BRITISH GENERIC MANUFACTURERS ASSOCIATION

# Strengthening the resilience of the global supply chain

## Foreword

**The COVID-19 crisis has presented challenges to society which were unimaginable even less than a year ago. The global scale and all-pervading nature of the virus has required swift and drastic measures to try keep people safe and healthcare systems from being simply overwhelmed.**

**Peter Ballard**
**Chair**

At the peak of the first wave in the UK, the pandemic derailed all sense of normality. It thrust healthcare and its supply chains into the forefront of public consciousness as the NHS staff struggled to keep pace with patient demand with the resultant knock-on effect to the medical supply chain.

The efforts of those at the vanguard of care have been extraordinary but despite this, the toll has been severe and far-reaching, and many lessons will need to be learned in the weeks, months, and years ahead.

Generic medicines, which were central to the treatment of patients impacted during the peak of the pandemic, make up three-quarters of all prescription drugs in the UK. Ensuring wherever possible that products get to patients in the right place at the right time is the principal ethos of our industry.

However, this objective has been severely challenged as demand from the NHS earlier this year, as well as other countries, soared. In some cases, our members told us that demand was 5-10 times higher than normal for certain ICU related medicines.

This coupled with logistical restrictions across the globe meant manufacturers had to work extremely hard not only to fulfil orders but ensure they made it to the UK. Stockpiles already prepared for a possible non-negotiated exit from the European Union were run down.

Sourcing of Active Pharmaceutical Ingredients (API) and logistics were other major hurdles for companies to navigate. Employment and transport restrictions, caused because of the pandemic across the globe, made it considerably harder for medicines to arrive in the right place.

Although supply was tight at times, and flexibility was needed within the NHS, patients did not go without the medicines required for intensive care and collaboration was a critical success factor ensuring medicines were able to reach where they were needed most.As an association, and along with our members, we interacted with many parts of Government and the NHS daily in coordinating actions. Elsewhere, we worked with our partners in the supply chain to reach solutions facilitated by some very pragmatic decisions by regulators to ensure products reached patients as quickly as possible.

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**Looking to the future, what cannot be lost is the strengthened collaboration and partnership between all connected to supply of medicines from manufacturers to pharmacists, and of course the NHS itself.**

Although we have moved away from the first peak, the crisis very much remains prevalent and the focus remains on seeking to create a vaccine which provides a level of immunity as well as increasing stocks in the short term. The challenges within the UK are far from over. Complacency cannot be afforded, and it is critical further measures are considered to mitigate what might lie ahead due to this pandemic or other crises. We also need to be cognizant on what impact leaving the European Union will have in the short and long-term for medicines supply.

Looking to the future, what cannot be lost is the strengthened collaboration and partnership between all connected to supply of medicines from manufacturers to pharmacists, and of course the NHS itself.

This document looks at what our industry contributed during the first wave of COVID-19 to inform the lessons required to ensure both the UK and the generics industry are adequately prepared for future similar incidents. We outline a range of recommendations that we believe Government and our stakeholder partners should examine in more detail to ensure medicines supply resilience under business as usual and future specific challenges. This would be brought together under a specific industrial strategy for the generic and biosimilar medicines industries.

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## Introduction

This report is intended to inform and provide a greater understanding of how the generic medicines market in the UK operates during normalised times. It also shines a light on how the industry performed during the peak of the first wave of the COVID-19 pandemic in the UK.

It is important to understand the issues the industry was faced with to inform and assess future policy and legislation. This also includes the context of the UK's departure from the EU's single market which we as an association estimate has already cost the generic industry £140m in additional investment and preparation.

To help inform future discussions, the report also looks at how the market works and answers key questions such as why all medicines for the UK are not manufactured here and will that change in the future?

