Supported by the Andhra Pradesh Pollution Control Board and the Indian Government's Department of Pharmaceuticals, it tackled a range of topics under the broad heading of "*Green chemistry and engineering enabling greater business value for an environmentally responsible pharma supply chain*".[92] At the event, Nordea presented the bank's expectations with regard to cleaner manufacturing and improved transparency and accountability throughout the pharmaceutical supply chain.

Following the sessions with auditors and CEOs, in May 2017 PSCI organised a conference for supply chain partners in Hyderabad covering a range of topics including process safety management, environmental performance, industrial hygiene, ethics and labour. Over 150 participants representing more than 70 suppliers were present, indicating high interest among local pharmaceutical suppliers.

Despite these broadly positive developments, and evidence that some companies are beginning to take the pharmaceutical pollution crisis more seriously, a significant part of the industry remains in denial about the extent of the problem and has repeatedly hit back at evidence that pharmaceutical pollution is creating an environmental and public health crisis in India. For example, in response to the Changing Markets Foundation's findings in October 2016, the head of the drugs industry lobby group Pharmexcil (India's Pharmaceutical Export Promotion Council) stated that reports linking water pollution to factories making antibiotics were inaccurate and that drug factories were in compliance with local environmental rules [93], further claiming that "'vested interests' were campaigning against Indian pharma players in view of the 'strong' advantages and the export potential of the country going forward."[94] The team of German scientists and documentary film-makers who visited Hyderabad in late 2016 also had difficulty engaging with the companies featured in their documentary. Those few that did respond to their enquiries denied everything and questioned the findings.[95]

In May 2017, the Hyderabad-based Bulk Drug Manufacturers Association (BDMA) published preliminary findings from a two-year study on the link between pharmaceutical production and the development of drug-re-

The Indian drugs industry lobby has disputed the findings from a number of scientific investigations in Hyderabad over the past few years

(credit - Norddeutscher Rundfunk)

sistant bacteria denying that pharmaceutical manufacturing clusters (PMCs) in and around Hyderabad are playing a role in fuelling drug resistance.[96] However, commenting on the BDMA's study, the German microbiologist Christoph Lübbert highlighted several significant flaws in the analysis, and called the conclusions "questionable and inaccurate."[97] Further doubt was cast on the findings by Professor Joakim Larsson, one of the leading authorities on the link between pharmaceutical manufacturing discharges and the spread of AMR, in November 2017. [98]

Local activist and campaigner K. Chidamberum, who leads the civil society organisation Citizens for Better Patancheru Constituency was also unconvinced by the industry study: "Our groundwater continues to be contaminated and agriculture stands affected. While industrial units can claim there is no chemical discharge, the waterbodies continue to receive inflows clearly loaded with chemicals." [99]

C. Indian Pharma and the US Food and Drug Administration (USFDA)

In recent years the Indian pharmaceutical industry has set its sights on expansion into foreign export markets, making particularly striking inroads in the United States: between 2005 and 2015, Indian pharmaceutical exports to the US increased twentyfold, from US$0.3 billion to US$5.9 billion.[100]

The Economic Times of India reports that the Indian pharmaceutical industry currently earns around 50% of its revenues from exports. Of the sector's total exports of US$16.8 billion during the year 2016-17, the majority of these, accounting for 40.6% were to the American continent followed by 19.7% to Europe, 19.1% to Africa and 18.8% within Asia.[101]

According to 2014 presentation by Pharmexcil, the top 10 Indian pharmaceutical exporters are Dr. Reddy's Laboratories, Lupin, Mylan, Aurobindo, Cipla, Hetero, Sun Pharmaceuticals, Glenmark Generics, Ranbaxy Laboratories and Serum Institute of India.[102]

Aurobindo, a company which has featured prominently in several pollution scandals, makes around 44% of its sales from its US business, according to Reuter.[103] Furthermore, the company is looking to increase its market penetration over the coming years – in July 2017, The Hindu reported that it is looking to expand further into the US and Europe over the coming 3-4 years, with the aim of enlarging its share of the generics market.[104]

Other Indian players also have their sights set on expansion, especially in terms of increasing export volumes from India to the US. Their efforts will be boosted by the fact that many branded drugs are going off patent during 2017-19, which confers a special advantage on the Indian industry.[105] With this expansion comes the promise of ever-greater profits; in April 2017 the director-general of Pharmexcil predicted that Indian pharma exports will total US$20 billion a year by 2020.[106]

However, it also leaves the industry subject to international regulations and standards; as the Indian pharma industry has become more exposed to overseas markets, its financial success has become much more dependent on the approval of its products by the US Food and Drug Administration (FDA) and European medicines agencies, such as the UK's MHRA, France's ANSM and Italy's AIFA. Although inspections are currently focused on the respect of Good Manufacturing Practices (GMP), which currently exclude waste water management or other environmental indicators, several organisations, including the German Environmental Agency (UBA)[107] and the Swedish Medical Products Agency[108] have called for GMP to be extended to include environmental criteria.

Since 2012, the US FDA has stepped up its inspections in generics manufacturing countries – most notably India and China. According to the Indian online publication LiveMint, inspections in India increased from 108 in 2009 to 290 in 2015.[109] The US FDA has also expanded the scope of its inspections to reportedly include "lapses such as inappropriate clothing of employees, improper washing conditions and inadequate lighting."[110] Increased US scrutiny of its overseas pharmaceutical suppliers was part of a move to ensure that internationally manufactured products were subject to the same quality standards as US manufacturers.

Credit: Norddeutscher Rundfunk

The increase in inspections has resulted in a rise in the number of non-compliance reports issued to companies that have rattled the industry. In March 2017, the US FDA published a blog post stating that "quality issues are an ongoing challenge for the Indian pharmaceutical industry".[111] Of 42 warning letters issued by the US FDA's Office of Manufacturing Quality in 2016, nine went to Indian facilities. In the past year, a slew of observation letters have been dispatched to pharmaceutical companies including Aurobindo and Dr Reddy's.[112] Warning letters are issued when the FDA finds that a manufacturer has significantly violated FDA regulations. Observation letters, also known as Forms 483, are issued if, upon inspection of a facility, the FDA has observed any conditions or practices that may cause the product being manufactured to become adulterated or injurious to health. Upon receiving a Form 483, pharmaceutical companies must reply to the FDA outlining how they

plan to rectify these issues.

In May 2017, Hyderabad-based NGO Save Our Urban Lakes (SOUL) wrote to the head of the US FDA requesting copies of the Forms 483 served on companies in and around Hyderabad noting that the "socially and environmentally irresponsible behaviour of the bulk drug manufacturers [is] causing immense harm to human health" and urging the FDA to include the verification of waste management practices in their inspections.[113]

While US FDA inspections still fail to capture environmental impacts of pharmaceutical manufacturing, the financial impact of negative observations on the Indian pharmaceutical giants can be clearly seen. Offending companies have seen their stock price plummet in the wake of receiving FDA observations; conversely, once a company resolves the issue, its stock rises once again. The long-term damage of not remediating issues swiftly is pronounced; the Economic Times (India) estimated in February 2017 that regulatory charges from the US "wiped out nearly Rs15 billion (around EUR199 million) worth of market cap of the top five drug companies over the past one year".[114]

The financial sway of the US FDA over Indian Pharma could be a powerful tool for incentivising the clean-up of the industry. As the US FDA noted in its March blog post, "India's regulatory infrastructure must keep pace to ensure that global quality and safety demands are met."[115] And Indian Pharma companies are taking note, adapting their practices to ensure ongoing access to one of the world's largest drug markets.

D. Pharma City and local communities' resistance

In light of the persistent pollution problems, the government of the state of Telangana plans to shift polluting factories in Hyderabad to 19 land parcels (essentially villages) to a new 'Hyderabad Pharma City' at Mucherla, in the Ranga Reddy District, south of the city's outer ring road.[116] It is expected that the new site will host between 900 to 1,000 pharma companies.[117] Officials claim that the new plants will operate 'zero liquid discharge' systems and there are also plans to set up common effluent treatment plants (CETPs) with a capacity of 250 million litres a day.

In June 2017, Telangana information technology and industries minister K.T. Rama Rao made a personal pledge that "the state government itself will take care of effluents let out by companies" and also suggested that the location of the Pharma City, 40km from Hyderabad airport, and outside of the city, means that there will be less impact on local residents.[118] This seems to contradict a 2015 statement from local government officials that "villages would develop similar to Hyderabad once the Pharma City comes up."[119]

In 2015, villagers from the surrounding settlements in Mucherla, Saireddygudem, Hanmaspally, Kurmidda, Thadipatri and Kadtal launched protests against the new development[120] and India's Opposition Congress Party has raised concerns about these new plans, notably in relation to the failure to seek local inhabitants' consent[121], which is required where "red category" industries such as the pharmaceutical industry are concerned.[122] The Government's response was to call on Congress members "*not to make irrational claims that were not warranted at this juncture when several companies were venturing to put in investments in the project*" – indicating that the Government is putting financial considerations ahead of the protection of people and the environment.[123]

Officials claim that they have received inquiries "from companies across the world" keen to set up units at the Pharma City, with one senior employee at the Telangana State Industrial Infrastructure Corporation (TSIIC) stating that: "Owing to the low costs, multi-national companies are making a beeline to Pharma City".[124]

However, local residents are fearful that history will simply repeat itself. At a round table conference organised by Hyderabad-based NGO Save Our Urban Lakes (SOUL) in May 2017, local activists expressed the view that the new Pharma City will "turn the land toxic" and shift polluting industries from one area to another.[125] More recently, there have also been protests against pharmaceutical industry expansion in Nalgonda, south-east of Hyderabad[126] and Dothigudem."[127]

In October 2017, a public hearing on the environmental impact of the Pharma City was held during which a number of protesters were detained by police.[128] Former vice-chairman of the National Disaster Management Authority (NDMA) Marri Shashidhar Reddy heavily criticised the environmental impact assessment drawn up by the Environmental Protection Training and Research Institute (EPTRI) and called for a new public hearing on the basis of a more robust study. Feedback and submissions from the hearing are currently with India's ministry of environment and forests which is responsible for providing the requisite environmental clearances for the project.[129]

Batte Shankar, also known as "Musi Shankar", has been campaigning for 15 years against the pollution of the Musi River by pharmaceutical factories

Interview with Batte Shankar

The investigation team interviewed the Sarpanch[130] of the village of Edulabad, Batte Shankar, also known as "Musi Shankar" in reference to the name of the river which runs through Hyderabad. Edulabad is located a few kilometres outside Hyderabad's outer ring road and approximately 20km downstream from the discharge point of the Amberpet sewage treatment plant, often described as Asia's biggest such facility [131], on the Musi River. As well as generating enormous amounts of pollution, the plant has destroyed fishing and farming livelihoods and caused major health problems in Edulabad. Fish in the village tank regularly die when chemical effluent flows into the water body.[132]

Batte Shankar has been Sarpanch of Edulabad since 2012 and was previously a youth activist who was instrumental in campaigning and mobilising community protests about pollution of the Musi. He began working on the issue when in 2002 all the fish in the Edulabad village tank died suddenly after river pollution entered the tank. He collected water samples and had them tested at a laboratory, and the results indicated significant toxic chemical residues in the water. The villagers had begun suffering from a specific set of health problems: cancers, miscarriages, eye problems, skin conditions, brain development problems in children, and he was told that the chemicals in their river water were responsible.

