



Brussels, 18.9.2019  
SWD(2019) 335 final

**COMMISSION STAFF WORKING DOCUMENT**

**EVALUATION**

**of the**

**European Medicines Agency's fee system**

{SWD(2019) 336 final}

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## Abbreviations

AER	Adverse event reporting
ATMP	Advanced Therapy Medicinal Product
CAP	Centrally authorised product
CAT	Committee for Advanced Therapies
CHMP	Committee for Medicinal Products for Human Use
COMP	Committee for Orphan Medicinal Products
CVMP	Committee for Medicinal Products for Veterinary Use
DCP	Decentralised procedure
EASA	European Aviation Safety Agency
ECA	European Court of Auditors
ECHA	European Chemicals Agency
ECU	European Currency Unit
EDQM	European Directorate for the Quality of Medicines & Healthcare
EEA	European Economic Area
EMA	European Medicines Agency
EMEA	European Agency for the Evaluation of Medicinal Products, also known as the European Medicines Evaluation Agency. Former name of the EMA
EU	European Union
FDA	U.S. Food and Drug Administration
HMA	Heads of Medicines Agencies
HMPC	Committee on Herbal Medicinal Products
HTA	Health technology assessment
IMP	Incident management plan
MAH	Marketing authorisation holder
MBDG	EMA Management Board data gathering
MNAT	Multinational assessment team
MRL	Maximum residue limit
MRP	Mutual recognition procedure

MUMS	Minor use and minor species
NAP	Nationally Authorised Product
NCA	National Competent Authority
NUI	Non-urgent Information
OPC	Online public consultation
PASS	Post-authorisation safety study
PDCO	Paediatric Committee
PIP	Paediatric investigation plan
PMF	Plasma master file
PO	Purchase order
PRAC	Pharmacovigilance Risk Assessment Committee
PRIME	PRIority MEdicines
PSUR/PSUSA	Periodic safety update report (single assessment)
PUMA	Paediatric use marketing authorisation
RA	Rapid alert
SME	Micro, small and medium-sized enterprise
VAMF	Vaccine antigen master file
VMP Regulation	Veterinary Medicinal Products Regulation (Regulation (EU) 2019/6)
WHO	World Health Organization

## Glossary

<i>Term or acronym</i>	<i>Meaning or definition</i>
Abridged application	An application for a new marketing authorisation for a medicinal product for human or veterinary use should normally be accompanied by a ‘full dossier’ (see further below in this table). However, in certain instances applicants are permitted to submit a medicinal dossier that does not include all of the results required for a full dossier. This is called an abridged application. An applicant can choose to submit an abridged application instead of a full dossier when the results of an already authorised medicine are relevant to the new medicinal product and when reference can be made to these results. See also ‘generic’, ‘biosimilar’ and ‘full dossier’.
Additional activities	Both EMA and NCAs undertake activities additional to the activities that were covered by the data gathering exercise of the EMA Management Board. These ‘additional activities’ do not concern time spent in and preparatory work for committees and working parties, nor any of the procedural activities covered by the external study. For more information, see Section 5.
Administrative fee	Fees charged on a one-off basis by EMA to undertakings for the provision of the following administrative services: negative administrative validation of an application, issuing of certificates outside of procedures, notifications of parallel distribution and variation worksharing.
Advanced Therapy Medicinal Product (ATMP)	Medicinal products for human use based on genes, cells or tissues used to diagnose, prevent or cure diseases or to replace, repair or regenerate human tissue.
Advanced Therapy Medicinal Product (ATMP) classification	Any applicant developing a product based on genes, cells or tissues may request a scientific recommendation of the Agency with a view of determining whether the referred product falls, on scientific grounds, within the definition of an advanced therapy medicinal product. The Agency shall deliver this recommendation after consultation with the Commission and within 60 days after receipt of the request.
Annual fee	Fees charged annually by EMA to undertakings for services related to the maintenance of a valid marketing authorisation (e.g. databases). Two types of annual fees exist: (1) an annual fee for centrally authorised medicinal products (CAPs) for human and veterinary use (CAP annual fee) and (2) a pharmacovigilance annual fee for nationally authorised medicinal products (NAPs) for human use.
Basic fee	The full applicable fee before reductions (fee incentives) or additional amount (for the assessment of additional strengths, pharmaceutical forms or presentations) have been applied. See also under ‘procedural fee’.
Biosimilar application	A biological medicinal product that is highly similar to an already authorised biological medicine (‘the reference product’) and for which not all test results need to be provided as for a full dossier. A biosimilar application is a type of abridged application. See also ‘abridged application’ and ‘full dossier’.

CAP annual fee	See under ‘annual fee’.
Centrally authorised medicinal product (CAP)	Medicinal products authorised at European Union level. The marketing authorisation is granted by the European Commission and is valid in all Member States.
Coordination group	The coordination groups for human medicinal products (CMDh) and veterinary medicinal products (CMDv) were set up for the examination of any questions relating to nationally authorised medicinal products, specifically related to disagreements on the grounds of potential serious risks to public health between Member States on pending initial marketing authorisation and variation procedures. The tasks also include certain pharmacovigilance activities related to nationally authorised products.
European Currency Unit (ECU)	This was the official monetary unit of the European Communities. It was an artificial, electronic unit based on a basket of the national currencies of twelve EU Member States. The ECU was replaced by the euro on 1 January 1999 at the value of 1 EUR = 1 ECU
Extension of marketing authorisation (line-extension)	Procedure via which any of the following changes are made to an already existing authorisation: <ul style="list-style-type: none"> <li>• Changes to the active substance, strength, pharmaceutical form, and/or route of administration;</li> <li>• Other changes specific to veterinary medicines to be administered to food-producing animals or the change or addition of target species.</li> </ul>
Full dossier	An application for a new marketing authorisation for a human medicinal product should normally be accompanied by results of pharmaceutical (physico-chemical, biological or micro-biological) tests, pre-clinical (toxicological and pharmacological) tests and clinical trials (Article 8i of Directive 2001/83/EC). In the case of veterinary medicinal products these are results of pharmaceutical (physico-chemical, biological or micro-biological) tests, safety and residue tests, pre-clinical and clinical trials, and tests assessing the potential risks posed by the medicinal product for the environment (Article 12j of Directive 2001/82/EC). Applications that are submitted in accordance with these requirements are called a ‘full dossier’. See also ‘abridged application’.
Generic application	Application for a medicine containing the same active substance(s) and used at the same dose(s) to treat the same disease(s) as an already authorised medicine (‘the reference medicine’). A generic application is a type of abridged application. See also ‘abridged application’ and ‘full dossier’.
Health technology assessment (HTA)	HTA bodies provide recommendations on medicinal products and other health technologies with regard to their properties and direct and indirect impact as well as unintended consequences. It is mainly aimed at informing policy and decision-making in health care, especially on how best to allocate funds in terms of reimbursement.
Inspection	Medicine developers and (future) marketing authorisation holders should ensure that they and any parties working for them comply with standards set out in Union legislation and guidelines for good

	clinical practice (GCP), good laboratory practice (GLP) and good manufacturing practice (GMP) for investigational and to be authorised or already authorised medicinal products. Compliance with these standards is verified by the national competent authorities during (GCP/GLP/GMP) inspections. When it concerns products that are to be authorised or have been authorised via the centralised procedure, the EMA is responsible for coordinating the inspections by NCAs.
Management Board data gathering (MBDG)	In March 2014 the EMA Management Board set up a Data Gathering Steering Group to gather evidence on the time spent by staff of the EMA Secretariat and NCAs on EMA-related activities, to support the evaluation of the EMA fee system by the European Commission.
Maximum residue limit (MRL)	The maximum concentration of a residue of a pharmacologically active substance (veterinary medicine) which may be permitted in food obtained from an animal exposed to that substance.
Micro, small and medium-sized enterprise (SME)	The following definition is not specific to the pharmaceutical sector, but instead applies EU-wide (Commission Recommendation 2003/361/EC):  Microenterprise: company which employs fewer than 10 people and which has an annual turnover and/or annual balance sheet total not exceeding €2 million.  Small enterprise: company which employs fewer than 50 people and which has an annual turnover and/or annual balance sheet total not exceeding €10 million.  Medium-sized enterprise: company which employs fewer than 250 people and which has an annual turnover not exceeding €50 million and/or a balance sheet total not exceeding €43 million.
Minor use/minor species (MUMS) and limited market	Veterinary medicines for the treatment of rare diseases in major animal species (cattle, sheep, pigs, chickens, salmon, cats and dogs) and for the treatment of minor animal species.
Nationally authorised medicinal product (NAP)	Medicinal products authorised at the national level in one or more Member States. The marketing authorisation is granted by the relevant National Competent Authority(ies) of the Member State(s) where the application is made.
Orphan designation	The procedure via which it is evaluated whether a medicinal product fulfils the criteria of an orphan medicinal product.
Orphan medicinal product	Medicine used to diagnose, prevent or treat life-threatening or chronically debilitating diseases that are either rare or unlikely to generate sufficient return to justify the necessary investment, and where no satisfactory or better alternative already exists within the European Union. A condition is defined as 'rare' if it affects no more than five in 10 thousands people in the EU.
Paediatric investigation plan (PIP); waiver; deferral; modification	Development plan drawn up by a pharmaceutical company containing information on how that company intends to gather data on the use of the medicine concerned in children. The aim is to ensure that data are gathered that are necessary to approve use of a medicine in children.  Normally, a PIP is required with each application for authorisation

	<p>of a new medicine. However, under certain circumstances the applicant may request the EMA to waive or defer the PIP. A waiver is granted if the development of a medicine in children is not needed or not appropriate, such as for diseases that only occur in adults. A deferral allows the applicant to delay development in children until, for instance, enough information is gathered about its effectiveness and safety in adults.</p> <p>An approved PIP can be modified at a later stage as knowledge increases or if it is proven that the implementation of the PIP is impossible or no longer appropriate.</p>
Parallel distribution	The distribution of a centrally authorised medicine from one Member State to another by a company other than the owner of the medicine.
Peer-review(er)	One of the members of the CHMP or CVMP is appointed to review the scientific evaluation of the rapporteur and co-rapporteur conducted during the first phase of applications for a marketing authorisation and extensions of existing marketing authorisations, with the purpose of ensuring the quality and consistency of these evaluations. The peer-reviewer especially focusses on the draft list of questions compiled by the rapporteurs for the relevant scientific committee.
Periodic Safety Update Report (Single Assessment) (PSUR/PSUSA)	Reports containing information and a critical analysis on a benefit-risk balance of an authorised medicinal product. The report is compiled by the owner of the marketing authorisation and submitted to the relevant competent authority for evaluation. Based on the assessment of a PSUR, the relevant competent authority can determine whether actions are needed to protect public health, for instance via the update of information for patients and health care professionals.
Pharmacovigilance	The monitoring of adverse effects (safety) of medicines or any other medicine-related problem after their placing on the market, with the aim to identify, assess and prevent such problems.
Pharmacovigilance annual fee	See under ‘annual fee’.
Pharmacovigilance procedural fee	Procedural fee related to pharmacovigilance activities (assessment of PSUR, PASS, pharmacovigilance referrals). See also under ‘procedural fee’.
Pharmacovigilance referral	Referral (arbitration) related to the safety of a medicine. See further under ‘referral’.
Post-authorisation safety study (PASS)	A study carried out after a medicine has been approved in order to gain more information on its safety or to measure the effectiveness of measures taken to reduce safety risks.
PRiority MEDicines (PRIME)	A voluntary scheme launched by the European Medicines Agency in 2016 to enhance support for the development of medicines that target an unmet medical need or that offer a major therapeutic advantage over existing treatments. Via participation in this scheme developers of medicines receive early and proactive support from EMA to optimise development plans and accelerate scientific evaluation with the aim of early access to patients. This scheme also provides fee incentives for scientific advice requests for PRIME products from micro-sized enterprises and SMEs as



	well as academic sector applicants.
Procedural fee	Fees charged by EMA to undertakings on a per-service basis.
Protocol assistance	Protocol assistance is a special form of scientific advice specifically available for developers of orphan designated medicines. See further under ‘scientific advice’ and ‘orphan designation’.
(Co-)Rapporteur	Scientific committees appoint one of their members as rapporteur and may appoint a second one as co-rapporteur to lead the scientific evaluations of applications submitted to the EMA. The rapporteurs are responsible for drafting the assessment reports submitted to the committees for discussion and adoption.
Referral (arbitration)	Procedure initiated to resolve issues such as concerns over the safety of an already authorised medicine or to resolve disagreement among Member States on the benefit-risk balance of a new medicine under evaluation. Referrals can be initiated by the European Commission, a Member State or the owner (marketing authorisation holder) of the product.
Renewal	A new marketing authorisation is only valid for five years from the date the Commission notifies the marketing authorisation holder the authorisation has been granted. An application for renewal of the authorisation shall be submitted timely (i.e. nine months before its expiry date) to ensure it remains valid. Once renewed, the marketing authorisation is valid for an unlimited period, unless the Commission decides, on justified grounds relating to pharmacovigilance, including exposure of an insufficient number of patients to the medicine concerned, to proceed with one additional five-year renewal.
Scientific advice	The EMA can give advice to a developer on the appropriate tests and studies in the development of a medicine. This helps to facilitate the development and approval of a medicine.
Scientific services	Services provided by EMA upon application for any scientific advice or opinion by a scientific committee other than those related to scientific advice, initial marketing authorisation, inspection, variation, extension, renewal, referral, maximum residue limit, transfer of marketing authorisation, or the maintenance of a marketing authorisation. This includes any evaluation of traditional herbal medicinal products, any opinion on medicinal products for compassionate use, any consultation on ancillary substances, including blood derivatives, incorporated in medical devices, and any evaluation of plasma master files and vaccine antigen master files.
Synthetic baseline	A synthetic baseline is used to determine costs to EMA and NCAs incurred for EMA-related activities in a ‘typical year’. The synthetic baseline “neutralises” differences in the reporting of data for EMA and NCAs. This was necessary to ensure that, for activities where NCAs are involved, the number and type of activities is the same for EMA and NCAs in the ‘typical year’.
Theoretical fee	A benchmark cost-based fee used in the evaluation and calculated based on combined estimated costs for EMA and NCAs to conduct a particular activity in a ‘typical year’, using weighted average costs for NCAs. See also ‘weighted average’.

Typical year	The model used to calculate EMA and NCAs' cost and income made use of a so-called 'typical year' in order to compare those costs and income. It is assumed that a 'typical year' is a representative year for EMA and NCAs under the current regulatory framework in terms of types and frequency of the various activities occurring.
Unitary costs and unitary fees	Costs to EMA and NCAs or fees charged to industry for a given activity, such as the evaluation of a marketing authorisation application or variation.
Variation; Type IA, IB and II	<p>Change to the terms of an existing marketing authorisation, e.g. the change in manufacturing site, the addition of an indication, the replacement of an excipient of the medicinal product.</p> <p>Type II variations concern major changes which may have a significant impact on the quality, safety or efficacy of the medicinal product. These variations require approval by the relevant competent medicine authority before they can be implemented.</p> <p>Type IA variations concern minor changes which have only a minimal impact or no impact at all on the quality, safety or efficacy of the medicinal product. These variations do not require approval by the relevant competent medicine authority prior to implementation ('Do &amp; Tell').</p> <p>Type IB variations concern changes that are neither Type IA nor Type II variations. These variations require approval by the relevant competent medicine authority before they can be implemented.</p>
Weighted average of NCAs' costs	In the model calculating costs and income of EMA and NCAs for a 'typical year' NCAs costs were determined as a weighted average of costs estimated for various NCAs, using as weight the frequency of involvement of the NCAs.

# 1. INTRODUCTION

## 1.1. General context

A medicinal product for human or veterinary use may only be placed on the market in the European Union (EU) when a marketing authorisation has been issued either by a competent authority of a Member State for its own territory (national procedure) or when an authorisation has been granted by the European Commission for the entire Union (centralised procedure). In addition, once a medicinal product has been authorised and placed on the market, its safety profile continues to be monitored throughout its entire lifespan (pharmacovigilance).

Under the centralised procedure, the applicant submits an application dossier to the European Medicines Agency (EMA or ‘the Agency’). The Agency comprises seven scientific committees<sup>1</sup>, a Secretariat, an Executive Director and a Management Board. The relevant scientific committees of the Agency, composed of experts appointed by the Member States, assess the application and prepare a scientific opinion. Based on that opinion the European Commission adopts a decision regarding the authorisation of the medicinal product concerned. If an authorisation is granted, it is valid throughout the EU.

Under a national procedure, new medicinal products are authorised in one or more Member States by the national competent authorities (NCAs) for their own territory. The role of EMA’s committees is restricted to the safety monitoring of nationally authorised medicines (pharmacovigilance) in procedures that also cover one or more centrally authorised products and, in case of disagreement between NCAs, to providing a scientific opinion on the topic at issue.

The Secretariat of the Agency provides technical, scientific and administrative support for all the committees and working parties and ensures appropriate coordination between them. It further provides technical and administrative assistance to the coordination groups of the Member States’ authorities. The Agency also has other technical, scientific and administrative tasks defined in its Founding Regulation (Regulation (EC) No 726/2004)<sup>2, 3</sup>.

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<sup>1</sup> These concern the Committee for Medicinal Products for Human Use (CHMP), Committee for Medicinal Products for Veterinary Use (CVMP), Pharmacovigilance Risk Assessment Committee (PRAC), Committee for Orphan Medicinal Products (COMP), the Committee on Herbal Medicinal Products (HMPC), the Paediatric Committee (PDCO), and the Committee for Advanced Therapies (CAT).

<sup>2</sup> Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency: OJ L 136, 30.4.2004, p. 1–33

<sup>3</sup> For the full list of EU and EEA NCAs and for more information on the regulatory framework for marketing authorisation procedures, please refer to respectively Annex 2 and 3.

The Agency's budget is composed of (1) a contribution from the Union, (2) a contribution from third countries (Member States from the European Economic Area (EEA)) participating in the work of the Agency, (3) fees paid by undertakings (i) for obtaining and maintaining Union marketing authorisations and for other services provided by the Agency and (ii) for services provided by the coordination group as regards the fulfilment of its pharmacovigilance tasks, (4) charges for other services provided by the EMA, and (5) Union funding in the form of grants for participation in research and assistance projects.<sup>4</sup>

EMA charges fees to applicants for scientific advice, assessment of applications for a marketing authorisation, changes to existing marketing authorisations (variations and extensions) and a number of other pre- and post-authorisation procedures, as well as annual fees for the maintenance of already authorised medicines. Pharmacovigilance activities for nationally authorised medicines for human use conducted at EU level are also financed by fees paid by marketing authorisation holders (MAHs). Overall, the vast majority of EMA's activities are currently funded through fees, charged to pharmaceutical companies in their capacity of applicants and holders of marketing authorisations.

EMA remunerates NCAs for the scientific assessment of 'rapporteurs' appointed by the EMA scientific committees.<sup>5</sup>

The EMA fee system<sup>6</sup> is established by EU legislation. The main legislative and non-legislative provisions governing EMA's fee system are laid down in:

- **The EMA Founding Regulation:** Regulation (EC) No 726/2004, which provides the sources of income constituting EMA's revenue (see further above) and which lays down that NCAs should be remunerated in accordance with a scale of fees established by the EMA Management Board;
- **The main Fee Regulation and its Implementing Rules:** Council Regulation (EC) No 297/95<sup>7</sup>, and its Implementing Rules<sup>8</sup>, which together provide the rules and amounts for fees charged to undertakings and for remuneration paid to NCAs for obtaining and maintaining Union marketing authorisations and for other services provided for centrally authorised medicines for human and veterinary use;

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<sup>4</sup> Article 67(3) of Regulation (EC) No 726/2004, as last amended by Regulation (EU) 2019/5 of the European Parliament and of the Council of 11 December 2018 (OJ L 4, 7.1.2019, p. 24–42).

<sup>5</sup> Article 62(3) of Regulation (EC) No 726/2004.

<sup>6</sup> Throughout this report the term 'EMA fee system' is used to refer to both the fees charged by the EMA to industry and the remuneration of NCAs paid by the EMA for the EMA-related activities that the NCAs undertake.

<sup>7</sup> Council Regulation (EC) No 297/95 of 10 February 1995 on fees payable to the European Agency for the evaluation of medicinal products: OJ L 35, 15.2.1995, p. 1–5

<sup>8</sup> Rules for the implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures: [EMA/MB/57356/2018](#)

- **The Pharmacovigilance Fee Regulation:** Regulation (EU) No 658/2014<sup>9</sup>, which provides the rules and amounts for fees charged to industry and remuneration paid to NCAs for pharmacovigilance activities conducted at Union level for nationally and centrally authorised medicines for human use;
- **The SME Regulation:** Council Regulation (EC) No 2049/2005<sup>10</sup>, which provides the rules for and levels of fee incentives (partial and full fee waivers and deferrals) for applicants fulfilling the definition of a micro, small or medium-sized enterprise (SME) as defined in Commission Recommendation 2003/361/EC<sup>11</sup>.

In addition, several pieces of sectorial legislation impact the fees charged to applicants, i.e. the Paediatric Regulation (Regulation (EC) No 1901/2006)<sup>12</sup>, the Orphan Regulation (Regulation (EC) No 141/2000)<sup>13</sup>, and the Advanced Therapy Medicinal Products (ATMPs) Regulation (Regulation (EC) No 1394/2007)<sup>14</sup>, which provide for fee incentives (partial and full fee waivers and deferrals) and activities exempted from fees for certain types of medicinal products.

For a detailed overview of the legislative and non-legislative provisions governing the EMA fee system, including those laid down in sectorial legislation, please refer to Annex 4.

## 1.2. Purpose and scope

The EMA fee legislation has not been evaluated since 2005. According to the EMA Founding Regulation (Article 86a), the Commission has the obligation to review by 2019 the regulatory framework for fees payable to the Agency in relation to medicinal products for human use and veterinary medicinal products and to put forward, as appropriate, legislative proposals with a view to update that framework.

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<sup>9</sup> Regulation (EU) No 658/2014 of the European Parliament and of the Council of 15 May 2014 on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use: OJ L 189, 27.6.2014, p. 112–127

<sup>10</sup> Council Regulation (EC) No 2049/2005 of 15 December 2005 laying down, pursuant to Regulation (EC) No 726/2004 of the European Parliament and of the Council, rules regarding the payment of fees to, and the receipt of administrative assistance from, the European Medicines Agency by micro, small and medium-sized enterprises: OJ L 329, 16.12.2005, p. 4–7

<sup>11</sup> Commission Recommendation of 6 May 2003 concerning the definition of micro, small and medium-sized enterprises (2003/361/EC): OJ L 124, 20.5.2003, p. 36–41

<sup>12</sup> Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004: OJ L 378, 27.12.2006, p. 1–19

<sup>13</sup> Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products: OJ L 18, 22.1.2000, p. 1–5

<sup>14</sup> Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004: OJ L 324, 10.12.2007, p. 121–137

Previous evaluations of (aspects of) the EMA fee system have not reported major shortcomings in the fee system, but indicated a need for clarification of some funding mechanisms for unpaid activities and whether such funding should take place at EU or national level.<sup>15</sup> In several of their reports on the annual accounts of the EMA the European Court of Auditors has noted the need to introduce a system of remuneration for services provided by Member State authorities based on their real costs.<sup>16</sup>

The purpose of this evaluation is to examine in a comprehensive way the functioning of the EMA fee system as laid down in the relevant bodies of legislation and implementing arrangements. The analysis provides a basis from which to consider the need for reform of the fee and remuneration system, and to consider which elements of the fee system might be specifically targeted for reform.

This evaluation addresses specifically the fee system, and does not include the underlying regulatory framework governing the authorisation, maintenance and monitoring of medicinal products.

The evaluation assesses the strengths and weaknesses of the fee system by focusing on the extent to which fees and remuneration amounts are founded on a sound economic basis, whether they are fair and proportionate, whether the system avoids unnecessary administrative burden and whether it is financially sustainable in the future. It addresses those questions with reference to the Better Regulation criteria effectiveness and efficiency, relevance, and coherence. The criterion of EU added value was not evaluated. Although there are implicit benefits for Member States of being part of the centralised regulatory system, the EMA Founding Regulation, which governs this regulatory system, is not within scope of this evaluation. In addition, the criterion of EU added value is not considered applicable to the evaluation of the fee system itself; the Agency is a European decentralised Agency established under Union legislation and hence the decision on its funding and charging of fees is to be taken at the EU level. Only the Union can act to enable the Agency to charge fees.

As required by legislation, this evaluation analyses the relationship of the services provided with the underlying costs.<sup>17</sup>

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<sup>15</sup> [Evaluation of the European Medicines – Final report - January 2010 by Ernst & Young](#): pages 11, 125 and 198

<sup>16</sup> See the European Court of Auditors reports on the annual accounts of the European Medicines Agency for the financial years [2006](#) (Report on the annual accounts of the European Medicines Agency for the financial year 2006 together with the Agency's replies (2007/C 309/07), OJ C 309, 19.12.2007, p. 34–39), [2010](#) (Report on the annual accounts of the European Medicines Agency for the financial year 2010, together with the Agency's replies, 2011/C 366/06, OJ C 366, 15.12.2011, p. 27–32) and [2011](#) (Report on the annual accounts of the European Medicines Agency for the financial year 2011, together with the Agency's replies, 2012/C 388/20, OJ C 388, 15.12.2012, p. 116–122).

<sup>17</sup> Article 12 of the Fee Regulation (Council Regulation (EC) No 297/95) provides that '[a]ny review of the fees shall be based on an evaluation of the Agency's costs and on the basis of the related costs of the services provided for by the Member States. Those costs shall be calculated in accordance with generally accepted international costing methods, which shall be adopted in accordance with Article 11(2).' In addition, Recital 7 of the Pharmacovigilance Fee Regulation (Regulation (EU) No 658/2014)

The scope of the evaluation covers the fee system of the EMA and the way in which it funds activities carried out by the Agency including the remuneration paid to NCAs, as specified by the main Fee Regulation and its Implementing Rules and the Pharmacovigilance Fee Regulation. Cross-cutting fee incentives for SMEs provided for in the SME Regulation as part of the overall EU policy to support SMEs are also taken into account. However, the SME Regulation itself is not within scope<sup>18</sup>. Specific fee incentives set in separate sectorial legislation for orphan designated medicines, ATMPs, and paediatric medicines were included in the calculations of fee income for EMA but are not part of the evaluation as such. The fee incentives are one of the provisions set in these sectorial legislative acts which, together, aim at reaching the individual objectives of these regulations. Therefore, the evaluation of these fee incentives can only be part of an evaluation of the entire legislation that provides for these incentives<sup>19</sup>. Similarly, the mechanism of the Union budget contributions set in the EMA Founding Regulation and the Orphan Regulation<sup>20</sup> as well as existing sources of EMA income other than fees are not evaluated but are used as fixed variables in the models used for the evaluation (see Section 4).

