

A Review on Impact of Covid-19 on Pharmaceutical Industry

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Abstract: All countries and industries continue to cope with unparalleled challenges presented by novel coronavirus (COVID-19), a specific area of concern has been the uncertainty surrounding the impact of the COVID-19 pandemic on the global and Indian supply chains of the pharmaceutical industry. The COVID-19 crisis has demonstrated the importance of establishing a risk management system that focuses on assessing future risks resulting from the loss of a supply chain among countries. This review focuses on the role of the Indian pharmaceutical industry towards the pandemic. This review investigates the economic effect of COVID-19 across segments and what it implies for the pharmaceutical industry.

Keywords: Coronavirus, social distancing, manufacturing operations, transmission, precautions, lockdown, vaccines

INTRODUCTION

Corona viruses are a large family of viruses which may cause illness in animals or humans. The most recently discovered disease causes coronavirus covid 19.[1]

It is the infectious disease caused by the most recently discovered corona virus. This new virus and disease were unknown before the outbreak began in Wuhan, China, in December 2019. Covid-19 is called SARS-CoV-2 (with SARS standing for 'severe acute respiratory syndrome).[1]

The Coronavirus SARS-CoV-2 is an RNA molecule. SARS-CoV-2 RNA has a protein on its surface ('corona'-shaped) which latches onto a receptor called in the lining of the lung. Covid-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so it's important that you also practice respiratory etiquette (for example, by coughing into a flexed elbow).[1]

Most people infected with the Covid-19 virus will experience mild to moderate respiratory illness and may recover without requiring special treatment. The best way to prevent and slow down transmission is be well informed about the Covid-19 virus, the disease it causes and how it spreads. Symptoms of COVID-19 include fever, dry cough, and headache. COVID-19 patients exhibit respiratory symptoms and there are many deaths due to this disease. Individuals with existing health problems and older persons have a high likelihood of developing severe illness.

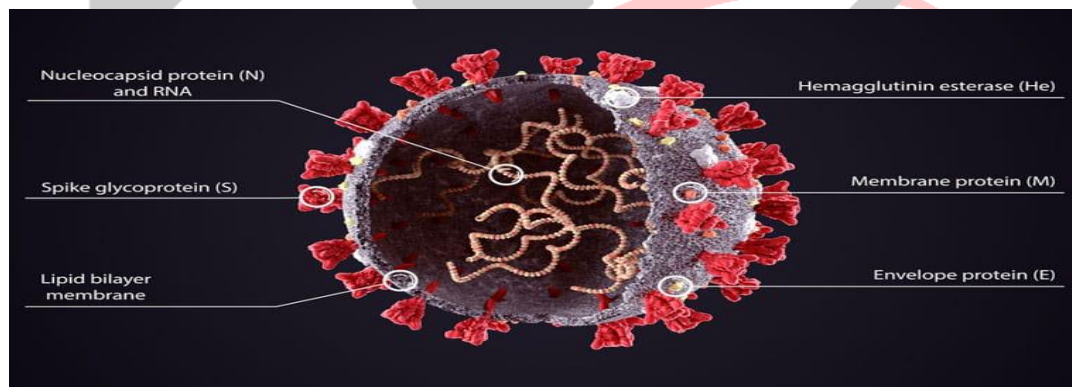


Fig.No.1 Coronavirus

The COVID-19 pathogen spreads mainly through direct contact with nose discharges or saliva droplets expelled when a patient sneezes or coughs.[2] Customs measures to combat this pandemic included banning the export of masks, medical gown, gloves, disinfectants, soap, detergents and alcohol, and expediting the issuance of clearance permits for imported items related to coronavirus and exemptions from custom tariffs.[2] COVID-19 has affected the pharmaceutical industries, pharmaceutical business, clinical trials.[3]

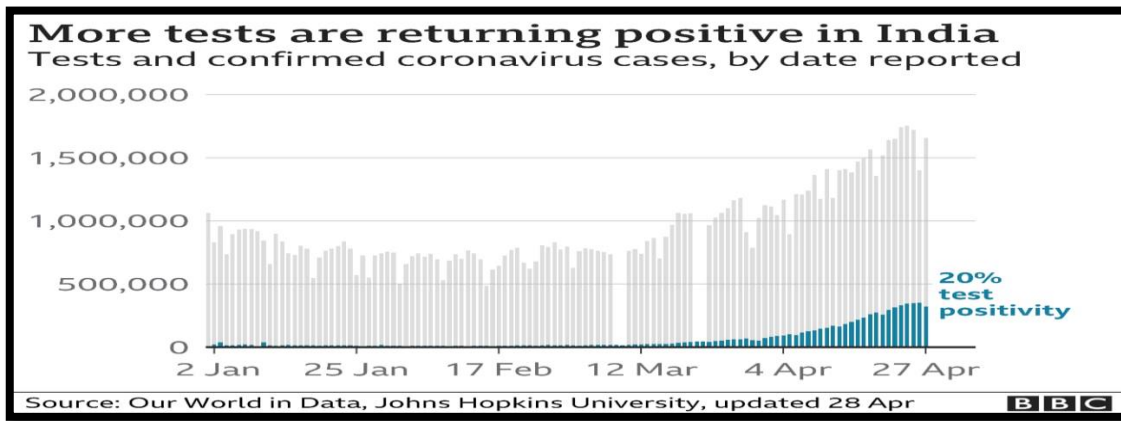


Fig. No. 2 confirmed coronavirus cases

Various Variant of Covid 19:

Viruses, like SARS-CoV-2, change over time and will continue to change the more they circulate. Sometimes, variants of the virus may develop.[4]

A variant is where the virus contains at least one new change to the original virus. Some variants of the coronavirus, such as Delta and Omicron, are spreading more easily between people. We know we can protect from the virus and its new variants by[4]:

- Getting vaccinated when it's your turn
- Keeping a safe distance
- Opening windows when possible
- Wearing a mask
- Covering coughs and sneezes

Delta Variant:

Delta is currently the predominant variant of the virus in the United States. Below is a high-level summary of what CDC scientists have recently learned about the Delta variant. More information will be made available when more data are published or released in other formats.[5]

The Delta variant is highly contagious, more than 2x as contagious as previous variants. Some data suggest the Delta variant might cause more severe illness than previous variants in unvaccinated people. In two different studies from Canada and Scotland, patients infected with the Delta variant were more likely to be hospitalized than patients infected with Alpha or the original virus that causes COVID-19. Even so, the vast majority of hospitalization and death caused by COVID-19 are in unvaccinated people.[5]

