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CONNECTING & SUPPORTING PHARMA ACROSS EUROPE

Position paper 2021

Enhancing the Role of European Small and Medium Sized Enterprises (SMEs) for their Contribution in Making Affordable Medicines Available to European Patients.

Table of Content

1 Policy Objective

Enhancing the Role of European Small and Medium Sized Enterprises (SMEs) for their Contribution in Making Affordable Medicines Available to European Patients.

2 Introduction to Europharm SMC

Europharm SMC is the official European Association representing Small and Medium Sized pharmaceutical companies in the EU.

Europharm SMC supports and defends the interests of its members, in achieving a legal and political framework compatible with the interest of SMEs in the global pharmaceutical industry.

Europharm SMC encourages and assists companies to develop co-operations and other forms of synergies with partners across national borders.

Europharm aims at working towards improving economic frame conditions specifically oriented to company size and less to pharmaceutical fields of activity (e.g. general matters of taxation, co-operation with companies and institutions representing the interests of mid-sized businesses).

3 Importance of Pharmaceutical SMEs in Europe

In the pharmaceutical sector, SMEs are the motor of innovation and play a major role in the development and distribution of new medicines for patients.[1] SMEs are a major source of innovation to address rare diseases: 42% of the medicines that were recommended for marketing authorization in the past ten years were orphan medicines.[2]

SMEs applications for the marketing authorization of new medicines account for approximately 10 to 15% of the overall number of applications. More than one in two medicines developed by SMEs that were recommended for marketing authorization in the past ten years contained a new active substance; this shows that SMEs are an important source of medicines that have the potential to address patients' unmet medical needs.

Pharmaceutical SMEs also play an important role in Europe on the revival of the economy, by creating employment and new market opportunities, in the segments of manufacturing, supply chain and therapeutical innovation of medicinal products. Tailor-made support to help them grow and innovate is essential. At all stages of development, small businesses struggle more than large enterprises to get finance and reassure sustainability and resilience to secure supply for patients in an ever more demanding environmental legislative framework, fierce competition and significant deterioration of pricing & reimbursement conditions in some EU countries.

On the grounds of the decisions taken at the European level, pharmaceutical SMEs have to be seen as an important resource to be further stimulated, considering not only their

[1] SME Annual Report 2018-2019
[2] EMA SME Office Annual Report 2019

industrial value as manufacturers and distributors of medicinal products, their capacity to deliver high value jobs but also considering their ability to, develop innovative technologies on essential well established active ingredients and to cover therapeutical areas where multinational companies are less active in, such as orphan drugs and even to some extent, to start, new innovative research activities in critical areas of unmet need such as those of antimicrobial resistance and new threats to mankind.

Whereas on the one hand, globalisation and networking are key words for success, on the other, SMEs experience new needs to face this challenge – from the need for swifter information exchange and the search for cooperation partners, to the need for logistic support in R&D, product registration and drug production and distribution – which in order to be successfully overcome, will require a strong sense of union and close cooperation amongst SMEs across the national borders, but also the need for a strong financial and educational infrastructure from the European institutes to ensure global competitiveness and resilience of SMEs

From the perspective of the local governments and European institutions, there has been a strong will, underlined in several European Commission Communications, to promote and enhance competitiveness of the small and medium-sized companies, but more needs to be done

4 SMEs Future Challenges

Key challenges that SMEs face in all phases of their lifecycle with regards to funding, cost of regulation and reduction of regulatory burden, identified in SMEs stakeholders' consultations have been addressed through actions planned at EU level. The measures aim to promote innovation, unlock potential investments and help small and medium-sized enterprises to grow.[3]

In May 2017 EMA published an action plan for 2017-2020 for small and medium-sized enterprises (SMEs) built on measures introduced to support SMEs pursuant to Commission Regulation (EC) No 2049/2005.

The action plan addressed the following challenges:

- awareness of the EMA SME initiative
- training and education
- support to innovative medicines' development
- engagement with SMEs, EU partners and stakeholders.

Indeed, through the SME Office at EMA, registered SMEs (close to 2000 companies) receive assistance and support in identifying the most relevant guidance, and advice on regulatory strategy for a product development or authorization.

However, under the current circumstances and particularly due to the economic consequences of the pandemic, SMEs are the most vulnerable companies, and therefore, further active measures need to take place to support SMEs with financial and regulatory

[3] EMA Action Plan 30rd May 2017

measures to ensure economic survival and support of SMEs in all stages of medicines' development, and in the manufacturing and distribution activities.

5 Europharm's proposal for enhancing SMEs' competitiveness and viability

5.1 Ensure the profitability of SMEs and strengthen the competitiveness of European SMEs

5.1.1. Stimulate new business synergies, support and promote international expansion of SMEs to other EU countries and ROW.

