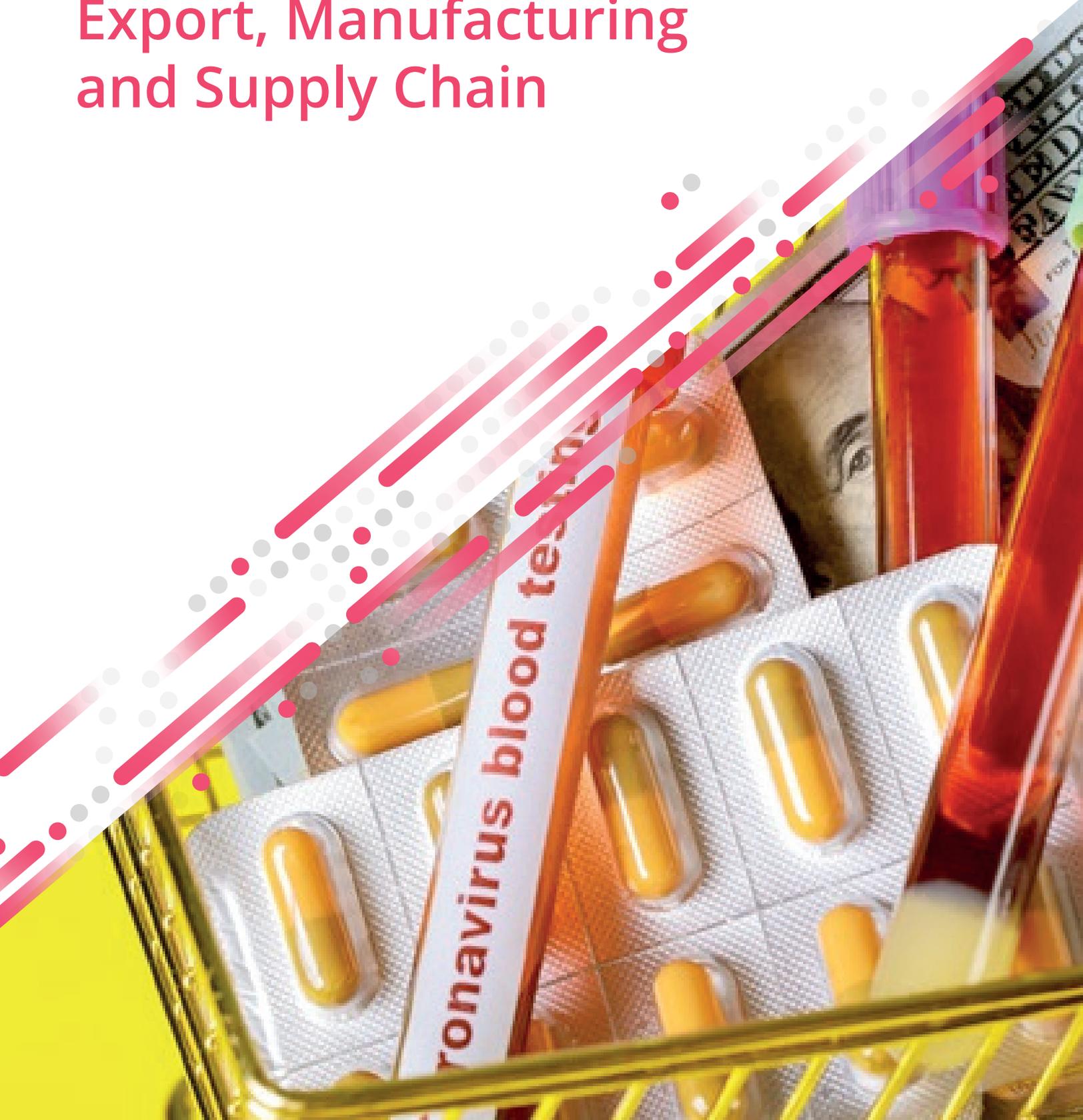


Export, Manufacturing and Supply Chain



India Curbs Exports Amid Coronavirus

Restricted Products Include Paracetamol API And Formulations

Executive Summary

India has published a list of APIs and formulations for which exports will be restricted, with immediate effect. The move comes against the backdrop of growing concerns over the off-patent industry's supply chain given the ongoing pressures caused by the coronavirus outbreak.