As regards NCAs, this evaluation only covers activities of NCAs contributing to the EMA and, regarding NCAs' income, only remuneration paid by the EMA. The geographical coverage includes NCAs from all EU and EEA Member States.

EMA activities related to both human and veterinary medicines are considered. However, an analysis of the new Veterinary Medicinal Products (VMP) Regulation (Regulation (EU) 2019/6)<sup>21</sup>, which introduces new and amended regulatory procedures, will apply as from January 2022. This regulation and its impact on veterinary fees are therefore not within the scope of this evaluation. They will be considered in relation to assessment of the relevance of the EMA fee system.

The evaluation covers the full period since the start of the intervention in 1995. However, the review of the level of fees in relation to costs incurred by EMA and NCAs for their services provided are based on a time data gathering over the year 2016 and a cost data gathering relative to the same year.

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stipulates that '[a]ny future revisions of the pharmacovigilance fees or other fees levied by the Agency should be based on a transparent and independent evaluation of the costs of the Agency and the costs of the tasks carried out by the national competent authorities.'

<sup>18</sup> It should be noted that any new legislative proposal by the European Commission is systematically subject to the SME test which analyses the possible effects on SMEs.

<sup>19</sup> The Commission is currently evaluating separately both the Orphan and Paediatric Regulation, including the fee incentives and fee exemptions provided for by these regulations (Ref. Ares(2017)6059807 – 11/12/2017).

<sup>20</sup> Article 67(3) of Regulation (EC) No 4726/2004 provides that the EMA receives a general Union budget contribution and Article 7(2) of Regulation (EC) No 141/2000 provides that the EMA additionally receives a special Union contribution to waive, in part or in total, all fees for orphan designated medicines.

<sup>21</sup> Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC: OJ L 4, 7.1.2019, p. 43–167

## **2. BACKGROUND TO THE INTERVENTION**

### **2.1. Intervention logic**

The intervention subject to this evaluation is the EMA fee system, as governed by Union legislation as described in Section 1. The structure and operation of the fee system, including remuneration paid to NCAs and fee incentives applied, are based on how medicinal products are authorised and monitored at Union level. The EMA fee system underpins the functioning of the Agency; without it there would be no budget with which the Agency could operate, and thus no EU-level authorisation system for medicinal products. In designing the fee system, the interests of applicants had to be balanced with the cost of employing the experts who carry out the authorisation process, and those of citizens who need access to effective and affordable medication when they fall ill.

More specifically, the fee system was designed to meet four needs:

1. To provide a sound financial basis for the Agency and its activities, including fair remuneration for the services provided by NCAs;
2. To ensure a level-playing field for industry in terms of access to EMA's services, and thus to promote competitiveness;
3. To facilitate the development and marketing of safe and effective medicines for patients; and
4. To limit the administrative burden generated by the fee system to the minimum.

The sections below outline the objectives pursued by the fee system, their translation into actions, and the positive results to which they were expected to lead.

#### **Ensuring a sound financial basis for the Agency:**

To put it simply, the Agency needs sufficient income to cover its costs. EMA's costs can be broken down roughly into two main categories:

1. The costs for activities carried out in-house by the Agency's own staff; and,
2. The remuneration paid to NCAs for the work they do through EMA's scientific committees and other working groups, which are responsible for evaluating applications, among other crucial tasks.

In order to fund these activities, the Founding Regulation laid down that pharmaceutical operators should pay fees to the Agency for obtaining and maintaining a Union marketing authorisation, as well as for other services provided by EMA. The level of fees, which would be set by the Council, should be sufficient to cover all costs. As a result, the fees laid down vary according to the service provided by the Agency. In addition, a contribution to the Agency's budget from the Union was planned from the very outset, so as to make it possible for EMA to grant special fee reductions and exemptions in certain cases where these might be deemed to be in the public interest.



These provisions were accompanied by the explicit condition that EMA's revenue and expenditure should be more or less in balance on an annual basis.

Over time, it was foreseen that the tasks of the Agency would be liable to change, and that the costs involved might also vary, so provision was made for the possibility of adjusting existing fee levels, and for introducing new types and levels of fee. This flexibility has since been used extensively, the greatest single change coming with the new pharmacovigilance activities assigned to EMA in 2010<sup>22</sup>, for which a whole new set of fees was created.

The NCA experts are remunerated for the services they provide to EMA in accordance with a fixed scale of fees established by the EMA Management Board, and laid out in the Implementing Rules of the Fee Regulation. These could likewise be subject to change and adjustment in response to changing circumstances.

Both the fees paid by industry to EMA, and the remuneration paid by EMA to the NCAs, were understood to be set in such a way that they corresponded to the costs actually incurred in providing the service concerned. In addition, fee levels were made subject to annual review and adjustment by reference to the inflation rate. The result expected was that neither EMA nor the NCAs would make a profit on the activities they carry out, but nor would they make a loss. In this way, the fee system sought to ensure that the financing of EMA was sustainable both in terms of EMA's own budget, and in terms of the willingness of NCAs to continue to collaborate with the Agency.

### **Creating a level-playing field for industry:**

The EMA fee structure was designed to be transparent and proportionate. It was expected that if this was achieved, then it would be perceived as fair and legitimate by payers (applicants and marketing authorisation holders), who would understand why they were being asked to pay the amount in question, and how their money was being spent. This legitimacy would in turn contribute to the perceived value of the services provided by EMA, and to the readiness of pharmaceutical operators to channel their authorisation requests through the Agency. It was also intended that fees should be set at a level which meant that procedural costs were not a factor in determining whether applicants chose a national authorisation procedure rather than the centralised procedure.

The pharmaceutical industry is not homogenous, however. Companies vary in size and financial means. In order to ensure that the EMA fee system provided a level playing-field, it was necessary to allow for the possibility of varying fees not only in relation to the complexity and cost of the service provided, but also to the means of the applicant. Provisions were therefore introduced to reduce or waive fees for SMEs, and to defer their payment pending the outcome of the application. It was expected that this would level the playing field, at least where authorisation applications were concerned, between dominant industry players and emerging SMEs. The same concern was reflected in the

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<sup>22</sup> The new legislation on pharmacovigilance for medicinal products for human use authorised via the national or central procedure was adopted in 2010 but started to apply as of July 2012.

decision to charge lower fees for all veterinary medicinal product procedures, since the market for veterinary medicines is much smaller than that for human medicines.

It was expected that these measures would produce a system in which central authorisation would be an attractive option not only for large companies, but also for SMEs, and in which competitiveness and innovation in the European pharmaceutical industry would thus be stimulated.

### **Facilitating the development of safe and effective medicines:**

Ensuring that citizens have access to safe and effective medicines assumes that the Agency carries out its tasks with the highest possible level of competence and vigilance. This in turn depends upon its financial stability, and its ability to compensate NCAs adequately for the essential expertise they provide. However, there were also other factors, which could interfere with the delivery of safe, and effective medicines by the EMA fee system, and which specific measures were therefore introduced to address.

Some of these measures were introduced via the fee system itself, whereas others were introduced via separate sectorial legislation not directly part of the current intervention (see further down). Those stemming from the fee system make it possible to grant incentives to SMEs, and also on a case-by-case basis to meet exceptional circumstances, and for imperative public or animal health reasons. The latter allows the Executive Director of the EMA to decide on fee incentives for human and veterinary medicines used for instance in pandemic situations, rare diseases and/or for small markets. For example, some veterinary medicinal products address only small markets such as those treating parasitic mites in honey bees or cancer in cats, and the revenue they could reasonably be expected to generate is unlikely to always cover the costs of their research and development. This concern was reflected in the decision to provide fee incentives to address the lack of veterinary medicines for the treatment of minor animal species and uncommon diseases.

It was expected that these incentives, including those provided by sectorial legislation described further below, would encourage the production of medicines for populations and/or diseases that might otherwise be neglected, and would ensure that appropriate products would be available to meet emergency situations in a timely manner.

### **Limiting the administrative burden generated by the fee system:**

It was intended that the fee system resulting should combine flexibility and proportionality with relative simplicity and easy applicability. By ensuring that fees charged were transparent, that the fee structure was not arbitrary or inconsistent but reflected the underlying regulatory framework and was coherent with its central objectives, and that the administrative processes involved were straightforward and user-friendly, it was hoped to achieve a balance between simplicity and complexity. The expected outcome was that the fee system would be well accepted by all stakeholders, EMA, NCAs and pharmaceutical industry and that pharmaceutical industry would consider whatever administrative burden might be created proportionate to the benefits

and advantages they gained from the central authorisation procedure, and would thus be inclined to use that procedure whenever it might be appropriate.

### **Fee reductions and exemptions provided by sectorial legislation:**

While some medicinal products address huge markets such as those used to treat high blood pressure in humans, others are only relevant to very small populations, and the revenue they could reasonably be expected to generate is unlikely to always cover the costs of their research and development. As a result, sectoral legislation was used to introduce a series of incentives, including measures which allow EMA fees to be reduced or waived, for specific types of medicinal product – those targeting rare diseases (the Orphan Regulation) or certain paediatric indications (the Paediatric Regulation) or those offering new treatment opportunities (the ATMP Regulation). The expected outcome is that patients regardless of their condition or age receive the same quality of treatment.<sup>23</sup>

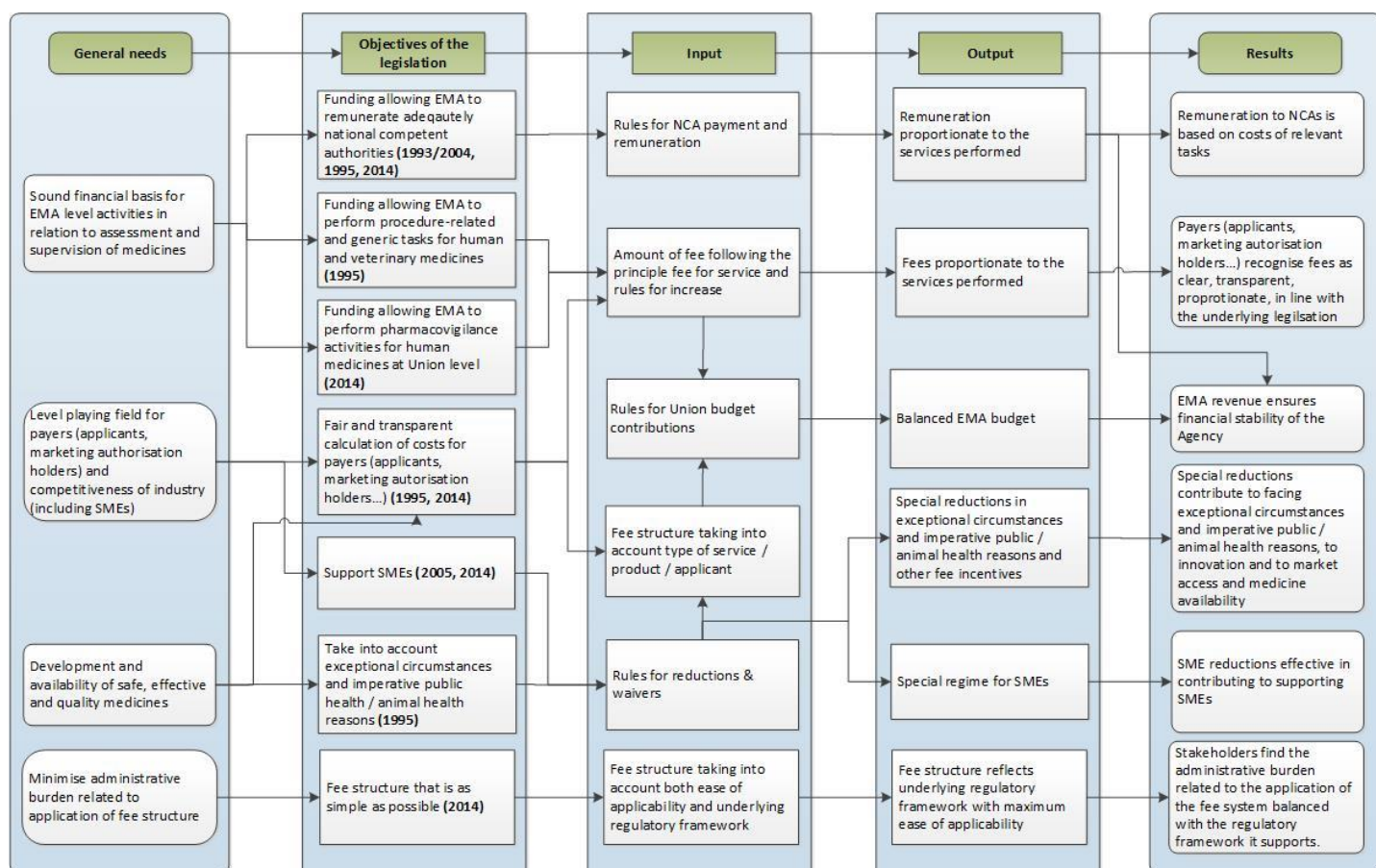
These sectorial regulations, including their provisions for fee incentives and activities that are free of charge, are not part of the intervention and therefore, as already stated in Section 1, not within scope of this evaluation. Nevertheless, they have an impact on several aspects of the intervention, i.e. on fees charged to industry, EMA's income from fees and Union contributions and NCA remuneration (see Section 3.1). These fee reductions and exemptions are therefore taken into account as fixed variable for the calculation of fee income in assessing cost-effectiveness of the fee system (see Section 4). Also, reduction in EMA's fee income due to the provision of fee reductions and exemptions, including activities free of charge, for orphan designated medicines, paediatric medicines and ATMPs, as well as for SMEs and for exceptional circumstances and imperative reasons of public or animal health, needs to be balanced by Union budget contributions to ensure financial stability for the Agency. Hence, fee reductions and exemptions provided by sectorial legislation impact on elements of the intervention.

Figure 1 below summarises the paragraphs above by visualizing the needs identified, the objectives of relevant legislation, the fee system inputs created by this legislation, and the intended outputs and results of the fee system. Under 'objectives of the legislation' years are included in each box to indicate to which regulation the objective concerned relates. More specifically, '1993/2004' refers to the (initial and current) Founding Regulation, '1995' refers to the Fee Regulation, '2005' refers to the SME Regulation, and '2014' refers to the Pharmacovigilance Fee Regulation.

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<sup>23</sup> Recital 2 of Regulation (EC) No 141/2000, Recital 4 of Regulation (EC) No 1901/2006, and Recitals 1 and 5 of Regulation (EC) No 1394/2007

**Figure 1: Schematic representation of the intervention logic**



## 2.2. Baseline – the entry into force of the fee system

The Agency was established by the ‘1993 Founding Regulation’ (Council Regulation (EEC) No 2309/93<sup>24</sup>). The Agency became operational only in 1995 once the Union regulation on fees payable to the Agency was adopted, in order to ensure adequate resources with which to carry out all of its main tasks.<sup>25</sup> Therefore, the baseline for this evaluation is the situation at the entry into force of the main Fee Regulation in 1995. The fee system evolved over time via amendments to the Founding Regulation, the Fee Regulation and the adoption of the Pharmacovigilance Fee Regulation and SME Regulation. The individual amendments to the fee system are not used as different points of comparison but considered in their entirety as evolving baseline.

<sup>24</sup> Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products: OJ L 214, 24.8.1993, p. 1–21. This regulation was later repealed by the previously mentioned Regulation (EC) No 726/2004, the current EMA Founding Regulation.

<sup>25</sup> [First general report on the activities of the European Agency for the Evaluation of Medicinal Products of 1995, as adopted by the Management Board on 6 March 1996](#): page 11

## **Fees charged by EMA:**

**The entry into force of the Fee Regulation (1995):** The 1993 Founding Regulation of the Agency provided that its budget consists of industry fees and a contribution from the EU. Details on type and level of fees were laid down in the Fee Regulation, adopted in 1995.

The Fee Regulation established fees charged on a per-service basis, for the purpose of this document also referenced as ‘**procedural fees**’. Fees were payable to the Agency for: (1) initial marketing authorisations; (2) inspections; (3) variations to an existing marketing authorisation; (4) renewals of an existing marketing authorisation; (5) extensions of an existing marketing authorisation; (6) transfers of an existing marketing authorisation to another MAH; (7) referrals (arbitration); (8) maximum residue limit (MRL) (veterinary medicines only).

For initial marketing authorisations for human and veterinary medicinal products, reduced basic fees applied to applications for medicinal products, which did not require a full dossier.<sup>26</sup> In addition, procedural fees for veterinary medicines were generally set at a lower level than those for medicines for human use.

Altogether, the Fee Regulation recognised a total of 23 different basic procedural fees ranging from ECU<sup>27</sup> 5,000 to ECU 140,000. Further, a supplementary fee could be charged for each additional strength or pharmaceutical form for applications of the same medicinal product, up to a certain ceiling specified in the Fee Regulation. This additional fee ranged from ECU 5,000 to ECU 20,000. As explained in Section 2.1, the amounts for the procedural fees were determined based on the principle that they should not be a determining factor for the applicant for an authorisation where there is a choice between a centralised procedure and a national procedure<sup>28</sup>.

**Amendments to the Fee Regulation and its Implementing Rules (1999, 2005):** Since 1995, the Fee Regulation has been amended several times, mostly to adjust the fee levels in relation to the inflation rate. However, the number and type of fees charged were also changed twice. The 1999 and 2005 amendments to the Fee Regulation<sup>29</sup> aimed at ensuring coverage of EMA costs connected with the authorisation and supervision of

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<sup>26</sup> More specifically, reduced fees applied to applications submitted in accordance with Article 4(8)(a) or (b) of Council Directive 65/65/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 22, 9.2.1965, p. 369–373). This article provided that for certain types of medicines the results of pharmacological tests, toxicological tests and clinical trials may be substituted for published references or data.

<sup>27</sup> The European Currency Unit (ECU) was the official monetary unit of the European Communities. It was an artificial, electronic unit based on a basket of the national currencies of twelve EU Member States. The ECU was replaced by the euro on 1 January 1999 at the value of 1 EUR = 1 ECU.

<sup>28</sup> See the recitals of the Fee Regulation.

<sup>29</sup> Council Regulation (EC) No 2743/98 of 14 December 1998 amending Regulation (EC) No 297/95 on fees payable to the European Agency for the Evaluation of Medicinal Products: OJ L 345, 19.12.1998, p. 3–8 ; Council Regulation (EC) No 1905/2005 of 14 November 2005 amending Regulation (EC) No 297/95 on fees payable to the European Medicines Agency: OJ L 304, 23.11.2005, p. 1–9

medicinal products. These costs had increased due to the introduction of new tasks for the EMA and the amendment of existing ones, most notably following changes in pharmaceutical legislation (the 1993 Founding Regulation was repealed by the 2004 Founding Regulation).

In detail, existing fees were amended and new fees were introduced for scientific advice (1999) and scientific services (2005), and the single fee for Type I variations was replaced by two separate fees for Type IA and Type IB variations (2005). In addition, both an **annual fee** for maintenance activities (e.g. development of central databases, safety monitoring) and **administrative fees** were introduced (1999). The annual fee was set at ECU 20,000 and ECU 60,000 for respectively veterinary and human medicines. The Management Board was tasked to classify and specify the levels of the administrative fees in the Implementing Rules, which weren't to exceed ECU 5,000. In addition, an **indexation mechanism** for automatically adjusting fees in relation to the inflation rate was introduced (2005).

Further, the Management Board and the Executive Director of the EMA were given **additional flexibility** to adapt certain basic fee levels, within certain limits and under clearly-defined circumstances, to the particular situation of the application and the related product. The circumstances were included in the Implementing Rules.

**Entry into force of the Pharmacovigilance Fee Regulation (2014):** In 2010 new pharmacovigilance legislation was adopted for medicines for human use authorised via the national or central procedure.<sup>30</sup> This legislation, which started to apply as of July 2012, brought significant changes in the safety monitoring of these medicines in the EU by introducing new and amended pharmacovigilance activities. It also empowered EMA to charge fees for pharmacovigilance activities to holders of marketing authorisations, including for specific Union pharmacovigilance activities of the coordination group. These fees should fund EMA's horizontal tasks, such as literature monitoring, IT tools and the provision of information to the public, but not tasks carried out by NCAs for which they charge national fees.

In accordance with these provisions, the Founding Regulation was amended by adding that EMA's revenue should also consist of fees charged to undertakings for certain pharmacovigilance-related activities provided by the coordination group.<sup>31</sup> In addition,

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<sup>30</sup> Directive 2010/84/EU (OJ L 348, 31.12.2010, p. 74–99) and Regulation (EU) 1235/2010 (OJ L 348, 31.12.2010, p. 1–16) amended existing pharmacovigilance provisions in, respectively, Directive 2001/83/EC (on the Community code relating to medicinal products for human use: OJ L 311, 28.11.2001, p. 67–12) and Regulation (EC) No 726/2004 (Founding Regulation) and Regulation (EC) No 1394/2007 (ATMP Regulation). These two pieces of legislation were accompanied by Commission Implementing Regulation (EU) No 520/2012 on the performance of pharmacovigilance activities (OJ L 159, 20.6.2012, p. 5–25).

<sup>31</sup> See Article 1(18)(a) of Regulation (EU) No 1235/2010. Via this article, Article 67(3) was amended to: 'The Agency's revenue shall consist of a contribution from the Union and fees paid by undertakings for obtaining and maintaining Union marketing authorisations and for other services provided by the Agency, or by the coordination group as regards the fulfilment of its tasks in accordance with Articles 107c, 107e, 107g, 107k and 107q of Directive 2001/83/EC.' (emphasis added)

the Pharmacovigilance Fee Regulation was adopted in 2014 setting fees for pharmacovigilance activities at Union level in respect of medicines for human use authorised at the central and national level. It introduced **procedural fees** for the assessment of periodic safety update reports (PSUR/PSUSA), post-authorisation safety studies (PASS) and pharmacovigilance referrals. The applicable fees were set at €19,500 for PSUR/PSUSA, €43,000 for PASS and €179,000 for referrals. The latter could be increased by €38,000 per each additional active substance or combination of active substances as of the third active substance or combination of substances, with a ceiling of €295,400. An additional **pharmacovigilance annual fee** was established to finance EMA's pharmacovigilance activities relating to IT systems and literature monitoring. This fee only applied to nationally authorised products, since for centrally authorised products these activities are already covered by the annual fee charged under the Fee Regulation (see further above). The amount payable for each market authorisation holder was set to depend on the number of 'chargeable units'<sup>32</sup>, with a basic fee of €67 charged per chargeable unit. The fees set out in this Regulation were based on an evaluation of the Agency's estimations and forecasts as regards its workload and related costs, and on the basis of an evaluation of the costs of the work carried out by the NCAs.<sup>33</sup>

Unlike the Fee Regulation, the Pharmacovigilance Fee Regulation is not accompanied by implementing rules. Therefore, all provisions related to the type and level of basic fees, reduction of basic fees and NCA remuneration are laid down in the regulation itself.

The amendments to the Fee Regulation and introduction of the Pharmacovigilance Fee Regulation led to a stark increase in the number of basic (full and reduced) fees applied through the fee system.

### **Fee reductions and exemptions:**

**The entry into force of the Fee Regulation (1995):** The Executive Director could grant fee incentives on a case-by-case basis in exceptional circumstances and for imperative reasons of public or animal health for medicinal products with a limited number of applications. The general criteria for granting waivers and reductions were to be determined by the Management Board and included in the Implementing Rules. The Management Board decided that fee waivers and reductions should only be available for

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<sup>32</sup> Since the Pharmacovigilance Fee Regulation applies to both centrally and nationally authorised products, a harmonised definition of the concept of a 'marketing authorisation' across the EU is required in order to be able to levy pharmacovigilance fees in a consistent manner. However, such harmonised definition does not exist. For this reason, the chargeable unit was introduced, defining, for the purpose of charging pharmacovigilance fees, a unitary entry that can be considered equivalent to a single marketing authorisation. A single chargeable unit consists of a unique combination of the following dataset: (1) name of the medicinal product, as defined in point 20 of Article 1 of Directive 2001/83/EC; (2) marketing authorisation holder; (3) Member State in which the marketing authorisation is valid; (4) active substance or a combination of active substances; (5) pharmaceutical form. For instance, a medicinal product registered under the name <medicine X> containing simvastatin/ezetimib in film-coated tablets, owned by MAH Y and authorised in Poland and Latvia results in two chargeable units, because it is authorised in two different Member States.

<sup>33</sup> See Recital 6 of the Pharmacovigilance Fee Regulation.

orphan medicines for human use and comparable products for veterinary use (i.e. medicines for minor use/minor species (MUMS)), including the determination of certain MRLs of old products.<sup>34</sup>

**Amendments to the Fee Regulation and its Implementing Rules (since 1995):** In 2005, the possibility for the Executive Director to decide on total or partial fee exemptions was extended to orphan designated products, MUMS, the extension of existing MRLs to additional animal species, and medicines available for compassionate use.<sup>35</sup>

Since 1995, the Management Board amended the provision of partial or total fee reductions several times, changing levels for fee incentives and adding new ones. Some of these amendments were a direct consequence of changes in the Fee Regulation or the adoption of relevant cross-cutting or sectorial legislation (in the situation where the legislation provided for the possibility of total or partial fee waivers without specifying the level and/or conditions). Others followed from budgetary decisions by the Management Board to ensure a balanced budget for the Agency.

**Entry into force of the SME Regulation (2005):** The SME Regulation, which entered into force in 2005, specifies both the services of EMA that should be incentivised for SMEs, the condition(s) under which the incentive is applicable and the level of the incentive (e.g. 90% of the full fee). Additional fee incentives for SMEs were adopted by the Management Board and included in the Implementing Rules.

**Entry into force of the Pharmacovigilance Fee Regulation (2014):** The Pharmacovigilance Fee Regulation provides for fee reductions for SMEs for both its procedural fees (PSUR/PSUSA, PASS, referral) and its annual fee. It also specifies the conditions and levels of fee reductions that are applicable.

**Entry into force of sectorial legislation (2000, 2006, 2007):** Although not part of the intervention, the adoption of sectorial legislation (i.e. the Orphan Regulation (2000), the Paediatric Regulation (2006) and the ATMP Regulation (2007)), has contributed to the increase of fee incentives provided by the Agency and for the establishment of activities that are free of charge.