Even if the global EU Pharmaceutical trade balance shows a positive value of 122,031 Mio€, this value could be greater and there are many EU countries showing a negative balance[4] and this should be improved. Europharm's proposals are:

- Create incentives and special guidance from regulatory authorities for registration preparedness and submission and other investments made for expansion of local activity to other markets and/or export of their products
- Cooperate with associations which promote and enhance business partnerships and collaborations among SMEs and with other companies.

5.1.2. Economical sustainability of mature and essential products

All European countries are heavily involved in the provision and financing of their national health care system, and all are anxious to limit their expenditure.

In the last few years there has been an increase in the number of products withdrawn from the market upon decisions by the manufacturers. Attention should be given to this phenomenon by Healthcare authorities because this causes disruption on the patient and on the economic sustainability of the companies.

Whilst price setting mechanisms for new originator medicines, needs ample and further debate, focus should also be given to the mature products, not only generics, that are also rightfully part of the therapeutic arsenal. These mature products, mostly marketed by SME companies, have been suffering constant price constrains throughout the years due to aggressive tendering systems and external reference pricing systems across nations.

This has put a pressure on the pharmaceutical industry, which is forced to endure constant annual price decreases, leading often to product withdrawals due to exclusive economic issues as products become economically non-viable.

On the other hand, whilst prices spiral downwards, manufacturing costs increase, and furthermore, some APIs and raw materials have extensive price increase trends, especially in the case of APIs with a reduced number of worldwide manufacturers, or following implementation of more demanding regulation to upgrade on quality issues, such as that of nitrosamine impurities, or even subsequent to a crisis situation such as COVID-19.

[4] EFPIA Key Data 2020

The combination of the above factors has a major impact on SMEs' economical sustainability driving companies to withdraw products from the market, hereby jeopardizing patient access to safe and affordable medicines.

To promote the discussion on how to achieve smart spending and guarantee the economical sustainability of SME's, Europharm brings forward some ideas for European policymakers:

- Secure existing European production capacities by ensuring price stability for medicines whose active substances are produced in Europe;
- Determine the drugs whose sustainability of local supply is no longer ensured for economic reasons and find ways to restore it;
- An origin criteria could be introduced in hospital tenders in addition to the price criteria in order to support EU production and to stimulate the creation of local high value jobs.
- Better coordination among EU countries to ensure that pricing decisions taken by one country do not lead to domino effect in other countries with negative impacts on patient access to medicines and on company economical sustainability.

5.1.3 EU economic policy and financial incentives for EU MAHs sourcing finished products and/or APIs from European manufacturers

The EU is increasingly dependent on final product manufacture, active ingredients and raw materials originating from outside the EU. Most of API manufacturers (around 70%) are located in Asia (China or and India). As a result of this, the EU API sourcing exodus driven by the Pharmaceutical industry in the last 10 years drifted so as to procure in countries where the labor costs are much lower in comparison to EU countries. There are also difficulties of technical capabilities of some API manufacturers in complying with the latest GMP and GDP guidelines and other new requisites such as compliance with nitrosamine impurities, sourcing of starting materials etc.

This brings added risks to Europe regarding quality issues and potential shortages of medicines which has been clear in the current outbreak of COVID-19. Europe needs to bring together actions and incentives to relocate production of medicines and APIs to European territory in order to avoid disruption of the supply chain and reassure quality.

The economic policy should therefore be mobilized around the industrial objectives in light of the above factors. It is therefore suggested that Europe should set up a protected area, that allows to maintain and relocate to Europe certain strategic industrial productions for essential drugs. It would be based on the political will to preserve the European industrial capacity and to relocate the production of essential drugs (finished products and/or APIs) and also to support export activities.

This could be achieved for example:

- With a change in the pricing mechanisms in Europe which should ensure an acceptable price level and stability to guarantee long-term viability of the production and distribution in the European territory.

- With the development of an exceptional deduction on productive investments to be able to modernize and keep existing industrial sites competitive,
- With exemption from property tax and contribution on the added value of companies for a period of five years, for their production and storage sites,
- With a temporary reduction at least for 3 years, on the tax on the turnover of the finished product

5.2. Secure supplies of essential drugs and reduce the risk of shortages

Efficient medicines supply chains are integrally linked to strong health care systems. Adequate human resources, sustainable financing, comprehensive information systems, and coordinated healthcare partners and institutions are key components to ensure uninterrupted availability and accessibility of essential medicines.

Europharm's proposals to reduce the risk of shortages are:

1) Transparent information exchange between member states' authorities and the pharmaceutical industry on available stocks and demands in order to allow for efficacious management of production and supply chains.
2) To focus on drugs of strategic health interest and to establish obligations of reinforced stock. However, it should be noted that in order to secure a buffer stock this represents a significant financial investment for SMEs and there should therefore be an EU funding for the extra investment made in producing buffer stock for emergency situations.
3) A Under emergency situations such as that of Covid-19 pandemic, reduce the time window for the return of pharmaceutical products within the shelf life

It is in common practice that most distributors and pharmacies and hospitals, return medicinal products that have limited shelf life (less than six months) and return all such stock to the manufacturer/ MAH.