India's government has published a list of active pharmaceutical ingredients and formulations for which exports will be restricted, with immediate effect.

The move comes against the backdrop of growing concerns over the off-patent industry's supply chain given the ongoing pressures caused by the coronavirus outbreak, which has brought into focus the global reliance on China for APIs and has also led to concerns over the prospect of shortages within India for products that rely on Chinese imports.

In the notice published by India's directorate general of foreign trade on 3 March, 13 APIs and formulations are switched from 'free' to 'restricted' status, without elaboration.

These include paracetamol, tinidazole, metronidazole and acyclovir. Vitamins B1, B6 and B12 are also affected, along with progesterone, chloramphenicol, erythromycin salts, neomycin, clindamycin salts and ornidazole.

"Export of the specified APIs and formulations made from these APIs...is hereby restricted, with immediate effect and until further orders," the notice states.

US Food and Drug Administration commissioner Stephen Hahn said during a US Senate hearing on 3 March that the agency was reviewing the Indian export restriction notice to determine whether it would affect the US drug supply.

Global Supply Chain Under Pressure

Sandoz CEO Richard Saynor had recently labeled as "concerning" reports from India that prices for basic medicines such as painkillers and antibiotics were rising by up to 70% as a result of a tightening supply situation for Chinese APIs caused by the coronavirus outbreak. (Also see "Sandoz Pledges Price Stability Amid Coronavirus" - Generics Bulletin, 27 Feb, 2020.)

Midway through February, European off-patent industry association Medicines for Europe said it saw a "limited immediate risk to production or supplies in Europe" as a result of the coronavirus outbreak. However, the association acknowledged that if the situation continues and results in an extended shutdown period for Chinese suppliers of APIs and intermediates, "we cannot exclude an important impact on supplies due to the potential market effects of the crisis." (Also see "EU Off-Patent Industry Sees 'Limited Immediate Risk' From COVID-19" - Generics Bulletin, 19 Feb, 2020.)

Medicines for Europe has also suggested that a "simplified and quicker" procedure for registering an alternative source of API supply should be made available in urgent cases of adding a new API supplier as part of actions to mitigate supply-chain disruption. (Also see "Regulatory Measures Could Mitigate EU Coronavirus Risks" - Generics Bulletin, 19 Feb, 2020.)

More recently, the US Association for Accessible Medicines insisted it was actively working to mitigate coronavirus-related disruptions to the supply chain, with contingency planning a “top priority” for generics and biosimilars firms. AAM interim CEO Jeff Francer said that “diversifying the supply chain and ensuring there is no single point of failure is key to these efforts.” (Also see “AAM Working To Mitigate Coronavirus Effects” -

Generics Bulletin, 2 Mar, 2020.)

Sanofi recently announced plans to create the world’s second-largest API manufacturer to help ease European drugmakers’ dependence on supplies of raw materials from China and India. (Also see “Sanofi API Unit Expects \$1bn Sales By 2022” - Generics Bulletin, 28 Feb, 2020.)

AAM Working To Mitigate Coronavirus Effects

US Association Says Contingency Planning Is A 'Top Priority'

Executive Summary

The US Association for Accessible Medicines says it is actively working with industry stakeholders to mitigate coronavirus-related disruptions to the off-patent industry's supply chain, with contingency planning a "top priority."

The US Association for Accessible Medicines says it is actively working to mitigate coronavirus-related disruptions on the off-patent industry's supply chain, with contingency planning a "top priority" for generics and biosimilars firms.

"AAM is working closely with all stakeholders, including the US government, to mitigate disruptions to patient access," the industry association told Generics Bulletin.