### **Union budget contributions:**

**Entry into force of the Founding Regulation (1993, 2004):** In accordance with its Founding Regulation, EMA has received a Union contribution from the very beginning which balances shortfalls in EMAs budget due to fee incentives or fluctuations in fee

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<sup>34</sup> [First general report on the activities of the European Agency for the Evaluation of Medicinal Products of 1995, as adopted by the Management Board on 6 March 1996](#); page 13

<sup>35</sup> Proposal for a Council Regulation amending Regulation (EC) No 297/95 on fees payable to the European Medicines Agency (COM(2005) 106 final) ; Amending Council Regulation (EC) No 1905/2005 (OJ L 304, 23.11.2005, p. 1–9)



income. Amendments to the Founding Regulation did not affect the provision of this balancing contribution.

**Entry into force of sectorial legislation (2000, 2006):** Although not part of the EMA fee system, the relevant sectorial legislation is shortly described here in regards their provisions regarding Union subsidies for reasons mentioned under Section 2.1. The Orphan Regulation (2000) introduced a **specific orphan contribution** to be used exclusively by the Agency to waive, in part or in total, all the fees payable for orphan designated products.<sup>36</sup> This orphan contribution is distinct from the general Union contribution provided for by the Founding Regulation.<sup>37</sup> Further, the Paediatric Regulation (2006) stipulates that the general Union contribution should cover the work of the Paediatric Committee (PDCO), including scientific support provided by experts, and of the Agency resulting from the implementation of the Paediatric Regulation, including assessments of paediatric investigation plans (PIPs), scientific advice and any fee waivers provided for in that regulation.<sup>38</sup>

### **NCA remuneration:**

**Entry into force of the Founding Regulation (1993):** In accordance with the 1993 Founding Regulation<sup>39</sup>, the Management Board decided in 1995 that 50% of the full procedural fee would be allocated to the remuneration of NCAs for their scientific services, to be equally divided between the NCA of the rapporteur and co-rapporteur.<sup>40</sup>

**Amendments to the Fee Regulation and its Implementing Rules (1999):** When the annual fee was introduced via an amendment of the Fee Regulation, it was also specified that part of this annual fee would have to be allocated to NCAs in accordance with rules to be adopted by the Management Board.<sup>41</sup> Following this, the Management Board decided on a distribution of this fee whereby 30% of the full applicable fee is paid to the rapporteur and co-rapporteur (15% each) for the medicinal product concerned for the production of annual safety reports and other supervisory tasks<sup>42, 43</sup>.

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<sup>36</sup> Article 7(2) of Regulation (EC) No 141/2000, the Orphan Regulation.

<sup>37</sup> Article 57(1) of Council Regulation (EEC) No 2309/93, later repealed by Article 67(3) of Regulation (EC) No 726/2004, the Founding Regulations of the EMA.

<sup>38</sup> Article 48 of Regulation (EC) No 1901/2006, the Paediatric Regulation.

<sup>39</sup> Article 53(3) of Council Regulation (EEC) No 2309/93, the 1993 Founding Regulation.

<sup>40</sup> [First general report on the activities of the European Agency for the Evaluation of Medicinal Products of 1995, as adopted by the Management Board on 6 March 1996](#): page 14

<sup>41</sup> Amending Council Regulation (EC) No 2743/98: OJ L 345, 19.12.1998, p. 3–8

<sup>42</sup> [Fifth general report on the activities of the European Agency for the Evaluation of Medicinal Products of 1999, as adopted by the Management Board on 1 December 1999](#): page 19

<sup>43</sup> Amending Council Regulation (EC) No 2743/98 provided in its recitals that '[w]hereas an annual fee must be introduced to ensure coverage of the costs connected with the supervision of authorised medicinal products; whereas a given part of this fee will have to be allocated to the competent national authorities required under the terms of Regulation (EEC) No 2309/93 to supervise the market on behalf of the Community; whereas, moreover, the rules for distribution amongst those authorities will

The above mentioned decisions of the Management Board were laid down in the Implementing Rules.

**Entry into force of the Pharmacovigilance Fee Regulation (2014):** The Pharmacovigilance Fee Regulation provides that NCAs of the rapporteur and co-rapporteur, including those within the coordination group, receive a fixed amount of procedural fees. It further stipulates that where a fee incentive applies, this amount is reduced proportionally. NCAs do not receive a share in the pharmacovigilance annual fee as it is intended to cover activities that only involve EMA staff.

### **Quantitative output in terms of EMA budget and NCA remuneration:**

In 1995, EMA's initial year of operation, the Management Board adopted an initial budget of ECU 14.4 million. Industry fees amounted to ECU 4.0 million of EMA's total income (27.8%). In 2014, pharmacovigilance fees added €1.4 million to EMA's budget (0.5%), as compared to €216.3 million from non-pharmacovigilance fees (79.6%).

In 1995, the general Union contribution amounted to ECU 10.2 million, including ECU 650,000 from the EU enlargement budget and ECU 750,000 released from the reserve by the European Parliament at the end of 1995 (70.5%) to be used for the financing of fee waivers. The first orphan contribution provided to the Agency in the year 2000 was set at €1.0 million, which constituted 1.8% of EMA's total budget.

Total remuneration paid to NCAs in 1995 equalled ECU 3,6 million. In 2014, remuneration of pharmacovigilance activities was introduced, amounting to €1.5 million, as compared to €94.6 million of remuneration paid for non-pharmacovigilance activities in that same year.<sup>44</sup>

The paragraphs above present a summary of the evolution of the legislative and non-legislative provisions governing the fee system. For more information, see Annex 4.

### **2.3. Other comparators and referenced information**

Several other comparators and references are used to review the EMA fee system against the evaluation criteria. These are shortly described below.

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have to be adopted by the Agency's Management Board in accordance with the procedure laid down in this Regulation'.

<sup>44</sup> Figures quoted for 1995 are based on those published in (1) the [First general report on the activities of the European Agency for the Evaluation of Medicinal Products of 1995, as adopted by the Management Board on 6 March 1996](#) (pages 13 and 18) and (2) the [Third general report on the activities of the European Agency for the Evaluation of Medicinal Products of 1997, as adopted by the Management Board on 3 December 1997](#) (Annex 6). Figures quoted for 2014 are based on those published in the EMA Budget Report for [2016](#) to ensure use of final data.

### **Previous analyses of (aspects) of the EMA fee system:**

- ***2004 EMA analysis of the fee system:***

Following a change in the tasks and responsibilities assigned to EMA in 2004<sup>45</sup>, the fee system was evaluated by EMA to assess whether it was still fit for purpose.<sup>46</sup> Based on EMA's findings the Commission prepared the 2005 amendment of the Fee Regulation as described in the previous section.

- ***2010 external study on the EMA:***

A 2010 external study on the evaluation of the EMA, commissioned by the Commission, included some aspects related to the fee system, allowing to (partially) address certain questions under the evaluation criteria.<sup>47</sup>

- ***European Court of Auditors reports on EMA's annual accounts:***

In their annual accounts of the EMA, the European Court of Auditors (ECA)<sup>48</sup> also repeatedly made comments on elements of the fee system specifically related to NCA remuneration.<sup>49</sup>

The observations of the 2004 EMA analysis of the fee system, of the 2010 external study on the EMA and of ECA are not listed here but included in Section 5 to provide a reference for the findings of the current evaluation of the fee system where relevant. However, when using these sources of information as reference, it should be kept in mind that the fee system has changed significantly since 2004/2010, most notably through the Pharmacovigilance Fee Regulation in 2014 and a recent amendment of the Founding Regulation (see Section 3).

### **The fee systems of other agencies:**

The fee systems of several other agencies are used to evaluate EMA's fee system in regards fee structure, NCA remuneration and the provision of fee incentives for SMEs.

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<sup>45</sup> This change resulted from a change in pharmaceutical legislation, whereby the 1993 Founding Regulation (Council Regulation (EEC) No 2309/93) was repealed by the 2004 Founding Regulation (Regulation (EC) No 726/2004).

<sup>46</sup> Report to the European Commission on financing the European Agency for the Evaluation of Medicinal Products – Endorsed by the Management Board on 11 March 2004 (not published) ; See also section 2.2 of the Explanatory Memorandum accompanying the Commission proposal for a Council Regulation amending Regulation (EC) No 297/95 on fees payable to the European Medicines Agency {SEC(2005)407} /\* COM/2005/0106 final - CNS 2005/0023 \*/.

<sup>47</sup> [Evaluation of the European Medicines Agency – Final report – January 2010 \(Ernst & Young et Associés\)](#)

<sup>48</sup> The ECA is the EU's independent external auditor looking after the interests of EU taxpayers. It checks whether EU funds are collected and used correctly and helps to improve EU financial management.

<sup>49</sup> See the European Court of Auditors reports on the annual accounts of the European Medicines Agency for the financial years [2006](#) (OJ C 309, 19.12.2007, p. 34–39), [2010](#) (OJ C 366, 15.12.2011, p. 27–32) and [2011](#) (OJ C 388, 15.12.2012, p. 116–122).

- ***European Chemicals Agency***

The revenue of the European Chemicals Agency (ECHA) consists of a Union contribution, fees paid by undertakings and any voluntary contribution from the Member States.<sup>50</sup> ECHA works in a similar way as the EMA. It has an Executive Director, Management Board, a Secretariat and several scientific committees. The members of the committees are experts put at ECHA's disposal by the Member States, who perform evaluations as rapporteur and co-rapporteur. Commission Regulation (EC) No 340/2008<sup>51</sup> sets the amounts and rules for payment of the fees and charges levied by ECHA for the registration, evaluation, authorisation and restriction of chemicals. Commission Implementing Regulation (EU) 2018/895<sup>52</sup>, which amended ECHA's Fee Regulation, provides in its recitals that the structure and amount of the fees shall take account of the work required to be carried out by ECHA and the competent authorities and shall be fixed at such a level as to ensure that the revenue derived from them when combined with other sources of revenue is sufficient to cover the cost of the services delivered.

In addition, the 'ECHA Fee Regulation' provides for reduced fees and charges for SMEs for all their services. Reductions are broken down by the size of the business. In addition, SMEs can receive further reductions in the case of some joint submissions.

The regulation further stipulates in its Article 14 that a proportion of the fees and charges collected shall be transferred to competent authorities of the Member States as compensation for the work of the rapporteur and co-rapporteur and for any related scientific and technical support. The regulation does not indicate the exact proportion or amount, but provides that this should be set by the Management Board on the basis of workload involved (Article 15).

ECHA's Fee Regulation is not accompanied by implementing rules.

- ***European Aviation Safety Agency***

The revenue of the European Aviation Safety Agency (EASA) consists of a contribution from the Union and from third countries, fees paid by applicants for certificates and approvals issued, maintained or amended by the Agency, and of charges for publications, handling of appeals, training and any other service provided by EASA. Commission

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<sup>50</sup> Article 96(1) of Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC: OJ L 396, 30.12.2006, p. 1–849

<sup>51</sup> Commission Regulation (EC) No 340/2008 of 16 April 2008 on the fees and charges payable to the European Chemicals Agency pursuant to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the registration, evaluation, authorisation and restriction of chemicals (REACH): J L 107, 17.4.2008, p. 6–25

<sup>52</sup> Commission Implementing Regulation (EU) 2018/895 of 22 June 2018 amending Regulation (EC) No 340/2008 on the fees and charges payable to the European Chemicals Agency: OJ L 160, 25.6.2018, p. 1–5

Regulation (EU) No 319/2014<sup>53</sup> determines the matters for which fees and charges are due, establishes the amount of the fees and charges and the way in which they are to be paid. It stipulates in its recitals that the tariffs need to be adjusted in order to ensure a balance between the costs incurred by EASA for related certification tasks and services provided, and the revenues to cover said costs. It further provides that fees and charges should be set in a transparent, fair and uniform manner.

With regard to NCA remuneration, the ‘EASA Fee Regulation’ states that Member States may undertake certification tasks on behalf of EASA and that they will be reimbursed for this. However, it does not specify any rules on remuneration.

EASA does not offer fee reductions or exemptions for SMEs.

EASA’s Fee Regulation is not accompanied by implementing rules.

- ***US Food and Drug Administration***

The EMA fee system is compared with the US Food and Drug Administration (FDA) fee system in terms of flexibility for SMEs.

With regard to SMEs, FDA does not recognise individual definitions for micro, small or medium-sized enterprises. Instead, they offer reductions and exemptions to ‘small businesses’, which are enterprises of fewer than 500 employees, including employees of their affiliates. The FDA waives fees for SMEs for some first applications as defined by the Medical Device User Fee Act (MDUFA), Biosimilar User Fee Act (BsUFA), Prescription Drug User Fee Act (PDUFA) and the Animal Drug User Fee Act (ADUFA). In addition, it offers 25 to 50% reduction to fees defined by the MDUFA, except for the Annual Establishment Registration Fee. There are no fee incentives for SMEs defined by the Generic Drug User Fee Act (GDUFA) or the Animal Generic Drug User Fee Act (AGDUFA).<sup>54</sup>

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<sup>53</sup> Commission Regulation (EU) No 319/2014 of 27 March 2014 on the fees and charges levied by the European Aviation Safety Agency, and repealing Regulation (EC) No 593/2007: OJ L 93, 28.3.2014, p. 58–80

<sup>54</sup> For an overview of all FDA fee acts and fees levied, see the 'FDA User Fee Programs' at <https://www.fda.gov/ForIndustry/UserFees/default.htm> (link consulted April 2019)

### 3. IMPLEMENTATION / STATE OF PLAY

The complexity of the current EMA fee system stems from (1) the wide variety of services provided and activities carried out by the EMA, most of them in close cooperation with the NCAs, and (2) the several layers of legislation governing and impacting on the fee system.

Each year, EMA, with the involvement of NCAs, provides independent, science-based evaluations on a great number of centralised pre- and post-authorisation procedures for medicinal products for human and veterinary use, following the processes and procedures described in Annex 3. In 2017, 548 inspections were carried out, 667 scientific advices/protocol assistance (initial and follow-up requests) and 260 applications for orphan designation were received, 421 opinions on PIPs and PIP waivers were issued, 117 applications for marketing authorisation were evaluated, 6,739 variations and extension applications were received, 1,003 PSURs/PSUSAs recommendations were issued, 2,062 potential signals were reviewed, and the product information for 397 medicines was updated. In addition, work was undertaken at EMA level in the area of, among others, scientific guideline development, fighting antimicrobial resistance, EU Telematics, early access to medicines, improving medicines availability, stakeholder interaction, and bilateral interactions with non-EU regulators.<sup>55</sup>

This work is carried out by EMA's seven scientific committees (Committee for Medicinal Products for Human Use (CHMP), Committee for Medicinal Products for Veterinary Use (CVMP), Pharmacovigilance Risk Assessment Committee (PRAC), Committee for Orphan Medicinal Products (COMP), the Committee on Herbal Medicinal Products (HMPC), the Paediatric Committee (PDCO), and the Committee for Advanced Therapies (CAT)), its numerous working parties and scientific advisory groups and its Secretariat.<sup>56</sup> Members of the committees, working parties and scientific advisory groups are scientific experts put at the Agency's disposal by Member States, whereas EMA's staff members comprise the Secretariat.

All costs incurred by EMA for abovementioned activities, as well as remuneration paid towards NCAs for their scientific contributions as committee rapporteur or co-rapporteur, need to be financed from EMA's budget. This budget is composed of (1) a contribution from the Union, (2) a contribution from third countries (EEA Member States)

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<sup>55</sup> Figures given are for veterinary and human medicines combined, except for PIPs and PIP waivers, potential signals and the update of product information, which only concern medicinal products for human use. Sources: [Annual report 2017 – The European Medicines Agency's contribution to science, medicines and health in 2017](#) and the EMA [Annual activity report 2017 \(EMA/269647/2018\)](#).

<sup>56</sup> Article 56(1) of Regulation (EC) No 726/2004 establishes that the EMA comprises the CHMP, CVMP, PRAC, COMP, HMPC, PDCO and CAT, a Secretariat, an Executive Director and a Management Board. In accordance with Articles 56(2) and 56(3) of this same regulation, EMA's committees may establish standing and temporary working parties which they may consult on scientific issues and for providing scientific advice to undertakings as well as scientific advisory groups in connection with the evaluation of specific types of medicinal products or treatments.

participating in the work of the Agency, (3) fees paid by undertakings (i) for obtaining and maintaining Union marketing authorisations and for other services provided by the Agency and (ii) for services provided by the coordination group as regards the fulfilment of its pharmacovigilance tasks, (4) charges for other services provided by the EMA, and (5) Union funding in the form of grants for participation in research and assistance projects.<sup>57</sup>

Below follows a summary of the EMA fee system as currently in place, including a description of fees charged, NCA remuneration and Union subsidies. Although not part of the intervention, certain provisions related to fee reductions and exemptions in sectorial legislation (i.e. the ATMP, Orphan and Paediatric Regulation) are shortly referenced below as they affect income of EMA from Union contributions, fees charged to industry by EMA and costs incurred by EMA and NCAs.

For a more detailed account of the fee system and an overview of the legal provisions governing this system, see Annexes 4 and 5.

### **3.1. Structure and operation of the fee system**

#### **Fees charged by EMA:**

The fee system foresees fees charged on a one-off basis (i.e. fees charged on a per-service basis, for the purpose of this document also referenced as ‘procedural fees’, and administrative fees) and on an annual basis (annual fees).

**Procedural fees** are applicable to a specific set of services provided either before or after the granting of a marketing authorisation (‘pre- and post-authorisation procedural fees’), more specifically:

1. Fees are charged for non-pharmacovigilance activities for centrally authorised human and veterinary medicines. These activities concern: scientific advice and protocol assistance, initial marketing authorisation applications, extensions of marketing authorisations, variations to existing marketing authorisations, renewals of marketing authorisations, referrals (other than those related to safety issues), scientific services<sup>58</sup>, transfers of marketing authorisations, and inspections. In addition, for veterinary medicinal products fees are also charged for the establishment, extension or modification of MRLs.
2. Fees are charged for pharmacovigilance activities for nationally and centrally authorised medicines for human use. These activities concern: referrals related to safety issues, PSURs/PSUSAs and PASS.

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<sup>57</sup> Article 67(3) of Regulation (EC) No 726/2004.

<sup>58</sup> Scientific services include scientific opinions for the evaluation of medicinal products for human use intended exclusively for markets outside the EU, opinions on compassionate use, evaluation of traditional herbal medicinal products, consultation of ancillary substances incorporated in medical devices, certification of plasma and vaccine-antigen master files (PMF and VAMF), and certification of quality and non-clinical data relating to ATMPs developed by SMEs.

Specific fee levels exist for each type of procedural activity. In addition, for certain activities the fee system defines more than one fee level. The applicable level depends on the expected complexity of the underlying data that needs to be assessed.<sup>59</sup> In addition, procedural fees for veterinary medicines are set at a lower level (generally at 50%) than those for medicines for human use for reasons outlined in Section 2.1.

The above results in around 90 different basic procedural fees for medicinal products for human and veterinary use. Basic fee levels for human and veterinary medicines currently range from €3,200 to €291,800. Further, additional fees may be added to the basic fee for each additional strength, pharmaceutical form or presentation that needs to be evaluated. These additional fees currently range from €7,300 to €29,300 for non-pharmacovigilance activities and €40,020 for pharmacovigilance activities.<sup>60</sup>

**Annual fees** apply for horizontal post-authorisation activities related to existing marketing authorisations. Two types of annual fees exist:

1. An annual fee is charged for centrally authorised products (CAPs) for human and veterinary use. The CAP annual fee funds the Agency's pharmacovigilance and inspection staff costs (30% of the total fee), the sampling and testing of centralised products under the EDQM<sup>61</sup> - EMA scientific agreement programme<sup>62</sup> (up to 10% of the total fee), special activities determined by the EMA Management Board in consultation with the scientific committees (30% of the total fee), and the scientific services provided by NCAs at EMA's request (e.g. annual product reports or safety reports) and other activities carried out by NCAs under their Union obligations (30% of the total fee).
2. A pharmacovigilance annual fee is charged for nationally authorised products (NAPs) for human use. This fee is charged to fund EMA's costs for IT systems, in particular the maintenance of the EudraVigilance database, and medical literature monitoring.

The current fee system defines six levels of CAP annual fees, three for human medicines and three for veterinary medicines, whereby the latter are set at 33% of the CAP annual

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<sup>59</sup> For example, initial marketing authorisation applications for medicinal products containing a new active substance generate a higher fee than those for generic medicines.

<sup>60</sup> Fee amounts quoted for the current situation are those valid in April 2019.

<sup>61</sup> The European Directorate for the Quality of Medicines & Healthcare (EDQM) is responsible for supporting the basic human right of access to good quality medicines and health care in Europe. The EDQM protects public health by enabling the development, supporting the implementation and monitoring the application of quality standards for safe medicines and their safe use, which are recognised as a scientific benchmark world-wide.

<sup>62</sup> Since CAPs are authorised throughout the Union, a coordinated EU approach to controlling their quality is required. A contract governing an annual CAP Sampling & Testing Programme was signed by the EMA and EDQM. The EMA is the sponsor of the programme and has overall responsibility for it, whereas the EDQM coordinates the sampling and testing operations. EDQM duties include reporting the results and, if required, proposing follow-up actions, to the EMA. National inspectorates take the samples, and members of the EU/EEA official medicines control laboratories (OMCL) test the samples. Both inspectorates and OMCLs can be part of a national regulatory body or be separate bodies.



fee for human medicines. The level depends further on the type of underlying dossier.<sup>63</sup> CAP annual fees currently range from €8,600 to €104,600. The calculation of pharmacovigilance annual fees has not changed over the years, i.e. the amount payable for each MAH depends on the number of ‘chargeable units’. The basic fee per chargeable unit has slightly increased from €67 to €69 to adjust to inflation.<sup>64</sup>

**Administrative fees** apply for administrative services (1) where documents or certificates are issued outside the framework of services covered by ‘procedural fees’, (2) where an application is rejected following the conclusion of the administrative validation of the related dossier, (3) where the information required in the case of parallel distribution has to be checked, and (4) where worksharing arrangements are applicable to variations. With the exception of the latter, the levels of the administrative fees are the same for medicines for human and veterinary use. The classification and levels of the administrative fees are to be adopted by the Management Board within the range specified by the Fee Regulation and included in the Implementing Rules. A total of 13 different administrative basic fees apply, ranging from €290 to €7,290. In addition, where the activity concerns the provision of certificates, additional fees are charged for each additional set of certificate issued.<sup>65</sup>

Section 2.2 describes how the amounts for the fees under the two fee regulations were initially determined. These amounts are currently subject to rules for increase. First, as specified by both regulations, any review of the fees shall be based on a (transparent and independent) evaluation of the Agency’s costs and on the basis of the related costs of the services provided by the NCAs.<sup>66</sup> In addition, these amounts are reviewed annually by the Commission by reference to the inflation rate and adjusted as appropriate.<sup>67</sup>

For a complete list of fees currently charged, see Annex 6.

### **Fee reductions, exemptions and fee deferrals:**

Union legislation has introduced **partial or full fee waivers** for several types of applications. Further, the EMA Executive Director and Management Board have decided on additional fee incentives<sup>68</sup>, which are either specified in the Implementing Rules of the Fee Regulation or take the shape of Executive Decisions. Partial or full waivers are currently in place for: SMEs, orphan designated medicines, ATMPs, medicinal products for paediatric use (PUMAs), veterinary medicines for MUMS/limited markets, veterinary vaccines against certain epizootic diseases, multi-strain veterinary dossiers, core dossier for a pandemic influenza vaccine, generics, well-established use medicinal products,

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<sup>63</sup> Products authorised based on a full dossier are charged a higher CAP annual fee than those based on an abridged application.

<sup>64</sup> Fee amounts quoted for the current situation are those valid in April 2019.

<sup>65</sup> Fee amounts quoted for the current situation are those valid in April 2019.

<sup>66</sup> Article 12 of the Fee Regulation and Recital 7 and Article 15 of the Pharmacovigilance Fee Regulation.

<sup>67</sup> Article 13 of the Fee Regulation and Article 15(5) of the Pharmacovigilance Fee Regulation.

<sup>68</sup> In accordance with Article 9 of the Fee Regulation.

herbal medicines, homeopathic medicines, and multiple applications submitted on usage patent grounds.<sup>69</sup> In addition, EMA grants fee reductions and exemptions for applicants from the academic sector in the case of scientific advice procedures for products falling under the PRIority MEDicines (PRIME) scheme.<sup>70</sup>

Where an applicant could, in respect of the same fee, benefit from more than one category of fee reduction, the provisions which are the most favourable to the applicant apply.

Fee incentives applied range from a 10% to a 100% reduction of the full applicable fee depending on the beneficiary/type of product and the type of activity that is incentivised. For a complete overview, see Annex 7.

**Fee deferrals** exist for applications for medicinal products to be used in a human pandemic situation and for SMEs. In the case of SMEs, the payment of fees for their application for an initial marketing authorisation and for inspections is deferred until notification of the final decision on the marketing authorisation or until withdrawal of the application. In addition, where an application for a marketing authorisation is submitted for a medicine for which scientific advice was already given by the Agency, no fee is charged to the SME for the examination of that application if the marketing authorisation is not granted.

#### **Non-fee generating activities:**

Further, there are certain procedural activities for human and veterinary medicinal products for which **no fee** is foreseen under the current Union legislation. For medicinal products for human use these concern: the evaluation of orphan designations, procedures related to PIPs, ATMP classification, scientific advice procedures for medicinal products for paediatric use<sup>71</sup>, and non-pharmacovigilance referrals that are not triggered by the MAH<sup>72</sup>. Non-fee generating procedures for veterinary medicinal products under the

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<sup>69</sup> Article 9 and Annex VII of the Implementing Rules ; Decision of the Executive Director on fee reductions for scientific advice requests on PRIME products for SMEs and applicants from the academic sector ([EMA/63484/2016](#)) ; Executive Director's decision on fee reductions for designated orphan medicinal products ([EMA/317270/2014](#)) ; Revised policy for classification and incentives for veterinary medicinal products indicated for minor use minor species (MUMS)/limited market ([EMA/308411/2014-Rev.1](#))

<sup>70</sup> In 2016, the EMA launched the PRIority MEDicines (PRIME) scheme to support developers of medicinal products that may offer a major therapeutic advantage over existing treatments or may benefit patients without treatment options. This scheme also provides fee incentives for scientific advice requests for PRIME products from micro-sized enterprises and SMEs as well as academic sector applicants. See the Decision of the Executive Director on fee reductions for scientific advice requests on PRIME products for SMEs and applicants from the academic sector ([EMA/63484/2016](#))

<sup>71</sup> However, fees are set for scientific advice procedures for paediatric medicinal products that are also an orphan designated product or an ATMP.

