LESSONS FROM THE COVID-19 PANDEMIC

Enhancing Supply Chains to Ensure Consumer Access to Non-prescription Medicines

GLOBAL SELF-CARE FEDERATION

INTRODUCTION

According to Harvard Business School professor Willy Shih, the COVID-19 pandemic "exposed vulnerabilities in the production strategies and supply chains of firms just about everywhere. Temporary trade restrictions and shortages of pharmaceuticals, critical medical supplies, and other products highlighted their weaknesses."[1] Among the areas where COVID-19 had a major impact was the supply chain—from starter materials through active ingredients to finished products—of non-prescription medicines that are crucial to decreasing demands on the healthcare systems.

Initially, there was a surge in demand for popular non-prescription medicines across the globe, which, in turn, led to shortages in some geographies. At the same time, international freight shipment, both air and sea, was severely restricted and, consequently, the cost of international transportation of finished goods and product components reached record heights. Supply chain resilience was further tested, with product shortages exacerbated by exporter restrictions of starting materials and active substances. In addition, some governments began stockpiling certain products and many consumers filled their pantries in expectation of future shortages.

As supply chains were strained, the pandemic has also highlighted an issue of securing alternative suppliers or manufacturing facilities for key medicinal products. Such activities are generally part of good risk management procedures for most manufacturers. For instance, the sourcing of ingredients from one supplier (i.e., mono-sourcing) is a supply chain risk which emerged during the pandemic. Unsurprisingly, this led some governments to encourage local manufacturing to protect the needs of their own citizens, particularly for critical medications, which are primarily prescription only.[2] However, this interest, at times, spilled over into non-prescription medicines.