In our accompanying resilience report document we examine in detail our recommendations on what needs to adjust and adapt to ensure the UK is as prepared as possible for future challenges. Our view at the heart of this is the need for a proper industrial strategy for generic and biosimmilar medicines given that our industry provides 78 per cent of all prescription medicines.[1]

Areas examined under a potential strategy include:

- A strategic medicines reserve and / or buffer stock
- Intellectual property
- Procurement
- Regulation
- The UK manufacturing base

COVID-19 has presented unprecedented challenges, but it would unforgivable not to learn from those and apply that experience to the future. This paper in conjunction with our resilience report seeks to create awareness, provide solutions and engender discussions with Government and industry partners to do just that. We welcome debate, discussion, and engagement on all the areas included in this report. If you would like to get in touch visit our website:

www.britishgenerics.co.uk or

email info@britishgenerics.co.uk

1 https://www.nhsbsa.nhs.uk/statistical-collections/prescription-cost-analysis-england/prescription-cost-analysis-england-2019

**Generics are authorised to the same standards of safety, quality and efficacy as original branded drugs, and have to demonstrate in clinical studies that they are bioequivalent to the original product:**

## How does the UK Generic Market work?

A generic medicine contains the same active ingredient as the equivalent original branded drug and is marketed once the originator's patent protection has expired. Generics are authorised to the same standards of safety, quality and efficacy as original branded drugs, and have to demonstrate in clinical studies that they are bioequivalent to the original product: i.e., they deliver equal medical benefits to the patient.

Generic medicines are therefore normally interchangeable with the equivalent branded drug. On the rare occasions where this is not the case, the MHRA (Medicines and Healthcare products Regulatory Agency) requires generic medicines to have a brand name so that patients may be maintained on a single manufacturer's product.



Generic medicines make the drugs bill affordable and promote innovation. When an original branded drug loses its patent protection, generic equivalents are launched, typically by many manufacturers. The competition between these manufacturers drives down prices, often leading to a reduction of 90% or more within a few weeks.

The onset of generic competition also drives innovation. Because the originators know that their products will eventually face generic competition leading to a significant fall in sales and income, they need to research new medicines.

## Virtuous circle

This interaction between branded and generic medicines is a virtuous circle: today's new drug is tomorrow's generic, and that generic provides the headroom for investment in yet further new drugs as well as the commercial incentive to develop them.

Many countries in Europe determine the cost of their generic medicines by a range of mechanisms, including basing them on the price of the equivalent branded drug, tendering, or other forms of reference pricing. This stifles competition and reduces the number of companies in the market, leading to increased risk of shortages of medicines. It also delays generic entry to the market, costing health services money due to the later onset of generic competition.

In the UK, market prices are set by competition with no barriers to entry other than gaining the product's marketing authorisation based on its safety, quality, and efficacy. This leads to a vibrant multi-source market in generics, minimising the scope for shortages and delivering on average the lowest market prices in Europe – and beyond.

**At the heart of this is in our view the need for a proper industrial strategy for generic and biosimilar medicines given that our industry provides**

**78%**

**of all prescription medicines.**

## Reimbursement price

Unlike most of the rest of Europe, most generic medicines in the UK are marketed by the generic name or International Non-proprietary Name (INN). GPs are trained at medical school to write prescriptions by INN except where there is a clinical reason for doing otherwise. Hospital Trusts also encourage their GPs to prescribe generically to benefit from the savings due to the lower costs of generics.

The reimbursement price – i.e., the price paid by the NHS to the community pharmacist of most generics changes quarterly. It is set by the Department of Health and Social Care (DHSC) and is based on quarterly returns to the Department by all generic manufacturers showing the volumes sold of each product and the net revenues gained. DHSC sets the reimbursement price according to a formula that manages the profit made by pharmacists due to dispensing generic medicines.

In this way, GPs have incentives to prescribe generics and pharmacists have incentives to dispense them, whilst prices are based on competition with the minimum of government interference. This lack of bureaucracy ensures that the NHS benefits from high levels of savings due to early generic entry to the market. Other EU member states' more bureaucratic systems achieve lower savings and only after considerable delay.

## Competition and access

A key feature of the strong generics industry in the UK is that it introduces competition to the supply of prescription medicines making them more affordable to the NHS and enhancing their availability to patients.

According to NHS figures (NHS Digital), more than a billion items are prescribed generically every year. The increase of generic prescriptions, allied with a reduction in the net ingredients costs, means that overall savings to the NHS medicines bill have now passed more than £13 billion annually.[1]

Our industry's mission is centred around increasing patient access to life saving and life changing medicines. We do this by bringing competition to the medicines' marketplace at the molecule level when patents (and / or any data or market exclusivity) expire.