<sup>72</sup> For non-pharmacovigilance referrals, a fee amount is foreseen only when the referral is initiated by the applicant or the MAH and not if it is triggered by the Commission or a Member State. Non-pharmacovigilance referrals concern procedures in accordance with Articles 29(4), 30 and 31 of Directive 2001/83/EC, Article 13 of Regulation (EC) No 1234/2008 and Article 5(3) of Regulation (EC) 726/2004.

currently applicable legislation are: MUMS/limited market applications, referrals that are not triggered by the MAH<sup>73</sup> and pharmacovigilance procedures<sup>74</sup>.

### **Union budget contributions:**

EMA receives a general Union contribution which balances the EMA budget taking into account fluctuations in EMA's revenue. The general budget contribution is calculated taking into account the projected net fee revenues. It is adjusted annually in order to address increases or decreases in net fee income, thus balancing EMA's costs and revenues. The adjustment is done within a maximum amount defined within the seven-year EU budget framework.

Further, EMA receives a specific contribution to be used exclusively to address the fee incentives provided for orphan designated medicinal products.

### **Other sources of EMA income:**

The Founding Regulation was recently amended (2019) in regards sources of EMA income, allowing the Agency to also apply charges for other services provided.<sup>75</sup> This new provision has not yet been implemented. However, EMA's total budget currently does comprise sources of income other than those coming from fees and Union contributions, such as income received from administrative operations (e.g. organisation of seminars), external assigned revenue for projects and programmes, and revenue from miscellaneous sources (e.g. refunds and compensations).

### **NCA remuneration:**

The EMA remunerates NCAs acting as rapporteurs and co-rapporteurs appointed by the relevant EMA scientific committee for their scientific assessments. The NCA remuneration scheme as currently operated is rather complex and is linked to the type of fees charged. The different elements making up the scheme have not changed since their introduction over the years (see Section 2.2). In summary:

- Remuneration is paid to NCAs and not to individuals;
- For non-pharmacovigilance fee generating activities, the NCAs of the rapporteur and co-rapporteur receive 50% (25% each) of the full fee. This means that fee reductions do not affect the amount received by NCAs;
- For pharmacovigilance fee-generating activities, the NCAs of the rapporteur and co-rapporteur are remunerated a fixed amount, which in case of incentives is reduced in proportion to the incentive rate applied to the full fee;

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<sup>73</sup> Referrals for veterinary medicinal products are procedures in accordance with Articles 33(4), 34 and 35 of Directive 2001/82/EC, Article 13 of Regulation (EC) No 1234/2008 and Article 45 of Regulation (EC) No 726/2004.

<sup>74</sup> These concern: periodic safety update reports (PSURs), surveillance/signal detection, adverse event reporting (AER), rapid alerts (RA), non-urgent Information (NUI) and incident management plan (IMP).

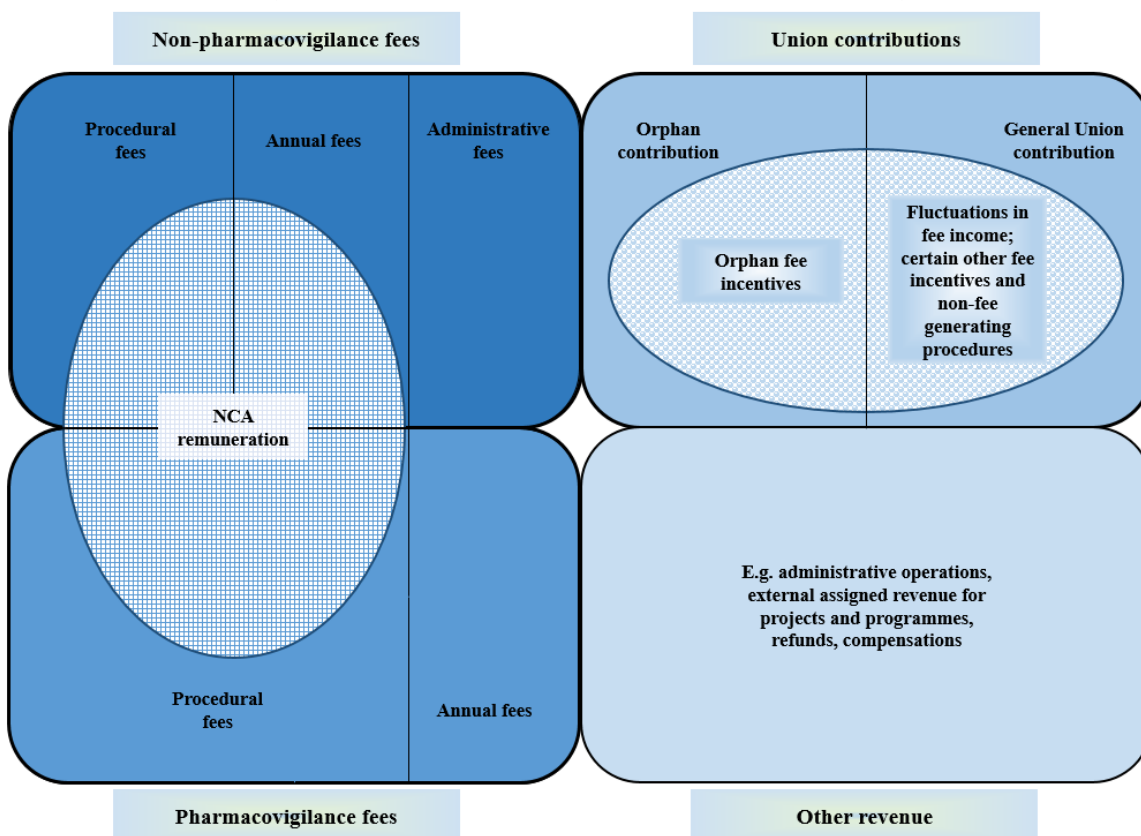
<sup>75</sup> Article 67(3) of the Founding Regulation, as amended via Regulation (EU) 2019/5.

- For services for which currently no fee is set in legislation, EMA does not charge a fee and NCAs acting as rapporteur or co-rapporteur do not receive remuneration. Also, no remuneration is received if an application for marketing authorisation submitted by an SME for a product for which previously scientific advice from EMA was sought ends negatively;
- The NCA of the rapporteur and co-rapporteur together receive 30% (15% each) of the CAP annual fee for scientific evaluation services provided at the request of the Agency (e.g. annual product reports and specific reporting for pharmacovigilance and safety reports). This share is also intended to contribute to other activities carried out by NCAs under their European Union obligations;
- Costs incurred for preparing and participating in committees and working parties, outside of procedures, are not remunerated;
- The pharmacovigilance annual fee is fully retained by EMA.

For a full list of the level of NCA remuneration per activity, see Annex 6.

Figure 2 below provides a visual presentation of all the above. The size of the different boxes does not reflect the actual amounts.

**Figure 2: Schematic representation of the EMA budget**



### **Implementation and operation of the fee system:**

The above described fee system is fully operated and implemented by the EMA. The EMA Management Board adopts the Implementing Rules of the Fee Regulation which specify, *inter alia*, detailed fee amounts and reductions and remuneration amounts for NCAs. From the operational point of view, EMA calculates the full fees applicable, applies fee reductions where relevant, collects fees payable by industry, calculates and pays out the amounts for NCA remuneration for their services provided, in line with the relevant provisions. For each fee-generating procedural activity, the EMA sends the applicant an invoice. In addition, for each fee-generating procedural activity involving NCAs, the EMA sends out 'purchase orders' to NCAs of the rapporteur and co-rapporteur stipulating the remuneration amount they will receive upon fulfilment of their obligation.

In order to aid payers in the understanding of the applicable fee, the EMA published two guidance documents: the 'Explanatory note on general fees payable to the European Medicines Agency' and the 'Explanatory note on pharmacovigilance fees payable to the European Medicines Agency'.<sup>76</sup> These documents explain the rules for fees and fee incentives and provide illustrative examples.

Involvement of the NCAs of the Member States in the operation and implementation of the intervention is limited to the actions and decisions taken by the EMA Management Board.<sup>77</sup> The Management Board takes decisions on the rules and amounts for NCA remuneration in relation to services covered by the Fee Regulation<sup>78</sup> as well as on the detailed conditions of fee incentives granted by the Executive Director in exceptional circumstances and for imperative reasons of public or animal health.<sup>79</sup> These decisions are reflected in the Implementing Rules, which are adopted by the Management Board.

## **3.2. State of play**

### **EMA revenue:**

**EMA's total revenue** increased to €317.4 million in 2017, the majority of which consisting of fees charged to pharmaceutical companies in their capacity of applicants and holders of marketing authorisations (87.9% or €278.8 million). This increase in EMA's fee income since 1995 can be attributed in part to an increase in volume of fee-

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<sup>76</sup> Explanatory note on general fees payable to the European Medicines Agency ([EMA/909567/2019](#)) ; Explanatory note on pharmacovigilance fees payable to the European Medicines Agency ([EMA/580301/2018](#))

<sup>77</sup> The Management Board is the supervisory body of the Agency, consisting of representatives of each Member State, the Commission and the European Parliament that act in the public interest. It sets the Agency's budget, approves the annual work programme and is responsible for ensuring that the Agency works effectively and cooperates successfully with partner organisations both within and outside the EU.

<sup>78</sup> Rules and amounts for NCA remuneration for services covered by the Pharmacovigilance Fee Regulation are established in the annex of that regulation.

<sup>79</sup> Articles 9, 11(1) and 11(2) of Regulation (EC) No 297/95.

generating procedures. This is partially due to the extension of the scope of the centralised procedure in 2004, making more types of products eligible for a Union marketing authorisation. In addition, EMA's budget was further impacted by the introduction of new fees via amendments of the Fee Regulation and the Pharmacovigilance Fee Regulation. Fee revenues mainly stem from fees charged in accordance with the Fee Regulation (in 2017, around 90% of the total sum of fees, or €251.2 million), with the remainder of fees charged under the Pharmacovigilance Fee Regulation (€27.6 million).<sup>80</sup>

**Total contributions from the Union** initially increased over the years but have decreased since 2010. Also the ratio fee income to Union contributions within EMA's total budget changed over time. In EMA's initial year of operation, fees contributed to 27.8% of EMA's income with 70.4% coming from Union contributions. However, already from the year 1998 onwards, the majority of EMA's income consisted of fees. In 2017, the proportion of fee income of EMA's total revenue equalled 87.9% (€278.8 million). At the same time, the proportion of the Union contributions gradually decreased to almost 9% (€28.5 million).<sup>81</sup>

As stated before, the first **orphan contribution** provided to the Agency in the year 2000 was set at €1.0 million, which constituted 7.4% of the total Union contribution and 1.8% of EMA's total budget. This amount has gradually increased over the years to €13.3 million in 2017, which equates to a proportional increase to 46.5% of the total Union contribution and 4.2% of EMA's total budget. The **general EU and EEA budget contribution** increased until 2008 but then started decreasing. More specifically, it dropped from its maximum of €43.3 million in 2008 to €15.3 million in 2017. This equates to a proportional reduction from 92.0% to 53.5% of the total Union contributions and 23.0% to 4.8% of EMA's total budget. This decrease is higher in rate than the increase in orphan contribution, which means that total Union contributions decreased over the past decade, both in actual amounts as well as in proportion to the EMA income from industry fees.<sup>82</sup>

The general contribution is a balancing subsidy that should cover shortfalls in EMA income through fees. The proportion of fee income of EMA's total revenue increased over the years, whereas the general balancing contribution decreased at an equal rate. The orphan contribution is to be used exclusively to address fee incentives provided for orphan designated medicinal products. Hence the increase in this contribution over the years is a direct result of an increase in procedural activities for orphan designated products for which fee incentives are applied to the full fee.

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<sup>80</sup> Figures quoted for 2017 are based on those published in the EMA Budget Report for [2019](#) to ensure use of final data.

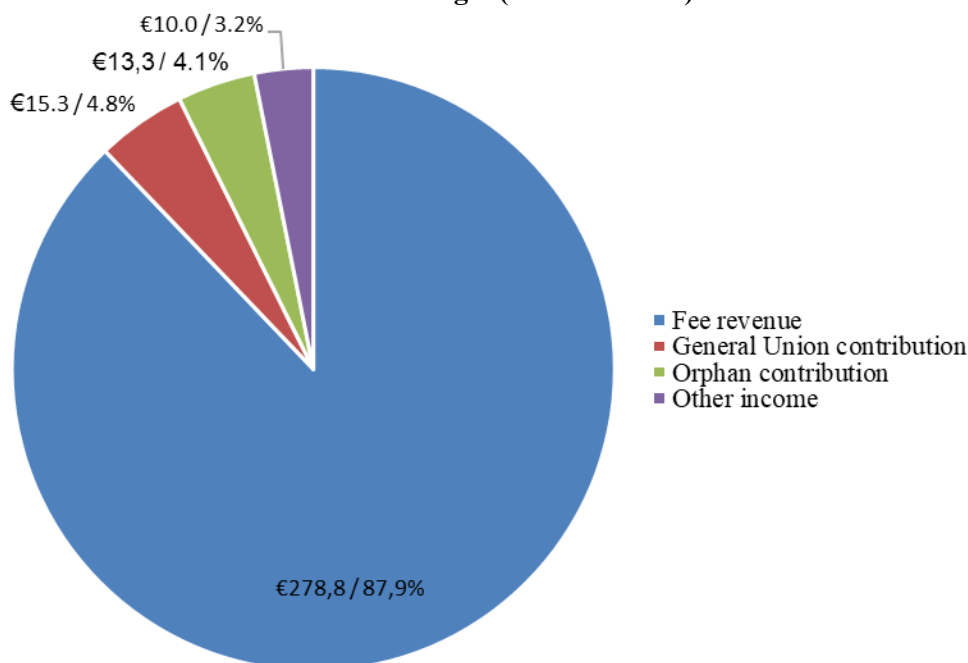
<sup>81</sup> Figures quoted for 2017 are based on those published in the EMA Budget Report for [2019](#).

<sup>82</sup> Figures quoted for 2000 are based on those published in the EM(E)A Seventh Annual Report [2001](#) (see Annex 6) and figures quoted for 2008 and 2017 are based on those published in the EMA Budget Report for respectively [2010](#) and [2019](#) to ensure use of final data.

Finally, a portion of EMA’s total revenue, 3.2% in 2017 (€10.0 million), comprises income from **other sources**.<sup>83</sup>

Figure 3 below shows the different sources of EMA revenue constituting EMA’s total budget in 2017 as described above.

**Figure 3: EMA’s sources of revenue in 2017 in both million euros and as percentage of the total EMA budget (€317.4 million)**



**NCA remuneration:**

Total annual NCA remuneration increased over the years to €114.7 million in 2017, corresponding to 41.1% of the total fee revenue received by EMA.<sup>84</sup> The vast majority of the total remuneration amount, i.e. €101.9 million or 88.8%, was related to non-pharmacovigilance activities.<sup>85</sup> This equates to 40.6% of the total fees EMA receives for such activities. The remaining amount, €12.8 million or 11.2%, came from remuneration for pharmacovigilance activities.<sup>86</sup> This equates to 46.4% of total fees EMA receives for such activities. See Figure 4 below, which shows the total amounts of EMA fee income (prior to NCA remuneration) and the totals amount of NCA remuneration as well as the percentage of NCA remuneration of EMA fee income. Figures shown are for total EMA

<sup>83</sup> Figures quoted for 2017 are based on those published in the EMA Budget Report for [2019](#).

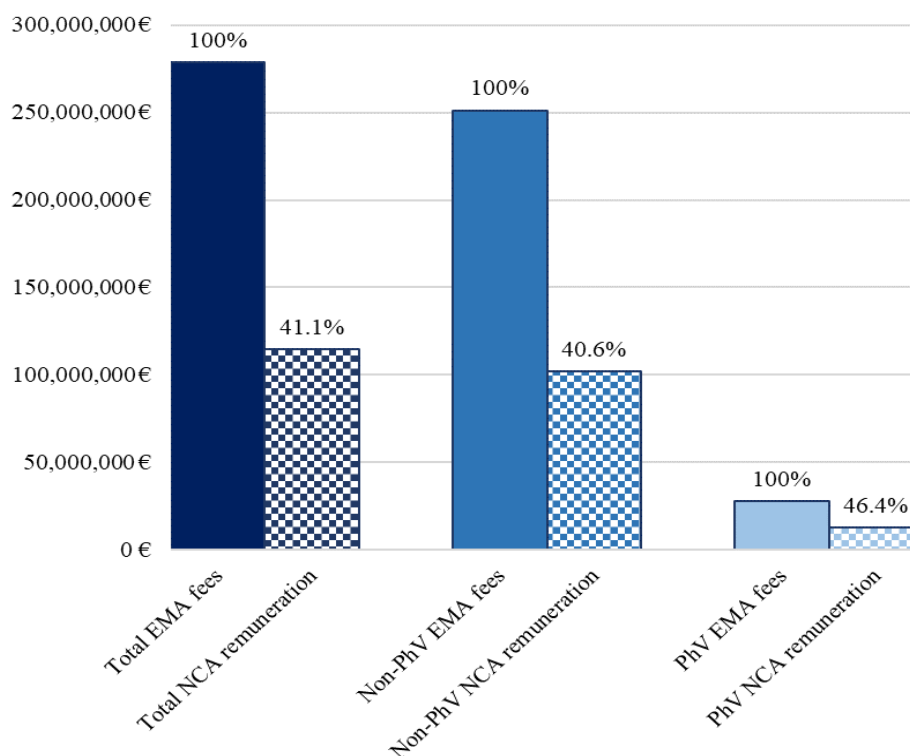
<sup>84</sup> Figures quoted for 2017 are based on those published in the EMA Budget Report for [2019](#).

<sup>85</sup> More specifically, the €101.9 million of remuneration was used to cover: (1) the expenditure to rapporteurs, co-rapporteurs, co-ordinators and inspectors and experts for the evaluation of medicines, in accordance with Article 62(3) of the Founding Regulation, and (2) the expenditure for sampling and testing of medicines by Member States under the EDAM-EMA scientific agreement, in accordance Annex V of the Implementing Rules which specifies that (up to) 10% of the annual fee should be allocated to such activities.

<sup>86</sup> More specifically, the €12.8 million of remuneration was used to cover expenditure to rapporteurs and co-rapporteurs for the evaluation of pharmacovigilance procedures, in accordance with Annex I of the Pharmacovigilance Fee Regulation.

fee revenue and remuneration as well as for those received for non-pharmacovigilance and pharmacovigilance activities.

**Figure 4: EMA fee revenue vs NCA remuneration in 2017: total, for pharmacovigilance (PhV) activities and non-pharmacovigilance (non-PhV) activities**



The reasons for increase of NCA remuneration since 1995 are the same as those specified for the increase of EMA's fee income, i.e. an increase in the volume of fee-generating procedures and the addition of new fees and new fee-generating procedures.

**Fee incentives:**

Since 1995, the provision of fee incentives by EMA to industry based on applicable fee amounts has increased significantly in total value to €30.2 million in 2017 (€13.3 million related to orphan designated products and €16.9 million related to other applications).<sup>87</sup> This is due to an increase of the number of procedural activities to which fee incentives apply. This increase is caused by a general increase in regulatory submissions to the Agency as well as by changes in the relevant legislative framework, including sectorial pharmaceutical legislation, and in decisions from the Management Board and Executive Director allowing for additional fee incentives.

<sup>87</sup> Figures for fee reductions for orphan medicinal products are derived from EMA's Annual report on the use of the special contribution for orphan medicinal products for the financial year 2017 (EMA/19529/2018)(no longer published). Figures quoted for other fee reductions are derived from EMA's Report on budgetary and financial management for the financial year 2017 ([EMA/838683/2017](#)).



In addition, several procedural activities are exempted from fees. Hence, the total annual ‘value’ of fee incentives and exemptions provided to industry based on current fee amounts is actually higher than the total annual value of fee reductions presented here.

### **Unintended and unknown effects:**

As explained in Section 2, fees charged to industry should be proportional to the assessment costs incurred by EMA and NCAs, and cross-subsidisation between procedures should be avoided. Available information described above suggests that the Union contributions are sufficient to cover the loss in revenue due to fee incentives, but this excludes coverage for non-fee generating activities. This may point towards non-fee-generating procedures being funded, at least in part, through other EMA sources of income. However, whether this is indeed the case and to which extent industry fees actually relate to costs incurred by EMA for the provision of the relevant services is difficult to assess. In addition, the 2010 study on the evaluation of the EMA commented on an imbalance between NCAs' costs and remuneration received, and the potential effects of this imbalance on future NCA engagement in (especially non-remunerated) EMA-level activities and sustainability of the regulatory system as a whole. In 2010, the same concerns were raised by the Heads of Medicines Agencies (HMA), the network of the heads of the NCAs<sup>88</sup>, and ECA also commented several times on such imbalance (see Section 5).<sup>89</sup> Before this evaluation, it has however never been fully investigated how remuneration received actually relates to costs incurred by NCAs for services provided.

Further, the fee system has not always proven to be effective in the timely adjustment to new tasks and responsibilities of the EMA. As described before, the Pharmacovigilance Fee Regulation entered into force two years after application of the new pharmacovigilance legislation. This meant that during a period of two years EMA and NCAs were not receiving fees and remuneration for services provided in accordance with that legislation.

The 2010 study on the evaluation of the EMA commented on the complexity of the fee structure and suggested that it may benefit from a simplification to lighten the administrative procedures, while keeping the fairness of fees as an important goal (see Section 5).<sup>90</sup> Since 2010, the fee system has gained in complexity by the adoption of the Pharmacovigilance Fee Regulation. This regulation specifically provides that the structure of the fees should be as simple as possible to apply in order to minimise the related administrative burden. Whether, in view of the different stakeholders, the

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<sup>88</sup> Heads of Medicines Agencies (HMA) position paper: [Role of the European regulatory medicines network and its relation to a revision of the fee regulation, December 15, 2010.](#)

<sup>89</sup> The European Court of Auditors reports on the annual accounts of the European Medicines Agency for the financial years [2006](#) (OJ C 309, 19.12.2007, p. 34–39), [2010](#) (OJ C 366, 15.12.2011, p. 27–32) and [2011](#) (OJ C 388, 15.12.2012, p. 116–122).

<sup>90</sup> Ernst & Young, 2010, Evaluation of the European Medicines Agency – [Final Report](#): pages 14, 124 and 202

complexity of the fee system balances fairness of fees charged and administrative burden of the application has however so far not been further investigated.

Finally, to which extent fee incentives currently provided truly contribute to and are relevant for the need for providing a level playing field for payers and for stimulating development and availability of medicines has not been investigated. As clarified in Section 1, with the exception of incentives for SMEs, fee incentives are not within scope of this evaluation. However, a separate Commission evaluation of the Orphan and Paediatric Regulation is currently ongoing which also covers the incentives provided therein.<sup>91</sup>

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<sup>91</sup> [https://ec.europa.eu/info/law/better-regulation/initiatives/ares-2017-6059807\\_en](https://ec.europa.eu/info/law/better-regulation/initiatives/ares-2017-6059807_en)

## 4. METHOD

The evaluation was supported by a study conducted by RAND Europe.<sup>92</sup>

The external contractor collected and reviewed quantitative and qualitative information. Different primary and secondary data sources were identified in an evaluation matrix covering all the evaluation questions. To collect data and views from the relevant stakeholders a consultation strategy was developed at an early stage of the evaluation process. A summary of the stakeholders' consultation, the number and composition of respondents and consultation outcomes are provided in Annex 10. An inter-service Steering Group on this evaluation was set up to steer, monitor and ensure the necessary quality of the external study and the overall process of the evaluation.

### 4.1. Data collection and financial modelling

#### Cost and workload data collection:

The evaluation used data from:

- An EMA Management Board Data Gathering initiative - MBDG (data collected for the year 2016 from EMA and NCAs on time spent by EMA staff and NCA staff on the vast majority of EMA procedures); It was considered that the procedures having occurred during the time period of data collection (mainly 2016) are representative enough of the system and that it would not be reasonable to further extend the data collection period;
- Data collected by the contractor of the study supporting the evaluation from EMA and NCAs (also for 2016) on the costs associated with the various EMA activities.

#### Consultation activities:

The external contractor used different stakeholders' consultation tools, which are summarised in Table 2 below. The results of these consultations are presented in Annex 10.

**Table 1: Consultation activities carried out**

Consultation tool	Targeted stakeholders/ participants	Time	Number of contributions/ participants
EMA consultation (interviews)	EMA Executive Director and Deputy Executive Director and representatives from several divisions: stakeholders and communication; administration, legal	23 and 27 March 2017	8 group interviews with 2 to 6 individuals each

<sup>92</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system – Final report: SANTE/2016/B5/021

	and audit; information management; Human Medicines Research and Development (R&D); Human Medicines Evaluation; Inspections and Pharmacovigilance; and Veterinary Medicines		
<b>NCA consultation</b>	47 NCAs	4 April - 30 May 2017	30 of 47 NCAs (based on a list provided by the EMA) participated in the survey (i.e. 63.8%), representing 23 Member States and 95% of all EMA-related activities in the reporting period
<b>Stakeholders on-line survey</b>	Pharmaceutical Industry Wholesalers association Research organisation Healthcare professional association Public Health NGO Patient association	5 May - 30 June 2017	44
<b>Online public consultation</b>	Public	2 May - 2 August 2018	51
<b>In-depth interviews with NCAs</b>	Austrian Medicines and Medical Devices Agency (Austria), State Institute for Drug Control (Czech Republic), Federal Institute for Drugs and Medical Devices (Germany), Paul-Ehrlich-Institut/Federal Institute for Vaccines and Biomedicines (Germany), National Institute of Pharmacy and Nutrition (Hungary), Medicines Evaluation Board (Netherlands), Medicines and Healthcare Products Regulatory Agency (United Kingdom), Agency for Veterinary Medicinal Products (France) and Health Products Regulatory Authority (Ireland).	3 July - 29 August 2017	0

To complement the evidence collected through primary sources of information, the final report on the evaluation of the EMA of January 2010 by Ernst & Young<sup>93</sup> was used for the analysis of the EMA fee system.

**The financial model of the EMA fee system** was developed with the purpose to examine the economic basis (cost-based nature) of the current fee and remuneration system. It models first the current situation and, beyond, looks into some scenarios on different modalities of applying the cost based principle to the EMA fee system, taking into account the effect of incentives.

Developing a financial model was needed in order to estimate the type and frequency of EMA activities happening one year, knowing that often procedures span beyond one year and payment of fees and remuneration of NCAs do not coincide in time. All revenues

<sup>93</sup> [Evaluation of the European Medicines – Final report - January 2010 by Ernst & Young](#)

and costs incurred by EMA were integrated in a ‘typical’ year. The need for the model was also driven by the lack of data on the costs NCAs incur for EMA activities – i.e. hourly rates for staff and time spent per type of procedure by NCAs.