He began to raise awareness in Edulabad, mobilising other villages along the Musi, and led a 5,000-strong march to the door of the Home Minister demanding that the Musi be declared a highly polluted river. The communities asked for effluent treatment plants to treat the pharmaceutical and other chemical wastes which were pouring down from Hyderabad's industrial zones into the river. The government partially acknowledged that there was a pollution problem and sanctioned the construction of a sewage treatment plant in 2002 (not the effluent treatment plant they had asked for), which was eventually constructed in 2004. A cleaning project for the river was also announced, and some potable borewells were provided for the communities affected. Shankar walked 150 km along the Musi mobilising further villages. The government then began the planning of an 18km pipeline which was intended to divert pollution from the Patancheru industrial area, a pharmaceutical manufacturing hub in Hyderabad's Medak District. This pipeline, once constructed in 2008 further severely compounded the existing pollution problems caused by effluent from other industrial zones within the valley catchment.

"The lake used to give us everything we needed. Of course, we can't say the same now […] We have been systematically denied the very basic things required for life. The air we breathe, the water we drink, and the food we eat. They're all polluted now."

Batte Shankar, Sarpanch of Edulabad - April 2017[133]

3. The investigation

This section presents results from water sampling adjacent to pharmaceutical plants and in water bodies in Hyderabad undertaken in September 2017. All samples were sent to Specialty Analytical in Oregon, United States, which provided protocols, and analysed the samples for concentrations of heavy metals and solvents commonly used in pharmaceutical manufacturing. The method used to test for solvents was US Environmental Protection Agency (US EPA) Method 8260 – a gas chromatography method which covers a wide range of solvents.[134]

Following the discovery of drug-resistant bacteria and high concentrations of APIs at some of the sites featured here by the Changing Markets Foundation and German researchers in 2016 and early 2017, the purpose of the sampling was to understand what other contaminants might be present in manufacturing discharges from pharmaceutical units in Hyderabad.

Pharmaceutical manufacturing is usually a very chemical-intensive process leading to the generation of significant quantities of toxic discharges. For example, previous studies on heavy metal concentrations in pharmaceutical effluent have found levels of lead, chromium, cadmium, zinc, cobalt, copper and nickel that were – in many cases - above the World Health Organisation recommended maximum contaminant concentration level.[135] The US EPA notes that lead and zinc are known to be used as precipitating agents.[136] Other metals used as process catalysts in pharmaceutical production include chromium, copper, nickel, palladium, platinum and rhodium.[137]

The US EPA has also identified "priority pollutants" including the solvents methylene chloride, toluene, chloroform, 1,2-dichloroethane, and phenol as being used in the manufacturing of pharmaceuticals. Solvents are used in two ways in extraction operations. Some solvents are used to remove fats and oils that would contaminate products. They are also used to extract the product itself.[138]

A. Summary of results

1. Findings

The sites sampled represent a cross-section of both plant-specific and public waterbodies. **Specifically, samples were taken at factories operated by the following pharmaceutical companies:**

- Aurobindo (Bachupally and Borpatla)
- Mylan (Pashamylaram and Jeedimetla)
- Dr Reddy's (Bollaram)
- Hetero (Gaddapotharam)
- SMS Pharma (Gaddapotharam)

And at the following waterbodies and locations:

- Isnapur Lake in Pashamylaram
- Circular tank and borewell in Gaddapotharam
- Borewell and effluent channel ('nallah') in Kazipally
- Hussain Sagar Lake in downtown Hyderabad
- Tributary of the Musi River at Edulabad
- Ramky Hazardous Waste Plant in Gaddapotharam

In comparison to previous sampling trips, it was apparent that some companies and particular plants are becoming more conscious of scrutiny over time and have adopted deterrent measures, whether enhancing their security or covering up perimeter gullies, potentially redirecting wastewater effluent underground.[139] As a result of this, fewer sample sets were collected than planned (17 out of a total of 31 visited sites). Furthermore, it was not possible to test 4 of the samples for the presence of solvents.

Sampling at Kazipally stream

Laboratory analysis identified the presence of a range of heavy metals and solvents consistent with pharmaceutical manufacturing or organic synthesis in most samples tested. In some cases, these substances were present at extremely high concentrations, orders of magnitude higher than maximum legal limits or safe exposure levels defined by the US EPA, Indian Bureau of Standards, WHO, European Union or Californian EPA. Several substances detected are associated with increased cancer risk and others with human toxicity at the levels determined in the samples. Worryingly, extremely high levels of hexavalent chromium (CrVI), a significant human carcinogen, were detected in several samples. Chromium(VI) does not break down or degrade easily and there is a high potential for accumulation in fish life.[140]

It is also important to note that many of the compounds detected are volatile, meaning there is possible inhalation exposure in addition to dermal contact or ingestion. Furthermore, there is growing concern about the possible synergistic effects of a wide variety of chemicals and pharmaceuticals that individuals could be exposed to. Combined exposure to chemical mixtures may have adverse effects on human health, even if each individual substance is below its own risk limit, and experts regard the predominant chemical-by-chemical approach currently used in risk assessment as insufficient to protect against the risks of combination effects.[141]

While the findings presented here only offer a snapshot of the situation in Hyderabad, it is clear that the wide range of chemicals at the levels detected by the laboratory is a result of improper wastewater and effluent management by industry. While some of the samples tested clearly point to the responsibility of the pharmaceutical industry as a source, with other samples, notably those taken from public water bodies, it is less clear which industry is responsible for the presence of these toxic substances. The pharmaceutical industry is not the only industry operating in the areas investigated. It has, however, been repeatedly exposed for improper waste management and even illegal waste dumping, as described in detail in previous chapters of this report.

Chemical profiles and regulatory limits for heavy metals and solvents investigated in this report are presented in the Annex

Findings for each site are presented below.

The information presented should be interpreted as follows:

Grey text: substance relevant to pharmaceutical manufacturing detected. While most of the heavy metals profiled are naturally occurring and can be expected to be present in the environment at moderate levels, the presence of solvents (which are man-made substances) at any level is indicative of industrial activity and poor/absent waste treatment.

Orange text: substance relevant to pharmaceutical manufacturing is present at levels above maximum contaminant or safe exposure limits defined by the US EPA, Indian Bureau of Standards, WHO, European Union or Californian EPA.

Red text: substance relevant to pharmaceutical manufacturing is present at very high levels exceeding maximum contaminant or safe exposure limits defined by the US EPA, Indian Bureau of Standards, WHO, European Union, or Californian EPA. All Hexavalent Chromium levels and the vinyl chloride reading are highlighted in red given their extreme toxicity.

Aurobindo III, Bachupally

The team sampled at the plant's front perimeter gully, which contained blackish flowing water and sediment, apparently emanating from the site.

The following substances were detected:

Arsenic: 3µg/l	Nickel: 32.4µg/l
Cadmium: 0.419µg/l	Zinc: 1280 µg/l
Copper: 341µg/l	Hexavalent Chromium: 16.1µg/l

Mylan III, Bachupally

The team had previously encountered high security at this site. However due to the monsoon there was some vegetation cover which enabled them to be shielded from the guardhouse at the front of the site and they were able to collect samples of black, deep fast-flowing water apparently emanating from the site.

The following substances were detected:

Arsenic: 8.41µg/l	Nickel: 4030µg/l
Cadmium: 2.73µg/l	Zinc: 5180µg/l
Copper: 5350 µg/l	Hexavalent chromium: 12.7µg/l

Mylan VII, Pashamylaram

This very large site is entered through a gate and has a high security presence and covered perimeter gullies. However the team managed to find an apparent effluent outlet to sample, emanating from under a perimeter wall at the back of the plant where it is bordered by wasteland. The wastewater was seeping from under the wall and had collected in a sizeable set of stagnant puddles as well as spreading out and sinking down into the surrounding boggy grass and weeds.

The following substances were detected:

Arsenic: 12.2µg/l	Benzene: 0.770µg/l
Cadmium: 0.162 µg/l	Toluene: 1.07µg/l
Copper: 77.4 µg/l	MTBE: 1.51µg/l
Nickel: 77.2µg/l	diisopropyl ether: 5.01µg/l
Zinc: 295µg/l	Isopropyl alcohol: 3.95µg/l
Hexavalent chromium: 22.8µg/l	trimethylsilyl fluoride 2.42µg/l
Acetone: 56.4µg/l	

Isnapur Lake, Pashamylaram

Isnapur Lake is located next to a large industrial area (Pashamylaram) which is home to numerous pharmaceutical companies as well as other industries. Local farmers water their livestock here (goats, cattle, waterbuffalo). The lake was very full due to monsoon rains. The team sampled at the point where the outlet from the Pashamylaram zone enters the lake itself from a nallah of fast-flowing blackish oily wastewater emerging from under the road.

