EFPIA Position Paper on EMA Fees

Executive Summary

EFPIA has recently developed its *Regulatory Road to Innovation (RRI)*[1] to contribute ideas to enhance the current European regulatory framework. In summary, the RRI's regulatory science proposals seek to ensure that the European regulatory system keeps pace globally with advances in science and innovation, as well as to address the unprecedented challenges in the fight against COVID-19. Adequate and appropriate funding of the European Medicines Agency (EMA) and National Competent Authorities (NCAs) is essential to support the effective operation of the European Medicines Regulatory Network (EMRN) and to ensure public health. In recent months, during the COVID-19 pandemic, society has been acutely reminded of the importance of a robust, resourced, efficient, and adaptable regulatory system. As such, EFPIA welcomes the ongoing evaluation[2] of the current EMA fees system to ensure that a suitably resourced EU regulatory system can fully support the innovative medicines of today and tomorrow. EFPIA members would support a revision of the current fee system that is consistent with the fundamental principles of **transparency, fairness & proportionality, sustainability, simplicity, and flexibility**.

EFPIA is mindful of the future needs of the network for a fee structure that facilitates **reductions in administrative burden**. EMA continues to provide important regulatory guidance and facilitations for medicine developers during the COVID-19 crisis. EFPIA considers that some of these streamlined measures will assist in resource preservation, for regulators and companies, over the longer term. EFPIA would support changes to the Fees system that enable simplification and maintain current levels of overall costs to companies for the same volume of submissions. To that end, and as mentioned in our response to the Commission's Inception Impact Assessment[3], EFPIA supports a proportionate annual maintenance fee that includes all Type IA/IB variations together along with additional changes to the rest of the fee structure to remove a number of anomalies that have developed over time.

EFPIA does not believe that efficiency savings alone will be enough to progress the most resource intensive regulatory advances outlined in EMA's Regulatory Science Strategy to 2025 (RSS)[4,5]. Importantly, EFPIA believes that appropriate implementation of this **regulatory science improvement agenda**, including through ongoing stakeholder engagement, are essential for future proofing the EU regulatory system. Therefore, EFPIA is willing to consider other changes to the Fees system that meet the above principles (including proportionality and fee-for-service) and that could provide EMA with additional financial resources to enact some of the medicine development recommendations from its RSS. Specifically, EFPIA is willing to consider potential funding models in the regulatory science areas

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[1] *In its Regulatory Road to Innovation* (RRI), EFPIA identified regulatory science actions within the existing legislative framework to deliver more treatments, safer, better, and faster by: encouraging the use of new types of clinical trials; allowing greater use of data from real world use; allowing ongoing dialogue and discussion about a medicine throughout development; and simplifying how medicines and other products are regulated. Further, RRI incorporates recommendations for scientific assessment and decision on marketing authorizations, oversight of global manufacturing chain and availability of medicines, drug-device combinations, biomarker validation, and unmet medical need. https://www.efpia.eu/about-medicines/development-of-medicines/regulations-safety-supply/efpia-regulatory-road-to-innovation/

[2] Commission Roadmap to EU Pharmaceutical Strategy: 2 June 2020, excerpt: *The pharmaceutical strategy will examine the need for legislative and non-legislative actions and EU investments. Legislative actions may encompass follow up to the initiatives which are already in preparation, such as the review of the legislation on medicines for rare diseases and children (Orphan and Paediatric Regulations), the legislation on fees for the European Medicines Agency. It could also include a targeted evaluation and subsequent review of the basic pharmaceutical legislation.*

[3] https://ec.europa.eu/health/human-use/legal-framework/ema_impact-assessment_en

[4] EMA Regulatory Science to 2025: Strategic reflection; April 2020

[5] Note the draft European medicines agencies network strategy to 2025: Protecting public health at a time of rapid change. EMA/321483/2020 was released in July 2020 for public consultation. Although this strategy incorporates some regulatory science concepts from RSS, since it is not yet final, EFPIA's Fees position proposals are written to coincide with several of the final RSS recommendations.

of PRIME, iterative advice, and dynamic regulatory assessment, to ensure availability of the additional regulator resource needed to support these processes. EFPIA considers that such models, if implemented, should (as with all other activities) also be gauged by ongoing measures of impact as per the transparency principle.

Introduction

Adequate and appropriate funding of the European Medicines Agency (EMA) and National Competent Authorities (NCAs) is essential to support the effective operation of the European Medicines Regulatory Network and to ensure public health. In fact, today, fee and charge generating regulatory activities account for around 86% of EMA's current total budget of €358.1 million[6]. Given its essential role in patient health, EFPIA considers that public monies should contribute a significant portion to achieving a well-resourced, robust EU regulatory system, and, many non-fee-generating activities and infrastructure investments should be supported by public budgets.