Unvaccinated people remain the greatest concern: The greatest risk of transmission is among unvaccinated people who are much more likely to get infected, and therefore transmit the virus. Fully vaccinated people get COVID-19 (known as breakthrough infections) less often than unvaccinated people. People infected with the Delta variant, including fully vaccinated people with symptomatic breakthrough infections, can transmit the virus to others. CDC is continuing to assess data on whether fully vaccinated people with asymptomatic breakthrough infections can transmit the virus. Fully vaccinated people with Delta variant breakthrough infections can spread the virus to others. However, vaccinated people appear to spread the virus for a shorter time: For prior variants, lower amounts of viral genetic material were found in samples taken from fully vaccinated people who had breakthrough infections than from unvaccinated people with COVID-19.[5]

For people infected with the Delta variant, similar amounts of viral genetic material have been found among both unvaccinated and fully vaccinated people. However, like prior variants, the amount of viral genetic material may go down faster in fully vaccinated people when compared to unvaccinated people. This means fully vaccinated people will likely spread the virus for less time than unvaccinated people.[5]

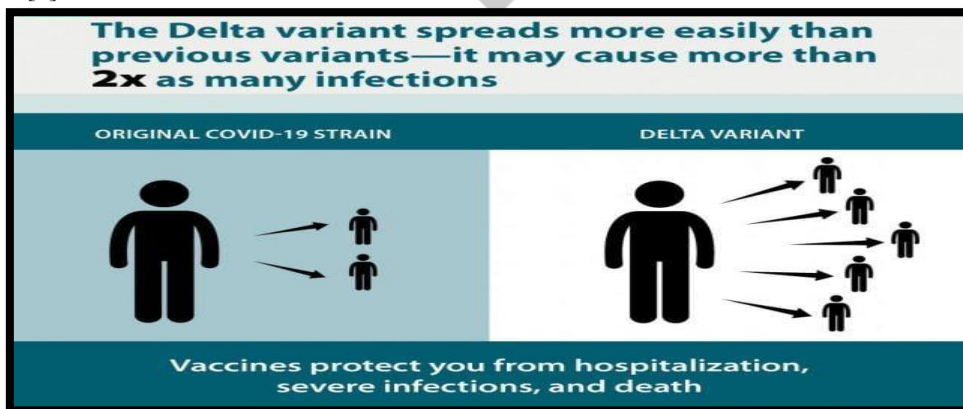


Fig. No. 3 Spread of Delta Variant

Omicron Variant:

The Omicron variant is a variant of SARS-CoV-2, the virus that causes COVID-19. As of December 2021, it is the newest variant. It was first reported to the World Health Organization (WHO) from South Africa on 24 November 2021. On 26 November 2021, the WHO designated it as a variant of concern and named it "Omicron", the fifteenth letter in the Greek alphabet. Omicron variant and other major or previous variants of concern of SARS-CoV-2 depicted in a tree scaled radially by genetic distance, derived from Nextstrain on 1 December 2021.[6]

The variant has an unusually large number of mutations, several of which are novel and a significant number of which affect the spike protein targeted by most COVID-19 vaccines at the time of the discovery of the Omicron variant. This level of variation has led to concerns regarding its transmissibility, immune system evasion, and vaccine resistance, despite initial reports indicating that the variant causes less serious disease than previous strains. The variant was quickly designated as being "of concern", and travel restrictions were introduced by several countries in an attempt to slow its international spread.[6]

Compared to previous variants of concern, Omicron is believed to be far more contagious (spreading much quicker), and spreads around 70 times faster than any previous variants in the bronchi (lung airways), but it is less able to penetrate deep lung tissue, and perhaps for this reason there is a considerable reduction in the risk of severe disease requiring hospitalization. However the extremely high rate of spread, combined with its ability to evade both double vaccination and the body's immune system, means the total number of patients requiring hospital care at any given time is still of great concern.[7]

The new variant was first detected on 22 November 2021 in laboratories in Botswana and South Africa based on samples collected 11–16 November. The first known sample was collected in South Africa on 8 November. In other continents, the first known cases were a person arriving in Hong Kong from South Africa via Qatar on 11 November, and another person who arrived in Belgium from Egypt via Turkey on the same date. As of 16 December 2021, the variant has been confirmed in more than 80 countries. The World Health Organization estimates that by mid-December, Omicron likely was in most countries, whether they had detected it or not.[7]

The FDA has published guidelines on how PCR tests will be affected by Omicron. Tests that detect multiple gene targets will continue to identify the tested as positive for COVID-19. S-gene dropout or target failure has been proposed as a shorthand way of differentiating Omicron from Delta.[8]

The variant may be identified by sequencing and genotyping. The BA.1 lineage, but not the BA.2 lineage, can be identified by S gene target failure (SGTF) of the TaqPath assay, a trait shared with subsets of SARS-CoV-2 Alpha variant.[38] Several other commercial assays can also be used, though they test for different amino acid substitutions.[9]

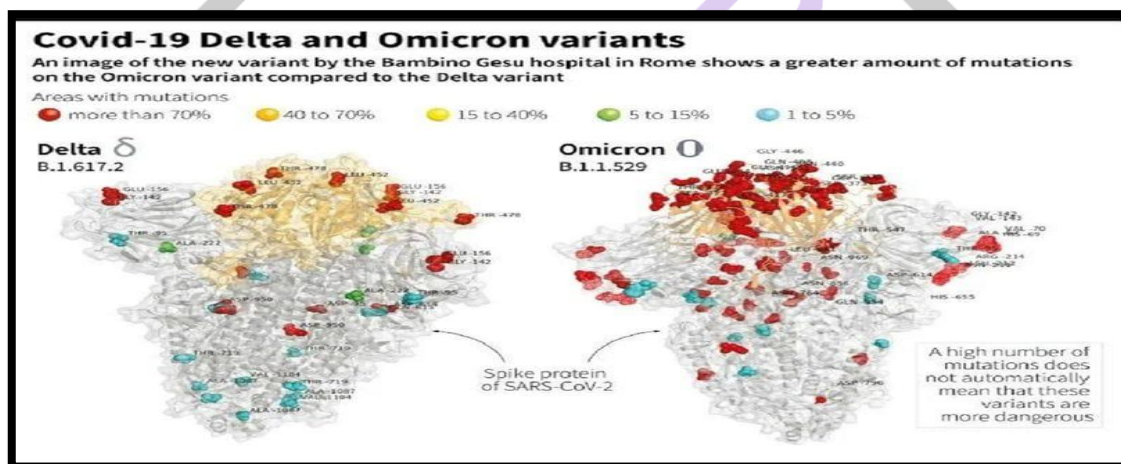


Fig.No.4 Spread of Omicron Variant

General Impact of Covid-19 on Pharmaceutical Industry:

Corona Virus (Covid-19) has almost impacted every industry, causing steep inroads into the global economy. Pharma industry is no exception. Let us understand the impact on the pharma industry. [10]

Cost of Drugs and Raw materials:

The impact of covid has created in China and the lockdown in India, United States, and other countries, further increases the chances of shoot up in the cost of raw materials and drugs. 13% of the brand and generic manufacturers are based out of China and according to the FDA, as of 2018, 24% of medicines and 31% of medical ingredients were imported from India.[11]

Example:

- The cost of Paracetamol in India has gone up to Indian Rupees 400-450 per kilogram from Rupees 250- 300 per kilogram
- The price of vitamins and penicillin have increased by 40- 50 % in India

If the current situation continues to prolong, the cost of essential drugs might increase in the US and other countries as well.[11]

Supply Chain:

Pharma supply chain is fragile, and the impact created by Covid-19 has brought it to limelight once again.[11]

There are two types of drugs -

Brand Name Drugs:

These are products protected with a reliable supply chain and profitable to the manufacturers.

Example:-Truvada

Generic Drugs:

The profit for these types of drugs is very marginal and the supply chain is lean. The API plant for these is often overseas with India and China dominating the API market. The API may be manufactured in a single plant and each stage holds very little inventory. The problem at any stage can cause drug shortage with the average drug shortage lasting for 14 months and there are cases where it has lasted for 3 year even.[11]

According to a recent survey, emergency care, anesthesia care, and pain management drugs are the drugs which mostly get affected due to shortage. The current situation might cause a shortage and increase in demands of certain medications such as Hydroxychloroquine and Chloroquine, which are most talked about during these pandemic times. It is believed that the shortage might not occur for now as companies have stocks at least for the next 5 months [11]

FDA Policies:

The Covid impact, demand for drugs and the lockdown in various countries may force the FDA to allow relaxation in a few areas:

- The review process of Generic medicine is lengthy, the demand and shortage created may also force minor changes
- The Federal law requires the manufacturers to notify the FDA about shortages when the circumstance arises. The rules do not apply to medical devices as it is manufactured at multiple plants. The shortage of devices during the pandemic might force the FDA to rethink on regulations on devices.
- FDA might also rethink the number of inspections on the overseas manufacturing plants .[11]

Example:-To maximize the number of respirators available, FDA and CDC recently announced that certain respirators regulated by CDC, but not by the FDA, can also be used.

Data & Analytics:

Pharma industry has an enormous amount of data, which also brings in various challenges

- Integrating siloed data and derive insights
- Infrastructure to leverage the power of Big Data
- Leveraging unstructured data
- Advance insights from clinical trails
- Data privacy
- Social listening[12]

The cost of drug development is skyrocketing, and the time taken for a drug to be launched is also high. The industry has been using data for years, but the challenge lies in leveraging its full potential. A large amount of clinical and molecular data available over the years can help in predictive analytics, which can be used to hasten the process of clinical trials and drug development. Companies are leveraging data and analytics, but the current situation might want them to use data even more efficiently for clinical trials, forecasting, and marketing. Infrastructure for big data and social listening will also play a key role.[12]

Real-World Data (RWD):

New drug development is estimated to cost which is up from 1 billion in 2013. On top of the cost involved, the time taken for development & clinical trials, might bring in more focus towards RWD.

Almost 95% of the companies are using RWD or will be using it by 2021. Data accessibility and security issues are a few of the challenges in using RWD, but it can be sorted out and will gain more popularity as companies and the regulatory bodies from here on might look to bring in innovative measures in clinical trials.

Clinical trials are gold dust for pharma but there are cases in the past where the drugs were pulled out from the market even after FDA approval. The main problem with clinical trial is it looks at a homogeneous population. To address this, FDA might relax the regulations on RWD.[13]

Digital Health:

Digital health might be the next big thing as telemedicine / video consultations, health related videos and apps are gaining popularity. Investments in online portals that help doctor-patient interaction will increase.[14]

Example of gaining digital:

- Well mind health (provides online courses for mindfulness-based cognitive therapy) has seen a recent uptrend in the purchase and enquires
- Due to the current pandemic situation, hospitals in the UK have been instructed by NHS England to increase telemedicine/video consultations
- Meditation apps Calm and Headspace have released free digital offerings to help people cope up with panic and anxiety.[14]

Primary and Secondary Market:

To control the drug shortages that occur often companies will reassess their strategies on the primary and secondary market for manufacturing.[15]

Short-Term Impacts:

Demand change, supply shortages, panic buying and stocking, regulation changes and shift of communication and promotions to remote interactions through technology and research and development (R&D) process changes can be seen as short-term impacts of COVID-19 on the health market.

- Demand change, which leads to shortage, in the case of induced demand and panic buying of oral home medications especially for chronic disease may be due to the pandemic (COVID-19-related), and also shortages due to supply-chain inconsistencies.[16]
- COVID-19-related: Increased hospitalization, incidence of COVID-19-related pneumonia and increased demand for assigning patients to ventilators, contributes to relate prescription medicine shortages. A medicine shortage is defined as a “supply issue that affects how the pharmacy prepares or dispenses a drug product or influences patient care when prescribers must use an alternative agent”. [16]
- On the global levels, many regulatory authorities announced confirmed shortage list, mostly including potential COVID-19 treatments and also associated pneumonia. For example, United States food and drug administration (FDA) shortage list included anti-COVID-19 potential pharmacotherapies, hydroxychloroquine (HQC) and chloroquine (QC), and also frequently prescribed medications for COVID-19 hospitalized patients with respiratory signs in critical care units, azithromycin, dopamine, dobutamine, fentanyl, heparin, midazolam, propofol and dexmedetomidine.[16]
- In addition, the American Society of HealthSystem Pharmacists (ASHP) announced an 11- medicine list of shortage; which mainly included hospital level antibiotics and anesthetic medications; including meropenem, ceftazidim, ampicillin and doxycycline, as antibiotics and vecuronium, rocuronium, as anesthetics. Also, this list included albuterol and fluticasone which are used to open airways in the lungs.[16]
- In global levels, the impact on medicine shortage was differed by medicine access level, retail and hospital-only, and type. Use of medicines currently being investigated in trials but not yet fully approved by FDA or so-called investigational treatments—including hydroxychloroquine, lopinavir+ritonavir, tocilizumab and sarilumab—had seen a two-fold increase in use over the past month, with 8 times higher use in hospitals. [16]

Long-Term Impacts:

Approval delays, moving towards self-sufficiency in pharm-production supply chain, industry growth slow-down and possible trend changes in consumption could be seen as long-term impacts of COVID-19 on the health and pharmaceutical market.