This competition reduces market prices, enhances security of supply, and fosters incremental and primary innovation–all of which support increasing patient access. Examples of innovation include new administrations and dosage strengths.

The evidence is that this sort of competition controls the price of medicines more effectively than direct intervention. We believe, therefore, that direct price control by the Government should only be employed where competition has been shown to be ineffective.

Looking at 40 originator products to come off patent since the start of 2014, the introduction of generics saw sales prices reduce by an average of 89% in this time.[2]

1 Based on BGMA analysis of NHS England prescribing data

2 https://www.britishgenerics.co.uk/oxera.html

**Every year more than a billion items are generically prescribed in England which equates to 78 per cent of all medicines patients receive.**

## How much of the UK's domestic supply of generics medicines are manufactured here?

Every year more than a billion items are generically prescribed in England which equates to 78 per cent of all medicines patients receive. Of those medicines, approximately 20-25% of them are manufactured within the UK.

Development and the subsequent production of generics in the UK has been undermined historically by a more stringent view than in other jurisdictions of what research can be done during the patent term of the originator, and a constant downward pressure on price, encouraging a shift in manufacturing base to lower cost markets..

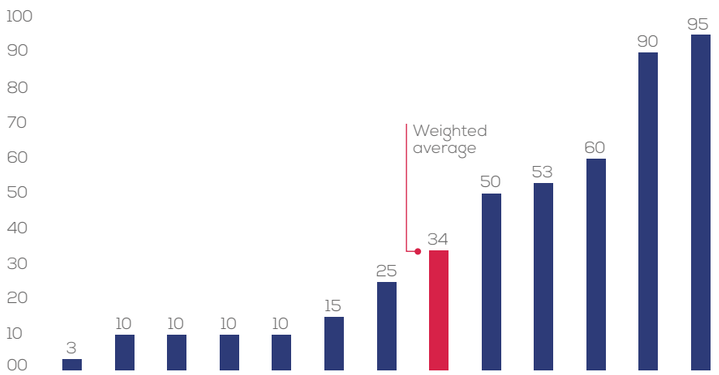
Historically, jurisprudence in the UK suggested that no research and development work could be undertaken to develop a generic medicines while a patent was in force.

In other countries, research and development was permitted: an approach that now applies in the UK too. This meant that research and development (R&D) has moved out of the UK followed by manufacturing. The location for R&D and commercial manufacture are closely linked.

The long-term consequence has become an increasing reliance on international supply chains rather than a core UK domestic base.

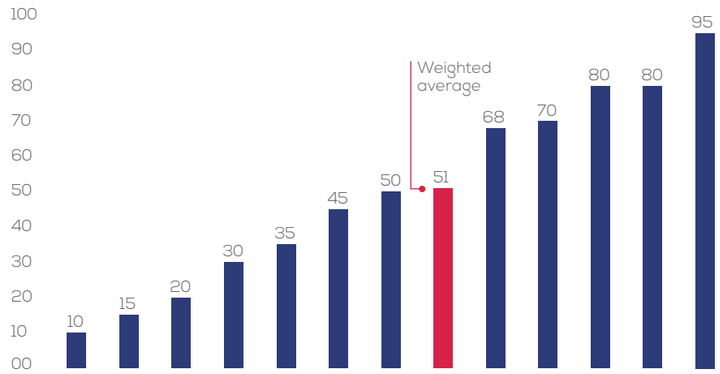
To illustrate this in a recent survey of our membership, we asked companies to show their reliance on India as an example of where a proportion of finished form products (FDF) are sourced from. The table below shows a wide variety of results with a weighted average of 34% – over a third of all medicines coming into the UK from India.

**% FDF sourced from India**






**% API from India**




**51%**

**of API was sourced from India, with a wide range from 10% to 95%.**

## API

The manufacture of the active pharmaceutical ingredients (API), which are the core of a medicine, has always been more international with the main centres in Italy and Spain, India and more recently China. In the past 15 years, generic manufacturers who are fully integrated from API through R&D to commercial production have grown. None of these companies is UK based. This has meant the manufacturing process has become increasingly globalised and has taken elements away from the UK relocating it firstly into parts of eastern Europe, and then further afield to places such as China and India.