The following substances were detected:

Arsenic: 12.3µg/l	Cadmium: 0.293µg/l
Copper: 41.4µg/l	Nickel: 414µg/l
Zinc: 296µg/l	Hexavalent chromium: 30.4µg/l
Acetone: 696µg/l	2-butanone: 57.8µg/l

Isnapur Lake is located next to a large industrial area

Benzene:0.430µg/l	Carbon disulfide: 33.8µg/l
Chlorobenzene: 3.23µg/l	Chloroform: 1.53µg/l
MTBE: 9.39µg/l	Toluene: 2.06µg/l
4,4-dimethyl-2-pentanone: 3.17µg/l	Dimethyl sulfide: 15.8µg/l
Isopropyl alcohol: 3.41µg/l	Sulfur dioxide: 100µg/l

Aurobindo IA, Borpatla

This is a vast and modern-looking site, a long way out from the older industrial zones, in the middle of a rural agricultural area, and with no other industrial plants visible nearby. There is very tight security. The footprint of the site is enormous and not all currently being used, but extensive groundworks are underway in some areas indicating new areas of expansion of the main buildings. There is a large pond of apparent effluent, with a strong chemical smell at the rear of the plant. The effluent may be reaching the pond via seepage from underground, or via underground pipes. According to an informant, in the rainy season the company dumps more blatantly into this external area via open pipe mouth holes which are visible in their perimeter wall.

The effluent lake behind the plant was considerably larger than on the previous visit, and full of black water. The team sampled at the lake edge. There are no other buildings anywhere near this lake and there is therefore a direct link to the company.

The following substances were detected:

Arsenic: 6.35µg/l	Copper: 30.2µg/l
Nickel: 46.1µg/l	Zinc: 79.7µg/l
Hexavalent chromium: 11.1µg/l	Acetone: 1090µg/l

The lake behind Aurobindo's Pharma Unit 1 is thickly coated in black tarry sediment

Closeup of the effluent at Kazipally tank

3,3,5-trimethylcyclohexanone: 3.70µg/l	diisopropyl ether: 7.81µg/l
Hexanal: 19.5µg/l	Isopropyl alcohol: 2.42µg/l
Pentanal: 2.64µg/l	Propanal: 4.35µg/l
Sulfur dioxide: 59.6µg/l	tert-butyldimethylsilanol: 2.94µg/l

Kazipally village borewell

The team sampled at the village borewell (sponsored by Hetero Labs), which is potentially in the same ground aquifer as the highly polluted borewell at Gaddopatharam village close by. A local said that the water was used for secondary purposes such as clothes washing, but another source told us that the water is not used for anything by the villagers – however it has not been sealed and the electricity has not been turned off. This is the case both for this well and for the borewell in Gaddopatharam village (see below). One explanation for not sealing the wells and shutting off the electricity supply to the pumps might be that if the PCB closes a well this would be an admission of the existence of a serious problem, which would imply some form of restitution and compensation.

The following substances were detected:

Arsenic: 1.18µg/l	Copper: 0.964µg/l
Zinc: 9.88µg/l	Acetone: 68.4µg/l
Isopropyl alcohol: 3µg/l	Sulfur dioxide: 55.3µg/l

Kazipally tank (effluent channel/nallah)

The team visited the large tank located at the edge of the village which has previously received the down flow of effluent from the Gaddopatharam industrial zone above at the head of the valley. This is not a concrete tank, but a manmade reservoir with earth banks. Due to campaigning by the villagers the effluent flow has now been rerouted through a new channel which bypasses the tank and continues on down the valley. At the same time the tank itself has had its lower side banks reinforced and now only a small outflow stream runs out of the tank, which is now theoretically only rainwater-fed. The team sampled at the new channel, which was filled with fast-flowing black water with a very strong and unpleasant chemical smell. The team tracked this open nallah as it passed the village, and were told that it continues down the valley, flowing on to Gandigudem lake, scene of a recent pollution leak and the mass death of thousands of fish, then on to Krishnareddy PET tank, then to the Isukavagu nallah which flows into the Manjira River, which is a tributary of the Godavari River.

The following substances were detected:

Arsenic: 862µg/l	Cadmium: 0.598µg/l
Copper: 317µg/l	Nickel: 370 µg/l
Zinc: 410µg/l	Hexavalent chromium: 19.5µg/l
2-butanone: 10.6µg/l	Benzene: 0.410µg/l
Carbon disulfide: 6.28µg/l	MTBE: 1.43µg/l
Toluene: 3.31µg/l	Chloroform: 4.24µg/l
Acetone: 7590µg/l	1,4-Dioxane: 6.11µg/l
1-Butanol: 29.3µg/l	2-Methyl-2-propanol: 23.6µg/l
2-methylcyclohexanone: 5.08µg/l	Dimethyl sulfide: 186µg/l
dimethyldisulfide: 8.34µg/l	Isopropyl alcohol: 85.3µg/l
methylthiobenzene: 2.72µg/l	triethylsilanol: 4.55µg/l
trimethylsilyl fluoride: 38.8µg/l	

Following the mass death of over 200,000 fish in Hyderabad's Gandigudem Lake in October 2017, a local official confirmed that "Preliminary findings suggest toxic chemicals from Kazipally Industrial area as cause of fishkill."[142] As a result of this, 14 companies in the Gaddapotharam and Kazipally industrial areas, most of which are pharmaceutical units, were issued with closure orders by the Telangana State Pollution Control Board. However, official documents seen by Changing Markets show that 15 other companies, including Hetero Pharma, Aurobindo and Mylan, which were earlier named in criminal charges brought by the local Fishermen Cooperative Society,[143] and which have consistently demonstrated poor environmental performance, escaped closure on the grounds that no harmful discharges were found.

Kazipally tank

Dr Reddy's I, Bollaram

The team sampled at a rear perimeter gully. The gully contained clearish shallow flowing water apparently emanating from the site. The plant is located in a highly degraded long-established industrial zone, which houses many heavily polluting industries including cement, paint, and chemicals.

The following substances were detected:

Arsenic: 3.17µg/l	Cadmium: 0.402µg/l
Copper: 12.1µg/l	Nickel:17.4µg/l
Zinc: 88.9µg/l	Mercury: 0.000267µg/l

Dr Reddy's II, Bollaram

The team sampled at a front perimeter gully, containing black sediment and flowing water apparently emanating from the site. There was high security at this site. The plant is located in a highly degraded long-established industrial zone, which houses many heavily polluting industries including cement, paint, and chemicals.

The following substances were detected:

Arsenic: 13.3µg/l	Cadmium: 18.4µg/l
Copper: 563µg/l	Nickel: 271µg/l
Zinc: 2360µg/l	Hexavalent chromium: 21.1µg/l

Gaddopatharam village borewell

The water from the borewell is bright yellow. In April 2017, villagers told the investigation team that it is undrinkable, and is not now even considered safe to use for "secondary purposes" such as clothes washing, since it gives the women skin conditions on their hands. For the same reason it is deemed unsuitable for watering animals or crops (in any case the villagers no longer grow viable crops since their soil is poisoned). The men explained that since their land is unusable, they are forced to work in the Gaddapotharam factories, but they are never given regular jobs, only intermittent and piecemeal "contract work". As a rule the factories do not employ locals for their regular manual work, they prefer to employ impoverished Bihari and other migrant workers as it is felt that locals will potentially mobilise and create labour problems.

Residents of Gaddapotharam village are forced to buy water even for secondary domestic purposes, as their own borewell water has become contaminated

These villagers now receive their "secondary purpose" water from another borewell some 2km away up above the zone – from an overhead water tank. Even this water is considered to be undrinkable, and drinking water is brought in by tanker (filtered/treated water from the Manjira tributary). They pay 5 INR per 20 litre can – and use 2 cans per day. They feel very bitter about the situation but perceive that regardless of which political leaders are in power, nothing will change for them. They reported that the PCB has taken samples from this borewell, but nothing happened as a result.

The team was told by a villager that the PCB have never sealed this pump, it is the villagers themselves who have taken the decision not to use it because environmental activists have warned them that it is dangerous.

The following substances were detected:

Arsenic: 5µg/l	Cadmium: 0.142µg/l
Copper: 0.899µg/l	Nickel: 10.5µg/l
Zinc: 669µg/l	Hexavalent chromium: 10900µg/l
Benzene: 127µg/l	1,2-Dichlorobenzene: 1.59µg/l

1,2-Dichloroethane: 21.8µg/l	1,2-Dichloropropane: 1.02µg/l
1,3-Dichlorobenzene: 2.99µg/l	1,4-Dichlorobenzene: 2.34µg/l
Chlorobenzene: 1780µg/l	Chloroform: 7.65µg/l
cis-1,2-Dichloroethene: 24.9µg/l	Isopropylbenzene: 1.85µg/l
MTBE: 13.6µg/l	Tetrachloroethene:13.9µg/l
Toluene: 1.89µg/l	Trichloroethene: 7.98µg/l

Laboratory testing found heavy metals and solvents present in the water of this common effluent tank at Gaddapotharam. Previous testing has also found antimicrobials and drug-resistant bacteria

Vinyl chloride: 24.7µg/l	diisopropyl ether: 96.9µg/l
Isopropyl alcohol: 21.3µg/l	trimethylsilyl fluoride: 40.7µg/l

It is important to note the extraordinarily high level of hexavalent chromium which was detected here, as well as the high levels of some solvents, including vinyl chloride.

Circular tank, Gaddapotharam

The circular tank is located at the corner of the Gaddapotharam industrial area (IA) close to the Hetero I and SMS Pharma sites (see below). As reported by The Hindu in November 2017, this tank is meant to serve as a temporary containment facility for toxic effluents from a dozen pharmaceutical companies. The effluent is then transferred from the tank to Patancheru Enviro Tech Limited (PETL), an effluent treatment plant around 20 km away, where it will be treated and released into Hyderabad's Musi river. However, as the article points out, it is not leak-proof and: "A natural rivulet takes the fluid in the well to the nearby Gandigudem lake, where

Kazipally's residents — mostly farmers and some pharma industry workers — raise fish to sell."[144]

Indeed, the investigation team witnessed first-hand how wastewater is channeled out of the IA from this well, and down into an open nallah which then heads down the valley towards the little village of Kazipally below (the Gaddopatharam IA is also called by some the Kazipally IA because of the village which is below it).