- Delayed approvals for non-COVID-related pharmaceutical products; as all countries, including Iran, are being under pressure of the crisis and their priority is COVID19 management, approval delays may be seen due to several month of application review postponements. In Iran, due to economic crisis, IML inclusion, registrations and reimbursement decisions was being made with a considerable delay; and this situation may maximize it. It also is affected by about one-month semi-closure of regulatory agencies.[16]
 - Moving towards self-sufficiency in pharma industry; potential shortages due to export bans in India and China, who are main suppliers of API and generics, made governments of many countries to consider self-sufficiency in supply chain and they have announced regulations to avoid shortages in such crisis.[16]
 - In this regards, on March 2020 the European commission has published a new guideline concerning foreign direct investment and free movement of capital from third countries; stating that foreign investments, especially those which affect the health market, in European Union (EU), must be subjected to risk-assessments to avoid any harmful impact on the EU’s capacity to cover the health needs of its citizens.[16]
 - Iran’s pharmaceutical industry was going towards self-sufficiency prior to this crisis; however, COVID-19 pandemic may lead to more importation restrictions and further regulation incentives for local manufacturing.[16]
- Pharmaceutical industry growth slow-down; Coronavirus pandemic resulted in economic slowdowns for many countries and this will possibly lead to pharma industry growth slow-down, which are sensitive to country economic growth.[16]

IMPACT	MIDDLE EAST	EU5 COUNTRIES	UNITED STATES
Short term	10.8% OTC category (cold, cough)	10.8% OTC category (vitamin, minerals)	Investigational treatment increased 2 fold
	40.3% personal hygiene	60.2% personal hygiene	Medicine used in hospital are 100% and 700% in January
	67% ICU medication	7.0% highest volume growth in ATC class	2 million excess prescription are used in hypertension, mental health, respiratory.

Long term	Pharma companies report delays in new trials.	Medicine growth account for 23% of interaction	Supply shortage of the covid 19 related complication treatment
	16% new trials & 32%delay new trials	Product launches delayed disrupted or impacted	Clinical trials existing delayed enrolment.

Table No. 1: short & long term impact

Impact of Covid 19 on Clinical Trials:

The COVID-19 pandemic caused major disruptions to clinical trial execution in India impacting key stakeholders across the industry. Investigative site capabilities experienced upheaval, driven by staff furloughs, social-distancing protocols, financial losses, and concerns over patient safety. Sponsors, CROs and other organizations that support drug development shifted to remote working environments. An estimated 80% of non-COVID-19 trials were stopped or interrupted as a result of the COVID-19 pandemic.[17] An April 2020 study suggests investigative sites demonstrated flexibility and ingenuity in adopting new approaches in order to cope with challenges presented by COVID, with over half of investigative sites transitioning to virtual approaches to interact with patients. More recently, follow-up studies performed in August 2020 have identified persistent impact of COVID, with over 60% reporting an “average” or greater level of impact on ongoing trials and initiation of new trials. [17]

The COVID-19 pandemic has disrupted the clinical trial research across the world. As in other aspects of life, the virus has severely affected the ability to conduct trials in safe and effective ways. This is especially true when considering that trials often deal with vulnerable populations who are most at risk from exposure to COVID-19. Thousands of trials have been suspended or stopped because of the difficulties in continuing under lockdown conditions, even as those restrictions have begun to ease in parts of the world. At the same time, the pandemic has seen an unprecedented reorientation in clinical trials research towards Covid 19.[17]

Both of those aspects—the disruption and the fast, effective readjustment to address a new challenge—ensure that the effects of the COVID-19 pandemic will be felt in clinical trials research long after the initial effects have faded. Therefore, there are now more opportunities for using remote healthcare including conducting virtual or decentralized trials, site-less clinical trials and use of other non-traditional approaches that do not involve in-person visits. This shift, driven by the effects of the pandemic, prompted the team at the Tufts Center for the Study of Drug Development to conduct a qualitative study researching the impact of COVID-19 on clinical trial execution.[18]

Region	No Enrollment	Lower	Same
Europe(n=7)	0%	86%	14%
US(n=10)	20%	60%	20%
Asia(n=5)	20%	20%	60%

Table no. 2 : Enrolling Patients in Ongoing Oncology Clinical Trials.

The study examined the effects of COVID-19 on clinical trials by gathering insights and perceptions from clinical operations professionals at pharmaceutical companies in the United States. The goal was to understand the modifications that organizations have made in response to the pandemic, especially with regard to remote or virtual approaches. In addition, the study explored how companies have approached planning and implementing remote and virtual approaches to trials, as well as their experience and lessons learned. Last, Tufts researchers sought to understand initial perspectives how COVID-19 will impact trial execution in the long-term.[19]

Recent FDA guidance (March 2020 and updated July 2020)³ acknowledged that the impact of COVID-19 may require companies conducting clinical trials to consider virtual patient visits or put new processes in place regarding their current protocols.

Supply Chain Disruption due to the Covid 19 :

The pharmaceutical supply chain is a very complex network, covering every step from new product development to patient delivery of medications at hospitals or retail pharmacies. Stakeholders in this complex system include government agencies, hospitals, clinics, drug manufacturers, drug distributors, insurance companies, retail stores, R&D companies, and the FDA. Overall, the goal of the pharmaceutical industry is to provide medications that can cure diseases, prevent infections, and maintain overall health. As of 2018, the global pharmaceuticals were a \$1.2 billion industry (Prowse, 2019). On average, pharmaceutical companies spend 17% of their revenue on R&D costs. Clinical trials are an extensive part of Investigational Medicinal Products (IMPs), and in recent years they have expanded globally. This adds another level of complexity to the supply chain because the trials must abide by local and global regulations. Once drugs have completed all necessary testing and are ready to be mass-produced, pharmaceutical manufacturers contract out Active Pharmaceutical Ingredients (APIs) to produce finished goods. APIs must come from trusted suppliers since there are significant health risks associated with errors in pharmaceutical products. Typically, third party logistics are used to transport the APIs to the manufacturing sites.