A recent survey of BGMA members showed that on average, 51% of API was sourced from India, with a wide range from 10% to 95% as demonstrated by the table below.

While this provides benefits in terms of cost to manufacture, it also means that supply chains are becoming longer and more stretched. This means they may be less resilient, and the recent global impact of COVID-19 has underlined the potential fragility of medicines supplies as countries restricted imports and closed borders to deal with the pandemic and prioritise their local populations.

## SPC

Some legislative improvements have been seen in recent years which have helped alleviate some of the previous restrictions. A good example of this is the Supplementary Protection Certificate (SPC) manufacturing waiver which came into effect on 1st July 2019. The SPC Regulation waiver allows – among other things – European generic and biosimilar medicines manufacturers to make and stockpile medicines within European Member States during the six months before patent expiry. This means they can launch a product in the European Economic Area on the day after expiry.

Despite some of the barriers, companies still see many advantages of being close to the market they want to sell to. They can be more efficient and nimbler, responding to market dynamics a lot more quickly. This is achieved by the UK companies adopting modern and highly efficient manufacturing technologies.

Equally, a diverse and flexible manufacturing base and supply chain is important in ensuring that local disruptions may be mitigated.

Looking to the future and how manufacturing capacity may change considering the current, and future potential pandemics, there are several factors which will influence bringing medicines development and manufacturing closer to the UK. If this is to happen we would like this to be in the context of a broader strategy for the sector. Environmental concerns could be one driver and shortening supply chains would help in this respect. The other key factor will be the supply of API which is the most fundamental element of any medicine. Rather than focusing solely on more manufacturing here, access to API supply closer to home or in the UK itself could be an integral way to strengthen supply chain resilience in the future.

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# The impact of COVID-19

At times it was close – and the pressures on the pharmaceutical industry were significant, evolved rapidly and changed course regularly – but at no point did the UK run out of medicines during the peak of the pandemic earlier this year. This was the result of a mix of partnerships, pragmatism and close collaboration between industry, the NHS, Government, regulators, and international organisations.

The headline issue was unprecedented demand – particularly for ICU medicines – along with the fact that clinically so much was being learned as the pandemic took hold.

A survey of our members showed that across a wide range of ICU medicines, supply in March and April was 145% higher compared to the same period last year. In individual products, this was significantly higher.

Generic manufacturers provide four in every five medicines in the UK and thus naturally our industry was at the forefront of the crisis. One senior NHS official recently described the generics industry as "the backbone of medicines supply" in the UK. As most treatments for Covid patients were via off-patent medicines, the demand on our industry's supply chains was unprecedented with the NHS often requiring five times more medicine than normal in some areas.

Added to this were huge challenges on transport, international border control, sourcing of ingredients and workforce issues, among others. We look at these challenges and the actions taken as context to the recommendations on policy change we make at the end of this report.

There were countless examples of companies going above and beyond to maintain supply including:

- One global company produced supplies of a critical medicine in two weeks that would normally require two years.
- Another has ordered four times its normal requirement from its suppliers so that they could quickly increase the availability of medicines to patients.
- Elsewhere, in cooperation with the NHS, one company moved its stocks into the distribution chain to make space to manufacture and store more.
- Another increased its global production capacity by 50% of one product while closing other non-essential lines. It also managed to secure extra quantities for the UK and fast tracked the drugs through customs.
- Another company paid £45k – a cost it absorbed completely – to ensure medicines were delivered to the NHS over the Easter Bank Holiday and supplies maintained.
- One global company put significant resource into sourcing ICU medicines on the priority NHS list for treating COVID-19 including antibiotics, anaesthetics, and a corticosteroid. Some of these were not medicines they marketed here but via close collaboration with international colleagues were able to divert stock into the UK.

## Specific challenges

A confluence of issues – some domestic, many international – came together in the run-up to and during the peak of first wave of COVID-19 to create scenarios not previously seen before. In response, the UK medicines supply industry played a crucial role in ensuring patients were able to access the treatments they needed.