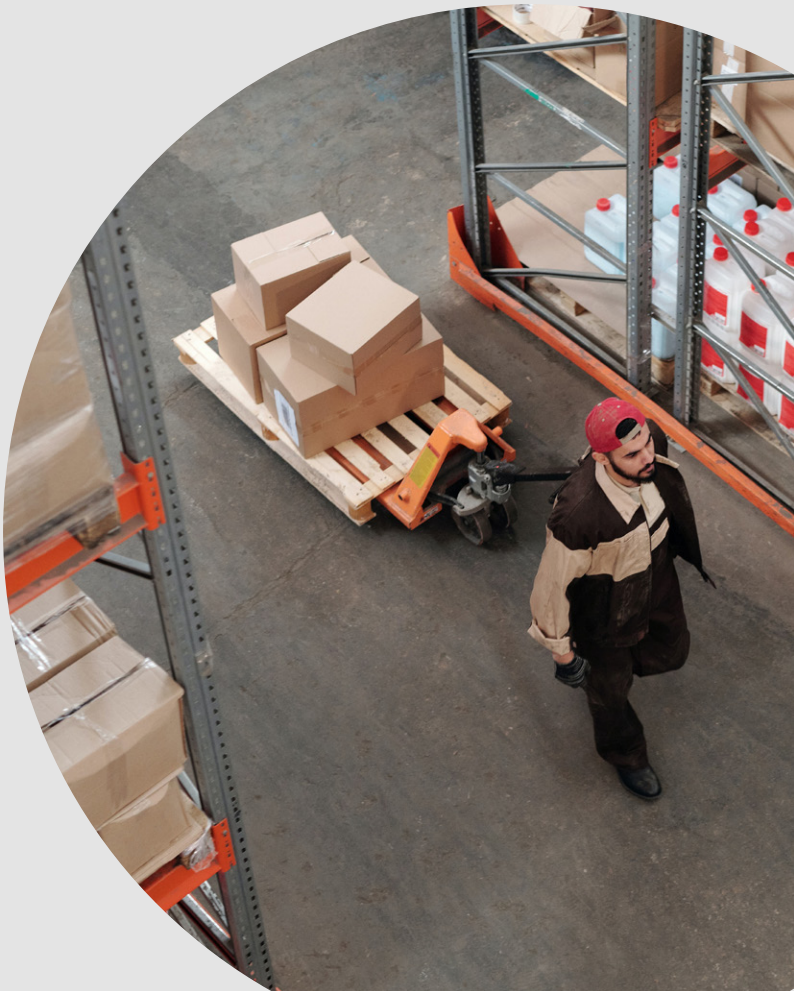
NON-PRESCRIPTION MEDICINES SUPPLY CHAIN CONTINUITY AND RESILIENCE

BACKGROUND

Once the COVID-19 crisis subsides, the Global Self-Care Federation (GSCF) recognizes that measures will need to be in place to ensure that the world is better prepared to react effectively to other similar emergencies, as well as to respond to the needs of consumers who have grown increasingly dependent on self-care. GSCF believes that many of the actions and collaborative efforts undertaken during the pandemic could, or should, become standard regulatory practice. Not every action was successful, but the fact that different practices emerged from various health authorities, provides ample opportunity to identify and share best practices at the country, regional, and global levels. Plus, the willingness to establish new or improved collaboration and communication, along with a better understanding of the importance of self-care products, suggests that there may be readiness to improve overall policies and regulations to help prepare for the next emergency and to improve standard regulatory and supply practices going forward.

As governments and regulators consider updating policies associated with non-prescription medicines supply chain sustainability and resilience, three interconnected principles should be applied:

- **Co-operation amongst governments and regulatory agencies and with manufacturers to create a closely connected, diverse, and resilient supply chain.**
- **Convergence of regulatory practices and principles amongst regulatory bodies in the regulation of self-care products, ensuring that consumers are able to obtain trustworthy, quality products.**
- **Reduction of the regulatory burden for new products with established APIs and for the life-cycle management of existing products, while keeping in place all effective provisions to ensure quality.**



DISCUSSION

CO-OPERATION AMONGST GOVERNMENTS AND REGULATORY AGENCIES AND WITH MANUFACTURERS TO CREATE A CLOSELY CONNECTED, DIVERSE, AND RESILIENT SUPPLY CHAIN

As previously discussed, the COVID-19 pandemic was highly disruptive to supply chains across different industries. One of the positive responses was the formation of new collaborations among regulatory authorities and manufacturers and the strengthening of existing collaborations at national and global levels. This resulted in greater awareness of the challenges being faced by authorities, manufacturers, and most importantly, consumers and patients during the COVID-19 crisis. It has also triggered health authorities and manufacturers to explore innovative solutions to these challenges.

On the other hand, governments, in some instances, found that national producers of finished goods and component materials were often less dependent on difficult to obtain source materials from suppliers in Asia, leaving them with a near-term advantage over multi-national manufacturers. This led to an interest by governments to encourage localisation or regionalisation of manufacturing of component materials and finished goods for many products. Local sourcing does come with some actual and theoretical advantages, not the least of which is its near-term impact on the local economy. And, theoretically, shorter supply chains may lead to greater predictability in delivery of critically needed products, particularly in times of crisis. Although there may also be some environmental advantages due to less need for freight transportation, this model comes with numerous challenges. As globalisation of supply chains is associated with lower costs of supplies, shorter supply chains carry economic implications. In some markets, local manufacturing may be impeded by poor infrastructure, human resource constraints and limited local technical capability. Mandated local sourcing may also be associated with decreased flexibility in materials since local supplies are typically dependent on single manufacturing sites. Another challenge is the cost of establishing and meeting current global good manufacturing practices (GMPs) which guarantee the quality of medical products. Finally, any move towards mandated local sourcing should be discouraged; when combined with protectionist measures such as mandatory purchasing of locally produced products, this could lead to international trade conflicts that could have unintended consequences on supply chains. Overcoming these challenges could inflate the cost of production, which means the final product may be available for a higher price, making it relatively non-competitive against potentially cheaper imports.

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Overall, GSCF believes that **it is critical that governments do not mandate the localisation of components of the supply chain and do not**

implement policies that would destabilize the supply chain for currently available medicines or take any measures that could undermine the complex arrangements between firms which allow for efficient delivery of medicines. Instead, to reduce over-dependence on dominant suppliers or regions, manufacturers **need greater flexibility for multiple sourcing sites both for active pharmaceutical ingredients and critical starting materials**. For instance, in the EU, manufacturers can exceptionally source starting materials, reagents, intermediates or active substances from suppliers not specifically mentioned in the marketing authorisation if that is necessary to prevent or mitigate shortages of supplies. In a second example, the Taiwan Food and Drug Administration allows a fast-track for registering additional active pharmaceutical ingredient (API) sources if there is concern of the sufficient product supply for the original API.