The finished goods are packaged and labeled before they are distributed to depots worldwide. It is also imperative for manufacturers in this industry to do constant quality checks on their product lines to prevent cross-contamination or improper labeling on the final

products. After the products are manufactured and packaged, they are distributed to pharmacies, either directly or through a wholesaler. Nearly 80% of all drugs require temperature-controlled transportation, known as cold chain logistics. It's been reported that 30% of all cold temperature products are damaged during their shipping process (Bird, 2018). Once the products arrive at their destination, they are put into inventory. Managing inventory levels at pharmacies is difficult because patients urgently Proceedings of the 5th NA International Conference on Industrial Engineering and Operations Management Detroit, Michigan, USA, August 10 - 14, 2020 © IEOM Society International demand the products, and the products also have an expiration date (Shoenfeld, 2019). There is a high turnover rate for products in the pharmaceutical industry, which increases the need for efficient flow throughout the entire system.[20]

Regulating the Pharmaceutical Supply Chain :

Although the United States has been able to emerge as a world leader in drug research and development, it is not leading manufacturing efforts. Most of the APIs and final goods are produced in China and India because the United States can cut manufacturing costs by 30-40% by outsourcing overseas. The FDA must closely monitor sites abroad, but this can be challenging for a variety of reasons. In recent years, quality issues with drugs have been responsible for 62% of all shortages (Pagliarulo and Lopez, 2018). As of 2013, the Drug Supply Chain Security Act (DSCSA) was put in place by the United States Congress to increase drug traceability. The DSCSA proposes that electronic product tracking and tracing be implemented into the pharmaceutical supply chain over the next ten years. It also increases the responsibility of the FDA in regulating the pharmaceutical industry.[21]

Pre-Covid-19 Pharmaceutical Supply Chain Challenges :

The U.S. pharmaceutical supply chain is a complex global system that requires producing high-quality products and where meeting demands is crucial. There are many challenges the supply chain faces in ensuring demands are met with quality and timeliness. Around 80% of active pharmaceutical ingredients and 40% of finished drug products are processed and manufactured overseas (Pagliarulo and Lopez, 2018). This importing of pharmaceutical drugs causes the adherence to FDA Regulations and transparency of the supply chain to decrease. The U.S. faces many challenges in transparency, compliance, and logistics. These issues are important to the U.S. because they cannot track the location of products in the supply chain system, whether the products are being held to the quality standards and regulations of the FDA, or whether demands are being met in quantity and in time. This ultimately leads to shortages in drug supply and low-quality goods.[22]

Drug Shortages:

The leading cause of drug shortages is manufacturing issues in quality and production. When the FDA finds poor-quality drugs, that medication can no longer be given to the consumer. The FDA also finds that production delays and discontinuations are becoming common in older drugs. For some pharmaceuticals, there is only one production site, and when that facility stops manufacturing a drug, there is no place else to have it manufactured. When these issues occur in manufacturing, the FDA must address the issues with the supplier (FDA, 2018).[22]

Transparency:

The transparency and visibility of drugs in the pharmaceutical supply chain is a massive problem in the U.S. because most pharmaceutical drugs are produced overseas, and the U.S. cannot track them. Without consistent regulations across all countries, there is no clear way for the U.S. to see where their products are throughout the Pharma Supply Chain. This causes problems because the U.S. cannot see what products are being produced when they are being produced, where their product is located, and if the product is being carried in the correct conditions. India and China are the most prominent suppliers for pharmaceuticals. The FDA is in contact with the Indian and Chinese manufactures, but they often receive little information on the current state of production at these manufacturing sites. Therefore, the DSCSA was created to maintain quality and transparency in the Pharma supply chain.[23]

Compliance to FDA Regulations:

With a global supply chain, ensuring compliance with specific regulations is difficult. The director of the FDA's Center for Drug Evaluation and Research, Dr. Janet Woodcock, testified to congress in 2019 that overseas production "creates vulnerabilities in the U.S. supply chain" (Blackburn, 2020). The FDA is tasked with ensuring foreign production follows Good Manufacturing Practices. However, with hundreds of manufacturing plants overseas, it is challenging to regulate production. The FDA sends quality violation notices to these manufacturers when they inspect inferior quality products, yet they cannot get these manufacturers to comply with the regulations. The FDA also has the leading cause of drug shortages is manufacturing issues in quality and production. When the FDA finds poor-quality drugs, that medication can no longer be given to the consumer. The FDA also finds that production delays and discontinuations are becoming common in older drugs. For some pharmaceuticals, there is only one production site, and when that facility stops manufacturing a drug, there is no place else to have it manufactured. When these issues occur in manufacturing, the FDA must address the issues with the supplier (FDA, 2018).[23]

Covid 19 Responses to Pharma Companies:

During these unprecedented times, pharmaceutical companies are responding to the rapid challenges arising from disruption in supply chains and the need to change business processes. If the current COVID-19 pandemic lasts for a medium/long span of time, it may impact the supply of active material and ingredients (mainly from China), as well as the import and export of pharmaceuticals. There is also the potential for negative impacts of both a medium- and longer-term nature on R&D and manufacturing activities, as well as delay on projects/programmes not related to the core supply chain/data management operations. While the full impact of

the global pandemic is still unknown, pharma companies need to respond, recover and thrive. The document contains key pointers that companies should make a note of during this crisis.[24]

Crisis Management Team:

Set up a crisis management team/PMO, responsible for taking decisions during a pandemic. The crisis management team can: – Assign separate sub PMO leads for SCM, plant ops, people, IT, regulatory, finance, and industry. – Define scenario planning, triggers for action, and responsibility/time lines for action (during and after lockdown). – Define communication plans for employees, customers, and vendors. Include key members from critical functions as a part of the crisis management team. Schedule meetings or calls among members of the crisis management team on a periodic basis to evaluate the current situation. Set up business continuity and recovery plans based on various scenarios. Get a confirmation from the health insurance company that employee insurance includes Covid-19 cover.[24]

People Management:

Set up a covid HR team to monitor the status of every employee in the organisation on the following parameters: – Where they are currently situated – Their health status – Their current activity status – Disclosure of their family members' health issues. Daily monitoring (across all locations). Launch a digital employee health declaration system to track employee well-being and comply with administrative reporting requirements. Set up a panel of doctors to provide virtual guidance to employees on health issues. (COVID HR team to monitor). Prepare a roster of employees operating in the plant on a rotation basis, keeping in mind risk assessment, location proximity, executive health reports, and annual checkup reports. Develop and disseminate/communicate strict protocols for staff working at plants and from home. Conduct a periodic medical checkup, including a thermal checkup/scanning at entry point for all employees. In case anyone is found positive for COVID -19, – Ask employees to track all contact with coworkers and visitors in case they develop symptoms.[24]

Plant and Warehousing Operation:

Identify and priorities the critical products to be manufactured as per customer/government requirements. Plan to maximize capacities in plants located in states with fewer cases of COVID-19. Evaluate the allocation of available labour between production shifts to maintain the safety and wellbeing of workers. Prioritize scheduled maintenance activity such as HEPA filters. Frame an SOP w.r.t. COVID-19, which states the additional steps that need to be taken to ensure sanitization. For instance, “First entry door of manufacturing area should be permanently kept open”. Routinely clean all frequently touched surfaces in the workplace, such as workstations, keyboards, telephones, handrails, and doorknobs. Discourage workers from using other’s phones, desks, offices, or other work tools and equipment, when possible. If necessary, clean and disinfect them before and after use. Provide disposable wipes so that commonly used surfaces such as doorknobs, keyboards, remote controls, desks, other work tools and equipment can be wiped down before each use. Frequently sanitizes all warehouses and hubs with appropriate disinfectants. Check all warehouse employees for symptoms of being unwell, and thermally scan all employees at entry. Ensure all employees handling pharma products wear face masks and gloves. To increase social distancing among employees, extend lunch hours. Stagger lunch hours by department. Increase the area required for the canteen. Demarcate seating/standing areas in the canteen with adequate distance. Provide cleaning staff with PPEs.[24]

Research and Development:

Identify the trials that could be affected by possible shutdowns at supplier or logistic interruptions. Incorporate COVID-19 risk and impact tracking into trial management plans. Communicate with investigators to understand the specific issues COVID-19 is creating at their sites (such as local lab testing capacity, patient retention, serious adverse event risks). Investigate alternative timing or locations, and priorities initiation of new investigator sites in countries with a low potential risk. Establish strong patient communication plans. Establish an internal regulatory perspective on COVID-19 to guide communications with institutional review boards and investigators. Understand from the regulators how to deal with enhanced event risk in currently enrolled patients.[24]

Insurance:

Revisit the coverage of existing policies. Obtain adequate risk covers for protection of employees, product portfolio, assets, etc. (if not availed earlier). Maintain proper documentation detailing the effects of an untoward event on business activities. Consult with insurers to understand the eligibility of claims due to the impact of COVID-19 on business activities.[24]

Finance Management:

Revisit the coverage of existing policies. Obtain adequate risk covers for protection of employees, product portfolio, assets, etc. (if not availed earlier). Maintain proper documentation detailing the effects of an untoward event on business activities. Consult with insurers to understand the eligibility of claims due to the impact of COVID-19 on business activities.[24]

Pharmaceutical Business impact due to covid 19:

Covid-19 could affect the supply of finished drugs as well as Active pharmaceutical ingredients (APIs) to the world. India are major suppliers of finished dosage products as well as API to the World. Factory lockdowns and logistics delays due to Covid-19 measures at ports may affect production and delays in shipping of APIs. With the coronavirus spreading globally, the Pharmaceutical industry will have serious impact on costing. API imports from Indian manufacturers have been a major cost advantage for global pharmaceutical companies, but the outbreak and Covid-19 spread to the EU could limit the supplies to the global manufactures thereby increasing the overall costs to global manufacturers and importers & there by impacting consumers.[25]

At operational level, obviously there is impact by way slowing down the operations due to delays in activities, social distancing, continuously wearing face masks, sanitization, minimum workforce etc. All this results in lowering productivity. However due to pandemic situation, Pharmaceutical products are in great demand & Pharmaceutical Industry is seeing silver lining in growing demand & business.[26]

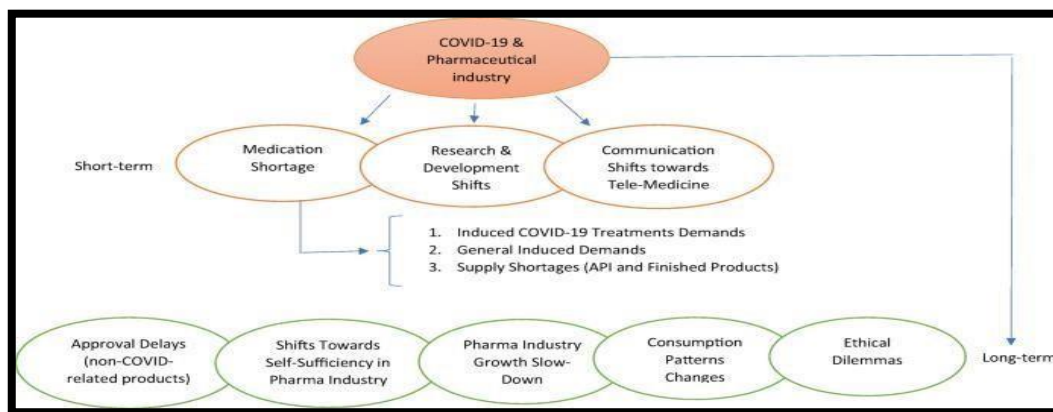


fig no.5 covid 19 and pharma industry.

Business Impact on Various Pharmaceutical Companies :

Johnson&Johnson's:

Positive Impact:-

Johnson & Johnson has committed to rapidly produce and supply more than one billion doses of a safe and effective vaccine globally. Our collaboration with Emergent is proof that we are moving quickly to deliver on that promise," Paul Stoffels, MD, vice chairman of the executive committee and chief scientific officer, Johnson & Johnson, said in the announcement.[17]

Johnson & Johnson first began efforts to research potential vaccine candidates in collaboration with Beth Israel Deaconess Medical Center (BIDMC), part of Harvard Medical School, when the COVID-19 sequence became available. Since then, various vaccine candidates have been tested.

Janssen and BIDMC went through preclinical testing for various vaccine prospects with the intent to identify possible treatments by the end March. Janssen's goal is to initiate a Phase 1 clinical study of a potential vaccine by the end of the year.

Most recently, Johnson & Johnson identified a lead coronavirus vaccine candidate and expected to initiate a Phase 1 clinical trial by September, the company announced at the end of March 2020.

The potential vaccine was discovered and the company had been working on since January through the expansion of its existing partnership between its Janssen Pharmaceutical Companies and the Biomedical Advanced Research and Development Authority (BARDA), part of HHS.

The vaccine selection also emerged from the scaling of the Company's manufacturing capacity with the goal of providing a global supply of more than one billion doses of a vaccine. The first batches of the vaccine could be available for severe patients in early 2021.

The announcement noted that Johnson & Johnson and BARDA will commit more than \$1 billion in funding for vaccine research, development, and clinical testing.

Alex Gorsky, chairman and chief executive officer at Johnson & Johnson, said that Johnson & Johnson is committed to ensuring the COVID-19 vaccine is available and affordable globally as quickly as possible.

Under the terms of the most recent collaboration, Johnson & Johnson will expand drug substance capacity. Emergent will provide drug substance manufacturing services with its molecule-to-market CDMO, starting this year, the announcement highlighted.[27]

Emergent will also reserve operations capacity to support commercial manufacturing of Johnson & Johnson's COVID-19 vaccine candidate by leveraging Janssen's AdVac and PER.C6 technologies beginning next year.

