

The Life Science Manufacturers Association, comprising companies that develop products for R&D, bioproduction and biotechnologies summarises a few considerations in the context of the current ongoing Substitution Study of the European Commission. We would like to highlight some of the specific considerations required by the life science value chain when it comes to substitution activities and challenges.

Question 1 – Substitution challenges of the current regulatory framework

- A one-size-fits-all approach for all industries overlooks technical variations, hindering successful substitution efforts and creating a disproportionate impact on society compared to human health and environmental gains.
 - Substitution overlooks nuance in how end-use performance expectations are challenged every day – both by the LSMA and our end customers. Products produced and used within the Life Science sector are often utilized beyond stated design specifications to enable scientific advancements and improve the health and welfare of society.
 - Substitution often comes with the additional complexity of the end-use going into highly regulated processes where performance changes can result in years-long re-validations, regulatory approvals, and market acceptance.
 - Cascading requirements for re-validations prior to pharma application should be applicable.
- Life Science Manufacturers must work hand-in-hand with our end-users to develop and validate alternative solutions, so such changes do not impact their applications (as illustrated in *Figure 1*).

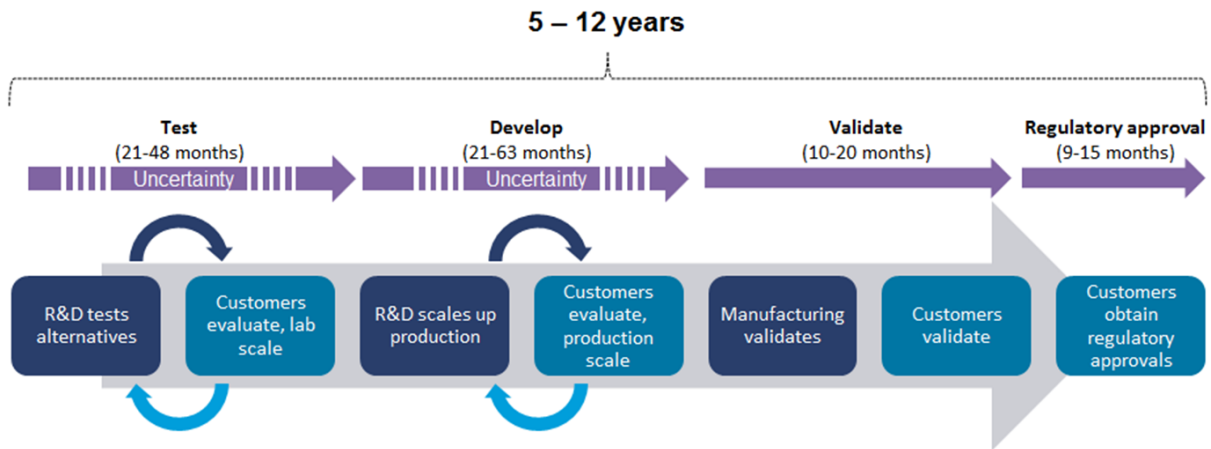


Figure 1 – Illustration of usual life science manufacturing timeline

- Successful substitution hinges on the commitment of article producers across global supply chains to collaborate towards innovative solutions that are practicable across all relevant sectors. This facet requires better understanding by regulators and support. Ideally, there should be a global alignment of regulatory actions on substances.

Disclaimer

This position paper has been prepared by the members of the LSMA in regard to the currently ongoing consultation process on *Strengthening the role of substitution planning in the context of REACH and other EU chemicals legislation* study by the European Commission. The content of this document is based on information known to us at the time of writing and may be subject to change.

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- Innovation and substitution can be highly time-consuming and unpredictable processes for the actors involved in Life Science Manufacturing. Furthermore, due to the varied and unpredictable performance requirements placed upon Life Science products, time-limited derogations, without regard to the technical progress of substitution are not suitable. Sectoral considerations need to be incorporated into substitution timelines and derogations.
- The Life Science Manufacturing sector supplies to industries and markets overseen by agencies such as EMA, which are subject to sectoral regulations such as the Medical Device Regulation, the In Vitro Diagnostic Devices Regulation, and the different medicinal regulations related to humans and animals. These companies often receive exemptions and derogations under REACH, whereas Life Science Manufacturers generally do not. Moreover, Life Science Manufacturers must indirectly comply with the aforementioned sectorial regulations. Therefore, this sector should be consistently covered by the exemptions and derogations granted to their clients, when relevant.
- The lack of certainty arising from unpredictable decision timelines in REACH authorisation/restriction processes impacts companies and hinders their ability to substitute and innovate. This unpredictability slows business decision-making and increases the risk of regrettable substitution by a selection of short-term alternatives.
- Additionally, the concept of "Suitable Alternative Generally Available" (SAGA¹) plays a crucial role in REACH authorization processes. However, applying this concept in Life Science applications presents unique challenges. SAGA overlooks sector-specific nuances where performance cannot be always predicted by perceived 'equivalent alternatives; and where the generally available criteria is rarely met. The availability of alternatives often hinges on sectoral regulation procedures, leading to significant delays surpassing REACH's authorization and restriction deadlines. It is important to understand that for uses covered by LSMA, neither performance nor time available for substitution can be compromised and this leads in most cases to a situation where the SAGA conditions are not met and hence it justifies the need for additional or extended derogations.
- Additionally, the "generally available" criterion can be difficult to meet due to overlapping sectoral regulations, which can significantly delay the development and approval of alternatives, exceeding REACH's authorization or restriction deadlines. For Life Science applications maintaining both performance and timely substitution is critical. This often leads to situations where the SAGA criteria are not fully met, potentially justifying the need for additional or extended derogations.
- In the case of complex Life Science instrumentation and equipment, substitution involves actors on many levels upstream of LSMA members. Each level has obligations ranging from new chemistry ideation, testing, and scale-up (in addition to registration and/or pre-manufacturing regulatory approvals), development of novel manufacturing processes adopting the new chemistry, obtaining global product certifications, and market acceptance before the substitution can be effectively implemented. Life Science Manufacturers have first-hand experience with substitutions taking more than 12 years to execute.