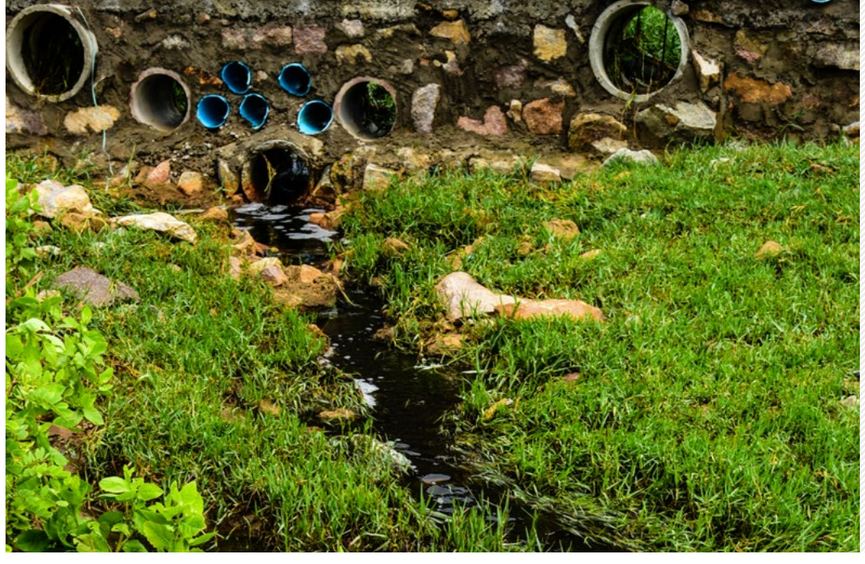
It is possible that wastewater from other pharma sites and industries will also be entering this well via interlinking gullies. The team sampled at the fast-flowing channel of black effluent that goes around the side of the stagnant tank, and continues on down towards Kazipally village tank.

The following substances were detected:

Arsenic: 441µg/l	Cadmium: 0.491µg/l
Copper: 30.2µg/l	Nickel: 208µg/l
Zinc: 482µg/l	Hexavalent chromium: 6.85µg/l
1,2-Dichloroethane: 5.05µg/l	2-Butanone: 42.9µg/l
4-Methyl-2-pentanone: 68.5µg/l	Benzene: 29µg/l
Chloroform: 324µg/l	MTBE: 97.9µg/l
Methylene chloride (Dichloromethane): 874µg/l	Acetone: 16700µg/l
Chloromethane: 2.02µg/l[145]	Bromochloromethane: 5.13µg/l
Carbon disulfide: 2.89µg/l	Chlorobenzene: 7.57µg/l
o-Xylene: 11.1µg/l	Toluene: 304µg/l
1,-Dioxane: 12.5µg/l	1-methylethyl ester acetic acid: 32.4µg/l
2-Methyl-2-propanol: 62.4µg/l	2-Methylcyclohexanone: 20.7µg/l
Acetonitrile: 76.4µg/l	diisopropyl ether: 107µg/l
Dimethyl sulfide: 345µg/l	hexaethyldisiloxane: 11.5µg/l
methyl ester acetic acid: 162µg/l	Tetrahydrofuran: 525µg/l
triethylfluorosilane: 13.9µg/l	triethylsilanol: 77.1µg/l
trimethylsilyl fluoride: 51.2µg/l	

Ramky Hazardous Waste Plant, Gaddopatharam

The Ramky plant is at the edge of the Gaddopatharm IA which contains multiple industries including pharmaceutical factories. The team entered waste ground at the rear of the plant. A steady stream of apparent effluent was



Effluent outlet pipes behind Ramky Hazardous Waste Plant

emerging from a pipe set into the wall of the plant, quite close to the roadside corner. The team went further along the perimeter wall and came to another point where multiple pipes were emerging from the same wall, and a much larger flow of black chemical-smelling water was flowing steadily from the plant into streams which stretched away across the waste ground forming stagnant pools and puddles. The sample was taken here, as close as possible to the wall. In April 2017, a local informant told the team he had personally witnessed tankers coming out of the zone on a regular basis in the evenings and dumping waste into the wasteland behind the Ramky plant.

The following substances were detected:

Arsenic: 51.7µg/l	Cadmium: 8.23µg/l
Nickel: 182µg/l	Hexavalent chromium: 6.01 µg/l
Zinc: 132µg/l	Copper: 28.8µg/l
Platinum: 0.130µg/l	Acetone: 522µg/l
Chloromethane: 1.09µg/l[146]	2-Butanone: 20.5µg/l
2-Methyl-2-propanol: 8.08µg/l	Dimethyl disulfide: 6.65µg/l
Dimethyl sulfide: 647µg/l	Isopropyl alcohol: 140µg/l
methyl ester acetic acid: 7.48µg/l	methylthiobenzene: 5.04µg/l
trimethylsilyl fluoride: 17.9µg/l	

Hetero I, Gaddapotharam

The team accessed the site from the rear, and took water samples from a location where apparent effluent exits the Hetero plant from a gully leading under the side gate. There was high security in operation at the plant, and the team were followed at a distance by personnel from the site.

The following substances were detected:

Arsenic: 28.7µg/l	Nickel: 124µg/l
Zinc: 45µg/l	Copper: 3.85µg/l
Hexavalent chromium: 5.17µg/l	1,2 Dichloroethane: 208µg/l
Benzene: 128µg/l	MTBE: 20.1µg/l
Methylene chloride (Dichloromethane): 33.1µg/l	Acetone: 896µg/l
Chloromethane: 4.69µg/l[147]	1,2-Dichlorobenzene: 1.73µg/l
Bromomethane: 3.76µg/l	Chlorobenzene: 10.5µg/l
Toluene: 5.53µg/l	1,4-Dioxane: 37.4µg/l
2,2,2-Trifluoroethanol: 7.54µg/l	diisopropyl ether: 30.4µg/l
Dimethyl sulfide: 723µg/l	isoproyl phenyl ketone: 8.55µg/l
trifluoromethylbenzene: 139µg/l	trimethyl silanol: 11.9µg/l
trimethyl silyl fluoride: 13.3µg/l	

SMS Pharma, Gaddapotharam

The team returned to the SMS Pharma site where they had earlier been threatened by security at the gate. This time they used a public access alleyway running along a side wall and managed to collect a sample without being seen. They were able to see apparent effluent clearly seeping from under the plant wall halfway along the alleyway, and collecting in puddles in the grass.

The following substances were detected:

Arsenic: 18µg/l	Zinc: 87.3µg/l
Cadmium: 0.270µg/l	Copper: 32µg/l
Nickel: 45.4µg/l	Toluene: 32300µg/l
Acetone: 4880µg/l	Chloromethane: 1.03µg/l[148]
4-Methyl-2-pentanone: 6200µg/l	Benzene: 1.62µg/l
Carbon disulfide: 4.41µg/l	Ethylbenzene: 2.18µg/l
4-Methyl-2-pentanol: 93.5µg/l	Benzaldehyde: 21.3µg/l
diisopropyl ether: 133µg/l	Dimethyl sulfide: 302µg/l
Isopropyl alcohol: 43.8µg/l	

Musi River, Edulabad

The team sampled at a spot, where a road crosses the river. Due to monsoon weather the river level was virtually as high as the road, and covered in effluent foam. There are many paddy fields in this area. Borewells in the village are no longer used for drinking or secondary purpose water, all water is brought in from the Manjira River.

Closeup of foam in the Musi River in Hyderabad

The following substances were detected:

Zinc: 25.6µg/l	Arsenic: 1.13µg/l
Cadmium: 2.03µg/l	Copper: 9.08µg/l
Nickel: 4.51µg/l	Hexavalent chromium: 9.38µg/l

Hussain Sagar Lake, Hyderabad

The team sampled from a spot at the corner of the lake. The lake level was very high following heavy monsoon rain.

The following substances were detected:

Arsenic: 0.776µg/l	Cadmium: 1.17µg/l
Copper: 1.74µg/l	Nickel: 3.39µg/l
Zinc: 8.52µg/l	Hexavalent chromium: 6.85µg/l
1,2-Dichloroethane: 3.47µg/l	Isopropyl alcohol: 3.16µg/l

Nallah beside Hussain Sagar Lake, Hyderabad

The team sampled at the point where there is a fast-flowing stream of blackish water coming from the Jeedimetla zone, before the junction where it joins with the lake water and flows on down towards Golnaka I&D.

The following substances were detected:

Arsenic: 7.29µg/l	Cadmium: 303µg/l
Nickel: 78.3µg/l	Copper: 538µg/l
Zinc: 2230µg/l	Hexavalent chromium: 6.85µg/l
Acetone: 614µg/l	1,2-Dichloroethane: 2.65µg/l
4-Methyl-2-pentanone: 20.4µg/l	Chloroform: 23.4µg/l
o-Xylene: 4.60µg/l	Toluene: 40.2µg/l
2-hexanol: 1.76µg/l	Dimethyl sulfide: 19.9µg/l
	Sulfur dioxide: 33µg/l

2. Discussion of results

These are troubling results indicating significant potential risk to human health, evidence of which many villagers described to the investigators. Toxic chemicals can be especially harmful to more vulnerable parts of the population, such as children and pregnant women. In addition, it is well documented that these chemicals also cause disruption of ecosystems, which often results in a loss of livelihoods for local villagers, as demonstrated by repeated incidents such as massive fish die-off, and acute poisoning of soils, which prevents agricultural activity and causes disease and miscarriages in livestock.

Many samples showed the presence of volatile synthetic organic compounds* (SOC), most frequently several SOCs were found. The resultant compounds are often found from industrial discharges or waste materials. Chlorinated solvents, including break-down products, were noted. These chemicals have a significant human toxicity/cancer risk, both from ingestion and inhalation. The levels indicate little treatment of the solvents is occurring, or very heavy burdens of these solvents are overwhelming the waste treatment technology in use.