Trend data demonstrate that the EU regulatory system is falling behind in several important global measures of effectiveness (e.g. approval timelines, use of expedited pathways, acceptance of innovative study designs). Most recent benchmark data show that it takes around 423 days (median) for the EMA to approve a new active substance, compared to 243 days in the USA, 304 in Japan, 346 in Canada, and 346 in Australia. Also, during the most recent year, 68% of products approved by the US FDA followed an expedited pathway compared with only 7% for the EMA[7]. EFPIA does not believe that fees alone can address the regulatory system and resourcing challenges faced by EMA. Instead, long-term solutions will require a more fundamental shift in mindset, focus, collaboration, and policies. The EMA's Regulatory Science Strategy to 2025 (RSS)[4] offers a significant step in the right direction and, as such, EFPIA fully supports its implementation. The European Medicines Regulatory Network's Strategy to 2025 highlights "the need to ensure an appropriate funding model for the Network going forward and support recruitment, retention and development of staff with the right competencies".[5] EFPIA welcomes the ongoing evaluation of the current EMA fees system to ensure that a suitably resourced EU regulatory system can fully support the innovative medicines of today and tomorrow.

EFPIA members would support a revision of the current fee system provided that the following fundamental principles are met:

- **Transparency**: Changes to the fee structure should be based on a comprehensive, transparent and independent evaluation of the underlying costs of the services provided, projections of future developments and strengths and weaknesses of the current system.
- **Fairness & proportionality**: Fees must correspond to the service provided (i.e., "fee-for-service" principle) and should be fair and proportionate for all actors involved. While it is accepted that the majority of the EMA budget will continue to be derived from fees payable by Industry, some activities conducted by the Agency are part of its general mission to ensure public health and should therefore remain at least partly covered by the Community.
- **Sustainability**: In order to support public health and pharmaceutical innovation, the fee structure should ensure adequate availability of resources to support high quality scientific assessment by highly qualified experts within competitive timeframes.
- **Simplicity**: The fee system should be clear and simple in order to avoid unnecessary administrative burden for payers of the fees and for the EMA.

[6] https://www.ema.europa.eu/en/about-us/how-we-work/governance-documents/funding
[7] 2020 CIRS, R&D Briefing 77

- **Flexibility**: Reductions and waivers should be allowed for some procedures for certain justified categories of medicines and actors (e.g. orphan drugs and SMEs) or in exceptional circumstances (e.g. imperative reasons of public health).

EFPIA believes that efficiency improvements instituted to simplify the fee system would have a substantial positive resource effect on EMA and NCAs. Explicitly, the current fee system seeks to levy fees from Marketing Authorisation Applicants and Marketing Authorisation Holders (MAH), in a proportionate way, with lower fees being charged for simpler procedures requiring minimal or no scientific review and higher fees being charged as complexity of scientific review increases, with the highest fees being charged for assessment of Marketing Authorisation Applications (MAAs) for new active substances.

Whilst Industry absolutely agrees with the principle of levying fees in a proportional way, implementation of the current fee structure has resulted in some anomalies in the way this is applied that need amendment. In addition, an unintended consequence of the way in which fees are charged has resulted in significant levels of resource being diverted to process and invoice the simplest administrative submissions, resource that could be better utilised by all stakeholders to advance innovation and patient health.

This position paper proposes a potential way forward to deal with the anomalies in the current fee system and a new way to deal with the simpler, yet resource-consuming submissions which would free resources at the Agency previously tasked with administration of a complex fee system. The regulatory system resource and efficiency savings from EFPIA's proposal could then be redirected to essential public health initiatives such as RSS implementation and infrastructure investments.

Furthermore, EFPIA acknowledges the resource constraints that challenge the EMA's capabilities to implement the most resource demanding aspects of its regulatory science agenda. Hence, and corresponding with its underlying fees principles, EFPIA is prepared to consider potential new funding models to support more effective and sustainable performance in the regulatory science areas of PRIME, iterative advice, and dynamic regulatory assessment. Without adequate resources, EFPIA believes that it will not be possible to advance implementation of these RSS recommendations without further straining EMA's capacity and budget. At the same time, we believe that public funding should continue to support the progression of EMA activities, and any increase in fee-for-service charges should only be used to directly support these new regulatory actions and not be used as an offset for current or future reductions in public monies.

Proposals

1. Expansion of the Scope of the Annual Maintenance Fee

Fee levels for Type IA/IA_{IN}, so called "do and tell" variations and Type IB variations are low relative to other categories of chargeable procedures, but these variations numerically comprise the majority of submissions made to EMA that attract a fee. Although the experience of EFPIA member companies suggests that the number of Type IA variations submitted per MA per annum decreases over the lifecycle of the medicinal product (irrespective of the specific product or MAH), the overall number of these types of variations processed by the EMA on an annual basis has increased in recent years[8].