By presenting a 'typical' year, the model provides a good representation of the current situation and eliminates the effect of possible discrepancies between the number of activities involved and the payments received.

**Cost of NCAs and remuneration paid by EMA to NCAs.** Data was gathered by the EMA MBDG on the time needed by NCAs to process the vast majority of procedures. The hourly cost were reported in two groups: scientific experts and administrative staff. Average hourly rates across all NCAs were calculated and used to estimate the cost of the NCAs, based on the collected data. The average was weighted per the frequency of involvement of the NCAs within a given type of procedure.

Three overall groups of costs were calculated for NCAs: (1) procedural costs and (2) cost for attending scientific committees and working parties when not acting as (co-)rapporteur and (3) additional EMA-related activities. Only the costs in the first two groups were calculated based on unitary time data and cost data. The difference between total costs reported by the NCAs for their contribution to EMA and the costs calculated for the first two groups was branded “costs for additional EMA-related activities”.

The effect of incentives was not reflected on remuneration paid to NCAs in line with current practice (except for pharmacovigilance fees where the legislation provides for a proportionately reduced remuneration to NCAs).

**EMA revenue and costs.** Data from the MBDG was also used for time spent by scientific and administrative EMA staff on procedures. Cost data was provided by EMA and applied to time data to calculate costs. The amount of the EU budget contribution was fixed at the 2016 level (€16.8 million)<sup>94</sup> and the other sources of income were calculated as the difference to the overall budget of EMA. Both elements were used as a fixed variable in the scenarios. The effect of incentives on EMA revenue was calculated as an average incentive rate based on actual data provided by EMA.

The model made some assumptions. All revenues and costs are incurred in one financial year (typical year) in terms of number and type of procedures, including in terms of fee revenue received and remuneration to NCAs paid.

More information on the methodology is provided in Annex 8.

## 4.2. Limitations and robustness of findings

- The outcome of the EMA MBDG exercise was the main source of data on costs for EMA and NCAs. It covered the vast majority of existing procedural activities over a

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<sup>94</sup> EMA Budget Report for the financial year 2018, as adopted by the Management Board on 14 December 2017 ([EMA/MB/799068/2017](https://www.ema.europa.eu/en/documents/other/ema-budget-report-2018_en.pdf))

specific time period (i.e. 2016) but did not cover all of the activities that EMA and NCAs undertake. However, NCAs reported their overall cost for EMA activities. It was considered that the procedures having occurred during the time period of data collection (mainly 2016) are representative enough of the system and that it would not be reasonable to further extend the data collection period.

- The MBDG collected data per NCA. However, average time values from the MBDG data were used across all NCAs in the model as representative for all NCAs. For some activities there was wide variation in the times reported during the MBDG exercise (for example for Type II variations), therefore the costs calculated for individual NCAs may either not fully reflect the complexity of the work undertaken (represented by the time spent) or overestimate it, with a respective impact on the estimated cost. To mitigate the effect of this limitation, weighted averages were calculated in the cost calculations of the study supporting the evaluation, thus better reflecting the influence of various NCAs' cost structure on the estimated values used in the model.
- For veterinary medicines, data samples of the EMA MBDG were limited, with a large degree of variation across the reported values for some activities (for example for extension of a marketing authorisation). This is due to the structurally lower volume of activities undertaken relative to the human medicines area. The smaller samples mean that there is a higher degree of uncertainty associated with the calculated average time values that are used in the cost estimates, and hence with the cost estimates themselves. For the purposes of the evaluation, no mitigation measures were taken. Due to the low frequency with which veterinary procedures occur, it would have taken several more years to collect a more robust dataset for all veterinary activities, which was considered unfeasible.
- NCAs' data used as input in the modelling exercise were largely self-reported, and could not be triangulated with data from other sources. As a mitigating measure, information on the number of times an NCA completed a procedure as rapporteur or co-rapporteur was validated against data made available by the EMA in constructing the typical year<sup>95</sup>. However, such data could not be provided by EMA for unremunerated roles (e.g. PRAC rapporteur or co-rapporteur for CHMP procedures) and, hence, validation of data reported by NCAs in the survey on such roles was not possible. This may have an impact on the estimated cost of NCAs for procedures (e.g. any inconsistencies in the way the number of procedures was reported has an impact on the estimation of the overall cost of procedures) and, consequently, on the estimated cost for additional activities (because it is calculated as the total EMA-related cost less procedural costs less non-procedural cost for preparing for and attending committees and working groups).

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<sup>95</sup> Purchase orders (POs)

- NCAs reported their ‘additional activities’ in an unstructured way; it was not possible to either validate them and assess their relevance to EMA, or analyse potential duplication or calculate unitary costs. This limits significantly the possibilities for interpretation of this group of activities in terms of understanding their eligibility for remuneration and related cost estimations. The content of this group of cost requires therefore further analysis that the evaluation could not perform. As this was not anticipated, no specific mitigating measures were adopted apart from analysing this group of cost separately in the scenarios of a cost-based system.<sup>96</sup>
- In addition, there may be inconsistencies in the way NCAs filled out the survey, due to a difference in understanding of the data actually requested. For the gathering of data on roles other than the main roles contributing to the procedural activities, the contractor had only envisaged reporting for procedures completed as multinational assessment team (MNAT) member<sup>97</sup>, as PRAC rapporteur or co-rapporteur for non-pharmacovigilance procedures or as peer-reviewer. However, it is uncertain how NCAs have reported activities such as providing comments as commenting Member State (a possibility as part of the system that is used by some NCAs) or how PRAC (co-)rapporteurships for non-pharmacovigilance procedures were reported.<sup>98</sup> This may have distorted the calculations of the estimated procedural cost and, therefore, the estimated cost of additional activities of NCAs.
- Responses received to the survey on wider stakeholders cannot be understood as representative of the views of any particular group of stakeholders. Given the relatively small number of respondents (n=40), and the lack of responses from some types of stakeholders (namely healthcare professional organisations and public health NGOs), generalisations cannot be made.

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<sup>96</sup> Procedural cost and non-procedural committee time cost was calculated against unitary cost and time data which makes those calculations more reliable.

<sup>97</sup> See Annex 3 and 5.

<sup>98</sup> In the EMA MBDG exercise NCAs were requested to report time on this role under the main procedure to which it contributes.

## 5. ANALYSIS AND ANSWERS TO THE EVALUATION QUESTIONS

Costs and fee (revenue) shares presented and analysed in this section refer specifically to ‘EMA’ and ‘NCAs’. Using this convention, ‘EMA costs’ do not include the cost of remunerating NCAs and ‘NCAs’ costs’ mean the costs incurred by NCAs to provide EMA-related services. ‘EMA fee (revenue) share’ means the part of the fee (revenue) after payment of remuneration to NCAs and ‘NCAs’ share’ means the amount NCAs receive as remuneration for their EMA-related services.

### 5.1. Effectiveness and Efficiency

In the particular case of this evaluation, effectiveness and efficiency were analysed together as they are closely interlinked. Given the requirement of the legislation to be cost-based, fees are effective if they cover the costs of EMA and NCAs for their respective activities. To achieve this, the fee system has to be efficient, i.e.: fees have to be sufficient to fulfil EMA and NCAs’ needs whilst minimising the costs for undertakings. Therefore, the analysis of effectiveness and efficiency cannot be separated.

#### **EQ1: To what extent do the fees charged correspond with EMA costs?**

Overall, the fees charged to industry enable EMA to: undertake the procedural activities within its remit; provide remuneration to NCAs for their activities in line with the legislative requirements; and to cover some additional cross-cutting and horizontal activities. The total fees are not, however, sufficient to cover all of EMA’s activities. The EU and EEA budget contributions and revenues from other sources in effect finance additional activities that EMA undertakes. For NCAs, the total value of remuneration they receive from EMA covers the aggregate costs of the procedural activities that they undertake, as well as in aggregate almost half of the costs of the additional EMA-related activities that they report undertaking (i.e. in addition to procedural activities and time spent in working groups and committees when not being rapporteur/co-rapporteur). The aggregate costs for NCAs’ involvement in working groups and committees outside procedures are not covered. However, whether and to what extent these “additional” activities and the involvement in committees and working groups outside procedures should be part of NCA remuneration is still to be assessed.

Using average cost-based fees for procedural activities undertaken by EMA would help to balance unitary full fees against costs. However, other EMA income would need to be increased as compared to current revenue to balance its costs, which would have an impact on EU and EEA budget contributions or industry fees. In terms of EMA expenditure for NCA remuneration, average cost-based fees would cover procedural costs for NCAs overall, but not for all individual NCAs.

The question is addressed by looking at the alignment of fees charged with the services performed and an assessment of whether total fees earned enable the EMA to meet its



costs (taking into consideration the availability of EU and EEA contributions) as well as whether the remuneration paid to NCAs allows them to meet the costs of EMA-related activities. The costs, fees and number of procedures used in the results refer to the EMA “typical year” (Section 4). They do not aim to reproduce costs and fees reported in EMA and NCA accounts but are estimated values based on data provided by EMA and NCAs using an activity-based costing approach and with reference to the current fee legislation and rules.

The question looks at the total EMA expenditure, including providing remuneration to NCAs.

The assessment of alignment between fees charged and costs of services provided was performed primarily through the quantitative assessment of the current financial situation. The assessment focused mainly, though not exclusively, on procedural activities covered by the MBDG exercise. Alignment was assessed in two ways. Firstly, for both EMA and NCAs, the share of total fees each receives in aggregate for procedural activities was compared with the total costs to each of undertaking those activities (Table 2). Secondly, the average annual costs and fee revenues were compared for individual activities, activity by activity.

The assessment of total fees received indicates that the EMA fee share for procedural activities (i.e. excluding annual fees) for both human and veterinary medicines (€103.7 million/year) is sufficient to cover the costs to EMA of these activities (€81.6 million/year). These figures exclude NCA remuneration. This does not necessarily imply that industry fees are too high or that NCA remuneration is too low as EMA undertakes additional activities, some of which also procedural, for which they receive no fee income.

The total remuneration received by NCAs for undertaking procedural activities (excluding annual fees) for both human and veterinary medicines activities (€92.1 million/year) exceeds the costs for these activities (€87.3 million/year). This does not necessarily imply that NCAs are overpaid, however, as they undertake additional activities for EMA, some of which also procedural for which they currently receive no remuneration.

**Table 2: Total annual costs and remuneration for procedural activities for the current financial model over one typical year (€million/year)**

		Current financial model		
		Human medicines	Veterinary medicines	Total
<b>EMA</b>	Cost of procedures*	74.9	6.7	81.6
	Share of industry fees from procedural activities*	100.3	3.4	103.7
<b>NCA</b>	Cost of procedures	83.1	4.2	87.3
	Remuneration from procedural activities	89.2	2.8	92.1

*Source: Study supporting the evaluation of the EMA fee system<sup>99</sup>*

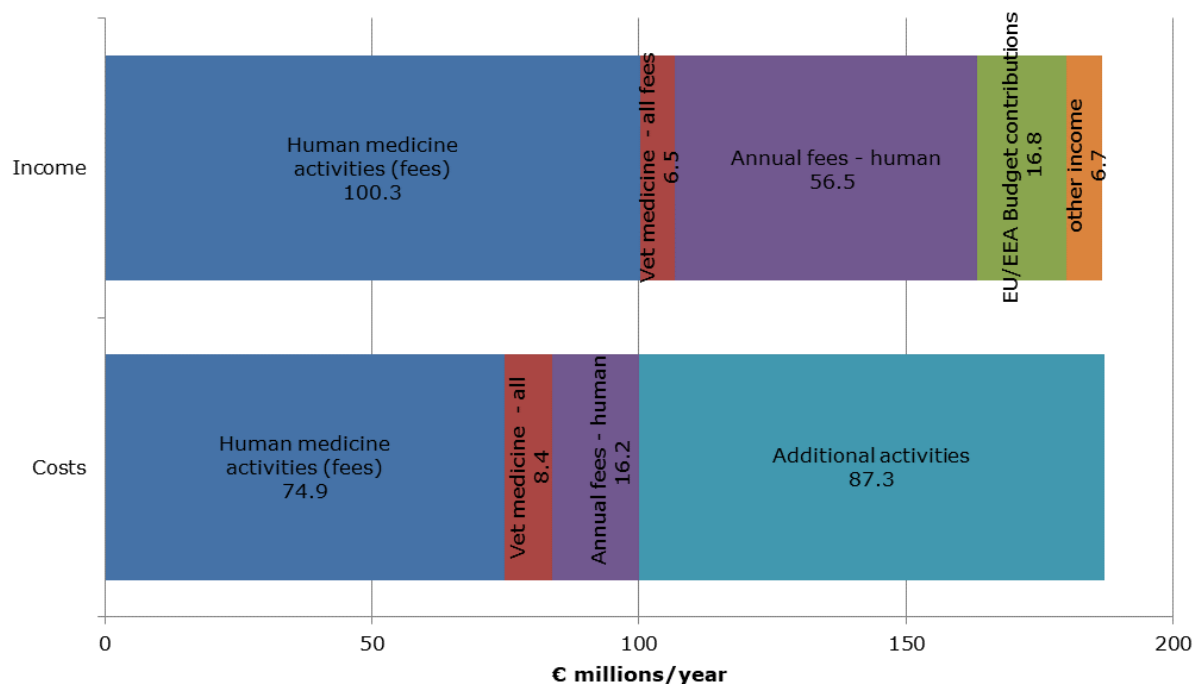
\* These values exclude NCA remuneration. Procedural activities include all activities listed in Question 17 and Question 18 of the NCA survey<sup>100</sup>. EMA reported combined cost and fee information for inspections for human and veterinary medicines. In the typical year, these were allocated to human and veterinary medicines in proportion to the procedures reported by NCAs.

The EMA share of fees for procedural activities (excluding annual fees) for human medicines only (€100.3 million/year) is sufficient to cover the costs to EMA of these activities (€74.9 million/year). However, the EMA share of fees for procedural activities for veterinary medicines (€3.4 million/year) is not sufficient to cover the costs to EMA for these activities (€6.7 million/year). An overview of EMA fee income and costs over one typical year under the current financial model is provided in Figure 5.

<sup>99</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system – Final report: page 38

<sup>100</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system – Final report: Appendix 5

**Figure 5: EMA income (fee revenue and EU/EEA budget contributions) and costs over a modelled typical year under the current financial model\* (€millions/year)**



*Source: Study supporting the evaluation of the EMA fee system<sup>101</sup>*

**Note:** EMA fee income is equal to total fee income net of incentives and NCA remuneration. NCA remuneration is not included as a cost in the figure above.

\*All numbers refer to the typical year, where the EU budget contribution reflects the actual total contribution in the year 2016. 'Other income' was calculated as a residual and corresponds to an estimated value in the typical year of other sources of revenue for EMA, such as external assigned revenue for projects and programmes or revenue from administrative activities and ancillary services.

The breakdown of the additional activities undertaken by EMA is listed in Table 3.

**Table 3: Additional activities undertaken by EMA and their costs**

Additional activities	Total costs (€)
Databases for use outside EMA: EudraVigilance, EudraPharm - Corporate + telematics	32,925,859
Guidelines for good practice	9,814,140
(Non-Guideline) Published information for healthcare professionals, patients and general public	6,869,224
EU Network Training Centre	830,681
Public Health activities: e.g. Anti-Microbial Resistance, Stakeholders, PRIME (PRIority MEDicines), Health Technology Assessment, and SME etc. and Animal health	13,197,488
Projects which create costs – Innovation Medicines Initiatives (IMI), GRIP, European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)	4,253,720

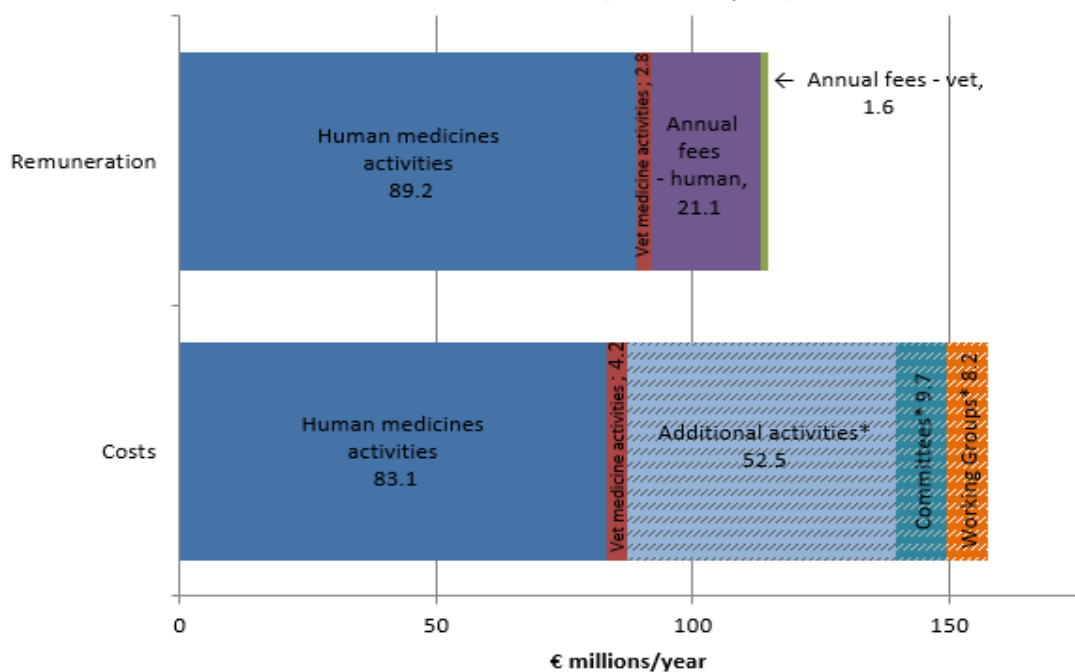
<sup>101</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system - Final report: page 50

Transparency on non-fee generating areas e.g. access to documents and publication of clinical trials	7,121,070
Literature monitoring (Pharmacovigilance)	758,840
Signal detection (Pharmacovigilance)	4,936,648
International activities	4,056,230
Coordination group (CMD) Human & Veterinary	2,555,085
<b>Total</b>	<b>87,318,985</b>

*Source: Study supporting the evaluation of the EMA fee system<sup>102</sup>*

The total remuneration received by NCAs for undertaking procedural activities for human only medicines activities (€89.2 million/year) is sufficient to cover the total costs of these activities (€83.1 million/year). The total remuneration received by NCAs for undertaking procedural activities for veterinary medicines activities (€2.8 million/year) is less than 70% of the costs they incur for veterinary medicines activities (€4.2 million/year). When annual fees are taken into account, NCA remuneration (€4.4 million/year) is approximately equal to costs. An overview of total NCA remuneration and costs over one typical year under the current financial model is provided in Figure 6.

**Figure 6: Total NCA remuneration and costs over a modelled typical year under the current financial model (€millions/year)**



*Source: Study supporting the evaluation of the EMA fee system<sup>103</sup>*

*\*The eligibility for remuneration of committees and working parties and the additional activities declared is still to be analysed.*

<sup>102</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system – Methodology Note: page 24

<sup>103</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system - Final report: page 52. For the purpose of this Staff Working Document, Figure 12 of the Final report was amended with regard to the presentation of the order of NCAs' costs.

As provided in Section 4, the €52.5 million of “additional activities” costs shown in Figure 6 represent the total cost declared by NCAs as “EMA-related” minus the calculated cost for procedures minus the calculated cost for non-procedural time spent in EMA committees and working parties. A draft list of additional activities as reported by NCAs contains activities such as databases, surveillance of safety of medicines and other safety-related activities, training, drafting of guidelines, activities related to herbal medicinal products or advanced therapy medicinal products, and committee activity in roles other than rapporteur/co-rapporteur.

However, the list of these activities needs further refinement and analysis in order to assess, according to legislation, which of the reported activities, if any, and their respective costs qualify for remuneration by EMA and consequently should be taken into account. Similarly, the eligibility for remuneration of costs incurred for committees and working parties needs further analysis.<sup>104</sup>

At a granular level of the purely procedural part of the cost, i.e. per type of procedure, the picture becomes more complex, reflecting both the complexity of the regulatory system in the EU and the EMA fee system. There are many different procedural activities, some of which are charged full fees<sup>105</sup>, some of which have reductions or waivers applied (either on the basis of applicant type, e.g. SMEs or micro-enterprises, or on the basis of product type, e.g. orphan, ATMP or PUMA)<sup>106</sup> and some of which are exempted from fees (e.g. PIPs, compliance checks, orphan designations)<sup>107</sup>. In a per-procedure cost-based situation, incentives and exemptions result in activities for which costs cannot be covered (fully or at all) and so other sources such as EU budget contribution and annual fees fund these costs, both for EMA and for NCAs.

In particular, EMA or NCAs’ costs for initial marketing authorisations are not covered, although they are currently associated with the highest fees relative to other procedural fees. For other activities, such as scientific advice, fees cover costs for NCAs but do not fully cover EMA costs. For yet other procedures, such as inspections, fees cover EMA costs, but do not cover the costs incurred by NCAs. Finally, some activities have fees that are higher than the cost of that particular activity. Type II variations are the most notable example of this; fees for these activities well exceed costs both for EMA and NCAs. The EMA and NCAs’ shares of costs and fee revenues for one year after incentives are applied under the current financial model are illustrated in Figure 7 (human medicines) and Figure 8 (veterinary medicines).

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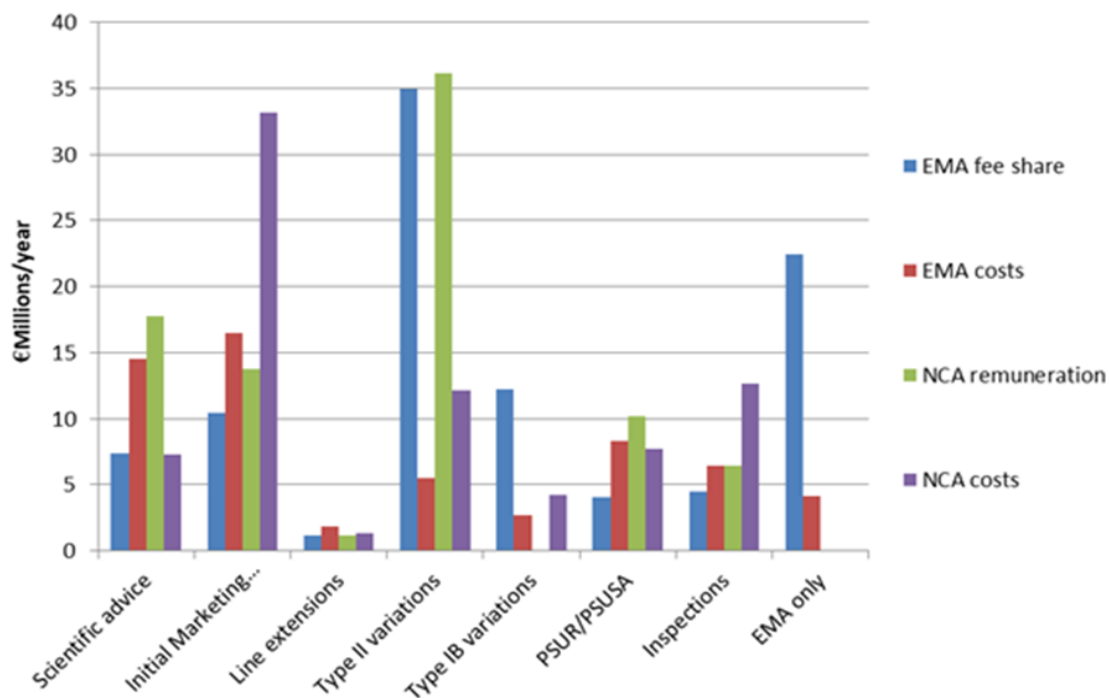
<sup>104</sup> As explained in Section 3.1, currently NCAs receive a contribution for some additional activities via their share of the annual fee. These additional activities concern scientific evaluation services provided at the request of the Agency (e.g. annual product reports and specific reporting for pharmacovigilance and safety reports) and other activities carried out by Member States under their European Union obligations. However, costs incurred for their involvement in committees and working parties are currently not remunerated.

<sup>105</sup> See Annex 4

<sup>106</sup> See Annex 5

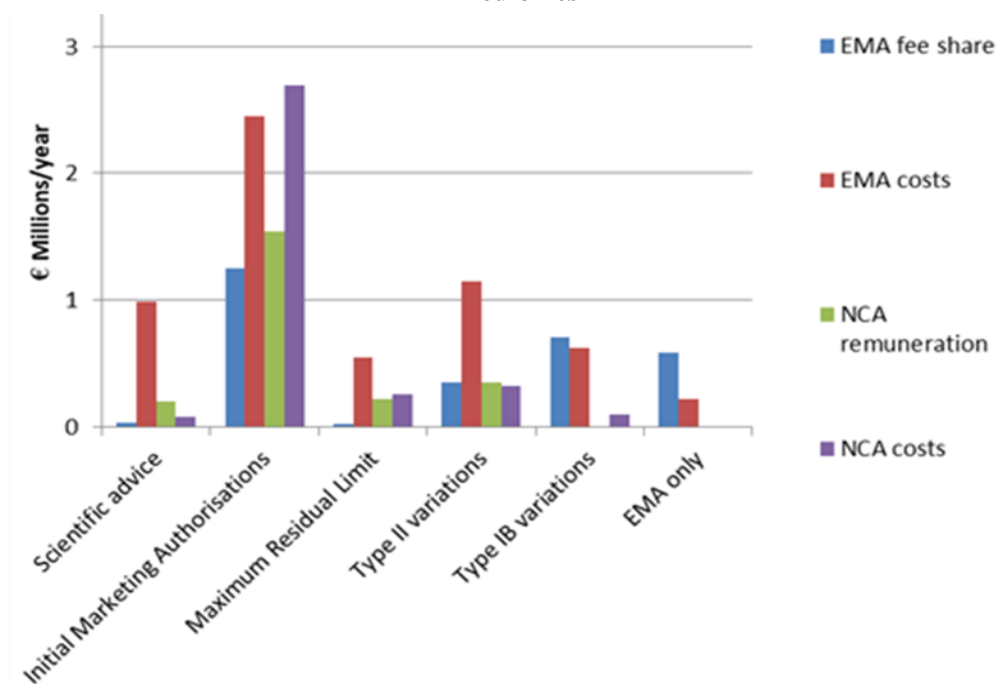
<sup>107</sup> See Annex 4

**Figure 7: EMA and NCA shares of purely procedural costs and fees over one typical year after incentives have been applied under the current financial model – human medicines<sup>108</sup>**



*Source: Study supporting the evaluation of the EMA fee system<sup>109</sup>*

**Figure 8: EMA and NCA shares of purely procedural costs and fees revenue/income over one typical year with incentives applied under the current financial model – veterinary medicines**



*Source: Study supporting the evaluation of the EMA fee system<sup>110</sup>*

<sup>108</sup> NCAs reported inspections for veterinary medicines and human medicines separately. They were combined in the EMA data reporting. In the ‘typical year’, these were allocated to human and veterinary medicines for EMA in proportion to the procedures reported by NCAs.