Under exceptional circumstances or in emergency situation the following factors should be taken into account:

- The authorities should prevent any wholesaler or hospital to refuse a delivery for a product with a shelf life less than 6 months
- To facilitate the national authorization of importation of stock where applicable. A harmonized approach may facilitate authorization and supply to prevent stock-outs.
- Measures such as donation of these medicines with short expiry date should be promoted. This will not only make the medicines available to the patients in countries where it is needed but also reduce the medicinal waste.

5.3 Regulatory procedures simplification & administrative assistance

5.3.1 EU Wide regulatory harmonization, flexibilization and simplification of regulation

Under the current outbreak due to COVID-19, it has been important to simplify European regulation, as witnessed by several documents aimed at streamlining and simplification adopted in the recent months.

The cost of regulatory life-cycle management of the marketing authorizations has become a huge burden for SMEs especially micro and small companies with reduced resources.

Lessons learnt from the very positive regulatory measures implemented during the COVID-19 crisis management whereby EMA has allowed for simplification and streamlining of some of the regulatory activities and on the other hand, have also recognized and increased the discretionary power of the QP and responsible person on GMP and GDP matters, should be considered as a future, post-pandemic, measure.

The overall idea would be to rely more on the Industry's compliance to rules and regulation and increase the authorities' surveillance and inspectorate activity. Do & tell variations should be expanded to more situations on risk-based criteria. This would reduce the number of variations and thus regulatory burden on SMEs, without jeopardizing safety or increasing risk on the quality concerns.

Thus, Europharm supports the introduction of regulatory flexibility measures and a bigger reliance on QPs' decisions by empowering them with more discretionary power to decide on a risk-based approach on GMP and GDP variations.

5.3.2 Apply the principle of proportionality of costs associated with the implementation of new regulation

The implementation of the Falsified Medicines Directives was without a doubt a key step forward in combatting medicine falsification and further guaranteeing patient's safety.

The implementation of this Directive impacted the competitiveness of SMEs due to the huge investments done for the implementation especially for companies with a very low turnover or operating in just one market.

Taking this into account, Europharm apply that the European commission should reflect on the principle of proportionality and impact on SMEs when new regulations are passed.

In these situations, SMEs, would recommend that costs of implementation should be proportional to the size of the company or alternatively be financially supported. These costs shouldn't be an obstacle to implementation of new regulations and shouldn't limit SMEs development.

5.4 Research and Development and Incremental Innovation

5.4.1 Accelerate the possibilities of repositioning certain molecules

It is possible to carry out a screening of the existing pharmacopoeia to examine the opportunity of repositioning certain existing molecules, sometimes old, in order to find immediate therapeutic solutions. Scientific strategy of investigating existing drugs for additional clinical indications should be considered during these times via "drug repositioning". This repositioning action must be initiated as soon as possible since it will benefit patients as it adds new indications to existing drugs for lower costs compared to de novo drug development.

This work could be undertaken through a partnership between EU SMEs, the NCA and several public research units given that clinical research groups recognizing efficacy of these "old" drugs for new indications often face an uphill struggle due to a lack of funding and support because of poor structural and regulatory support for clinical drug development.

Europharm proposes:

- To stimulate innovation including incremental innovation vs breakthrough innovation and R&DI (incremental research and development). Example: new pharmaceutical formulations, new devices & drug combinations, new therapeutic indications for existing mature products etc.
- To provide access and assistance to integrated European compassionate use programs and PRIME
- To support and promote research collaborations between academia, research centers and industry.

5.4.2 Guidance and assistance on regulatory issues and scientific advice at an early stage of R&D.

"Encouraging small enterprises to engage in dialogue with us early in the product development is a priority for EMA as the input we provide allows them to optimize their development program and generate high quality data on a medicine's benefits and risks".[5]

SMEs fully endorse this EMA SME office statement and reiterate that it is very important for SMEs to address EMA and NCAs for guidance on regulatory issues and scientific advice at a very early stage of development, even when still in pre-clinical stage.

5.4.3 To simplify and facilitate access to EU funding programs

SMEs need support for guidance's and advances for research program specifically dedicated to SMEs. It is of utmost importance to simplify the access to EU funding and to have a homogeneity all over Europe for clinical trial and support for product development and research.

- Provide research & development incentives for SMEs investing in R & D for unmet medical needs.
- Adapt current regulatory framework to new technologies and advances in science
- To support through funding R & D in major threats to mankind such as biological threats (viruses and bacteria multi-resistant to conventional antibiotics)

[5] EMA SME office Newsletter

- Create incentives and funding programmes to stimulate inn- house R & D activities and making them easily accessible to SMEs. Grant and non-grant support via the European Regional development fund ERDF or other programmes from the EU budget.
- Manufacturing investments (new equipment and software acquisitions, serialization, nitrosamine monitoring etc) and buffer stock mandatory production (such as demanded during the covid crisis) should be supported by government or at European integrated level

Approved by Europharm Board

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