Whilst these variations are minor by definition, the numbers involved result in the need for significant resourcing levels at both the Agency and MAH simply for processing and invoicing purposes, which

[8] Total Type 1A and IB variations for medicinal products submitted to the EMA centralised authorisation increased from around 1,000 in 2007 to around 3,000 in 2018.

seem disproportionate since minimal or no formal scientific review is required. A predictable and equitable fee structure which significantly reduces the administrative burden associated with their financial processing by companies and EMA, while supporting the appropriate level of regulatory oversight, would benefit all.

EFPIA's proposal to streamline variation system and expand annual maintenance fee:

- Replace Type IA and Type IB variation fees with an expanded annual maintenance fee for all MAs, based on the xEVMPD database (at the formulation level):
  - The adoption of a single charge per MAH per MA would be much simpler to operationalize and predictable to apply, for both the EMA and companies. Furthermore, this model supports improvements in efficiency though process optimisation by decoupling the direct association between income and the number of variations.
  - There is also precedent for this type of approach, which has already been adopted for the assessment of minor variations by some EU Member States e.g. Austria, Netherlands, and Sweden.
- The following types of procedures would be included in the expanded annual maintenance fee since they comprise routine maintenance activities for all MAs:
  - PV activities
  - Renewals
- The expanded maintenance fee could be reduced for products no longer subject to renewal to reflect the decreasing number of minor changes made to MAs during their lifecycle as products become more established. Specifically, EFPIA proposes:
  - Implementation of a tapered maintenance fee system, with a decrease in fees after 5 years and a further decrease after 10 years to reflect the decreasing workload
- MAAs authorized as true duplicates (identical Module 3, same indications) would be subject to the lower Tier III level maintenance fee throughout their lifecycle to reflect the fact that no additional scientific review is needed compared to the original MA
- The annual maintenance fee-based system should be applicable to Orphan Medicinal Products, Conditional MAs and Authorisations under Exceptional circumstances since they require similar levels of maintenance activities as other MAs

The introduction of the new, expanded annual maintenance fee to cover variation activities would adequately and appropriately, in conjunction with current levels of Union contributions, be utilized to fund EMA's overall responsibilities. It is envisioned that a review of this new expanded annual maintenance fee would also need to be undertaken at certain time points e.g. after 1 and 3 years to ensure that it is set at an appropriate level to meet the aims outlined in this paper.

2. Other Changes to Current System, if an Expanded Annual Maintenance fee cannot be adopted

If adoption of an expanded annual maintenance fee is not possible, then some additional modifications to the current system are needed to eliminate additional anomalies. These comprise:

- The need for a "bulk transfer fee" covering bulk changes of Company name or administrative address following a merger or other corporate change applying across a MAH portfolio. Such a fee category would reduce the invoicing and payment burden associated with the hundreds of virtually identical purely administrative submissions needed when companies are involved in such changes.
- The need for a cap on the level of fees that can be charged for grouping of Type IA/IB so that fees do not exceed the fee for a single Type II variation.

3. Consideration of potential funding models for the regulatory science areas of PRIME, iterative advice and dynamic regulatory assessment

EFPIA is ready to assist the EU Medicines Regulatory Network and its stakeholders in implementing the RSS through our commitment of time, energy, talents, and ideas. Previously within its comments on the draft RSS, EFPIA stated that it "would value the continuation of the EMA's stakeholder engagement, including the full participation of HMA/NCAs, frequent status updates and outreach technology platform meetings, throughout the 5-year implementation phase of the RSS 2025 plan"[4]. Further, EFPIA is willing to consider potential new funding models in the regulatory science areas of PRIME, iterative advice, and dynamic regulatory assessment to ensure availability of the additional regulator resource needed to support these processes. EFPIA assesses that any new funding model in these areas would likely require a targeted amendment to the current EMA Fees Regulation. However, these potential changes are considered here with the understanding that an amendment to Regulation 726/2004 or Directive 2001/83 would not be necessary since the EU legislation provides EMA with the general ability to collect fees from undertakings "for obtaining and maintaining Union marketing authorisations for human and veterinary medicinal products and for other services provided by the Agency"[9], which is applicable to PRIME, iterative advice, and dynamic regulatory assessment. Once fully implemented, EFPIA considers that new fees-for-service funding models for PRIME, iterative advice, and DRA would allow a company the choice as to whether to request a service(s) for a product and, if applicable, then to remit the related fee(s). Whereas today for PRIME, for instance, associated regulator activities are not directly paid by a dedicated fee-for-service payment, which may limit its level of application and overall use.