"Supply continuity is a part of the daily manufacturer's scheduling and planning," the AAM pointed out. "As it is a top priority for our members, they spend considerable time and resources each day proactively planning for contingencies, including potential disturbances, and then adjust their ordering and scheduling needs appropriately."

"Manufacturers of generic and biosimilar medicines are committed to being part of the solution to global health issues," the AAM insisted.

The AAM's statement comes shortly after European off-patent industry association Medicines for Europe said it saw a "limited immediate risk to production or supplies in Europe" as a result of the coronavirus outbreak.

However, the association acknowledged that if the situation continues and results in an extended shutdown period for Chinese suppliers of APIs and intermediates, "we cannot exclude an important impact on supplies due to the potential market effects of the crisis." (Also see "EU Off-Patent Industry Sees 'Limited Immediate Risk' From COVID-19" - Generics Bulletin, 19 Feb, 2020.)

Just last week, Sandoz pledged to maintain stable pricing for coronavirus-related essential medicines that it markets, amid ongoing concerns over the potential short-term and longer-term impacts of the outbreak on the supply chain. (Also see "Sandoz Pledges Price Stability Amid Coronavirus" - Generics Bulletin, 27 Feb, 2020.)

Interim CEO Francer Says Firms Are Minimizing Disruption

AAM interim CEO Jeff Francer – who recently took over as head of the association following the departure of Chip Davis (Also see "Davis Steps Down As AAM's Chief" - Generics Bulletin, 12 Feb, 2020.) – said that "as global public health experts are working to map the spread and impact of the novel coronavirus COVID-19, AAM will work closely with stakeholders, including the US government, to help ensure that patients in the US may continue to access FDA-approved generic and biosimilar medicines with the same quality and consistency that has served this country so well for decades."

"With regard to COVID-19," Francer emphasized, "AAM and its members are first and foremost committed to the health of the American people by minimizing any possible disruption to access to life-saving and health-maintaining generic and biosimilar medicines."

Citing US Food and Drug Administration data on the supply chain, Francer said that it was “critical to understand where our medicines come from” as the industry considered “the challenges this pandemic presents to the drug supply.” He noted that 13% of brand and generic active pharmaceutical ingredient facilities were located in China, while the country accounted for 15% of the 1,079 API facilities worldwide that made the 370 drugs on the World Health Organization’s Essential Medicines List that were marketed in the US.

“Threats to our drug supply are not new, whether they be a virus or a hurricane, and our manufacturers practice careful planning and have systems in place to mitigate them,” Francer said. Underlining that pharmaceutical companies “spend considerable time and resources proactively planning for contingencies and then adjust their ordering and scheduling needs appropriately,” he insisted that “diversifying the supply chain and ensuring there is no single point of failure is key to these efforts.”

“While no one could have predicted that an outbreak would seemingly close all of China,” Francer acknowledged, “an event such as the coronavirus outbreak is handled by our member companies in the same manner as other emergency situations, with an immediate review of their individual supply chains. Our members may then make the adjustments necessary to minimize disturbances to supply, manufacturing and distribution.”

“Even with so much planning and anticipation, as COVID-19 evolves, so will the operational realities facing all manufacturers,” Francer concluded. “Generic drug makers remain vigilant and are closely monitoring this significant public health crisis. And AAM stands ready to work with leaders

in government and medicine to help ensure continued patient access.”

FDA Announces Coronavirus-Related Shortage

Francer also highlighted that the FDA had recently announced the first drug shortage related to an API site affected by coronavirus, although it did not identify the manufacturer or product.

FDA commissioner Stephen Hahn stressed that there were “other alternatives that can be used by patients,” adding that the FDA was “working with the manufacturer as well as other manufacturers to mitigate the shortage.”

“We will do everything possible to mitigate the shortage,” Hahn insisted.

Hahn also explained that, since 24 January, the FDA had been in touch with more than 180 drug manufacturers, “not only to remind them of applicable legal requirements for notifying the FDA of any anticipated supply disruptions, but also asking them to evaluate their entire supply chain, including APIs and other components manufactured in China.”