For some chemicals, the risk is less known, as many of these compounds are less studied for human/ecological risk, but certainly exists. The presence of Acetone, 2-butanone, MTBE, and chlorinated chemicals other than Tetrachloroethene, trichloroethene, 1,2-dichloroethane, and vinyl chloride are typical for pharmaceutical or chemical synthesis manufacturing. The latter 3 compounds are degreasing solvents associated with general industrial processes, but have a higher associated risk (cancer) than many of the other detected compounds.

The presence of mixtures of chemicals shows a lack of adequate water treatment prior to discharge (or potentially no treatment whatsoever). Depending on the water flow in receiving water bodies, and the distance from the effluent source, the actual concentrations of these chemicals from the discharge source could be many magnitudes greater that the concentrations detected in samples.

Hexavalent chromium was detected in a number of locations. Chromium(VI) is a significant human carcinogen, and levels determined indicate a major risk. There is a tendency for most hexavalent chromium to undergo natural attenuation and convert in most cases to less toxic trivalent chromium. The fact that hexavalent chromium is present can be indicative of long-term disposal of high concentration waste, or ongoing contributions from sources. Overall, the samples presented have significant chemical contamination, presenting a substantial human and ecological risk potential. Through ingestion and inhalation (due to the high volatility of the solvents), and in some cases dermal absorption, risk is present. Minimising human contact to this water is highly recommended.

** Volatile organic compounds are chemical solvents or cleaners (and their byproducts) that are derived from petroleum products. They are man-made contaminants that arise from industrial processes.*

Overview of results from recent studies investigating pharmaceutical pollution in Hyderabad

Locations	Sampling sites	Findings from Gothwal and Shashidhar paper (2016)	Changing Markets investigation (October 2016)	Findings from Lübbert study in Infection journal (2017)	Changing Markets investigation (September 2017)
		Tested for concentration of antimicrobials	*Tested for bacteria resistant to specific antibiotics*	*Tested for drug-resistant bacteria and concentration of antimicrobials*	*Tested for heavy metals and solvents (heavy metals indicated were found at levels above regulatory limits, as were many solvents)*
Bachupally / Jeedimetla	Mylan III	–	–	–	Hexavalent Chromium, Zinc, Nickel, Copper
	Aurobindo III	–	–	–	Zinc, Hexavalent Chromium, Nickel
Borpatla Zone	Aurobindo IA (site perimeter)	–	–	–	Hexavalent Chromium, Nickel , Zinc, Solvents
Rudraram Zone	MSN Pharmachem (Rudraram)	–	–	Resistant bacteria and antimicrobials detected	–
	MSN Pharmachem	–	–	Resistant bacteria and antimicrobials detected	–
Pashamylaram Zone	Isnapur Lake	–	Resistance to cephalosphorins and fluoroquinolones detected	Resistant bacteria and antimicrobials detected (including highest reading of fluconazole ever recorded in the environment)	Arsenic, Nickel, Zinc, Hexavalent Chromium, Solvents
	Mylan VII	–	–	–	Arsenic, Nickel, Zinc, Hexavalent Chromium, Solvents
Patancheru/ Bollaram Zone	Dr Reddy's II	–	–	–	Nickel, Zinc,Hexavalent Chromium
Gaddapotharam Zone	Mylan I	–	Resistance to cephalosphorins and fluoroquinolones detected at large lake in vicinty of plant	–	–
	Borewell in Gaddapotharam village	–	–	–	Zinc, Hexavalent Chromium, Solvents Arsenic, Cadmium
	Circular well/tank Gaddopatharam	–	Resistance to fluoroquinolones detected	Resistant bacteria and antimicrobials detected	Arsenic, Nickel, Hexavalent Chromium, Solvents, Zinc
	Ramky Hazardous Waste Plant	–	Resistance to cephalosphorins detected	–	Arsenic, Cadmium, Nickel, Hexavalent Chromium, Solvents

Locations	Sampling sites	Findings from Gothwal and Shashidhar paper (2016)	Changing Markets investigation (October 2016)	Findings from Lübbert study in Infection journal (2017)	Changing Markets investigation (September 2017)
		Tested for concentration of antimicrobials	*Tested for bacteria resistant to specific antibiotics*	*Tested for drug-resistant bacteria and concentration of antimicrobials*	*Tested for heavy metals and solvents (heavy metals indicated were found at levels above regulatory limits, as were many solvents)*
	Hetero I	–	–	–	Arsenic, Nickel, Hexavalent Chromium, Solvents
Gaddapotharam Zone	Borewell in Kazipally Village	–	–	–	Solvents
	SMS Pharma Unit 1	–	–	–	Arsenic, Nickel, Solvents
	Effluent channel, Kazipally Village	–	Resistance to cephalosphorins and fluoroquinolones detected	–	Arsenic, Nickel, Zinc, Hexavalent Chromium, Solvents
Bonthapally Zone	Hetero	–	Resistance to cephalosphorins detected	–	–
Central Hyderabad	Hussain Sagar Lake (channel leading to Golnaka I&D)	–	Resistance to cephalosphorins and fluoroquinolones detected	–	Hexavalent Chromium, Solvents
	Hussain Sagar Lake (nallah)	–	Resistance to cephalosphorins and fluoroquinolones detected	–	Cadmium, Nickel, Zinc, Hexavalent Chromium, Solvents
	Golnaka I&D	–	Resistance to cephalosphorins and fluoroquinolones detected	–	–
	Amberpet STP side outlet	–	Resistance to cephalosphorins, carbapenems and fluoroquinolones detected	–	–
	Amberpet STP discharge pipemouth	7 types of fluoroquinolones detected (including extremely high levels of ciprofloxacin)	Resistance to cephalosphorins, carbapenems and fluoroquinolones detected	–	–
Musi/ Edulabad Zone	Musi tributary at Edulabad bridge	–	Resistance to cephalosphorins, carbapenems and fluoroquinolones detected	–	Hexavalent Chromium
	Paddy field near Musi	7 types of fluoroquinolones detected	–	–	–
Polepally Zone	Aurobindo Unit VII	–	Resistance to cephalosphorins, carbapenems and fluoroquinolones detected	–	–

The global reach of Hyderabad's pharmaceutical industry

A substantial share of pharmaceuticals produced in Hyderabad and other manufacturing hubs across India are ending up in the hands of western consumers via health service providers and multinational pharmaceutical companies. As a series of recent reports have shown, global pharmaceutical supply chains are extremely complex and opaque, so mapping the journey of a pharmaceutical product from factory to pharmacy shelf is a challenging task. However, detailed examination of publicly available supply chain data, and evidence obtained through Freedom of Information (FOI) requests, has uncovered how antibiotics manufactured by companies in India and China (where the majority of the world's APIs are produced) are being exported to European and US markets, including the United Kingdom's National Health Service (NHS), French hospitals, German healthcare companies and US pharma giants CVS, Pfizer and McKesson.[149]

Supply chain case study: Aurobindo

AUROBINDO
Committed to healthier life!

Based in Hyderabad, Aurobindo Pharma Ltd. is one of India's largest vertically integrated pharmaceutical companies and its 4th largest producer of generic drugs.[150] Specialising in anti-infectives, it manufactures both active pharmaceutical ingredients (APIs) and finished dose products. Through its large network of subsidiaries, the company has a significant global presence, employing 15,000 people from over 30 countries[151], and exporting products to over 150 countries around the world. Its commercial focus is on export markets, with more than 87% of its revenues derived from international activities.[152] Drug production is mainly located around Hyderabad (18 manufacturing facilities) but the company also has manufacturing capacity in other parts of the world (3 manufacturing facilities in the U.S., 1 in Brazil).

Aurobindo has a sizeable market presence in the U.S., both through its own brands and those of its customers. Customs data shows multiple exports to the U.S. from Aurobindo's plants in Hyderabad. For example, in July 2016, a consignment of over 9 tonnes of the antibiotic Amoxicillin clavulanate potassium from Aurobindo's Unit VII plant in Polepally, a site identified in the Changing Markets Foundation's "Superbugs in the Supply Chain" report[153] as harbouring drug-resistant bacteria, arrived at Aurobindo's U.S. subsidiary Aurobindo Pharma USA, Inc..[154] In April 2015, over 8 tonnes of Amoxicillin clavulanate potassium were shipped from Aurobindo's Unit VII directly to U.S. pharma distribution giant McKesson, whose major customers include the retail giant CVS.[155] The combination of Amoxicillin and clavulanate potassium is used to treat a range of different infections, such as sinusitis, pneumonia, ear infections, bronchitis, urinary tract infections, and infections of the skin. Aurobindo's Units III, V, and XII in Bachupally, and its Unit VI in Chitkul also frequently export antibiotics to McKesson. All of these plants are located a short distance away from the critically polluted industrial area of Patancheru on the outskirts of Hyderabad.

Aurobindo also has numerous links with EU markets both through its own subsidiaries and through drugs supplied to third parties. In France, for example, Aurobindo products are sold under the brand name Arrow Génériques, while in the UK they are marketed under various brands including Milpharm Ltd., Actavis, Arrow, and Aurobindo. Across Western Europe (specifically in France, Italy, Spain, Portugal, Belgium, Germany and the Netherlands) it sells Indian-manufactured drugs under the Actavis brand[156], following its purchase of Actavis' European operations in 2014 – although some of those brands have since been merged with others. This is the case of Arrow Génériques, for example, which has superseded Actavis France. Through these different brands, Aurobindo markets its products to many large purchasers of antibiotics, including the UK's National Health Service (NHS) and French hospitals.[157]

Through information gained from freedom of information (FOI) requests filed in summer 2016, it was revealed that Milpharm, Actavis, Arrow, and Aurobindo-branded antibiotics are being purchased by Barts Health and Cheshire & Wirral Partnership NHS Trusts. For example, Barts Health NHS Trust has Milpharm (for Cefalexin, Co-Amoxiclav, Flucloxacillin, and Valaciclovir) among its listed suppliers. The Cheshire and Wirral Partnership NHS Trust purchases Co-Amoxiclav from Aurobindo, as well as Cefalexin from Arrow Generics.