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While the effects of the COVID-19 pandemic continue, GSCF believes governments and regulatory agencies should, first and foremost, **prioritize patient and consumer needs**. This starts with **greater international co-operation on mitigating supply chain challenges** at both national and international levels. Doing so would improve the non-prescription medicines industry's ability to make trustworthy, quality self-care products available to consumers and patients during the current and future crises, as well as the post-pandemic period. The hope is that today's collaborative climate among health authorities and between health authorities and manufacturers could serve as a catalyst for codification of such policies and regulations. This proactive approach, which could extend to other parts of government, such as customs, needs to be long term, collaborative, and coordinated, as well as include many of the improvements designed to be implemented in times of crisis and beyond. In addition, increased action by the **World Trade Organization to both coordinate and arbitrate export restrictions that impact global supply chains is warranted**. Finally, as mentioned previously, **the World Health Organization needs to step forward and encourage and guide regulatory agencies in the development of "emergency preparedness protocols" for future emergencies**. The emergency preparedness protocols would include recommendations for appropriate regulatory procedure postponements, as well as plans for the rapid creation of new regulatory guidance designed to address issues associated with emergencies.

One of the innovations established during COVID-19 that should be maintained is the institution of **single points of contact at regulatory bodies, which served to enhance coordination between manufacturers and the regulator**, as occurred in the EU during the pandemic. This was particularly valuable in ensuring clear and rapid communication of supply chain issues resulting in increased trust and more rapid problem solving.

CONSISTENCY AND CONFORMITY AMONGST REGULATORY BODIES IN THE REGULATION OF SELF-CARE PRODUCTS, ENSURING THAT CONSUMERS ARE ABLE TO OBTAIN TRUSTWORTHY, QUALITY PRODUCTS

The regulatory frameworks governing self-care products, including non-prescription medicines, are extremely varied and inconsistent from country to country. As a result, the list of OTC medicinal products available for self-care on different markets changes. A survey of 4,400 consumers during the COVID-19 pandemic across Italy, Germany, Spain, and the UK indicated that consumers are increasingly interested in having more non-prescription medicines at their disposal, not only for their personal ability to self-treat, but also to ease the strain on national health systems.[3]

As consumers desire greater availability of self-care products, GSCF believes that a key step to ensure global supply of critical healthcare products and cross-border access is moving towards **greater convergence at the global level with regards**

to the regulation of non-prescription medicinal products. This includes **global mutual recognition among worldwide regulators**, perhaps implemented through currently existing collaborations such as the International Coalition of Medicines Regulatory Authorities or the International Conference of Drug Regulatory Authorities.

Another example of greater consistency and conformity at the international level has been the UK's EC Decision Reliance Procedure (ECDRP) for marketing authorisation and post-approval variations. It was established in 2021 to recognise the successful completion of procedures for the same medicinal products by the regulatory authorities of its former partners in the European Union (EU). Although these initiatives are primarily targeted at providing patients with early access to new and advanced medical therapies, such models could be extended to non-prescription medicines to support greater international co-operation for mutual recognition between regulatory authorities. The subsequent regulatory reliance between jurisdictions upon prior approvals would help new non-prescription medicines reach intended markets quicker and facilitate post-approval changes.

Correspondingly, low- and middle-income countries, which currently depend on substantiated regulatory approvals within developed economies and the issuance of certificates of free sale could instead rely on mutual recognition between regional authorities or similar schemes. As an example, the newly formed African Medicines Agency could begin developing greater harmonization within the African Union (AU), hopefully leading to an increase in the availability of non-prescription medicines across the AU.

REDUCTION OF THE REGULATORY BURDEN FOR NEW PRODUCTS WITH ESTABLISHED APIS AND FOR THE LIFE-CYCLE MANAGEMENT OF EXISTING PRODUCTS, WHILE KEEPING IN PLACE ALL EFFECTIVE PROVISIONS TO ENSURE QUALITY

Regulatory agencies ensure that Good Manufacturing Practices (GMP) standards are met by all manufacturers and for all approved products, including non-prescription medicines. They also supervise Good Clinical Practice (GCP) and Good Pharmacovigilance Practice (GVP) standards. These three sets of standards are collectively known as GxP.

GSCF believes that the fact that much is known about these medicines provides a significant opportunity to **reduce a regulatory burden on introducing new products with established active substances as well as on the life-cycle management of existing products based on learnings from the practices adopted during the COVID-19 pandemic**. It is also an opportunity to implement practical changes that might lessen the impact of future crises and ensure that consumers have uninterrupted access to products they use on a regular basis.