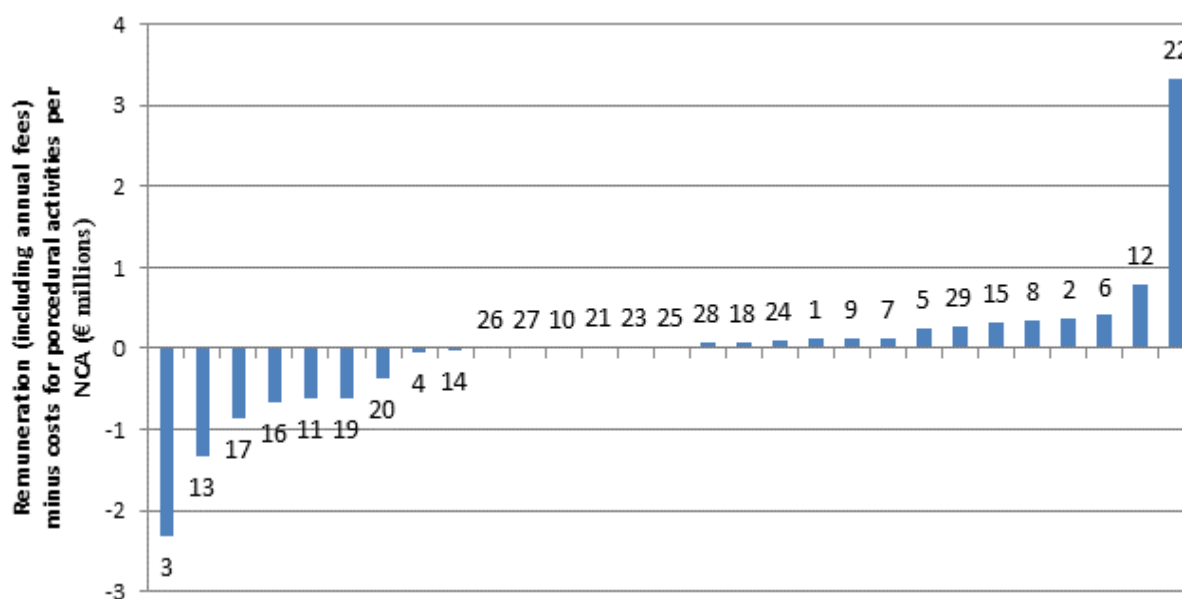
<sup>109</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system – Final Report: page 44

Thus, the more granular-level finding of the purely procedural cost is that the current fee system is not cost-based.

Under the current financial model fees are not always shared between EMA and NCAs in proportion to their costs. Scenarios that tested an average per-procedure cost-based approach show that such an approach would result in EMA and NCAs receiving a lower share of fee revenue for some activities and a higher share for others.

Figure 9 compares, for the typical year, the distribution of deficits and surpluses for procedural activities (as in procedural remuneration minus procedural costs) for the 29 NCAs that provided data for the study<sup>111</sup> based on average NCA costs.

**Figure 9: Distribution of annual remuneration for procedural activities minus annual costs for individual NCAs when modelling average cost-based remuneration for the typical year**



*Source: Study supporting the evaluation of the EMA fee system<sup>112</sup>*

**Note:** Each bar on the horizontal axis represents the cost recovery for one NCA for procedural activities. Negative values on the vertical axis indicate costs are not recovered, and positive values indicate that they are recovered in excess. NCAs are numbered in the figure only to provide a reference to Figure 10; the numbers do not have any other significance in the analysis.

The average cost-based remuneration of procedural activities only, (excluding annual fees), would cover costs related to procedural activities for NCAs overall, but not for all individual NCAs. Individual NCAs might be left with a financial ‘surplus’ or ‘deficit’ depending on whether their individual costs are below or above the average costs across all NCAs and on the types of procedures they provided services for. As shown in the

<sup>110</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system – Final Report: page 45

<sup>111</sup> See Annex 2 for more details on the NCAs involved in the study. The NCAs that provided data undertook the vast majority (95%) of all EMA activities in the reporting year. In addition, the amounts were scaled up by the study team to cover 100% of the procedures in a typical year.

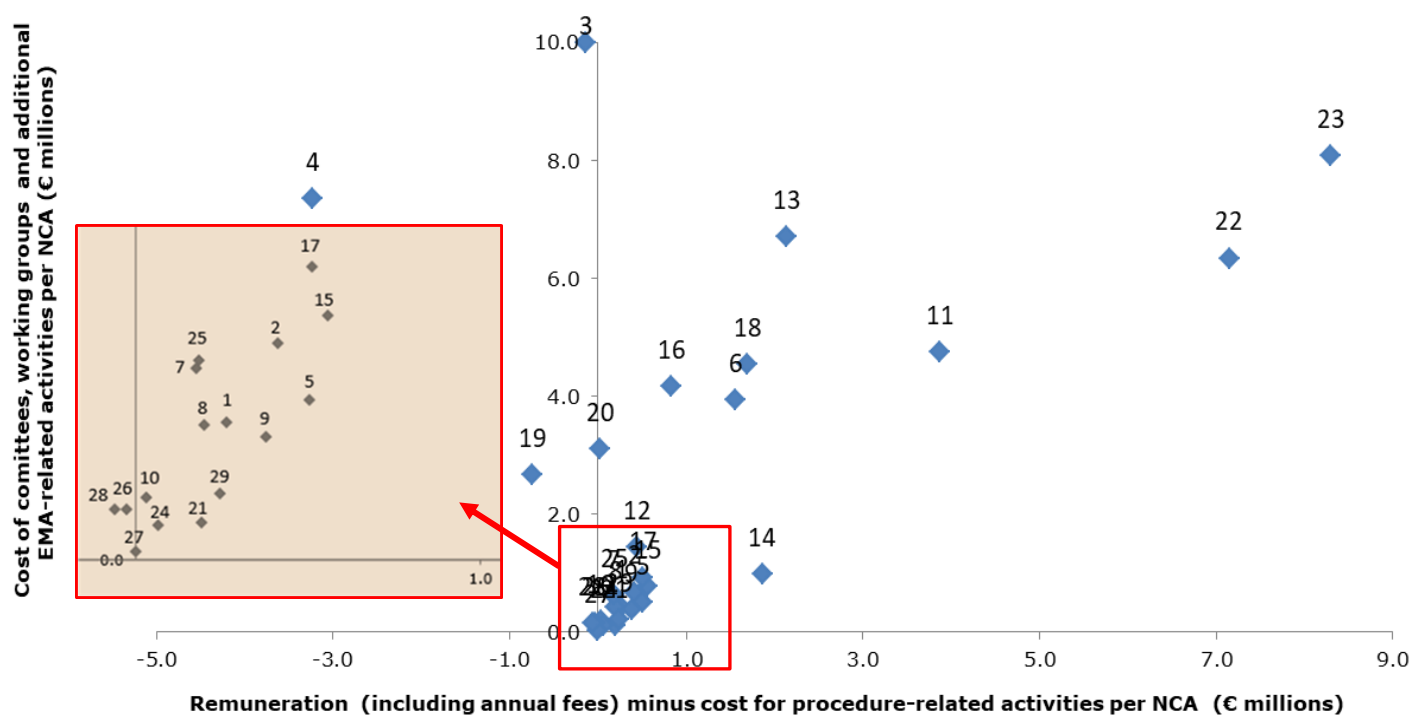
<sup>112</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system – Final Report: page 57

figure, for 19 of 29 individual NCAs (on the right hand-side of the picture, from NCA no. 27 to NCA no. 22), the modelled average cost-based remuneration covers costs for procedural activities.

It is to be noted that remuneration amounts differ across types of procedure, in line with the respective fee charged, and often they do not equal to the costs actually incurred. Consequently, high involvement in procedural activities does not necessarily correspond to equally high level of remunerations.

Whilst Figure 9 shows the distribution of deficits and surplus for procedural activities, Figure 10 takes more dimensions into account and shows the balance between (i) the costs for any other non-procedural, non-remunerated activities undertaken by the NCAs (preparation and attendance to committees, working groups; any additional activities) (y-axis), and (ii) the (negative or positive) residual of the total remuneration received, as in total remuneration (consisting of NCAs' share of both procedural fees and annual fees) minus the costs for procedural activities (x-axis) minus the costs for procedural activities.

**Figure 10: Comparison of total remuneration (i.e. NCAs' share of procedural and annual fees) net of procedural costs (x-axis) and total costs declared (procedural activities, attendance to committees and working parties and other unremunerated additional activities) (y-axis) for individual NCAs (◆) in the typical year**



*Source: Study supporting the evaluation of the EMA fee system<sup>113</sup>*

The scatterplot shows that, for example, NCA no. 22, after covering its costs for the procedural activities undertaken, still has a positive residual of ca. €7 million out of the total remuneration received from EMA (x-axis). This residual largely covers the costs for all non-procedural activities undertaken, which amount to just over €6 million (y-axis).

<sup>113</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system – Final Report: page 55



Therefore, in this specific case, fee-related remuneration from EMA can cover also the costs of unremunerated activities, including additional activities. The chart shows that for some NCAs overall declared costs exceed remuneration. The NCAs that receive the highest level of remuneration also have high additional costs (top right). In some cases, all unremunerated work can be funded through remuneration from EMA for fee-generating activities, but this is not always the case. The five NCAs for which remuneration is sufficient to cover all their costs either have low procedural activity costs and low costs for additional activities or overall costs are offset by high remuneration.

NCA costs vary across individual NCAs, with the consequence that some NCAs receive fees that cover their costs, while others experience a shortfall. This situation remains the same under scenarios that test an average cost-based fee system, as wage and other cost levels vary considerably between countries. However, the principle of applying average cost-based fees for procedural activities would by definition mean that total NCA remuneration would be equal to the total costs of these activities. Any individual NCA might be left with a financial deficit or surplus depending on their individual costs compared to the average NCA cost. A comparison of unitary full fees for the main activities under the current financial model and average cost-based fees (typical year) is provided in Figure 11 (human medicines) and Figure 12 (veterinary medicines).

Figure 11 shows the relative unitary full fees (that is the fees per individual procedure: fee per initial marketing authorisation, fee per Type II variation, etc.) for the main activities for human medicines. The inner ring of Figure 11 represents the distribution of fees in euro per procedure under the current financial model. Under the current financial model, unitary full fees are determined as per the currently applicable legislation (see Sections 2 and 3). For this study, the values used are averages based on full fee revenue provided by EMA (i.e. less detailed than the actual variety of amounts charged). The outer ring represents what fees per procedure could look like when modelling the principle of average cost pricing.

The fees for initial marketing authorisations are by far the highest fee in both cases. The fees would be even higher than under the current financial model using average cost pricing as current fees do not fully reflect the costs of these procedures (€442,400/procedure when modelling average cost pricing compared with €243,500/procedure under the current financial model). These numbers are based on data provided by EMA that takes into account variable fee components that depend on pharmaceutical strength and form. Type II variations have high fees under the current financial model for human medicines but the model shows that these would be significantly lower under average cost-based fees (€18,100/procedure when modelling average cost pricing compared with €72,600/procedure under the current financial model). In line with current legislation, no fees are charged for the paediatric and orphan designation activities included in the modelling exercise.<sup>114</sup> However these activities incur costs. The corresponding average cost-based fees modelled for these activities are

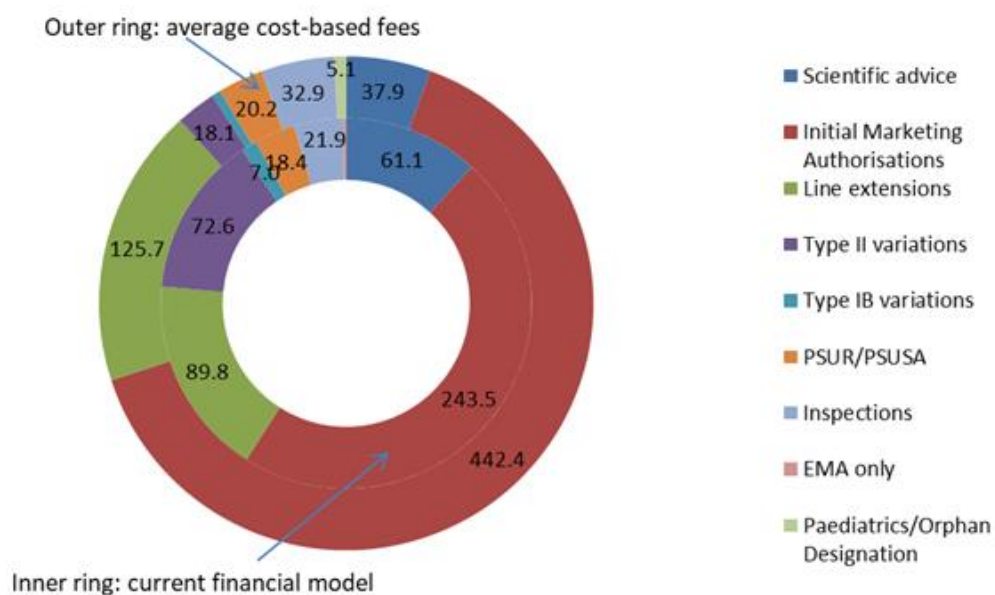
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<sup>114</sup> PIP-related and orphan designation procedures.

included in the outer ring only. In addition, under the current financial model, there are no fees or NCA remuneration associated with scientific advice activities for paediatric products that are not also an ATMP or orphan products. The cost of these to EMA and NCAs are included in the average cost-based full fees for scientific advice.

The same fee comparison is presented in Figure 12 for veterinary medicines. Here, for initial marketing authorisations, the same proportion of fees for both current fees and when modelling average cost-based fees indicates that current fees already reflect the high cost of these activities (€215,800/procedure when modelling average cost pricing compared with €137,100/procedure under the current financial model). NCAs and EMA incur costs for PSURs for veterinary medicines but no fees are charged for these under current legislation. The corresponding average cost-based fees modelled for these activities are included in the outer ring only.

**Figure 11: Comparison of unitary full fees for human medicine procedural activities for current financial model and when modelling average cost-based fees (€ thousand/procedure)**

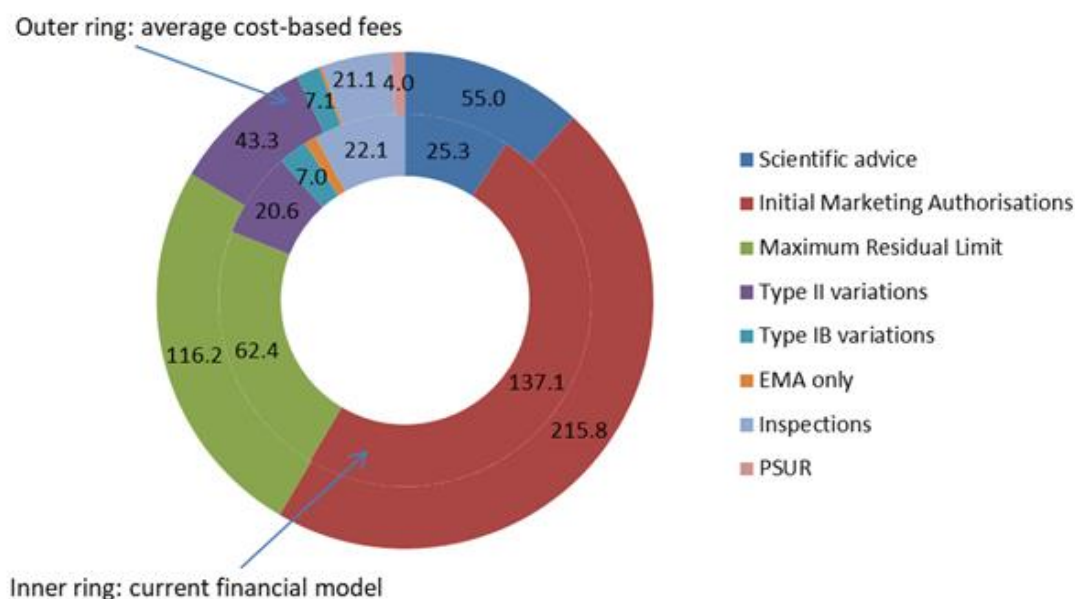


*Source: Study supporting the evaluation of the EMA fee system<sup>115</sup>*

**Note:** The outer ring represents average cost-based fees. The inner ring represents the current financial model.

<sup>115</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system – Final Report: page 46

**Figure 12: Comparison of unitary full fees for veterinary medicine procedural activities for current financial model and when modelling average cost-based fees (€ thousand/procedure)**



*Source: Study supporting the evaluation of the EMA fee system<sup>116</sup>*

**Note:** The outer ring represents average cost-based fees. The inner ring represents the current financial model.

**EQ2: To what extent does the current financial model allow the EMA to effectively perform the activities in its remit?**

The evidence indicates that the current financial model (including income from industry fees, EU budget contribution and other sources of revenue) provides an adequate financial basis to the EMA to perform both procedural and additional (cross-cutting and horizontal) activities for human and veterinary medicines. The budgetary principle of universality particularly contributes to the efficient financing and effective performance of EMA activities. There is no evidence that the EMA is hindered in its activities by the charging and remuneration arrangements.

The question is addressed by looking at whether the financial model enables EMA to perform tasks related to procedural activities within its remit as well as additional supporting activities (e.g. cross-cutting, horizontal).

Under the current financial model, EMA fee income from procedural activities is sufficient to enable it to undertake tasks for procedural activities related to human medicines, but not for veterinary medicines (EQ1, Table 2). Total fees for procedural activities and annual fees are however sufficient to cover all costs for procedural activities (EQ1, Figure 5). At the activity level, however, EMA fee income does not generally align with the costs of undertaking the activities for human medicines (EQ1, Figure 7) and veterinary medicines (EQ1, Figure 8). The incentives applied to the full

<sup>116</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system – Final Report: page 47

fees for an activity in a given year also have an impact on the ability of EMA to perform procedural activities. Under the current fee system, the EMA share of fee income is equal to the fee income once incentives have been applied and the NCA remuneration has been paid. For some activities, such as scientific advice, with high incentives, EMA recovers only part of its costs directly from the fees for scientific advice (EQ1, Figure 7). This is partly due to full fees not being cost-based but this would also be the case when modelling average-cost pricing due to incentives because the full fees before incentives are applied are based on average costs in such modelling. However, it should be noted that the distribution of the financial burden of incentives differs for fees for pharmacovigilance activities, where incentives are applied prior the remuneration of NCAs, reducing the remuneration amounts paid to the NCA rapporteurs.

EMA representatives are overall satisfied with the alignment of the current financial model and their activities. However, they indicated that in some instances covering procedural costs can be difficult, e.g. in the case of complex initial marketing authorisations where additional time and resources are required to carry out the assessment and where, therefore, procedural costs cannot be covered by the specific fee charged. Considering that EMA fee income is determined from actual fee income from industry net of incentives, once NCA remuneration has been paid, EMA has to rely on additional income from annual fees and the EU and EEA budget contributions to address any shortfall.

Furthermore, evidence shows that the current financial model enables the EMA to undertake and perform also additional tasks (EQ1, Figure 5). According to EMA representatives, one of the key pillars of the current fee and remuneration system in EMA's financial model is that it allows the EMA to take on new or different aspects of their work as well as to undertake cross-cutting activities. In addition, EMA interviewees emphasised that the current financial model provides sufficient flexibility in terms of the budget principle of universality, which ensures stability of their work. In the current model this is considered particularly important in the case of waived or reduced fees for SMEs and for specific types of products.

**EQ3: To what extent does the current financial model allow the EMA to remunerate the NCAs adequately for the activities they perform?**

The findings show that there is alignment between the total remuneration provided to NCAs and costs they incur, in aggregate, for procedural activities as well as almost half of the aggregate costs for the additional activities that NCAs reported to be EMA-related. However, it would not be sufficient to cover all of the aggregate costs for the reported additional activities and the aggregate costs for activities related to their participation to committees and working groups outside procedures. Whether and to what extent these “additional” activities and the involvement in committees and working groups should be covered by EMA remuneration is still to be assessed.

Furthermore, at the individual NCA level, remuneration is also sufficient to cover the costs of procedural activities, as well as committee and working group activities and additional activities, for some but not all NCAs (Figure 10).

At the level of individual activities, NCA remuneration is sufficient to cover the costs of some but not all activities.

The question is addressed by looking at the alignment between NCAs' remuneration and the actual costs they incur for the activities they perform. Furthermore, it looks at evidence of any issues regarding the current model's ability to adequately remunerate NCAs and compares the EMA system with that of similar EU agencies.

Under the current financial model, total remuneration provided to NCAs is sufficient to cover all of their procedural activities, as well as part of their reported additional activities (EQ1, Figure 9). It is to be noted that for procedural activities NCAs are remunerated only for the roles mentioned in the relevant legislation. For example, for initial marketing authorisation applications only the roles of CHMP rapporteur and co-rapporteur have a legal basis for remuneration, whilst costs incurred for other roles, such as CHMP peer-reviewer, PRAC rapporteur and PRAC co-rapporteur, are not addressed. Further, for pharmacovigilance activities NCA remuneration is reduced when incentives apply to the full fee (see EQ2). Nonetheless, evidence shows that the aggregated remuneration to NCAs, exceeds the aggregated costs of undertaking procedural activities requested by EMA, both for remunerated and unremunerated roles and despite incentives applied to pharmacovigilance activities (EQ1, Figure 9).

However, when looking at the individual NCA level, remuneration is sufficient to cover the costs of procedural activities, as well as the equivalent of costs incurred for committee and working group activities only for 19 out of 29 NCAs that provided cost information for this study. The remaining 10 do not cover their costs for procedural activities with the remuneration they receive. Possible explanations include varying national cost structures, varying workload involved in individual procedures of the same type and the fact that remuneration from the annual fees is not included. When remuneration from annual fees is also included, only 5 NCAs do not cover procedural activity costs (EQ1, Figure 9 and 10).

At the activity level (e.g. initial marketing authorisations, variations, scientific advice procedures), fees are not aligned with the actual costs to NCAs for the activities they perform (EQ1, Figure 7 and 8), with the fees for some activities effectively funding the costs of others, including those such as PIPs and orphan designation applications for which no remuneration is paid. Although individual NCAs do not undertake the same and the same number of procedural activities, the funding works to some extent across NCAs as almost all cover their costs. This may be explained by the fact that some procedures may be underpaid and other overpaid, each NCA being involved in a different mix of procedures, combined with different cost structures across NCAs.

Besides participation in EMA working parties and committees, NCAs also reported additional non-procedural EMA-related activities. Whilst remuneration would cover the costs for participation to working parties and committees, it is not sufficient to cover the costs of all the additional non-procedural additional activities declared (EQ1, Figure 6). However, further analysis is needed to understand the content of these additional activities and to assess whether the inclusion of (some of) these activities in the cost calculation is backed by a legal basis in the current regulatory framework.

The above issues were also highlighted in the 2010 external study on the evaluation of the EMA, which commented on a widely varying level of contribution from one NCA to another and on an imbalance between NCA's costs and remuneration. The main problem identified in the funding of EMA-related activities was that of non-fee generating activities, such as assessments of PIPs and orphan designations. The noted imbalance was especially considered an issue for NCAs funded through fees as well as veterinary agencies because of the fact that veterinary fees are generally set at a lower level than those for medicines for human use.<sup>117</sup> The HMA raised the same concerns in a 2010 position paper on a revision of the fee system.<sup>118</sup> Similarly, the European Court of Auditors repeatedly noted the need to introduce a system of remuneration for services provided by Member State authorities based on their real costs.<sup>119</sup>

EMA representatives acknowledged the difficulties some NCAs face due to a lack of remuneration for some procedural activities (e.g. PDCO and COMP related procedures). NCAs interviewees emphasised that they find such unremunerated activities important and they are willing to undertake these activities for this reason. However, three interviewees among the NCAs (NCAs no. 5, 19 and no. 24 in Figure 9 and 10) noted that they would prefer or may potentially have to decrease their engagement in these unremunerated activities in future as they are not able to fully fund their costs with remuneration amounts provided by the EMA. The 2010 study commented that if NCAs were to reduce their engagement due to lack of financial resources this would affect the sustainability of the regulatory network as a whole and, therefore, also directly impact EMA. At the same time, NCAs considered the return on investment regarding their involvement in EMA activities as clearly positive, in terms of scientific interest, but also in terms of exchange of experience.<sup>120</sup>

The data gathering and calculations were made while the UK was member of the EU and of the various EMA committees. The conclusions are based on overall average

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<sup>117</sup> Ernst & Young, 2010, Evaluation of the European Medicines Agency – Final Report: pages 10, 11, 97, 124, 125 and 198

<sup>118</sup> Heads of Medicines Agencies (HMA) position paper: [Role of the European regulatory medicines network and its relation to a revision of the fee regulation, December 15, 2010.](#)

<sup>119</sup> European Court of Auditors reports on the annual accounts of the European Medicines Agency for the financial years [2006](#) (OJ C 309, 19.12.2007, p. 34–39), [2010](#) (OJ C 366, 15.12.2011, p. 27–32) and [2011](#) (OJ C 388, 15.12.2012, p. 116–122).

<sup>120</sup> Ernst & Young, 2010, Evaluation of the European Medicines Agency – Final Report: pages 121 and 122

calculations and it is therefore not expected that UK's withdrawal would impact significantly the results of the evaluation. The effect of the redistribution of the UK NCAs portfolio to other NCAs should nevertheless be included in cost calculations, should an amendment of the EMA fee system be considered.

Turning to other agencies, similar to EMA, ECHA works with national competent authorities that conduct work as rapporteurs and co-rapporteurs of the agency's committees. A proportion of the fees and charges collected should be paid to the respective NCAs. The ECHA Fee Regulation provides that the maximum proportion of the fees and charges to be transferred to the competent authorities of the Member States are set by the Management Board of ECHA following a favourable opinion from the Commission. National correction coefficients (percentages) are applied to transfers to the individual Member States to adjust for differences in national costs for providing services due to differences in salary and overhead costs in each Member State, with Finland as the baseline country (100%).<sup>121</sup> The aim is to reach a balance between remuneration paid to Member States and costs for their services. It should be further analysed whether and to which extent the national correction coefficient for remuneration applied by ECHA would be relevant in the case of EMA.