Question 2 – Validating objectives of the substitution framework

- A future framework should consider the efficiency of all stakeholders active within the wider supply chain, in addition to the Member States and the EU Commission.
- The project's primary objectives should incorporate incentives aimed at facilitating the transition to safer alternatives while addressing sector-specific requirements. For instance, fostering

¹ See [Assessment of Alternatives: Suitable Alternative Available in General & Requirement for a Substitution Plan](#), 27 May 2020

innovation and augmenting R&D funding for technically feasible substitutes would provide crucial support to industries.

- The renewal of restriction derogations under Title VIII of REACH should be granted based on a lack of scientific and technical progress. It is therefore vital that the provisions governing the use of substitution plans in both REACH authorisations and restrictions include clear conditions for a revision clause to give the needed certainty when embarking on a costly and challenging substitution process.
- Recognising the diverse needs and challenges of each sector to accomplish substitution, adopting a sectoral approach is proposed.
- Incorporating realistic timelines into REACH restrictions would ultimately advance the objectives of the substitution framework. Mechanisms in the framework should improve the information available to dossier submitters to allow them better scope Restrictions and to propose realistic derogation timeframes.

Question 3 – Early information needs on uses, exposure and alternatives to enhance regulatory substitution timelines:

- Ensure the confidential repository of full material declarations for all articles. While ideally, the EU could centralize disclosures for all parts used in millions of products, acknowledging the current limitations, this initiative should focus on establishing mechanisms to accommodate late data submissions.
- Facilitate early discussions on alternatives to streamline regulatory processes.
- Drawing from recent experience on the uPFAS consultation, it would be useful to involve all value chain actors in dialogues and consultations from the beginning, especially component manufacturers and input suppliers, as well as SMEs.
- Similarly, enhancing the RMOA process is important to enable the industry to provide information and ensure that future risk management actions take into account potential impacts on the supply chains.

Question 4 – Legal/Voluntary substitution planning requirements

- Substitution planning should expand beyond REACH authorizations to include restrictions, focusing on fostering sector-specific substitution plans. These would also assist regulators in charge of preparing restriction dossiers to propose upfront derogations for sectors such as the life science value chain.
- To facilitate the process, developing a standardized substitution plan template and accompanying guidance is highly recommended. However, we should also consider alternative approaches, such as performance-based criteria, to ensure the greatest enablement for our industry.
- Voluntary substitution planning, led by pioneering companies and subsequently expanded through collaborative efforts within sectors, can generate momentum for substitution initiatives. At the same time, voluntary substitution should also bring financial incentives via grants or tax relief.
- However, any collaborative efforts will be severely limited by competition law and mechanisms introduced for substitution planning will need to account for this. “Cutting edge” sectors such as Life Science with small numbers of companies will be more restricted in collaboration than commodity or consumer sectors.

Question 5 – Effectively implementing the substitution plan

- Collaborative industry efforts have the advantage of streamlining safer alternatives and collectively responding to the demands. However, mechanisms to provide substitution plans for company-specific uses are required, especially for innovative, prospective or commercially sensitive uses that are critical for society.
- Sector-wide joint plans can be effectively developed and coordinated within industries where there is an acknowledgement of problematic substances and a commitment among companies to drive change.
- To address concerns regarding anti-competitive behaviour and safeguard innovators' interests, measures such as new block exemptions may be necessary. Implementing strict regulations on collaboration and data management, overseen by a neutral third party, can mitigate anti-competitive practices and safeguard confidential information.

Question 6 – Responsible actors in preparing, reviewing and monitoring the implementation of substitution plans

- Collaboration among key stakeholders throughout the value chain, including customers, suppliers, academia, micro-, and small- and medium-sized enterprises is vital for the development of substitution plans.
- To ensure transparent and inclusive decision-making processes, representatives from diverse sectors should assess the appropriateness of plans.
- Continuous monitoring of (sectoral) substitution plans, particularly within specific sectors, is key to maintaining effectiveness, adapting to emerging challenges, aligning with evolving regulatory standards, and promoting industry compliance and environmental sustainability.

For further information and inquiries, please contact the LSMA at info@lsma.org or visit their website at www.lsma.org.