“Also, as part of our efforts, the FDA has identified about 20 other drugs which solely source their APIs or finished drug products from China. We have been in contact with those firms to assess whether they face any drug shortage risks due to the outbreak. None of these firms have reported any shortage to date. Also, these drugs are considered non-critical drugs.”

“The FDA is using all our existing authorities to address COVID-19,” Hahn concluded, “and we welcome the opportunity to work with Congress to further strengthen our response capabilities and emergency preparedness.”

In particular, he pointed to “four specific proposals” included in the Trump administration’s latest budget that would “better equip the FDA to prevent or mitigate medical product shortages.”

These were: lengthening expiration dates to mitigate critical human drug shortages; requiring risk-management plans for certain drugs, thus

helping to identify supply-chain vulnerabilities; improving data-sharing and requiring more accurate supply-chain information; and establishing reporting requirements for device manufacturers, given that the agency “does not have the same authorities for medical device shortages as it does for drugs and biological products.”

European Coronavirus Planning Requires 'Structured Dialog'

Stakeholders Forum Is Urgently Needed To Plan For Extended Outbreak

Executive Summary

European off-patent industry association Medicines for Europe has called on the European Commission to urgently establish a "structured dialog" involving industry stakeholders, to help plan for an extended outbreak of coronavirus.

A "structured dialog" is urgently needed between industry, the European Commission, member states and regulators to "plan for a possible extended duration" of the coronavirus outbreak, according to off-patent industry association Medicines for Europe.

Writing to the European Commissioners for health and food safety, the internal market and crisis management, Medicines for Europe director general Adrian van den Hoven and president Christoph Stoller emphasized that "we do not see any short-term risk to production or supplies in Europe."

The association had in mid-February identified only a "limited immediate risk to production or supplies in Europe" but pointed to the possibility of more significant longer-term effects depending on the duration of the outbreak. (Also see "EU Off-Patent Industry Sees 'Limited Immediate Risk' From COVID-19" - Generics Bulletin, 19 Feb, 2020.)

"We have a large manufacturing capacity in Europe that supplies 67% of prescription medicines," the letter states. "We are coping with the challenges and are prioritizing the supply of medicines to patients as is the mission of our association." However, it acknowledges, "the uncertainties regarding future developments

warrant us to take precautionary measures."

As such, the letter calls for a structured dialog "to enable regulatory flexibilities to address potential shortages related to active pharmaceutical ingredient production problems, notably the possibility for emergency variation procedures and accelerated regulatory reviews for both active ingredients and for finished products and to move products across different EU markets."

Medicines for Europe recently set out a series of policy recommendations that it says could help to mitigate the risks of the coronavirus outbreak in Europe. (Also see "Regulatory Measures Could Mitigate EU Coronavirus Risks" - Generics Bulletin, 19 Feb, 2020.)

Such a dialog could also be useful as a channel to exchange information regarding specific pharmaceutical needs – such as antivirals and antibiotics – to address the outbreak, the letter suggests, adding that "we have noted that many of the products proposed to address the virus under the recent Innovative Medicines Initiative proposal are produced by our membership."

Suggesting that a Europe-wide dialog could be enacted through the recently-established EU executive steering group on shortages of medicines caused by major events – which met for the first time on 4 March – Medicines for Europe also advises that individual member states should "establish parallel dialogues with Medicines for Europe national associations."

"The combined exchange of national and EU-level information between manufacturers and authorities would be essential to tackle any

challenges for medicines supply," the letter insists.

No Clarity Yet On Chinese Production

Acknowledging the significance of China as "a major producer of pharmaceutical inputs, notably of APIs and intermediate products," Medicines for Europe concedes that "we do not yet have full clarity on the production situation in China because workers are returning in small batches to factories, in accordance with the public health rules in the country."