**EQ4: To what extent is a balance struck between a fee and remuneration system based on actual costs and simplicity of the fee system?**

The fee system is very complex and detailed; changes of underlying legislation along the years, whilst providing for simpler and more structured processes for procedural activities, in some cases have increased the complexity of the fee system. EMA commented on the high level of complexity encountered in implementing the system. Nonetheless, the majority of stakeholders consulted still find the fee system fairly easy to understand and transparent. However, looking more closely, the perception of whether the fee system is clear and transparent differs between large pharmaceutical companies and SMEs, highlighting the need for simplification of the system in order to make it more accessible to all industry categories. Furthermore, NCA representatives, wider stakeholders and respondents to the online public consultation suggested that, overall, fees charged to industry are proportionate to services provided in most cases, with the exception of some specific areas where more proportionality would be needed (e.g. initial marketing authorisations and variations).

In assessing the simplicity of the system, the analysis focused mainly on whether stakeholders found the system easy to understand. However, "clear/easy to understand" and "complex" should be considered as two separate factors, as the fact that the system can be found straightforward and easy to understand for professionals does not preclude that it is still very complex and granular.

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<sup>121</sup> ECHA uses the correction coefficients applied by the European Commission to adjust staff salaries as a baseline coefficient and adapts it for Finland as baseline country.

Therefore, in this context, complexity can be defined by the fragmented structure of the fee system, both in consideration of the multiple legislative and non-legislative documents making up the overall system (see Sections 1 and 2) and the granular breakdown of fees categories, levels, and incentives to be taken into account in the determination of both the amount to be charged to industry and the remunerations to be paid to the NCAs involved.

The current fee system provides around 90 different basic procedural fees for medicinal products for human and veterinary use ranging from €3,200 to €291,800 (as provided in Section 3.1). This is without counting the additional amounts that may be added to these basic fees if the application covers more than one pharmaceutical strength/potency, presentation or form.

Initially, the EMA fee system was only governed by the Fee Regulation. In their 2004 analysis of the fee system, EMA found that the use of graduated fees enabled to better reflect the actual level of scientific input and service provided. EMA concluded that, in light of the principle of proportionality, such flexibility could be further extended to other types of fees. This conclusion was reflected in the 2005 amendment of the Fee Regulation.<sup>122</sup> The Fee Regulation has not been amended since. However, over the years, it has been accompanied by several pieces of cross-cutting and sectorial legislation, establishing additional fee incentives for SMEs, orphan designated medicines, medicines for children and ATMPs. Furthermore, in 2014 the EMA fee system expanded to pharmacovigilance activities. These additional layers, whilst allowing for a more detailed breakdown of fees and fee incentives, also add to the complexity of the fee system (i.e. a higher number of specific fee amounts to be calculated). An example of this is the evolution of fee incentives for SMEs. Initially, exemptions and reductions were the same across SMEs. Currently, however, fees for non-pharmacovigilance and pharmacovigilance post-authorisation activities are broken down by company size. In addition, the EMA launched the PRIME (PRiority MEDicines) scheme in 2016 to support developers of medicinal products that may offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options. The scheme offers additional fee reductions for scientific advice requests for micro enterprises and SMEs as well as applicants from the academic sector.

The 2010 study on the evaluation of the EMA commented on the complexity of the fee structure. It found that, independently of the fee levels, the fee structure, including the rules for NCA remuneration, is complex as a result from consecutive regulations.<sup>123</sup> According to several EMA representatives, the complexity of the fee system is a result of the detailed breakdown of fees and the underlying complexity of the activities

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<sup>122</sup> Report to the European Commission on financing the European Agency for the Evaluation of Medicinal Products – Endorsed by the Management Board on 11 March 2004 (not published) ; See also section 2.2 of the Explanatory Memorandum accompanying the Commission proposal for a Council Regulation amending Regulation (EC) No 297/95 on fees payable to the European Medicines Agency {SEC(2005)407} /\* COM/2005/0106 final - CNS 2005/0023 \*/.

<sup>123</sup> Ernst & Young, 2010, Evaluation of the European Medicines Agency – Final Report: pages 14, 124 and 202



themselves. While EMA interviewees agreed that detailed incentives as well as a breakdown of fees by activity contribute to fairness, they also raised concerns that too much granularity of fee amounts could lead to an overly complex fee system. By contrast, a flat fee system is considered simpler, but interviewees also noted that a flat fee could lead to less fairness and proportionality. Several interviewees (both from NCAs and EMA) found that changes to legislation made the fee system less flexible in some cases (e.g. the amended pharmacovigilance legislation does not allow fee reductions after 30 calendar days from the date of the invoice<sup>124</sup>). Some EMA representatives indicated that they would prefer an overall revision of all legislative documents and consolidating them into one coherent piece of legislation.

Despite the high level of complexity of the system, stakeholders that are accustomed to the fee system find it understandable. The survey of wider stakeholders including industry representatives showed that more than half of the respondents consider the fee system to be straightforward and easy to understand whereas only about a quarter disagrees with the statement, and the rest being either neutral or indicating to not know. Among these, respondents from large pharmaceutical companies in particular found the fee system straightforward and easy to understand, with almost three quarters agreeing/strongly agreeing. By contrast, less than half of SME and one third of research organisation respondents agreed, while about a third of SME and research organisation respondents disagreed. Such differences between industry/organisation categories may be related to the respective level of experience and workforce available and the intricate system of incentives applicable to SMEs and research organisations. This highlights the need for simplification, harmonisation and consequent decrease of administrative burden for such structures. The results of the online public consultation mirrored the ones of the wider stakeholders' survey, indicating that the majority of the 51 respondents (69%) felt that the EMA fee system rules are clear and easy to understand.<sup>125</sup>

The fee system is also generally found to be clear and transparent. In the survey of NCAs, 63% of the respondents agreed that the fees charged are transparent. Similarly, the majority of respondents to the wider stakeholder survey (54%) agreed that the fees are transparent. Of those who agreed, the vast majority are large pharmaceutical company representatives (72%), while the majority of SME representatives were neutral (57%), with only 29% of SME consultees agreeing. As for the point discussed above, such discrepancy between industry categories highlight the need for further support to SMEs and simplification of the system to make it more accessible to users. The results of the online public consultation show that the majority of respondents (67%) also felt that the operation of the EMA fee system is transparent.<sup>126</sup>

However, the majority of NCA respondents reported that there are a few specific areas where more transparency is needed, especially for the breakdowns of the fees charged to

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<sup>124</sup> Articles 8(1) and 8(2) of Regulation (EU) No 658/2014.

<sup>125</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system - Final report: pages 72 and 73

<sup>126</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system - Final report: page 74

industry from which they can expect a 50% share, expected remuneration in case of reductions and incentives applied, and timing of remuneration.

While NCA representatives, wider stakeholders and respondents to the online public consultation suggested that, overall, fees charged to industry and services provided are proportionate, there are some specific areas that are perceived as lacking proportionality. Wider stakeholders across stakeholder type (i.e. large pharmaceutical companies, SMEs, representatives of research organisations as well as representative groups) highlighted some individual activities which they felt were not proportionately charged, such as variations, initial scientific advice, transfers of MAH, among others. Although half of respondents to the online public consultation (n=36; excluding respondents who chose the answer option ‘do not know’) agreed or strongly agreed that the EMA fee system reflects the overall costs of the services, but they also highlighted specific areas where more proportionality is needed, especially with regards to variations.<sup>127</sup> Already in 2010 similar concerns were noted. Human pharmaceutical companies commented that, with the exception of fees for scientific advice, fees were generally considered to be fair and appropriate to the services provided. Veterinary industry, however, were more critical towards the fees charged, noting that the centralised system may prove less attractive for their products as the veterinary market is more fragmented and country-specific.<sup>128</sup>

**EQ5: To what extent does the fee system enable needs to be met in exceptional circumstances or under particular priorities/imperatives?**

The analysis shows that key elements of the current fee system are its ability to respond to exceptional circumstances and a certain degree of flexibility to allow doing so. More specifically, the current fee system provides enough flexibility to the EMA to fund their EMA-related activities to meet particular needs, such as activities related to orphan designated medicines, products for paediatric use and advanced therapies. The combination of Fee Regulation and Implementing Rules is considered to be important to enable a certain degree of flexibility with regards to, for example, fee reductions and exemptions. However, changes to the pharmacovigilance legislation decreased the level of flexibility on fees charged for exceptional circumstances. The current fee system is not flexible enough to accommodate fluctuations in NCAs’ workload and, more specifically, the changes in time and budget needs related to increasing complexity of the activities undertaken. Finally, stakeholders from industry, academia and representative organisations are satisfied with the provisions made in exceptional circumstances or under particular priorities/imperatives (i.e. partial or full fee waivers), but they highlighted areas where more incentives and focus on particular user groups are needed, such as incentives for academic institutions as well as remuneration for representatives of non-profit and patient organisations.

<sup>127</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system - Final report: page 76

<sup>128</sup> Ernst & Young, 2010, Evaluation of the European Medicines Agency – Final Report: pages 14 and 156

The question is addressed by looking at whether reductions and exemptions enable authorisations for special categories of medicinal products that are prioritised by the EU and whether the fee system provides flexibility for exceptional circumstances, as well as by analysing any evidence of satisfaction with the provisions made in exceptional circumstances or under particular priorities/imperatives.

The current fee system provides enough flexibility to the EMA to finance all activities and to meet particular needs, such as activities related to ATMPs, orphan and paediatric medicines as well as support to SMEs. EMA representatives reported that this flexibility, and in particular the availability of EU budget contributions, is crucial to fully operating regardless of fee income fluctuations. The 2010 study also concluded that the balancing mechanism of the EU budget contribution is a guarantee for the various stakeholders, and EU citizens in particular, that the Agency will achieve its objectives without being potentially affected by external fee fluctuations and, therefore, contributes to sustainability of the Agency's resources.<sup>129</sup> Available information as described in Section 3.2 suggests that the amount of general EU budget contribution is approximately equal to the total value of non-orphan fee incentives (orphan related fee incentives are covered by the dedicated contribution). However, it is to be noted that this does not take into account costs for non-fee generating procedures, which have to be funded through other EMA sources of income.

The Fee Regulation allows for the granting of reductions and exemptions of fees on a case-by-case basis 'under exceptional circumstances and for imperative reasons of public or animal health [...] by the Executive Director after consultation of the competent scientific committee'.

Therefore, EMA representatives noted that the flexibility provided by the combination of the Fee Regulation and Implementing Rules is key in order to enable them to provide fee reductions and exemptions not foreseen in the legislation.

However, EMA interviewees indicated that although amendments to the pharmacovigilance legislation made the fee system more cost-based and simpler, changes also included restrictions regarding fee reductions under exceptional circumstances, hindering the level of flexibility at adjusting fee levels following regulatory changes.

Furthermore, several NCA representatives consulted indicated a lack of flexibility of the current fee system when it comes to fluctuations of the workload needed for accomplishing an activity, as remuneration to NCAs is not adjusted in such situations. There are indications that variance in workload is often tied to the increasing complexity of activities resulting from new and complicated innovations and advances in science (e.g. gene therapy, personalised medicines), resulting in more complex substances to be assessed, possibly requiring involvement of more committees or scientific advisory groups. NCA respondents consider these elements not to be reflected in the current fee and remuneration system.

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<sup>129</sup> Ernst & Young, 2010, Evaluation of the European Medicines Agency – Final Report: pages 110 - 112

Finally, in the online public consultation, respondents highlighted areas where industry and academic representatives require more flexibility, such as payment timelines and sharing of costs between MAHs.

Respondents of the wider stakeholder survey confirmed that the specific fee arrangements made for particular types of medicines (orphan medicines, veterinary medicines for MUMS, medicines for paediatric use, etc.) are appropriate (38% agree/strongly agree; 35% neutral; 27% disagree/strongly disagree). However SMEs were less satisfied with fee arrangements compared to other stakeholder groups (20% agree/strongly agree; 30% disagree/strongly disagree). Similarly, academic and non-profit institutions expressed a higher degree of dissatisfaction (25% agree/strongly agree; 50% disagree/strongly disagree).

Finally, in the online public consultation, the overall extent of agreement on the adequacy of the incentives and support provided by the EMA fee system was higher (58% agree/strongly agree). The 2010 study on the evaluation of the EMA found that fee waivers and reductions are considered extremely important by all stakeholders in order to maintain innovation.<sup>130</sup>

**EQ6: To what extent are SMEs supported through effective reductions in their costs to use the centralised system?**

Indicators such as numbers of registered SMEs and marketing authorisations to SMEs suggest that the current support to micro enterprises and SMEs in the form of fee incentives and administrative guidance enables them to access and participate in the centralised system. Comparison with ECHA shows that ECHA's and EMA's fee system both break their reductions down by the size of the enterprise (micro, small and medium-sized enterprises), providing significantly higher reductions to micro-sized businesses.. However, EMA offers higher fee reductions and exemptions that are not provided to SMEs in the ECHA fee system.

The question is addressed by looking at whether SMEs are able to participate in the centralised system without undue burdens, more specifically looking at responses to stakeholder consultations, analysis of number of registrations and number of submissions to EMA and comparison of definitions and incentives applied by other European (ECHA) and international (FDA) agencies.

More than half of the wider stakeholders surveyed prefer a fee system that is cost-based (55% agree/strongly agree; 13% disagree/strongly disagree). Among these, agreement was significantly higher among large pharmaceutical company representatives and industry organisations (73% agree/strongly agree; 27% neutral). By contrast, only 31% of SME representatives agreed (31% neutral; 31% disagree/strongly disagree; 8% do not know). Several stakeholders highlighted the importance of incentives for micro, small and medium-sized companies to ensure that the regulatory system remains accessible

<sup>130</sup> Ernst & Young, 2010, Evaluation of the European Medicines Agency – Final Report: page 161

also to SMEs.<sup>131</sup> This clearly highlights the importance of incentives for the long-term sustainability of SMEs. This element should be accounted for in case of any future revision of the fee system.

Fee reductions and exemptions for SMEs were introduced in 2005. Wider stakeholders responding to the survey provided mixed answers on the appropriateness of the specific fee arrangements made for SMEs (0% strongly agree; 21% agree, 18% neutral; 10% disagree; 15% strongly disagree). Of these, stakeholders who identified their organisation as an SME were less satisfied than the group of respondents as a whole (31% strongly disagree; 23% disagree). Some respondents commented on the adequacy of the EU definition of an SME provided in Commission Recommendation 2003/361/EC, which was not in the scope of the evaluation.

The SME Regulation aims at reducing financial and administrative hurdles for SMEs to access and participate in the centralised system, recognising the specific situation of SMEs; such enterprises generally have limited financial means, lack experience with the centralised procedure, and are often innovative companies which can notably benefit from the pooling of scientific expertise at Union level.<sup>132</sup> Indicators such as numbers of registered SMEs and scientific advice provided to SMEs suggest that SME incentives and guidance provided by the EMA SME office enable them to participate in the centralised system. In 2006, the first year after entry into force of the SME Regulation, 108 companies were registered as SME. By 2017, their number had increased to 1893, which represents an increase of 1,653%. For human medicines, 194 scientific advice and protocol assistance were submitted by SMEs in 2017 as compared to 19 in 2006 (respectively 31% and 7% of all requests). For veterinary medicines 7 scientific advice were submitted by SMEs in 2017 as compared to 3 in 2006 (respectively 35% and 44% of all requests). The number of initial marketing authorisation applications for human medicines submitted by SMEs showed significant fluctuations in the past few years. However, an overall increase from 2 SME applications in 2006 to 20 in 2017 was seen. Out of 17 applications for marketing authorisation for veterinary medicines received by EMA in 2017, 6 were SMEs (35%).<sup>133</sup> Overall, SMEs are very active in submitting marketing authorisation applications and requests for scientific advice for veterinary medicines compared to non-SME businesses.

Comparison to ECHA shows that both ECHA's and EMA's fee system break their reductions down by the size of the enterprise (micro, small and medium-sized enterprises), providing significantly higher reductions to micro-sized businesses; this may present the advantage of providing a more targeted support to SMEs depending on their size. With regard to EMA's fee system, the SME Regulation itself does not offer different fee reductions for micro-sized businesses as compared to small and medium-

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<sup>131</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system - Final report: page 108

<sup>132</sup> See the recitals of the SME Regulation.

<sup>133</sup> SME Official annual report 2017 ([EMA/123438/2018](#)) ; Report on the 10<sup>th</sup> anniversary of the SME initiative ([EMA/155560/2016](#))

sized companies. Instead, such further breakdown is laid down in the Pharmacovigilance Fee Regulation and the Implementing Rules of the Fee Regulation.

Further comparison between ECHA and EMA shows, however, that the EMA offers greater fee reductions for SMEs. The EMA fee system also offers fee exemptions, which are not provided for SMEs in the ECHA fee system. Compared to the U.S. FDA, the EMA offers more incentives to micro-sized businesses and SMEs. Unlike the EMA, the FDA does not have a single definition for micro, small or medium-sized enterprises. This and the different markets make it difficult to analyse whether in the case of ECHA or the FDA the SME policy leads to different results in terms of SME participation to the system.

Based on this comparison, the provision of incentives for SMEs may be seen as a strength of the EMA fee system, offering more incentive and exemptions than others do. However, the analysis of the effects of the SME incentives would require a separate evaluation.

**EQ7: To what extent does the current financial model ensure the financial stability of the EMA?**

EMA's total revenue has steadily increased over the last ten years, with a clear decrease of EU budget contribution vis-à-vis revenue from industry fees. The current fee system overall enables EMA and NCAs to meet their costs for procedural activities, although some flexible funding across procedures is needed where fee incentives and exemptions are applied. In particular, the flexibility to fund non-fee generating/unremunerated and cross-cutting activities, as well as incentives for specific medicinal products and SMEs, are considered to be essential.

However, some elements of the fee system create challenges for its long-term sustainability. The remuneration provided to NCAs under the current financial model don't always cover all costs of activities NCAs declared as EMA-related.<sup>134</sup> Furthermore, the current fee system may not be able to adequately and timely address expected future needs for example due to increasing complexity of assessments related to innovative medicines.

This question is addressed by looking at the composition of the EMA revenue over time highlighting variations in fee revenue and EU budget contribution; the correspondence of fees charged with EMA costs and of remuneration provided with NCA costs, as well as the extent to which the total fees earned enable the EMA to meet its costs, (taking into consideration the availability of EU contributions). Furthermore, it looks prospectively at possible external factors that could hinder the future effectiveness of the fee system.

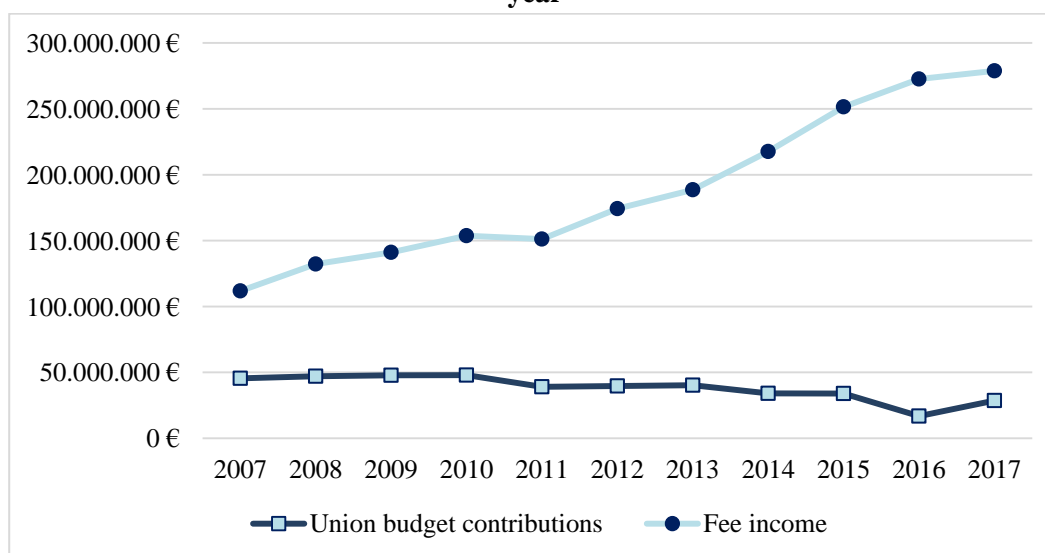
EMA's total revenue increased from €165.3 million in 2007 to €317.4 million in 2017, and the budget for 2018 as adopted by the Management Board was €337.8 million. The

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<sup>134</sup> As stated before, further analysis is needed on the content of the list of additional activities reported by NCAs as well as on their relevance for funding through fees and to which cost.

majority of this revenue consists of industry fees (see below). The majority of the total sum of fees in 2017 stemmed from activities under the Fee Regulation (around 90% or €251.2 million), with the remainder of fees charged under the Pharmacovigilance Fee Regulation (€27.6 million). Further income is received via Union budget contributions (general contribution and special contribution for orphan medicines). As shown in Figures 10 and 11, the proportion of fee revenue of EMA’s total revenue has increased over the last decade, from 67.6% in 2007 (€111.8 million) to 87.9% (€278.8 million) in 2017. At the same time, the proportion of the total Union budget contributions gradually decreased from 27.5% (€45.4 million) in 2007 to almost 9% (€28.5 million) in 2017. For 2018, the Management Board has adopted figures indicating that 90.2% of EMA’s budget consisted of fees, with a further 9.6% coming from Union contributions (respectively €304.5 million and €32.5 million).<sup>135</sup> Finally, a small portion of EMA’s total revenue, 3.2 to 7.4% between 2007 and 2017, comprises income from other sources, such as received from administrative operations (e.g. sale of publications and organisation of seminars), external assigned revenue for projects and programmes, and revenue from miscellaneous sources (e.g. refunds and compensations).<sup>136</sup>

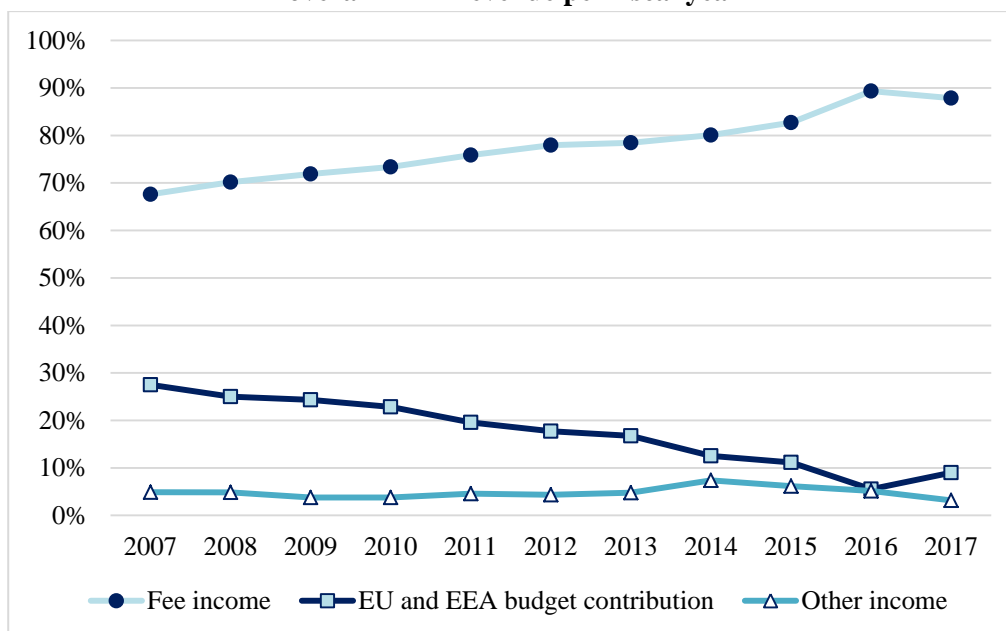
**Figure 13: Total amount of Union budget contributions and industry fees in euros per fiscal year**



<sup>135</sup> In 2016, EMA received a one-off rent rebate due to exchange rate fluctuations. This allowed a reduction in the balancing Union contributions. According to the EMA [Budget Report for 2016](#), the projected Union contributions for that year were higher, i.e. €25,151,000.

<sup>136</sup> Sources: EMA Budget Reports for [2009](#), [2010](#), [2011](#), [2012](#), [2013](#), [2014](#), [2015](#), [2016](#), [2017](#), [2018](#), and 2019. Figures quoted for 2007 – 2017 are based on those published for those years in the Budget Reports of 2009 – [2019](#) to ensure use of final data. The adopted figures for 2018 are based on the 2019 Budget Report.

**Figure 14: Percentage of Union budget contributions, industry fees and other revenue of the overall EMA revenue per fiscal year**



The current fee system enables both the EMA and NCAs overall to meet their costs for procedural activities (see Section 5.2). Furthermore, analysis shows that it enables the EMA and the NCAs to undertake cross-cutting activities, and hence to fund relevant activities that are not directly covered by a fee.<sup>137</sup> EMA representatives consider the flexibility to use overall fee revenue for activities and services provided a key pillar of the fee system, which ensures stability of their work. The availability of EU budget contributions also contributes to the stability of the fee system, as it enables the EMA to fully operate in cases of fee income fluctuations or when industry payments arrive later than expected. These findings are in line with those from the 2010 study which concluded that the balancing mechanism of the EU budget contribution is a guarantee for the various stakeholders (and EU citizens in particular) that the Agency will achieve its objectives without being potentially affected by external fee fluctuations and, therefore, contributes to the sustainability of the Agency's resources.

All eight interviewed NCAs as well as most of the NCA survey respondents indicated that they are not able to fund all EMA-related activities declared with payments received from EMA. As analysed under EQ1, the modelling exercise showed that, when looking at NCAs in aggregate, NCAs may use the remuneration they receive from EMA to cover (remunerated and non-remunerated) procedural activities and their share of annual fees to fund a portion of the additional activities they declared undertaking, but not costs associated with working groups and committees. As commented under EQ3, interviewed NCA representatives thus consider the current fee system not to be sustainable if the level of remuneration remains the same.

<sup>137</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system - Final report: pages 50 and 52



NCA representatives and wider stakeholder consultees identified areas that need more transparency, such as calculation of fees for industry submissions and detailed breakdown of fee invoices, detailed breakdown of calculation of NCAs remuneration (purchase orders), and timing of remuneration. According to them, increasing transparency in these operational areas could make the overall fee system more sustainable, as it would improve predictability and allow for better business planning and internal accounting. In the case of fees charged to industry, one large pharmaceutical company representative indicated that more clarity on the basis for fees is required.