In addition to sales of its own branded drugs, Aurobindo also exports APIs to third party importers in the EU. For example, its Unit I facility in Medak District, on the outskirts of Hyderabad, appears in EU import registrations for the antibiotic Cefuroxime issued to companies based in Greece, Cyprus, and Poland.[158]

Young girl with a bottle of contaminated groundwater, Gaddapotharam village

4. Policy Developments

While clearly a key element in tackling environmental pollution in the pharmaceutical supply chain, industry self-regulation has not been enough to change the situation on the ground. Voluntary measures typically lack a robust framework for tracking progress, a strict timeline or sanctions for bad behavior.

Despite promising statements of intent from some industry players, the reality is that most pharmaceutical companies are failing to curb irresponsible practices in their supply chains. What is more, the GMP framework, which is a condition for market access to lucrative EU and US markets does not take into account the environmental damage of pharmaceutical manufacturing in third countries. As the German documentary "*The invisible enemy – deadly superbugs from pharma factories*" clearly shows, foreign inspections frequently take place at polluting factories in Hyderabad and elsewhere but there is no scope for inspectors to make any observations about pollution they encounter at these sites. Incorporating environmental criteria into GMP was already identified as the best possible way forward by the Swedish Medical Agency in 2011.[159] It would provide a level playing field and ensure at the very least that regular independent inspections take place at those factories producing drugs for export.

The regulation of environmental emissions from the pharmaceutical industry is still in its infancy. Because most production of pharmaceutical APIs and raw materials takes place in developing and emerging countries where civil society is not as empowered to speak out against environmental scandals, problematic issues surrounding pharmaceutical production usually pass below the radar in the rich countries where many of these medicines are sold.

However, with global consumption of medicines rising year-on-year in step with a growing and ageing population, and the spotlight being shone on pollution in the pharmaceutical supply chain, more and more stakeholders are invoking the precautionary principle[160] in a bid to convince policymakers to crack down on environmental pollution. This is especially relevant in the light of evidence that antibiotic pollution contributes to the AMR crisis.

With regulators increasingly focused on adopting a "one health" approach in recognition of the fact that many interconnected factors (social, economic, environmental) affect human health, there are a number of existing and emerging policy and regulatory levers which will affect the way environmental concentrations of pharmaceutical substances are regulated in the coming years. This section will provide an overview of these, with a focus on the European Union, where policy-makers are currently exploring how to address this issue.

A. European Union

Legal obligations and civil society pressure have led to the adoption of two successive EU AMR action plans in 2011 and 2017 and will lead to a *Strategic approach to pharmaceuticals in the environment* in early 2018.[161]

The European Commission's own *Study on the risks of environmental effects of medicinal products* showed that pharmaceutical pollution is a significant problem for ecosystems and human health. Published in 2013, in preparation for the strategic approach, it noted that, while the pharmaceutical industry downplays the role production of pharmaceutical substances plays in their discharge into the environment, the amount of API releases from production facilities is "largely unknown." What is more, "Releases during manufacturing in non-EU countries, even if not directly linked with environmental effects on the EU territory, might be of relevance for the EU. In a globalised world EU citizens can be affected by the antimicrobial resistance developed in populations from those countries, notably in the case of antibiotics."[162]

The Swedish approach

In 2012, Sweden became the first country in the world to introduce environmental criteria into national contracts with pharmaceutical suppliers. Since then, Swedish procurement guidelines have contained special contract terms relating to the minimisation of environmental impacts in the manufacturing of pharmaceutical products.[163]

Under these terms, producers have to implement any necessary changes to procedures for minimising environmental impact within six months of signing a procurement contract.[164] The National Agency for Public Procurement guidelines state that necessary precautions include: adhering to national environmental, and health and safety legislation; control of discharges onto land and into water from the manufacturing plant (and frequency of reporting these measures); and open dialogue between contractors and suppliers with regard to their control over chemical discharges.[165] Additionally, and crucially, the procurement agreement includes a clause allowing for purchasers to inspect suppliers' facilities, either in person or via a third party.

As outlined by the Medical Products Agency of Sweden in 2011, the best way to proceed would have been to insert environmental controls into the framework of EU GMP as within that framework there already exists a well-developed and well-functioning inspection system for monitoring manufacturing.[166] However, since GMP can only be amended at the EU level, Sweden decided to proceed with public procurement measures as an intermediate tool to influence suppliers' behaviour.

EU action plan against the rising threats from Antimicrobial Resistance

As part of its "One Health" approach, the European Commission has to date adopted two five-year action plans to combat the rising threat of AMR. The first action plan ran from 2011 to 2016 and had 12 action points including cooperation with international partners regarding "reduction of the environmental pollution by antimicrobial medicines particularly from production facilities." With no evidence of progress on this action point (and many others) during the lifetime of the first plan, a new EU action plan on antimicrobial resistance was published in June 2017.[167]

The new EU AMR Action Plan notes that "The environment is increasingly acknowledged as a contributor to the development and spread of AMR in humans and animals, in particular in high risk areas due to human, animal and manufacturing waste streams, but strong evidence is still required to better inform decision-making in this area." It further states: "...the release of antimicrobials into the environment through human, animal

Hussain Sagar Lake, the largest water body in Hyderabad, started foaming in November 2017

An outflow into Isnapur Lake from the Common Effluent Treatment Plant (CETP)

and manufacturing waste streams should be assessed and new technologies developed to enable efficient and rapid degradation of antimicrobials in wastewater treatment plants, organic waste streams or the environment. [...] The AMR threat to public health and the social and economic burden it entails is even greater in developing countries."

NGOs were quick to point out the flaws in the Commission's approach, with the European Public Health Alliance highlighting a "major gap" in the Action plan where action on pharmaceutical industrial pollution is needed. Despite the fact that the Commission's own evaluation of the previous Action Plan (2011-2016) recognised this failing, the environmental dimension of AMR is still not addressed sufficiently. The new Action Plan claims that evidence on the impact of industrial pollution by pharmaceutical companies is lacking, and yet a series of reports released by the Swedish Government, Nordea and international NGOs show this to be untrue.[168] In its analysis of the new EU Action Plan, EPHA for example highlighted that the most credible solutions to this issue would be the introduction of environmental criteria in EU GMP and changes to procurement rules.[169]

Strategic Approach on Pharmaceuticals in the Environment

In the EU Water Framework Directive, which was adopted in October 2000, the European Commission was asked to prepare a strategic approach to the pollution of water by pharmaceutical substances by June 2015. At the time of writing this had been delayed for over two years and had still not been released, despite the publication of a wide-ranging study on the risks of environmental effects of medicinal products in 2013 which was meant to provide the basis of the strategic approach.[170]

Instead, in April 2017, the European Commission published a 'roadmap' on a strategic approach to pharmaceuticals in the environment, receiving feedback on its 4-week consultation from a number of stakeholders including NGOs and EU Member States (see box summing up Sweden's submission opposite).[171]

Swedish Government's submission to public consultation on the EU Strategic Approach Roadmap

"Further action is needed and anticipated in order to support a life cycle perspective in the manufacturing and handling of pharmaceuticals, where good manufacturing practice (GMP) is a cornerstone. Particular attention needs to be drawn to the fact that the release of agents with antimicrobial activity can contribute to the emergence of antimicrobial resistance (AMR), an increasing global threat for different sectors and sustainable development at large."

[...]Pharmaceuticals in the environment is an integral part of the Swedish environmental quality objectives adopted by the Swedish Parliament. In 2013 the Government adopted a milestone target. This is further elaborated on in a Government bill. The milestone target states that by 2020 there should be increased environmental considerations in the pharmaceutical legislation in the EU and the international arena."

In November 2017, the Commission opened a 12-week public consultation to receive feedback on a study carried out by Deloitte (*Options for a strategic approach to pharmaceuticals in the environment*) and on 30 possible policy options that were developed to respond to the Commission's mandate to develop the EU's strategic approach. Legislative options are still on the table and the public consultation is open until the end of February.[172] One of 10 main "action areas" identified is greener manufacturing, which includes an option to ensure that GMP address discharges of APIs into the environment, a review of the Best Available Techniques Reference documents relevant to the pharmaceutical industry to include emissions from manufacturing, etc.[173]

In May 2017, a coalition of NGOs, including the European Public Health Alliance (EPHA), Healthcare Without Harm Europe and the Changing Markets Foundation wrote to the European Commissioners responsible for the health and environment portfolios underlining the importance of introducing ambitious legislation to reduce pharmaceutical pollution, including the spread of AMR - a major global health crisis – and highlighting other potential unintended consequences arising from the release of increasing amounts of pharmaceuticals into the environment.[174]

Anil Dayakar, a local activist, surveys the environmental impact of a pharmaceutical plant on the outskirts of Hyderabad.

5. Conclusion

Amidst growing concern about the environmental and human health impacts of pollution in the global pharmaceutical supply chain, the objective of this report was to provide an updated snapshot of the situation on the ground in Hyderabad, one of India's main drug manufacturing hubs whose companies export to markets around the world.

On the basis of findings from two on-the-ground investigations (one in April 2017, during the dry season, and one in September 2017, during the rainy season), interviews with NGO experts and people living or working in the affected areas as well as in-depth analysis of media coverage and academic studies, this report concludes that the situation in Hyderabad has not improved since the publication of *Impacts of pharmaceutical pollution on communities and environment in India* in February 2016 – if anything, it has deteriorated. Furthermore, with plans afoot to expand the city's pharmaceutical production capacity over the coming years and the lack of credible regulation and measures to control manufacturing emissions, the future looks grim for the area's inhabitants.

Pollution continues to blight the lives of people living across the city. Local and national news outlets are saturated with stories of serious environmental incidents and damage to ecosystems, from lakes covered in industrial froth, to mass fish die-offs as a result of the presence of toxic chemicals in water bodies, many of which can be linked to pharmaceutical manufacturing activity.

The dumping of hazardous chemicals in a bid to cut waste treatment costs appears to be common practice across Hyderabad but countless reports tell of toothless regulatory bodies failing to discipline the offending industry players or investigate the root causes of the pollution. Following CSE's analysis that India's pollution monitoring and enforcement systems are in a "shambles", it is worrying to note that the authorities seem to be putting their faith in the industry to self-regulate its waste management.