- **PRIME –** EFPIA has been a strong supporter of PRIME as an important regulatory tool for innovation since its initial introduction. EFPIA appreciates the capacity demands that EMA and NCAs face in undertaking the resource-intensive regulator activities associated with each PRIME product (e.g. initial meeting, review of PRIME eligibility requests, ongoing responses to questions once a product is accepted into PRIME). EMA acknowledged these challenges and emphasised the scheme's importance in its RSS plans *to promote and invest in the PRIME scheme*[4]. Some actions included in EMA's plans may further increase demands on EMA and NCA resources. These include exploring opportunities for further engagement and collaboration with patients, healthcare professionals, academia and international partners, and exploring possible impact and benefits of expanding the earliest possible entry to the PRIME scheme to a wider range of applicants, including for new indications of existing products[4].

- **Iterative advice** - EFPIA believes that in the rapidly evolving landscape of medicine development an iterative, responsive regulatory dialogue with greater flexibility in the delivery of scientific advice and better alignment across stakeholders are needed to reflect the changing pace and process of innovation[10]. EMA also identified this as an important focus in its RSS recommendation to *diversify and integrate the provision of regulatory advice along the development continuum*[4]. To achieve this objective, EMA proposes some actions which may have resource implications for the associated processes and interactions with applicants/MAH. These include creating complementary and flexible advice mechanisms to support innovative product development also expanding multi-stakeholder consultation platforms; facilitating a more iterative advice framework that better addresses the continuum of evidence generation; and promoting more integrated medicines development aligning scientific advice, clinical trials approval and Good Clinical Practice oversight[4].

[9] Regulation 726/2004 and Regulation 2019/6

[10] If funding concepts such as iterative advice and dynamic regulatory assessment are introduced that increase proactive interactions and alignment, downstream EMA resources may be saved and redirected towards other Agency activities.

- **Dynamic regulatory assessment** – While the dynamic regulatory assessment (DRA) concept has evolved recently and is being discussed by many stakeholders including regulators, there is no consistently accepted definition. EFPIA considers DRA as a paradigm shift from the current approach to regulatory engagement, evidence generation and assessment across a medicine's lifecycle. DRA would facilitate iterative, tailored, and holistic exchange between medicine developers and regulators to support regulatory decision-making. This flexible mechanism will include the continuous, progressive provision and analysis of data as well as ongoing interactions with regulators across the EU system. The execution of DRA will evolve, with optimal application of the policies, processes, procedures, and digital tools (e.g., advanced analytics, algorithm-assisted decision-making) available at the time[11]. EMA has implemented some potential DRA approaches (e.g. rolling reviews) to facilitate the development and approval of medicines aimed at the COVID-19 pandemic. This and several of the DRA concepts may require consideration of new or adapted fee-for-service funding models and EFPIA is willing to discuss potential approaches. In fact, EMA has introduced a new fee model for rolling reviews, comprising a fee to initiate review, which will then be deducted from the respective fee payable for a marketing authorisation application for the same product, where such application is submitted by the same applicant.[12]

Conclusions

EFPIA has recently offered its proposals to enhance the current European regulatory framework in the *Regulatory Road to Innovation*. EFPIA considers that adequate funding of EMA and NCAs is essential to support the effective operation of the European Medicines Regulatory Network and to ensure public health. As such, EFPIA welcomes the ongoing evaluation of the current EMA fees system. Overall, EFPIA would support changes to the fees system that would result in a fairer, more transparent system that is sustainable, simple and flexible. A key measure to achieve this would be to introduce a proportionate annual maintenance fee that includes all Type IA/IB variations together with additional changes to the rest of the fee structure to remove a number of anomalies that have developed over time. The regulatory system resource savings from EFPIA's proposals could then be redirected to other future proofing initiatives such as implementation of some elements of the EMA's Regulatory Science Strategy to 2025. In addition, and corresponding with its underlying fees principles, EFPIA is prepared to consider potential new funding models to support advances in sustainable performance in the regulatory science areas of PRIME, iterative advice, and dynamic regulatory assessment.

[11] Source: EFPIA internal definition paper as further described: In the near term, the concept may be demonstrated with pilots that make use of existing EU telematics; longer term, the concept could be enhanced through cloud-based submissions of data. The ultimate goals are to enable smarter drug development, more timely availability of innovative medicines for EU patients, and real-time, evidence-based regulatory decision-making throughout a medicine's lifecycle.
[12] Rules for the implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures. EMA/MB/238467/2020 Rev. 1; Management Board meeting on 11 June 2020