A recent report by the Department of International Trade summarised the operating environment by saying: "The COVID-19 pandemic has seen the pharmaceutical sector affected by significant and distinctive shocks to both supply and demand, compounded by trade policy interventions in some countries that have impeded trade. Our evidence indicates, though, that UK supply chains for medicines have thus far proved to be resilient, partly due to actions taken by the UK Government".

## Transport

Aside from the manufacture of medicines, logistics was a major hurdle for companies to navigate during the peak of the crisis. Employment and transport restrictions, caused because of the pandemic across the globe, made it considerably harder for medicines to arrive in the right place.

Due to the closure of borders, our industry was faced with a major breakdown of its manufacturing and distribution supply chain. In Europe, the generics industry immediately called for medicines transport "green lanes" and worked to get clearance for trucks carrying medicines across EU borders to serve patients in need. The European Union listened to concerns and created guidance which said that Member States should preserve the free circulation of all goods. They should guarantee the supply chain of essential products such as medicines, medical equipment, essential and perishable food products, and livestock.

It also stated that transport workers, especially but not only those delivering essential goods, should be able to circulate across borders as needed and their safety should in no way be compromised. This was a swift and successful resolution which meant that trucks, which are a vital part of the medicines supply network, were not impeded and able to operate in relative normality.

Closed borders were also not just a European issue. The Indian Government also closed regional borders stopping trucks from travelling as well as shutting the port of Mumbai – a major international export hub. The pharmaceutical industry was able to speak to the UK Government about the impact of this on domestic medicines supply and they in turn were able to place this as a G20 resolution which helped resolve the situation.

Other transport issues arose elsewhere. For example, shipping or long-haul passenger flights are usually how most medicines reach the UK. However, with much of aviation stopping, companies were forced to take their own action including chartering flights themselves and looking at other routes to speed delivery. All these measures incurred considerable additional investment.

Again, the generic medicines industry called for the prioritisation of medicine and medical equipment in air cargo transport.

## Ingredients

Typically, manufacturers will hold significant levels of API – one of the key ingredients for making medicines. Companies may have as much as six months of API in stock. However, due to a variety of factors, supply of API has been more challenging in recent years before the emergence of COVID-19. This has included issues in China, which has seen factories close in urban areas to reduce climate impact.

This context ahead of the significant demand caused by COVID-19 meant manufacturers were under severe pressure to source the materials needed to manufacture medicines. Particularly, as those products used for ventilation are not normally produced in large quantities. Reserves of API were called on and stockpiling already undertaken by the industry for Brexit were also used in preperation for Brexit.

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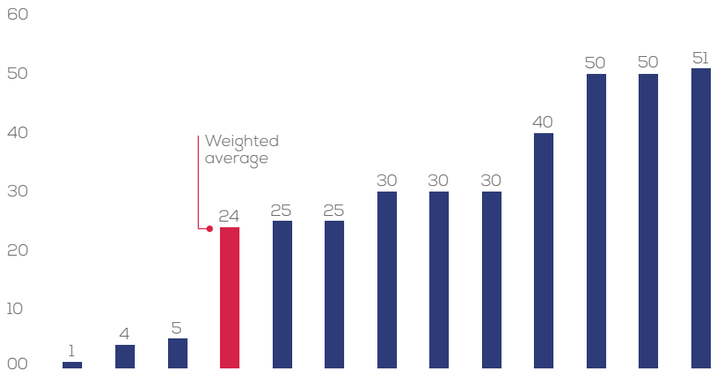
**Employment and transport restrictions, caused because of the pandemic across the globe, made it considerably harder for medicines to arrive in the right place.**

Issues were magnified by the decisions of some individual countries. For example, India, usually a major source medicines ingredients blocked all exports of API products to safeguard supplies for its own use. This also included a ban on some finished form products such as paracetamol.