Improving transparency, stamping out illegal waste dumping and improving effluent management are key to successfully tackling pharmaceutical supply chain impacts, whether social or environmental. The industry certainly has the means to do this: major players such as Aurobindo, Mylan, Dr Reddy's and Hetero – companies where testing of the water samples taken by the investigators found the presence of solvents and/or heavy metals – are all exporting large quantities of medicines to European and US markets. A recent article in The Hindu pointed out that even pharmaceutical companies themselves admit that the cost of complying with pollution norms is not more than 3-4% of production costs, and that the cost of waste treatment isn't the real issue.[175] The problem lies in insufficient regulations, lax implementation and the lack of accountability throughout the supply chain.

In an industry characterised by opaque and highly complex supply chains, improving transparency and trace-

ability stands out as a key priority for pharmaceutical companies. Other sectors including the electronics and textiles industries are already making headway on this; for example, many clothes retailers have introduced greater transparency and traceability in their supply chains since the Rana Plaza disaster in Bangladesh in 2013, including the public listing of the factories which they source from.[176] Innovations such as the supply

chain mapping tool launched in early 2018 by China's Institute of Environmental & Public Affairs and US NGO NRDC, which links named apparel brands to their suppliers' environmental performance, are redefining traceability and will likely extend to other sectors over time.[177]

Hyderabad's pharmaceutical pollution crisis is not just a local problem given that a significant share of medicines produced there are exported to global markets. While there is still only minimal transparency in the pharmaceutical supply chain, recent research has highlighted the numerous commercial links which connect

the city's drug manufacturers with multinational companies and health service providers in Europe and the United States.[178] These customers should address this as a supply chain issue and demand evidence of good environmental performance from the factories they are buying from.

Some pharma industry players acknowledge that they hold a share of responsibility for the impact of pharmaceuticals in the environment (most notably in relation to AMR), and have made a commitment to begin tackling the issue. However, the self-policing approach has not as yet been successful in tackling a challenge of such magnitude. Additionally, these initiatives do not, for the most part, represent the generics industry which produces a substantial share of our pharmaceuticals.

India plays a key role in global pharmaceutical production, and has also played a pivotal role in bringing affordable medicine to millions of people worldwide. However, in Hyderabad and other production hubs around the country this comes at an unacceptably high price for the people living in the vicinity of factories, the local environment, and even – given the global reach of antimicrobial resistance –the health and wellbeing of citizens around the world.

6. Annex

Chemical profiles – HEAVY METALS

Hexavalent Chromium

Chromium commonly occurs in two forms. Trivalent chromium (chromium III) is a naturally occurring element that is relatively stable and innocuous, and can be found in plants, animals, and soil. Hexavalent chromium (chromium VI) is far more dangerous for humans, and is usually created by anthropogenic causes. Hexavalent chromium compounds are used in pharmaceutical manufacturing, for example as reagents and pharmaceutical raw materials. Hexavalent chromium might also be used as an oxidant or for water treatment. Another possible link to the pharmaceutical industry is hexavalent chromium's use as a catalyst.

OEHHA research has shown increased rates of stomach cancer in people exposed to high levels of hexavalent chromium from drinking water; studies have also found a higher than average rate of lung and gastrointestinal cancers in workers who inhaled hexavalent chromium on the job. This chemical can damage DNA; according to the harmonised classification and labelling approved by the European Union, this substance is fatal if inhaled, is toxic if it is swallowed or comes into contact with skin, and may cause genetic defects, asthma symptoms and cancer. Hexavalent chromium is very toxic to aquatic life, with long-lasting effects; it is also a potential endocrine disruptor.

Regulatory Organisation	Regulatory limits for Chromium(VI) Carcinogenic	
WHO Drinking Water Guidelines	0.05mg/l	50µg/l
EU Drinking Water Directive	0.05mg/l	50µg/l
US EPA Maximum Contaminant Levels (MCLs) [Total chromium]	0.1mg/l	100µg/l
Bureau of Indian Standards [Total chromium]	0.05mg/l	50µg/l
California EPA MCLs	0.01mg/l	10µg/l
California EPA Public Health Goals	0.00002mg/l	0.02µg/l

Arsenic

Arsenic compounds are used in pharmaceutical manufacturing. Long-term exposure to inorganic arsenic through drinking water is associated with cancer of the lungs and bladder, and, to a lesser extent, cancer of the skin, liver and kidneys, as well as developmental defects, stillbirth, and spontaneous abortion, heart attacks, strokes and high blood pressure. The International Agency for Research on Cancer has classified arsenic as a carcinogen since 1980; according to the harmonised classification and labelling approved by the European Union, the substance is toxic if swallowed or inhaled, and is very toxic to aquatic life, with long-lasting effects. Arsenic is a potential endocrine disruptor.

Regulatory Organisation	Regulatory limits for Arsenic (As) Carcinogenic	
WHO Drinking Water Guidelines	0.01 mg/l	10µg/l
EU Drining Water Directive	0.01 mg/l	10µg/l
US EPA Maximum Contaminant Levels (MCLs)	0.01 mg/l	10µg/l
Bureau of Indian Standards	0.01 mg/l	10µg/l
California EPA MCLs	0.01 mg/l	10µg/l
California EPA Public Health Goals	0.000004 mg/l	0.004 µg/l

Nickel

Nickel is increasingly used as a transition metal catalyst in API manufacturing. The US Agency for Toxic Substances & Disease Registry outlines that long-term and high-level exposure to nickel has been linked to chronic bronchitis and reduced lung function. If ingested through water, nickel can cause adverse effects to the blood and kidneys. The California Environmental Protection Agency (CalEPA) categorises nickel as posing a health risk due to its developmental toxicity. According to the classification provided by companies to the European Chemicals Agency (ECHA), nickel causes damage to organs through prolonged or repeated exposure and is suspected of causing cancer. It is harmful to aquatic life, with long-lasting effects.

Regulatory Organisation	Regulatory limits for Nickel (Ni) Developmental toxicity (increased neonatal deaths)	
WHO Drinking Water Guidelines	0.07 mg/l	70µg/l
EU Drinking Water Directive	0.02 mg/l	20µg/l
US EPA Maximum Contaminant Levels (MCLs)	not defined	-
Bureau of Indian Standards	0.02 mg/l	20µg/l
California EPA MCLs	0.1mg/l	100µg/l
California EPA Public Health Goals	0.012 mg/l	12µg/l

Zinc

Zinc is widely used as a chemical catalyst in the pharmaceutical industry. Although naturally occurring in the environment, exposure to large amounts of zinc can be harmful, causing anaemia, stomach cramps and changes in cholesterol. According to the classification provided by companies to the European Chemicals Agency (ECHA), this substance is very toxic to aquatic life, with long-lasting effects. Zinc is also a potential endocrine disruptor. The WHO notes that zinc levels in surface water and ground water do not usually exceed 0.01mg/l (10µg/l) and 0.05mg/l (50µg/l) respectively.

Regulatory Organisation	Regulatory limits for Zinc (Zn)	
WHO Drinking Water Guidelines	3 mg/l	3,000µg/
EU Drinking Water Directive	not defined	-
US EPA Maximum Contaminant Levels (MCLs)	5 mg/l	5,000µg/l
Bureau of Indian Standards	5 mg/l	5,000µg/
California EPA MCLs	not defined	-
California EPA Public Health Goals	not defined	-

Copper

Copper can be used as a transition metal catalyst in API manufacturing. Copper is an essential nutrient, but is toxic at higher intake levels. The CalEPA categorises copper as a health risk due to its digestive system toxicity – nausea, abdominal cramps, diarrhoea and vomiting are all symptoms of mild copper poisoning. More serious cases of copper poisoning are reported as 'Indian Childhood Cirrhosis' (ICC), a condition primarily affecting children under the age of five, mainly in the Indian subcontinent. ICC can involve hepatic and renal necrosis, coma and even death. According to the classification provided by companies to the European Chemicals Agency (ECHA), this substance is very toxic to aquatic life, with long-lasting effects. It is toxic if inhaled, harmful if swallowed and causes serious eye irritation.

Regulatory Organisation	Regulatory limits for Copper (Cu) Digestive system toxicity	
WHO Drinking Water Guidelines	2mg/l	2000µg/l
EU Drinking Water Directive	2mg/l	2000µg/l
US EPA Maximum Contaminant Levels (MCLs)	1.3mg/l	1300µg/l
Bureau of Indian Standards	0.05mg/l	50 µg/l
California EPA MCLs	1.3mg/l	1300µg/l
California EPA Public Health Goals	0.3mg/l	300 µg/l

Chemical profiles – SOLVENTS

The samples were tested for a wide range of solvents relevant to pharmaceutical manufacturing, a selection of which are presented here.

Benzene

Benzene is highly flammable. It can can pass from water and soil into the air; it can also pass through soil into underground water sources. Breathing benzene can cause drowsiness, dizziness, and unconsciousness; ingesting high levels of benzene can cause vomiting, convulsions and death. Long-term exposure can cause anaemia and leukemia; the US EPA classifies benzene as a known carcinogen. According to the harmonised classification and labelling approved by the European Union, this substance may be fatal if swallowed, may cause genetic defects, damage to organs through prolonged or repeated exposure, and cancer. Benzene is also a potential endocrine disruptor.

Regulatory Organisation	Regulatory limits for Benzene Carcinogenic	
WHO Drinking Water Guidelines	0.01mg/l	10µg/l
EU Drinking Water Directive	0.001mg/l	1µg/l
US EPA Maximum Contaminant Levels (MCLs)	0.005mg/l	5µg/l
Bureau of Indian Standards	Not defined	-
California EPA MCLs	0.001mg/l	1µg/l
California EPA Public Health Goals	0.00015mg/l	0.15µg/l

Toluene

Toluene may affect the nervous system; low to moderate levels can cause tiredness, confusion, weakness, memory loss, nausea and loss of appetite. Long-term daily inhalation exposure to toluene may cause some hearing and colour vision loss, while repeatedly breathing toluene may permanently damage the brain. According to the harmonised classification and labelling approved by the European Union, this substance may be fatal if swallowed, and may cause damage to organs through prolonged or repeated exposure. The classification provided by companies to the European Chemicals Agency (ECHA) identifies toluene as potentially damaging fertility or causing damage to an unborn child. It is harmful to aquatic life with long lasting effects, and is also a potential endocrine disruptor.