According to information from the World Health Organization, Medicines for Europe says, "larger production sites will soon be fully operational, but smaller production sites, producing intermediates, are facing more difficulties." Meanwhile "logistical issues continue to be a challenge."

And addressing India's recent decision to restrict exports of certain key APIs and formulations – including paracetamol (Also see "India Curbs Exports Amid Coronavirus" - Generics Bulletin, 4 Mar, 2020.) – the association asserts that it is "concerned about the recent decision of India to impose export restrictions on certain active ingredients and medicines. While we believe that the scope of this measure will be limited in impact – affecting a small volume of exports to Europe – we are concerned about measures that clearly disrupt international co-operation."

The EU, US, India and China "should co-operate on global supply-chain manufacturing issues together with industry to maximize information and efficiency for all patients globally," Medicines for Europe insists, suggesting that "this could be facilitated by the WHO."

Guidance Needed To Maintain European Production

As Europe sees a growing number of coronavirus

cases, measures specifically geared to the region's medicines industry are needed to maintain production and logistics, Medicines for Europe argues.

Given that its members have production or laboratory sites "in all EU member states except Luxembourg," the association says, "we should provide clarity for all actors involved in medicines production."

Member state measures and decrees to limit the movement of people "should clearly recognize medicines production and logistics as essential," the letter insists, against the backdrop of nationwide lockdown measures recently imposed in Italy, a major supplier of APIs for the European market. "This will enable manufacturers to continue production and related cross-European logistics for the continued supply of medicines."

And where requested, there should also be guidance on how to maintain production and logistics while reducing the risk of the outbreak spreading, the letter urges, particularly given the significance of Italy as a center for API manufacturing.

"Our industry's major production centers in Italy are in the outbreak regions in the North of the country," the association points out, where "there are impacts on the availability of labor and concerns about logistics and transport in and out of the region."

While "our members in Italy have worked to maintain production and transport in the country for the most part," Medicines for Europe says, "the further spread of the virus to other regions in Europe close to our manufacturing sites would likely cause similar problems."

Therefore the association is calling on the Commission to provide clear guidance on transport and logistics issues “to avoid unnecessary disruptions.”

Need To Aggregate National Risk Assessments

With Medicines for Europe’s members having conducted national-level risk assessments in conjunction with local regulators, the association said it “strongly advises that the Commission and European Medicines Agency aggregate this information to assess the potential risks for supply if the outbreak continues. This would enable the Commission and inform manufacturers of potential supply problems and allow them to shift their manufacturing or their excess stocks to address the problem.”

Legal compliance issues limited the possibility for manufacturer associations to collect and share this kind of information, Medicines for Europe pointed out.

“This information could be used by the authorities to provide information to the whole manufacturing community on production and supply bottlenecks and to find manufacturers who could fill those potential gaps in the system,” the letter suggests.

Risk Of ‘Irrational Incentives’ For Stock Hoarding

Medicines for Europe also said its members had voiced concerns over the risk of hoarding within the distribution chain. “Although there

are no shortages, this disruption has an impact on the industrial market,” the association said, which “could create irrational incentives for stock hoarding.”

“We advise that the Commission and national authorities actively monitor this risk which could unnecessarily create shortages or stock-outs for patients,” Medicines for Europe urged. “There may also be a need to involve payers in this dialogue to address the economic impact of the outbreak on manufacturing which could have an impact further down the distribution chain.”

A possible decrease in the offer of APIs and intermediates “may result in sudden higher costs to produce medicinal products,” the association suggested, “which may need to be flexibly factored in the dialog with payers and authorities more generally.”

And for certain products, Medicines for Europe recommended considering the possibility of a bulk import exemption into the EU if these products are not widely commercialized in Europe – such as hydroxychloroquine – as “our members are marketing these products outside the EU where they serve a specific health need.”

“For these reasons, we call on you to enact the structured dialog with utmost urgency,” the letter concludes, emphasizing that stakeholders must “act now to prevent potential supply risks if the outbreak continues.”

For full coverage on Coronavirus from Generics Bulletin, please click here