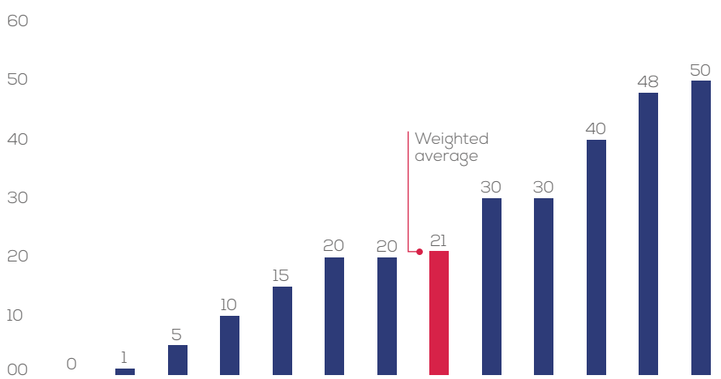
The impact was significant. We surveyed our members and asked what was the reduction in API supply because of the Indian ban during the peak of the pandemic? From the graph below, a weighted average showed nearly a quarter drop in availability of API.

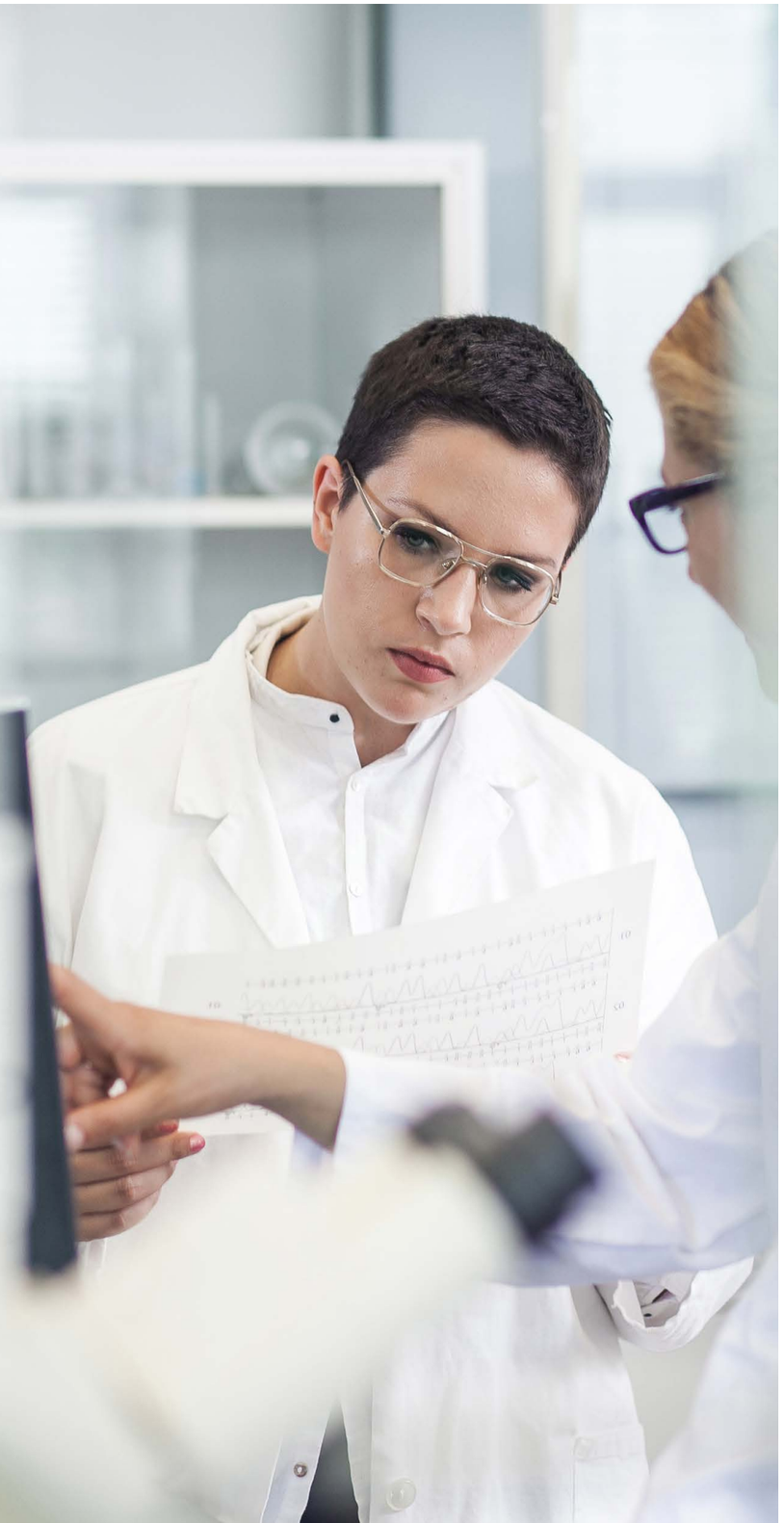
We also asked companies about the impact of the Indian export ban on their ability to supply finished form products (FDF). On average, companies found that there was a 21% reduction in supply of FDF product from India. Depending on the company, this ranged from 0% to 50%.