"For more than 20 years, Johnson & Johnson has invested billions of dollars in antivirals and vaccine capabilities. The COVID-19 vaccine program leverages Janssen's proven AdVac and PER.C6 technologies that provide the ability to rapidly develop new vaccine candidates and upscale production of the optimal vaccine candidate," the company stated.

"The same technology was used to develop and manufacture the Company's investigational Ebola vaccine and construct our RSV and HIV vaccine candidates, which are in Phase 2 or Phase 3 clinical development stages."

Negative Impact:-

Johnson & Johnson pharmaceutical company emerge weaker, dealing with delays in new product launches and with fewer resources to invest in R&D.

Johnson and Johnson is seeing significant disruptions in their business operations such as research and development, sales, and clinical trials.

While many pharmaceutical companies are profitable and will not need government assistance, some companies will emerge much weaker and experience delays in new product launches, with fewer resources to invest in research and development.

The study from the Pioneer Institute touched on four categories where the pharmaceutical industry will see the most downfall. Patient-provider interactions dropped more than 60 percent from early March to early April due to the pandemic, according to IQVIA highlighted in the study. The decrease in patient-provider interactions created a significant decline in the number of prescriptions. During March, there was a surge in patient stockpiling of medicines. In the months following, the volume of prescriptions has plummeted for both retail and mail order sales. Typical weekly prescription volume is around 79 million, but the last week of April saw volume drop to 68.9 million, IQVIA said.

Even solid pharmaceutical companies, including Eli Lilly and Company, said that the pandemic is going to harm its business in the future. so the pandemic has disrupted inperson sales and marketing. This is a problem especially for companies launching new drugs.

Johnsons and johnsons are experiencing a loss of medical conferences where companies can get create interest in their products by releasing data, distributing marketing material, promote their R&D pipelines, and otherwise mingle with key medical opinion leaders.

Nearly every market cap bracket fell in the first quarter for 600 global drug companies, Evaluate Advantage said in the report.

For the biotechnology sector specifically, biotech shares have generally declined. Some biotech stocks have increased on the basis of potential treatments or vaccines, such as Regeneron, Gilead, Moderna, and BioNTech, which partnered with Pfizer in midMarch on a potential vaccine.[28]

Eli Lilly's patients stockpiled treatments. But Merck cut its revenue estimates for 2020 by \$2.5 billion because two-thirds of its portfolio is physician-administered treatments.

These include vaccines, which generated over \$8 billion in sales during 2019, as well as their cancer drug, Keytruda.

Transmission Of Virus Covid-19 In Pharmaceutical Industry:

In Pharmaceutical Industry globally & efforts to overcome the challenges due to impact of Covid 19. The Pharmaceutical Industry is working tirelessly for Humanity safety. Hence our Pharmaceutical Industry is moving ahead with great confidence, as usual, to manufacture various Pharmaceutical products as well as Research & Development activities to develop the Vaccines & other products to combat the Covid 19 crisis.

People can catch COVID-19 from others who have the virus. The disease spreads primarily from person to person through small droplets from the nose or mouth, which are expelled when a person with COVID-19 coughs, sneezes, or speaks. These droplets are relatively heavy, do not travel far and quickly sink to the ground.

People can catch COVID-19 if they breathe in these droplets from a person infected with the virus. This is why it is important, as Social Distancing, to stay 1 meter to 2 meters away from a person who is sick depending upon space & situation. These droplets can land on objects and surfaces around the person such as tables, doorknobs and handrails.[29]

People can become infected by touching these objects or surfaces, then touching their eyes, nose or mouth. This is why it is important to wash your hands regularly with soap and water or clean with alcohol-based hand rub Corona virus SARS-CoV-2 (causative agent of the disease Covid-19) has severe impact & thus a global pandemic in 2020, leading to a lockdown globally.

A government imposed measures designed to slowdown the rate of infection, in order to reduce the pressure upon health services.[30]

Disinfection practices are important to reduce the potential of COVID-19 virus contamination in non-healthcare settings, such as in the home, office, schools, gyms, publicly accessible buildings, faith-based community centers, markets, transportation and business settings or restaurants. High touch surfaces should be identified for priority disinfection such as door and window handles, cafeteria and food preparation areas, counter tops, bathroom surfaces, toilets and taps, touch screen personal devices, personal computer keyboards, and work surfaces Since we are leaning more & more about new Corona 19 Virus every day, the information shared in this article may get updated based on experience & Global Experts advice. Eg. CDC USA & WHO has slightly different recommendations to use the masks or face shields as well as social distancing norms too.[31]

This article looks at various stages the Pharmaceutical Manufacturing Operation sites has to take care depending types of products & human involvement in such operations.

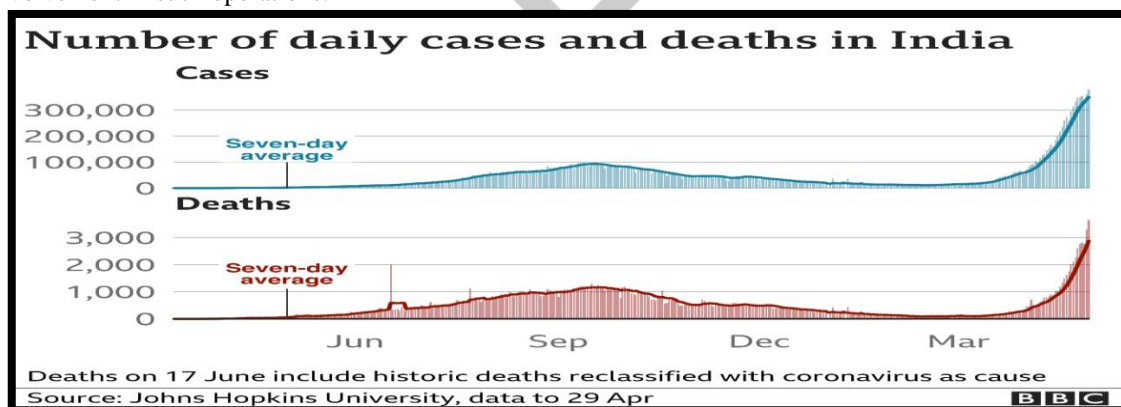


fig. no. 6 daily cases and deaths

Various operations like below have to be kept in mind:

- Supply chain of all input materials & finished products.
- Cleaning & sanitizing of Input Materials containers.

- Precautions during storage in warehouse.
- Precautions during sampling & testing.
- Necessary care during issue of Input Materials.
- Precautions while handling input materials during manufacturing operations Sanitization of all the areas.
- Social Distancing right from travel in Co. buses, entry & exit procedures, during Mfg./Packaging.[32]

Testing operations etc. in the plant. Important is SOP generations & trainings for all above activities to take all necessary steps/precautions during manufacturing & testing of products to avoid contaminations, virus spread & no one enters the plant with the Covid 19 infection. Impact of Covid-19 on larger Indian as well as Multinational players to be relatively limited.