Regulatory Organisation	Regulatory limits for Toluene Damage to unborn child	
WHO Drinking Water Guidelines	0.7mg/l	700µg/l
EU Drinking Water Directive	Not defined	-
US EPA Maximum Contaminant Levels (MCLs)	1mg/l	1,000µg/l
Bureau of Indian Standards	Not defined	-
California EPA MCLs	0.15mg/l	150µg/l
California EPA Public Health Goals	0.15mg/l	150µg/l

Chloromethane

Also known as methyl chloride, exposure to high levels of this solvent can cause serious problems to the nervous system, including convulsions and coma. It can also affect the liver, kidneys, and heart. The US EPA classifies chlomethane as a possible human carcinogen. According to the harmonised classification and labelling approved by the European Union, chloromethane is suspected of causing cancer, and may cause damage to organs through prolonged or repeated exposure. The classification provided by companies to the European Chemicals Agency (ECHA) identifies that this substance is suspected of damaging fertility or causing damage to an unborn child.

Methyl tert-Butyl Ether (MTBE)

MTBE is commonly found as vapour in the air; small amounts may dissolve in water and get into underground water sources. Drinking or breathing MTBE may cause nausea, nose and throat irritation, and nervous system effects. Studies in mice and rats suggest that drinking MTBE may cause gastrointestinal irritation, and liver and kidney damage. MTBE is a potential endocrine disruptor.

Regulatory Organisation	Regulatory limits for Methy-Tert-Butyl-Ether (MTBE) Carcinogenic	
WHO Drinking Water Guidelines	Not defined	-
EU Drinking Water Directive	Not defined	-
US EPA Maximum Contaminant Levels (MCLs)	Not defined	-
Bureau of Indian Standards	Not defined	-
California EPA MCLs	0.013mg/l	13µg/l
California EPA Public Health Goals	0.013mg/l	13µg/l

Vinyl Chloride

Vinyl chloride is a manufactured substance that does not occur naturally. it has been reported in groundwater as a degradation product of the chlorinated solvents trichloroethene and tetrachloroethene. Breathing high levels of vinyl chloride for short periods of time can cause dizziness, sleepiness, unconsciousness, and at extremely high levels can cause death. Breathing vinyl chloride for long periods of time can result in permanent liver damage, immune reactions, nerve damage, and liver cancer. The U.S. Department of Health and Human Services has determined that vinyl chloride is a known carcinogen.

Regulatory Organisation	Regulatory limits for Vinyl chloride Carcinogenic	
WHO Drinking Water Guidelines	0.0003mg/l	0.3µg/l
EU Drinking Water Directive	0.0005mg/l	0.5µg/l
US EPA Maximum Contaminant Levels (MCLs)	0.002mg/l	2µg/l
Bureau of Indian Standards	Not defined	-
California EPA MCLs	0.0005mg/l	0.5µg/l
California EPA Public Health Goals	0.00005mg/l	0.05µg/l

Methylene Chloride (Dichloromethane)

Breathing large amounts of methylene chloride may cause dizziness, nausea and a tingling or numbness of the finger and toes. A person breathing smaller amounts of methylene chloride may become less attentive and less accurate in tasks requiring hand-eye coordination. Skin contact with methylene chloride causes burning and redness of the skin. The World Health Organization (WHO) has determined that methylene chloride may cause cancer in humans; the US EPA has classified the solvent as a probable carcinogen. According to the harmonised classification and labelling approved by the European Union, this substance is suspected of causing cancer. Additionally, the classification provided by companies to ECHA identifies that this substance causes serious eye irritation, causes skin irritation and may cause drowsiness or dizziness. Methylene chloride is also a potential endocrine disrupter.

Regulatory Organisation	Regulatory limits for Methylene chloride (Dichloromethane)	
WHO Drinking Water Guidelines	0.02mg/l	20µg/l
EU Drinking Water Directive	Not defined	-
US EPA Maximum Contaminant Levels (MCLs)	0.005mg/l	5µg/l

Bureau of Indian Standards	Not defined	-
California EPA MCLs	0.005mg/l	5µg/l
California EPA Public Health Goals	0.004mg/l	4µg/l

Chloroform

Breathing chloroform can cause dizziness, fatigue, and headaches; breathing or ingesting chloroform over long periods of time may damage the liver and kidneys. It can cause sores if large amounts touch the skin. The US Department of Health and Human Services has determined that chloroform may reasonably be anticipated to be a carcinogen. According to the harmonised classification and labelling approved by the European Union, this substance is toxic if inhaled and harmful if swallowed, causes damage to organs through prolonged or repeated exposure, causes serious eye irritation, and is suspected of causing cancer. Additionally, the classification provided by companies to ECHA identifies that this substance is suspected of damaging fertility or an unborn child. Chloroform is also a potential endocrine disruptor.

Regulatory Organisation	Regulatory limits for Chloroform Hepatotoxicity (liver), nephrotoxicity (kidneys)	
WHO Drinking Water Guidelines	0.3mg/l	300µg/l
EU Drinking Water Directive	Not defined	-
US EPA Maximum Contaminant Levels (MCLs)	0.08mg/l	80µg/l
Bureau of Indian Standards	0.2mg/l	200µg/l
California EPA MCLs	Not mentioned	-
California EPA Public Health Goals	Not defined	-

1-2-Dichloroethane

Breathing or ingesting high levels of 1,2-dichloroethane can cause damage to the nervous system, liver, kidneys, and lungs and may cause cancer; the US EPA has determined that 1,2-dichloroetthane is a probable human carcinogen. According to the harmonised classification and labelling approved by the European Union, this substance is harmful if swallowed, causes serious eye irritation and skin irritation and may cause respiratory irritation and cancer. Additionally, the classification provided by companies to ECHA identifies that this substance may be fatal if swallowed and is toxic if inhaled.[179]

Regulatory Organisation	1,2-Dichloroethane Carcinogenic	
WHO Drinking Water Guidelines	0.03mg/l	30µg/l
EU Drinking Water Directive	0.003mg/l	3µg/l
US EPA Maximum Contaminant Levels (MCLs)	0.005mg/l	5µg/l
Bureau of Indian Standards	Not defined	-
California EPA MCLs	0.0005mg/l	0.5µg/l
California EPA Public Health Goals	0.0004mg/l	0.4µg/l

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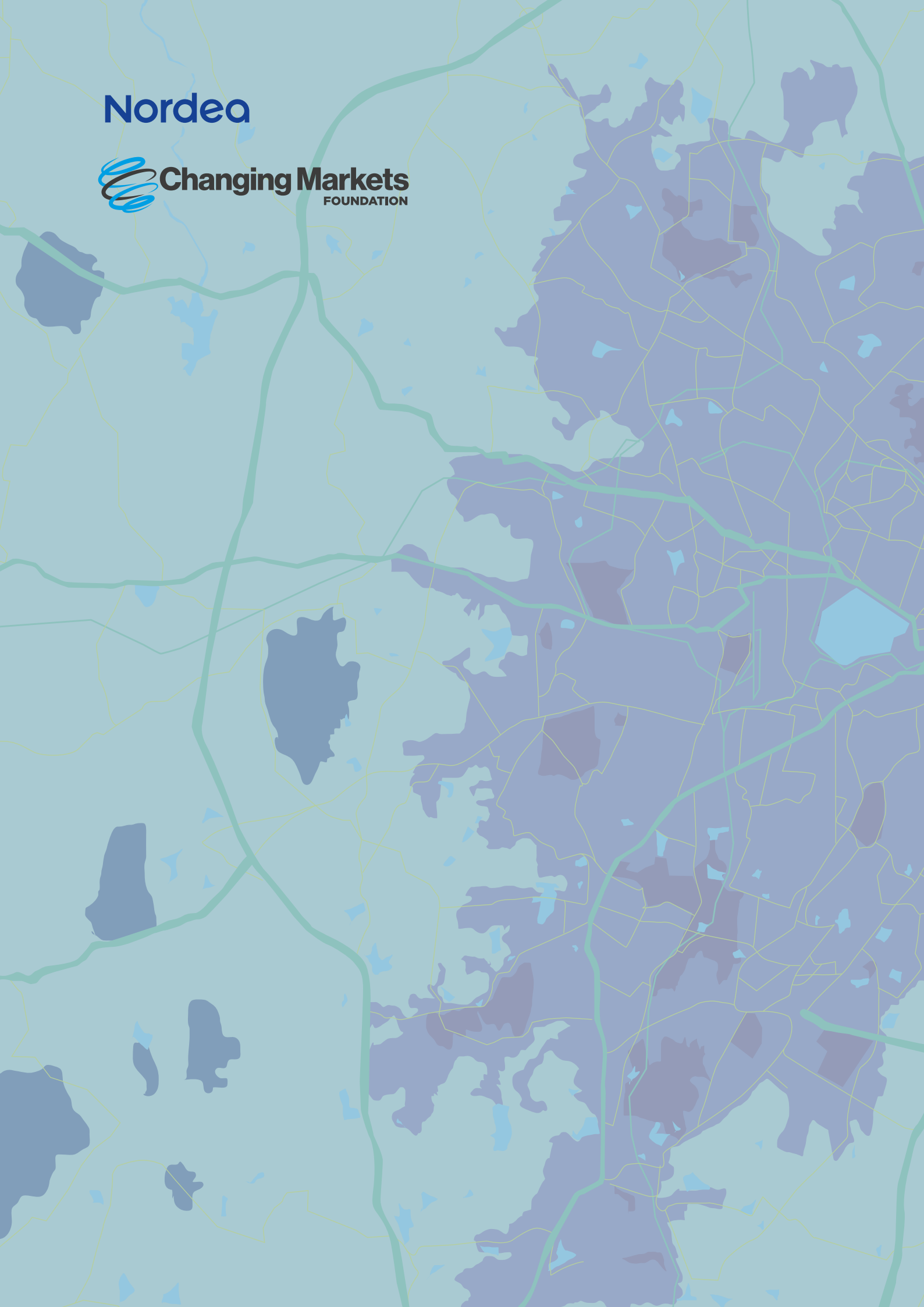
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