Historically, regulatory oversight of GxP has been managed through on-site visits by health authorities. During the early stages of the COVID-19 pandemic, despite a preference by European and US health authorities for on-site visits, regulators began conducting virtual inspections. These virtual visits are an innovative approach to maintaining rigorous GxP standards, while optimizing agency resources.

"Skip-testing", a process employed to reduce the analytical testing burden associated with frequency batch production, can easily be streamlined. Rather than test all batches within a given interval, the number of batches tested should be commensurate with risk. If potential risks have been identified and well understood, such that testing is expected to be consistent batch to batch, it may be appropriate to test pre-selected batches while 'skipping' the remaining ones. This reduction is justified by a visibly low risk of any batches failing specification. This is particularly true for non-prescription medicines, which are generally well-characterised due to their long history of use. **GSCF invites regulatory authorities to collaborate with manufacturers to develop a framework which defines when and how risk-based skip testing for finished product batches should be implemented**.

Current post-approval changes and renewal systems present many challenges as countries and regional regulators take vastly different approaches. This includes fragmented local regulatory requirements, inconsistent approval timelines, divergent regulatory decisions, irregular implementation periods,

bureaucracy, unnecessary administrative processes and sometimes even re-submissions or re-working. These circumstances result in disproportionately lengthy times for approvals, diverted resources and budgets for regulators (and manufacturers), and several versions of products approved globally with little added benefit to the consumer. GSCF believes that opportunities such as **global coordination of regulatory requirements, mutual reliance, recognition of prior applicable decisions by other regulatory agencies as well as other coordination initiatives would provide a more efficient environment for the management of post-approval changes and renewals**. COVID-19 led to regulatory pragmatism in some markets regarding the life-cycle management activities for self-care products, which, in turn, demonstrates that regulation of self-care products can be managed more effectively, without undue shift in risk to product quality and consumer safety.

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Post-approval regulation of non-prescription medicines, including **simplified approvals of variations, is also an area that can easily be modified** since risk management measures for these well-characterized products are generally understood. From a global perspective, where possible, post-approval changes should follow a common international system which is evidence- and risk-based and which establishes the same data requirements across regulatory authorities. Minor quality variations and other modifications requiring purely administrative changes should not require any regulatory approval prior to implementation. Agencies could either be notified in a periodic report or such changes should be maintained within the manufacturer's quality system and reviewed during inspections. For example, under the "do and tell" model in the EU, for a minor variation that has none or only a minimal impact on the quality, safety or efficacy of the medicinal product, the manufacturer must simply notify the regulatory authority within 12 months of the variation.

Variations of a moderate and major nature in terms of impact on quality and safety should be reviewed within set and predictable timelines before their implementation. In Europe, with regards to the evaluation within national phase procedures, health authorities could commit to a 30-day timeline to approve a single variation for simultaneous implementation everywhere. In the USA, Japan, and Australia, there is no regulatory licence renewal process for non-prescription medicines while in the EU and UK, renewals for non-prescription medicines are normally not required beyond five years after first marketing authorisation. Considering good pharmacovigilance practices worldwide and their well-established safety profile, the review of the safety of non-prescription products does not need to be done through a formal renewal. And, since quality aspects are continuously re-evaluated and updated through post-approval life-cycle management, the need for the licence renewal process should be deemed to be unnecessary.

Global coordination of regulatory requirements, mutual reliance, recognition of prior applicable decisions by other regulatory agencies as well as other coordination initiatives would provide a more efficient environment for the management of post-approval changes and renewals.

CONCLUSION

COVID-19 has exposed weaknesses in the global supply chain for many product categories, including non-prescription medicines. However, through innovative approaches implemented by governments, regulatory agencies, and manufacturers during the crisis, most shortages caused by supply chain issues were mitigated and avoided. To further enhance supply chain continuity and resilience for the future, both in emergency and normal times, it will be important for regulatory and other stakeholders to consider incorporating many of these innovations, as well as other best practices into standard practice. In the end, strong supply chains ensure that consumers can obtain safe and effective non-prescription medicines when needed, thus making the entire healthcare system more efficient and better able to serve individual patients, their families, and countries as a whole.