**% reduction in supply of API from India**




**% reduction in supply of FDF from India**





## Regulators

The COVID-19 pandemic posed unprecedented challenges to the continuity of medicines supplies. Therefore, targeted regulatory flexibility measures were needed to minimise shortages risks by for example permitting companies to swiftly source starting materials, reagents, intermediates or active substances from alternative suppliers, or add new manufacturing sites for scale-up, among other measures.

There were also many examples of companies switching manufacturing lines to try to ensure adequate levels of the right medicines were available. Guidance was also given to clinicians and the supply chain on how to maximise the use of these ICU medicines as well as the use of alternatives; and BGMA members worked with the NHS and others to ensure that demand and supply could be closely matched.

In the UK the medicines regulator MHRA responded to requests from industry for regulatory flexibilities to enable the supply of products. A programme of remote inspections was used to approve additional manufacturing sites. To allow rapid imports MHRA approved new licenses and changes to existing licenses in a few days compared to the usual three to six months.



## Looking to the future

Having outlined the issues and challenges presented by the first peak of the COVID-19 pandemic, it is critical we look ahead to see what needs to change to mitigate future potential issues. This report sets out proposals for enhancing the resilience of the generic and biosimilar medicines supply chain in a way that maximises the economic contribution of the industry to the UK.

Our ultimate resilience objective is to have a robust supply chain, able to supply medicines to patients as needed, with flexibility to be efficient at normal and enhanced levels of need.

Our overall conclusion is that there is no one single measure that delivers this on its own – the answer lies in a number of measures that mitigate the risks and bottlenecks in the existing supply chain, based on categorising medicines according to the supply risk that they present.

For this to be effective, there needs to be an industrial strategy for multi-source off-patent medicines. The elements of this can be found in the accompanying resilience report paper which outlines our recommended approach across a range of related areas.

> **Our ultimate resilience objective is to have a robust supply chain, able to supply medicines to patients as needed, with flexibility to be efficient at normal and enhanced levels of need.**

| | **Category 1 Medicines**<br>Low risk products due to indications and supply | **Category 2 Medicines**<br>Higher risk products due to importance and supply risk | **Category 3 Products**<br>Products most likely to come under pressure in pandemic |
|---|---|---|---|
| **Increased inventory** | Increase hospital trust stock holdings reversing the Carter Reforms | Buffer stocks of finished dosage form product | Medicines reserve of finished dosage form product and API |
| **Pro-resilience procurement** | Secondary care procurement policies to reward resilience and ensure plurality of supply | | |
| **Regulatory flexibilities & refocusing** | BAU regulatory flexibilities to instil supply chain resilience and flexibility of MAH response | | |
| | Off the shelf crisis flexibilities to be agreed and held in reserve for future crises | | |
| | Incentives through regulation and procurement to increase resilience through inspections of foreign API sites and level playing field quality, increased numbers of API and manufacturing sites on MAs, greater focus on the upstream supply chain | | |
| **Targeted investment in manufacturing** | | Targeted investment in manufacturing capacity of defined medicine types (e.g. sterile injectables, oral solid dose, etc), via capital grants, tax credits, etc | |
| **Pro-manufacturing IP policies** | Maintenance and extension of the SPC manufacturing waiver to make the UK a more attractive base for generic manufacture for export to non-patent protected markets whilst ensuring UK patent protection | | |
| **International cooperation** | International cooperation to aid medicines flows in times of crisis and to generate regulatory alignment and a global reference product to make generic registration in the UK more attractive post-Brexit | | |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