API supplies from China for Indian customers have gradually resumed with the Drug Controller General of India reaching out to companies to extend logistics support to airlift critical APIs from China.

Manufacturing facilities continue to operate with lower workforce and at lower utilization, companies have faced disruptions in outbound logistics and in the movement of raw materials and shipments within the country. Globally, the Pharmaceutical Industry is continuing to manufacture medicines for well-being of humanity.

The Pharmaceutical Industry is in operation to save human lives. Therefore it is essential to take all necessary precautions to take care of themselves as well as others surrounding.[32]

General precautions:

Entry, exit procedures during Covid-19 Traveling from home to industry and back to home at home (before travel to work place)

- Personal Hygiene is very important now than before.
- Wash hands with soap for minimum 20 seconds.
- Have items like personal sanitizable items
- Have minimum items... essential only
- Put face mask just before travel.
- Keep in mind Social Distancing
- Body temperature checks with calibrated/validated IR Thermometer.
- No Biometric access
- Cleaning/Sanitization
- Shoes Sanitization
- Self-declaration about health
- Social Distancing[32]



Fig no.7 precaution of covid 19

Sanitization/cleaning common areas at factory:

Includes washrooms, passages, office areas, change rooms cafeteria etc.

- Cleaning/Sanitization procedures/frequency
- Use of Hydrogen Peroxide/Sodium Hypochlorite

Sanitization of supplies. Quarantine measures for supply and storage of goods after sanitization of lockers.

Maintain a sanitization routine periodically especially in the common areas that include lunch area and common tables which will have to be wiped clean with disinfectants after every single use. Keep in, mind social Distancing here as well.[33]

Factory primary change:

- Line up with Social Distancing before entry to the factory.
- Follow Social Distancing. Use marked areas for Social Distancing.
- While opening the door avoid direct touch with hands.
- Use Fresh Face Masks
- Minimum number of persons at a time, as per SOP, while entry inside change room
- Hand/Feet sanitization
- Follow gowning SOP sequence
- Sanitization of hand-gloves/shoes.[32]

Factory secondary change:

- Minimum number of persons at a time, as per SOP, while entry inside change room
- Again sanitization & cleaning as per SOP [26]

- Use fresh face mask
- Follow Social Distancing During exit from factory
- Proper hand washing/sanitization
- De-gowning as per SOP
- Proper storing of used shoes
- Wearing own civil shoes/sanitization
- Use of Face Mask
- Follow Social Distancing
- Board the travel buses.[32]

At home:

- Hand washing
- Sanitization of personal items
- Used cloths to be discarded into bin for washing
- Have Bath.[32]

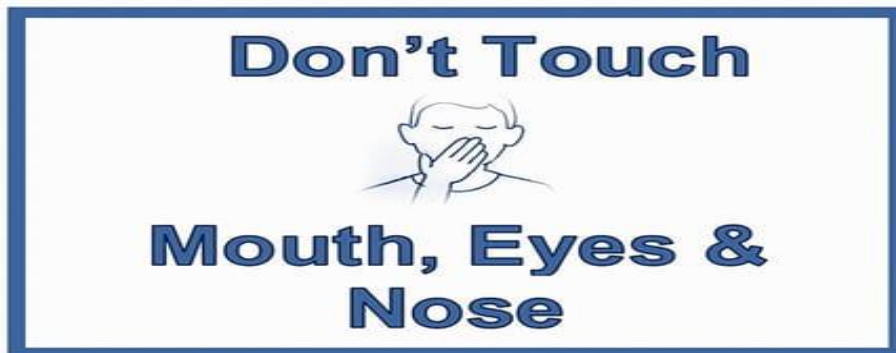


fig. no. 8 precaution of covid 19

Additional safety proactive measures in Pharma industry during Covid-19:

- Risk Based Assessment of All Procedures/ Processes for Personnel Protection in addition to The Product.
- Contactless operations to be considered like RFID based attendance and cafeteria services, hands free sanitizer dispensers, contactless temperature measurement, automatic taps and soap dispensers etc.[34]
- Educating and Training staff with Covid 19 precautions to be initiated via emailers, posters, social distance meetings.
- In the new Covid work culture, biometric fingerprint punching may be replaced by face recognition or card swiping to avoid physical touch.
- Thermal Scanners to be used location wise and temperature of all employees, contract workers & visitors entering the plants to be recorded.
- Common areas such as meeting rooms, elevators, reception, drop and pick-up points, cafeterias are floor-marked with social distancing circles to offer positional cues for visitors while standing or sitting.
- Field staff to Work from home.
- Work from Home to be initiated to reduce the number of staff in offices.[35]
- Employees above 55 & pregnant women employees, if any, may work from home.[35]
- Cafeteria furniture to be periodically sanitized. Zigzag seating has been facilitated in cafeterias and lunch breaks are now scattered over 4-5 hours.
- Employees to note primary and secondary contacts every day to keep a track of whom they are meeting.
- Create Helpline for all employees for any Covid-19 related support.
- Avoid face to face meetings. Essential meetings to be held in smaller groups via VC.
- Ensure items which can be sanitized only will be carried E.g. wallet, mobile, belt, eyeglasses, hand bags. Avoid unnecessary items.
- All vehicles and machinery entering the premise should be sanitized.[36]
- Medical insurance for the workers to be arranged.
- Work places shall have a gap of one hour between shifts and will stagger the lunch breaks of staff, to ensure social distancing.
- Social distancing in gatherings, meetings and training sessions.
- Not more than 2/4 persons (depending on size) to be allowed in lifts.
- Use of staircase for climbing should be encouraged.
- There should be strict ban of gunk, tobacco etc. and spitting should be strictly prohibited.
- There should be total ban on non-essential visitors at sites

Conclusion:

The corona virus disease continues to spread across the world following a trajectory that is difficult to predict. The health, humanitarian and socio-economic policies adopted by countries will determine the speed and strength of the recovery.

The COVID-19 global pandemic can may be associated with numerous short- and long-term impacts on the health market, mainly the pharmaceutical sector; which can be seen from both global and local perspectives.

The activities from COVID-19 are with a need to change the overall impression of pharmaceutical associations and even more together, reduce the dependence of the private pharma associations on alone suppliers like China.[30]

The pandemic of COVID-19 poses considerable crisis on the health markets, including the pharmaceutical sector; and identification of these effects, may guide policy-makers towards more evidence-informed planning to overcome accompanying challenges.

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