REFERENCES

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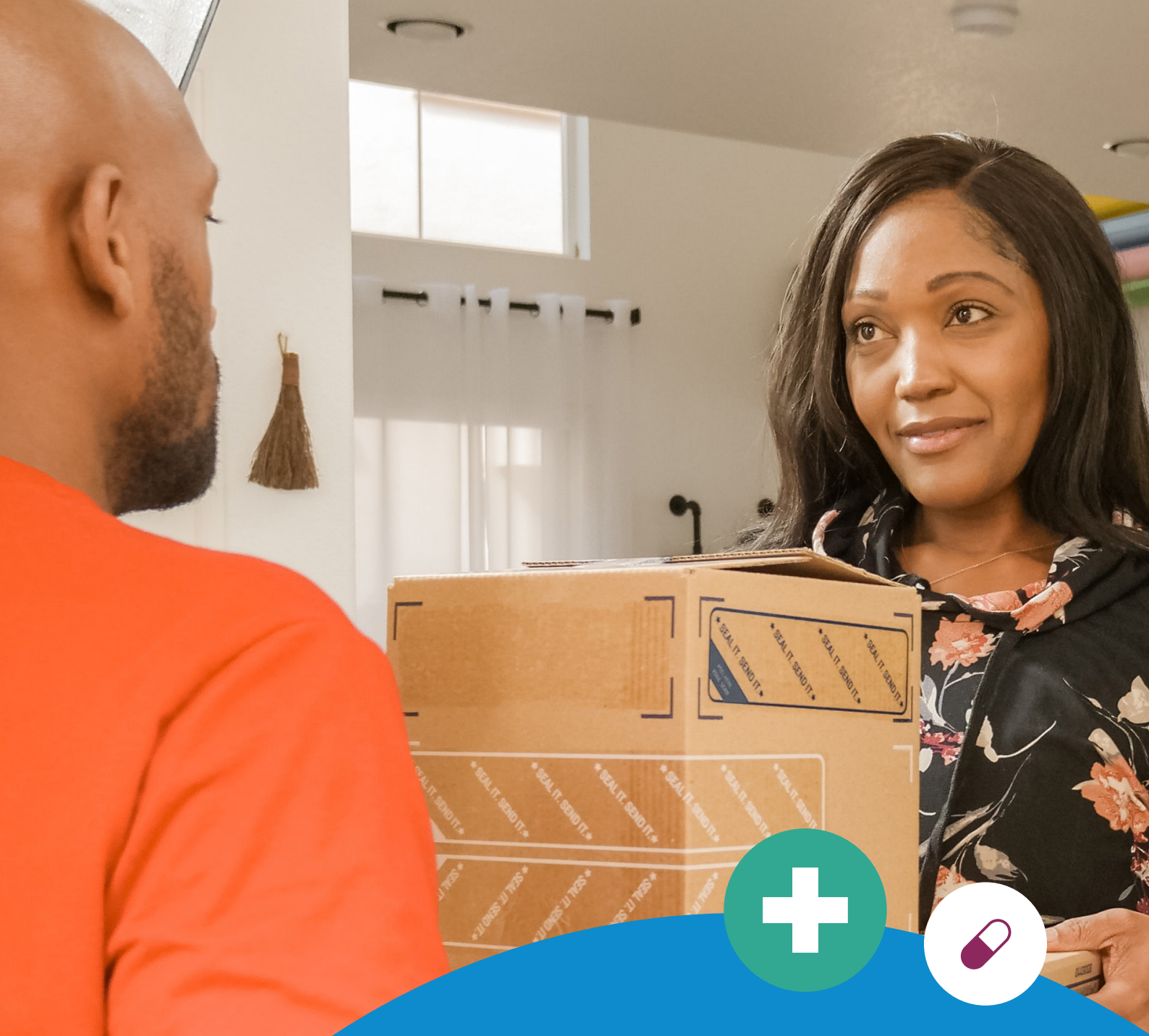

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GSCF is dedicated to a world where self-care provides individuals, families, and communities with the ability to manage their health and prevent diseases with or without the support of a health-care provider. Successful self-care provides individuals with greater choice of healthcare options and more accessible entries to care—e.g., through pharmacies; greater value for care when treating ailments and chronic conditions; and can lead to long-term better health outcomes. It also can decrease the burden on healthcare systems and professional medical personnel; increase freedom for innovation in healthcare; and make progress toward universal health coverage.

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