EMA interviewees noted that they have observed increasing complexity of coordination activities in the past years, raising concerns that the available budget might not be sufficient in the near future with the same level of other activities, as they expect that the level of complexity will increase even more. Similarly, several NCA representatives reported that procedures have become increasingly complex in recent years. In addition, interviewees noted that complex products more often require input from more than one committee and that the number of such cases has increased in the recent years. In addition, NCAs expect that the complexity of and workload for some activities will increase even more in the future due to new and more complicated innovations and advances in science. Some examples offered by interviewees were very innovative products without clinical data or with insufficient data, control activities for medicinal products (including falsified medicinal products, see Directive 2011/62/EU<sup>138</sup>), big data, analysis of real-world data and patient experience data (including how to address differences in data standardisation), health technology assessments, and companion diagnostic reviews. In the veterinary medicine sector, increasing complexity is also expected in activities related to monoclonal antibodies and stem cells.

## 5.2. Relevance

The assessment includes identification of mismatches between the originally acknowledged problems and needs that the EMA fee and remuneration system was designed to address. It compares the current fee system with existing needs to determine whether the fee system is still fit for purpose.

**EQ8: To what extent does the fee system address the problems and needs originally identified to fund the relevant legislative tasks of the EMA, including NCA remuneration?**

The current fee and remuneration system addresses most of the problems and needs identified at the time of the establishment of the EMA as well as requirements set out in the main legislation. The mixed funding model based on fees and EU budget contribution is considered relevant, as it provides a sound financial basis and flexibility to EMA to

<sup>138</sup> Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products: OJ L 174, 1.7.2011, p. 74–87

perform its activities. Furthermore, the fee system provides for remuneration to NCAs for undertaking EMA-related activities, although the fee charged and remuneration provided at the activity level are not cost-based across all activities. Whilst it enables NCAs in aggregate to cover their costs for procedural activities, it covers only partly the costs of additional activities declared by NCAs considered to be EMA-related and none of the costs for working groups and committees. Further analysis is needed to clarify whether these activities should qualify for remuneration.

The originally identified requirement to provide fee incentives to address public or animal health threats is in general met by the current fee system. Additional fee incentives introduced by EMA in later years indicate that the fee system responds to the requirement to allow fee reductions and exemptions under exceptional circumstances.

Specificities of the veterinary market are addressed by lower fees as compared to those for human medicinal products. However, at the level of individual activities those lower fees are not always justified by the underlying costs.

Furthermore, the need to minimise the administrative burden by adopting a fee structure that is as simple as possible is still relevant and not fully met by the current system. As a result of the introduction of various cross-cutting and sectorial pieces of legislation and the separate Pharmacovigilance Fee Regulation, the overall system is complex and heavy to implement.

This question is addressed by looking at the extent to which needs identified when the fee system was developed are addressed by the fee system.

Interviewed EMA and NCA representatives emphasised the importance of the fees to undertake EMA-related activities. The EMA annual budget reports show the relevance of the fee income to the overall budget of the Agency, with a steady increase over the last 10 years of the proportion of revenue from fees in the overall Agency's budget (from 67.6% in 2007 to 87.9% in 2017) (see EQ1).

EMA interviewees confirmed the importance of a system based both on fees paid by industry and EU budget contributions. The latter are found to be particularly important and still relevant, although decreasing in level, as they allow flexibility when it comes to funding activities and to counterbalance fee income fluctuations.

The fee system allows providing remuneration to NCAs for undertaking the majority of EMA-related activities. However, some EMA-related activities that NCAs reported undertaking are non-remunerated. Such activities include both legally required activities and other additional activities (see EQ1). EMA, NCA and wider stakeholder representatives overall agree on the need to remunerate NCAs for performing eligible EMA-related activities. They also indicated there is an imbalance between the amount of

fees and the costs of services they provide. This finding is substantiated by the outcome of the model calculations<sup>139</sup>, as shown in Figures 7 and 8.

The current fee and remuneration system offers lower fees for veterinary medicinal products compared to those for human medicinal products, thus addressing the originally identified need to take account of the specific nature of the animal health market and related issues. Some NCAs and EMA representatives noted that the current level of lower fees for veterinary medicinal products do not reflect the workload and complexity of services provided, and this misalignment between fees and costs is confirmed by the current evaluation (see EQ1). However, the decision to adopt lower fees for veterinary medicines was never linked to costs and workload but directly related to the specificities of the veterinary market. In this respect it is noted that some wider stakeholder respondents (large pharmaceutical companies, SMEs and industry organisation representatives) emphasised that the fee system should still remain proportionate to the size of the veterinary market. The originally identified need to address specificities of the veterinary sector by setting lower fees therefore seems still relevant.

Furthermore, the originally identified requirement to provide fee incentives to address public or animal health threats is in general met by the current fee system. Wider stakeholders and EMA representatives indicated that fee reductions in emergency cases are still relevant. In addition, the introduction of additional fee incentives by EMA in later years indicate that the fee system is capable to absorb the requirement to allow for fee reductions and exemptions under exceptional circumstances. In 1995, the Management Board adopted fee incentives for orphan designated products and comparable products for veterinary use, including the determination of certain MRLs of old products. Since then, the number of fee incentives adopted by EMA's Executive Director and Management Board under the relevant legal provision<sup>140</sup> has been significantly extended. In detail, partial or full waivers are currently in place for: SMEs, orphan designated medicines, ATMPs, medicinal products for paediatric use (PUMAs), veterinary medicines for MUMS/limited markets, veterinary vaccines against certain epizootic diseases, multi-strain veterinary dossiers, core dossier for a pandemic influenza vaccine, generics, well-established use medicinal products, herbal medicines, homeopathic medicines, and multiple applications submitted on usage patent grounds. In addition, EMA grants fee reductions and exemptions for applicants from the academic sector in the case of scientific advice procedures for products falling under the PRIME scheme. Some of these additional incentives were inspired by the adoption of new crosscutting and sectorial legislation, adding extra layers of fee incentives to those provided in said legislation, whilst others were introduced to address newly identified public or animal health needs. Decisions of the Executive Director and Management Board can be amended, revoked or added at any point in time in accordance with such needs, thereby changing the applicable types and levels of fee incentives and, as such, the fee system.

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<sup>139</sup> See Annex 8 for more information on the financial model.

<sup>140</sup> Article 9 of Council Regulation (EC) No 297/95

Finally, the current fee and remuneration system is complex and does not fully respond to the need of minimising administrative burden related to the application of the fee structure by adopting a simple system that takes into account ease of applicability whilst addressing the underlying regulatory framework. The introduction of several fee levels and several pieces of cross-cutting and sectorial legislation over the years as well as the more recent Pharmacovigilance Fee Regulation made the overall fee system fragmented, very granular and heavy to implement. EMA representatives commented on the complexity of the system and the consequent administrative burden related to its implementation. While they agreed that detailed incentives as well as a breakdown of fees by activity contribute to fairness, they also raised concerns that high granularity of fees leads to an overly complex system. As also stated under EQ4, already in 2010 the fee structure was considered complex as a result from consecutive regulations.<sup>141</sup> Since then the Pharmacovigilance Fee Regulation has added further to its complexity. Furthermore, there is evidence that SME representatives that responded to the wider stakeholder survey find the system less understandable and transparent than other categories of payers. This may indicate that categories of applicants benefitting of incentives (e.g. SMEs) find it difficult to navigate through the various pieces of legislation in determining the amounts they will be charged for their applications.

#### **EQ9: Is the fee system relevant in terms of current needs?**

While the fee and remuneration system is still relevant in relation to originally identified needs, new problems have been identified that are currently not taken into account. In particular, there are indications that the fee and remuneration system may not be flexible enough when it comes to ensuring future financial stability of EMA (EQ7).

A specific current need for the fee system is to consider changes brought by the underlying legislation by the new VMP Regulation. This regulation introduces changes to regulatory procedures for which the current fee system may not foresee fees. Related changes should be analysed separately in terms of their effects on the fee system.

Finally, stakeholders consulted confirm that there is no need for the establishment of a dispute settlement procedure between the EMA and industry.

This question is addressed by looking at whether current needs identified by EMA, NCAs and stakeholders are addressed by the fee system. These concern needs other than those originally identified when the fee system was developed.

As presented in the previous section, the current financial model enables the EMA to fund overall its activities, therefore it can still be considered relevant for the needs of the main stakeholders involved. However, EQ7 points to a newly identified need for more flexibility of the fee system in order to be able to adjust in future to the fast-paced environment in which the system operates.

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<sup>141</sup> Ernst & Young, 2010, Evaluation of the European Medicines Agency – Final Report: pages 14, 124 and 202

Further, the new VMP Regulation introduces changes to regulatory procedures for which the current fee system may not foresee fees. It also broadens the scope of veterinary medicinal products eligible for the centralised procedure, which in turn may affect the cost and income level of EMA and NCAs for activities related to veterinary medicinal products. These changes should be analysed separately in terms of their effects on the fee system.

In contrast to ECHA, the current EMA legislation does not foresee an administrative process for appeals for any natural or legal person affected by decisions taken by the Agency.<sup>142</sup> Whether there would be a need for such a dispute settlement procedure was investigated in this evaluation.<sup>143</sup> Stakeholders did not identify the need for a dispute settlement procedure between the EMA and industry. EMA representatives as well as respondents to the wider stakeholder survey did not refer to any disputes between different stakeholder groups. While EMA interviewees agreed that payers sometimes have queries, it was clarified that issues raised are usually quickly solved. Only one respondent to the online public consultation, a member of an industry organisation, indicated they thought that the EMA is not always objective in the decision of the amount of fees charged; however, no suggestions for a dispute settlement procedure were provided.

### 5.3. Coherence

Coherence refers to how well or not different aspects of a system work together (e.g. to achieve common objectives). The assessment of the fee system coherence is addressed: (i) internally (e.g. fee structure, remuneration levels) and (ii) with other EU policies.

#### **EQ10: To what extent is the fee system coherent internally?**

The fee system is overall coherent. Besides minor aspects, the Fee Regulation and its Implementing Rules are internally coherent. However, the Fee Regulation and the Pharmacovigilance Fee Regulation present some inconsistency in the approach to the calculation of fees and remunerations, as well as in the application of the incentives. The total fees charged for procedural activities align with the total costs for undertaking the activities. However, as noted elsewhere, the fee system is not cost-based at the level of specific activities. This contradicts the Fee Regulation which requires that the calculation of the amount of fees charged by the Agency must be based on the principle of the service actually provided. Finally, the current fee system is not coherent with the recent legislative amendments to the definition of sources of revenue for the Agency in the EMA Founding Regulation.

<sup>142</sup> In case T=573/10 the General Court clarified that the invoice sent by EMA to undertakings is an act/measure that can be subject to an action for annulment before the EU courts.

<sup>143</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system - Final report: page 94

This question is addressed by looking at the internal coherence of the fee system in terms of the fees charged, the internal coherence of the fee system in terms of the remuneration provided and internal coherence of the fee system in terms of the Agency's strategy and objectives.

Following recent changes to the regulatory framework of the EMA, there are elements of incoherence between the fee system and some of the new provisions introduced. The recent amendment of the Founding Regulation has redefined the sources of the Agency's revenue. Mainly, it recognised the possibility for the Agency to use also 'charges for other services' as a source of revenue. Currently the fee regulations of EMA do not include charges; such category could replace some of the existing fees or new charges could be added to the existing fees.

Overall, the Fee Regulation and its Implementing Rules are internally coherent. However, minor aspects of incoherence between the documents have been identified in relation to some of the wording used. The Fee Regulation introduces the term 'basic fee', which is 'the fee charged for the initial application for an authorization for a medicinal product plus a fee for each different strength and/or pharmaceutical form'. The Implementing Rules, however, uses 'applicable full fee' to describe initial application fees. The Fee Regulation also sets out that 'a ceiling should be established' for the fees for each additional strength and/or pharmaceutical form; however, no specification of such limits were found in the Implementing Rules.

The Pharmacovigilance Fee Regulation and the Fee Regulation on the general fees payable are generally coherent but present a number of inconsistencies. The two legal instruments show differences in the approach to calculation of fees and remunerations, as well as in the implementation of incentives. Unlike the Fee Regulation, the Pharmacovigilance Fee Regulation is not complemented by implementing rules. Instead, it includes the rules for fees, the fees to be charged to industry, applicable fee incentives for SMEs as well as the share of fees for rapporteurs and co-rapporteurs. By contrast, rules on NCA remuneration and fee incentives for SMEs are not addressed in the Fee Regulation at all, but are listed in the Implementing Rules (NCA remuneration and SME fee incentives) and in the SME Regulation (SME fee incentives). This situation affects the internal coherence in terms of measures and flexibility to govern those aspects within the EMA fee system; whereas a change in rules on and levels of NCA remuneration and SME incentives for pharmacovigilance activities require a co-decision procedure via Council and Parliament, for non-pharmacovigilance activities such change is decided on by EMA's Management Board, with the exception of incentives specified in the SME Regulation. Furthermore, for fees under the Fee Regulation, incentives are applied after remuneration to NCAs, leaving the related financial burden on EMA, whilst for fees under the Pharmacovigilance Fee Regulation the burden is shared between EMA and NCAs, with incentives applied before the remuneration for NCAs is calculated.

The Fee Regulation requires that the calculation of the amount of fees charged by the Agency must be based on the principle of the service actually provided. The fee system is not fully coherent with this provision. Although the total fees charged for procedural

activities align with the total costs of EMA and NCAs for undertaking the activities, at the individual activity level fees and costs are not always aligned. As discussed under EQ1, for some activities fees exceed total costs to EMA and NCAs for undertaking these activities whereas for others fees fall short of costs. In addition, some activities for which EMA and NCAs incur costs are free of charge.

No incoherence was found regarding the fee system, remuneration provided and the legislation determining the remuneration to NCAs. EMA, NCA and wider stakeholders did not refer to any inconsistencies regarding the fee system, the remuneration provided and the legislation. Similarly, a review of the Fee Regulation, the Implementing Rules and the Founding Regulation did not show any incoherence.

The Implementing Rules provide a list of activities for both the human medicines sector and the veterinary sector, for which rapporteurs and co-rapporteurs together receive 50% of the fees. Setting the remuneration amounts in the Implementing Rules corresponds with the general requirement in the Founding Regulation to provide remuneration for scientific services provided by NCAs. However, although NCAs receive the full (non-reduced) share of the fee for activities related to the general Fee Regulation regardless of exemptions or reductions, NCA interviewees noted that they do not receive remuneration for some scientific services provided, such as assessments related to applications for orphan designation, PIPs and MUMs/limited market. In that respect, the internal coherence with the abovementioned general requirement is negatively affected and may be improved.

#### **EQ11: To what extent is the fee system coherent with Member State fee systems?**

There is no evidence of overlaps or gaps between fees charged by EMA and fees charged by Member States for national activities.

The question is addressed by looking at whether the fee system is consistent and does not overlap with national fees.

There is no evidence regarding an overlap or gaps between fees for EMA-requested activities and fees charged for national activities. Views of EMA representatives, NCA interviewees and consultees as well as wider stakeholder survey respondents indicate that the fees charged for EMA-related activities do not overlap with fees charged for national activities. A review of the Fee Regulation and Implementing Rules does not indicate any potential overlaps between EMA and national fees. The Pharmacovigilance Fee Regulation determines that Member States should ‘not levy fees for the activities which are covered by Regulation (EU) No 658/2014’ and thus should not charge marketing authorisations twice for the same activity.<sup>144</sup> NCA interviewees confirmed that there is no

<sup>144</sup> Recital 8 of Regulation (EU) No 658/2014 provides: ‘This Regulation should only regulate fees which are to be levied by the Agency, whereas the competence to decide on possible fees levied by the national competent authorities should remain with the Member States, including in relation to signal detection tasks. Marketing authorisation holders should not be charged twice for the same pharmacovigilance activity. Member States should therefore not levy fees for the activities which are covered by this Regulation.’ This is consistent with Recital 24 of the Pharmacovigilance Regulation

double-charging for the activities regulated by the Fee Regulation nor for pharmacovigilance activities.

**EQ12: To what extent is the fee system coherent at EU level and with other EU policies?**

Overall, the fee system is coherent with sectorial and cross-cutting legislation. However, the fee system is not coherent with the new provisions introduced by the recent VMP Regulation. In addition, scientific experts supporting the PDCO are not compensated for their scientific support, contrary to the spirit of the legislative provision in the Paediatric Regulation. There is external coherence of the fee system with priorities set out in EU policies on SMEs and health.

The question is addressed by looking at the coherence of the EMA fee system with other sectorial and cross-cutting legislation, with similar European agencies, as well as with requirements set out in overarching EU policies.

The European Commission considers SMEs to be important players to ensure employment as well as to sustain and support wellbeing of EU citizens. The EU policy on SMEs sets out principles to ensure SME support such as the creation of an SME-friendly environment, financial incentives, and administrative support to SMEs. The current EMA fee system is coherent with this EU policy. More specifically, the SME Regulation outlines administrative support measures offered to micro enterprises and SMEs, such as the establishment of an SME office, the provision of workshops and training sessions, and the publication of a User Guide for SMEs. Further, the fee system provides for a wide range of fee incentives for SMEs. These are laid down in the SME Regulation, the Pharmacovigilance Fee Regulation and the Implementing Rules of the Fee Regulation. Overall, the fee system is also coherent with the sectorial legislation ruling the application of incentives for specific types of product.

The Orphan Regulation provides that ‘in order to facilitate the granting or the maintenance of a Community authorisation, fees to be paid to the Agency should be waived at least in part; the Community budget should compensate the Agency for the loss in revenue thus occasioned’. The implemented fee system is coherent with this provision. The existence of a dedicated EU contribution for orphan medicines complements the coherent implementation of the provisions set in legislation.

The fee system has been implemented to some extent in coherence with the Paediatric Regulation. This Regulation provides that the amount of the reduced fees for the examination of the application and the maintenance of a paediatric use marketing authorisation shall be fixed in accordance with the Founding Regulation.<sup>145</sup> In accordance with this provision, such reductions are specified in Annex VII of the Implementing

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(Regulation (EU) No 1235/2010) stating that EMA fees covering tasks of the Agency with regard to pharmacovigilance should not cover tasks carried out by NCAs for which such authorities charge fees.

<sup>145</sup> Article 47(1) of Regulation (EC) No 1901/2006.



Rules. However, the fee system's rules on NCA remuneration are not fully coherent with the Paediatric Regulation. This Regulation foresees that the general EU contribution shall cover the work of the PDCO and of the Agency; this includes scientific support provided by experts, the assessment of PIPs, scientific advice and any fee waivers provided for in that Regulation.<sup>146</sup> However, specific provisions for the remuneration of experts for their scientific support within this committee was never put in place, and currently the work on procedures undertaken by NCAs under this remit remains unremunerated (as shown in Section 3).

Finally, there is coherence also with the incentives applicable to ATMPs. Specific reduction rates for scientific advice and for marketing authorisation are provided by the ATMP Regulation<sup>147</sup> and are duly reflected in the Implementing Rules, as shown in Annex 7.

On the other hand, incoherence exists between the fee system and some of the new provisions introduced following the recent adoption of the VMP Regulation. The new regulation introduced substantial changes in the categorisation of procedures for the assessment and monitoring of veterinary medicinal products, especially for post-authorisation. The current fee system is not adapted to accommodate these changes as it may not provide relevant fees by EMA and remuneration paid to NCAs for regulatory procedures introduced or amended by the VMP Regulation.

The EMA fee system approach to the level of the fees in relation to costs is similar to those of ECHA and EASA. The Fee Regulation provides that the level of the fee charged by EMA should relate to the service actually provided. Rules on fees and charges payable to ECHA specify that the structure and amount of the fees provided need to take account of the work required to be carried out by ECHA and the competent authorities and should be fixed at such a level as to ensure that the revenue derived from them when combined with other sources of ECHA's revenue is sufficient to cover the cost of the services delivered. Similarly, EASA's tariffs need to be adjusted in order to ensure a balance between the costs incurred by EASA for related certification tasks and services provided, and the revenues to cover said costs. However, ECHA and EASA's approaches are more flexible in terms of adjusting the level of the fees to balance costs. Whereas ECHA and EASA fees can be adjusted via Commission measures, changing the level of EMA fees requires a co-decision procedure via Council and European Parliament.<sup>148</sup> ECHA fees were adjusted most recently in June 2018: application for authorisation fees were changed to 'better account of the amount of work involved in assessing the applications'.<sup>149</sup> The revision brought increased fees for each additional use covered by

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<sup>146</sup> Article 48 of Regulation (EC) No 1901/2006.

<sup>147</sup> Respectively in Articles 16 and 19 of Regulation (EC) No 1394/2007.

<sup>148</sup> Note that changing the level of EMA fees in relation to the inflation rate does not require a co-decision procedure; this is achieved via a Commission procedure (for fees laid down in the Fee Regulation) or delegated act (for pharmacovigilance fees).

<sup>149</sup> [ECHA/NR/18/41](#)

an application, but fees for additional applicants were removed to encourage joint applications. This element of encouraging joint application reflects the comment received from industry and academic representatives to the online public consultation (already presented in EQ5) requiring more flexibility, among other things, also for sharing of costs between MAHs. The applicability of such a measure to the EMA fee system could be analysed for any future revision of its fee system.

Furthermore, the fee system is overall coherent with other existing EU policies.

General coherence was found between the EMA fee system and the four main objectives of the third EU health programme (2014-2020).<sup>150</sup> The two fee regulations include supportive measures for the promotion of health and disease prevention; in particular, fee reductions and exemptions for medicinal products for the treatment of rare diseases and for paediatric purposes as well as for advanced therapies can be considered as important elements for achieving the third EU health programme's first objective. Similarly, both legislations have elements consistent with the remaining objectives, such as the support for fee exemptions and reductions in emergency cases, such as threats to public and animal health, as well as support for public health capacity-building through the European Commission's main objective for establishing the EMA, that is, to harmonise the regulation of medicines across the European Union and 'to improve the operation of the authorisation procedures for the placing of medicinal products on the market in the Community' (Regulation (EC) No 726/2004, L 136/1).

Similarly, the fee system is coherent with the priorities set out in the Strategic Plan of DG Health & Food Safety for 2016 to 2020.<sup>151</sup> The current fee system includes adequate measures including fee incentives to address threats to public health, including cross-border health problems. Furthermore, the EMA fee system's incentives and support measures for SMEs – which should particularly promote the development of innovative medicinal products by SMEs – as well as EMA's PRIME scheme and its related fee incentives indicate that the current fee system is overall aligned with DG Health & Food Safety's innovation priority. While health technology assessment (HTA) is not addressed in the current legislation on fees payable to the EMA, EMA interviewees and EMA-related documents and strategies show that the Agency has been collaborating with HTA

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<sup>150</sup> Regulation (EU) No 282/2014, L 86/6–7:

- to promote health, prevent diseases, and foster supportive environments for healthy lifestyles [...].
- [...] to protect Union citizens from serious cross-border health threats [...].
- [...] to support public health capacity-building and contribute to innovative, efficient and sustainable health systems [...].
- [...] to facilitate access to better and safer healthcare for Union citizens'

<sup>151</sup> DG Health & Food Safety 2016, 13–24:

- Specific objective 1.1: Better preparedness, prevention and response to human, animal and plant health threats.
- Specific objective 1.4: Effective, accessible and resilient EU healthcare systems.
- Specific objective 1.7: Increased EU influence in international fora.
- Specific objective 2.1: Effective EU assessment of medical products and other treatment.
- Specific objective 2.2: Stable legal environment and optimal use of current authorisation procedures for a competitive pharmaceutical sector and patients' access to safe medicines.

bodies since 2008 and intends to increase such engagement, reflecting one of the DG Health & Food Safety priorities.

## 6. CONCLUSIONS

Strengths and weaknesses of the current fee system have been assessed to show the extent to which fees and remuneration are founded on a sound economic basis, whether they are fair and proportionate, and whether the fee system avoids unnecessary administrative burden on fee payers. These questions were addressed with reference to four main evaluation criteria: effectiveness and efficiency, relevance, and coherence.

The key cross-cutting conclusions of the evaluation, taking into account the outcome of the study supporting the evaluation, are presented below per evaluation criterion.

➤ **The current fee system is generally efficient and effective but it is not cost-based at a granular level:**

The fee system allows EMA to meet its costs after remunerating NCAs, and there is no evidence that the EMA is hindered in its activities by the existing arrangements. EMA relies on both industry fees and EU budget contributions to meet its costs.

Total remuneration provided to NCAs covers the aggregate cost of their procedural activities and almost half of their aggregate costs for the additional activities they reported to undertake. However, if the total costs of such additional activities and the aggregate cost for their involvement in committees and working groups outside procedures were to be taken into consideration, the current aggregate remuneration would no longer be sufficient. Whether and to what extent these additional activities and the involvement in committees and working groups should be covered by EMA remuneration is still to be assessed.

At individual NCA level, there is a high degree of variation in the extent to which remuneration aligns with costs. NCAs that undertake veterinary activities only are less likely to cover their costs.

**At a granular level, the current fee system is not cost-based.** There are many different procedural activities. Fees for some procedures exceed the total EMA and NCA costs of delivering them. Fees for some other procedures fall short of costs. Furthermore, there are no fees for some procedural activities, especially with regards to PDCO and COMP related procedures.

Some fees may have incentives applied, or be exempted, for certain types of medicines and certain types of entities. Incentives and exemptions, and misalignment between fees and costs, result in activities for which costs cannot be covered (fully or at all) by fees. Hence, other sources of income, such as annual fees, support covering the costs for undertaking these activities, both for EMA and for NCAs. For veterinary medicines, average incentives are generally higher than for human medicines.

Fees are not always shared between EMA and NCAs in proportion to their respective costs incurred for delivering the activities.

**The fee system is complex and would benefit from streamlining.** The main Fee Regulation has not been amended since 2005. In the meantime, several pieces of sectorial legislation have been introduced establishing additional fee incentives. In addition, the introduction in 2014 of the Pharmacovigilance Fee Regulation expanded the fee system and added to the overall complexity.

Despite the complexity, the fee system is generally found understandable and fairly transparent. Minor operational areas needing more transparency have been highlighted by some stakeholders, especially in terms of provision of a detailed breakdown of the amounts charged to applicants as well as of the remunerations paid to NCAs.

**The current fee system provides a level of flexibility that is sufficient for the current operations of EMA and NCAs but it might not be enough to guarantee their future sustainability.** In particular, the flexibility to fund some non-fee generating or unremunerated activities, as well as incentives for specific medicinal products, such as orphan medicines, products for paediatric use and advanced therapies, as well as support for SMEs are considered to be essential. Equally, the lower fee levels for veterinary products, albeit not aligned to costs at the granular level, are viewed as important in order to support their development, bearing in mind the specificities of the veterinary sector.

However, the fee system lacks flexibility to address variance in workload needed to accomplish activities, mainly when it comes to new innovative products and general advances in science. This may be a challenge for future sustainability of the EMA including remuneration of NCAs. Hence, the fee system needs to provide more flexibility in order to accommodate future changes in the regulatory system.

➤ **The current fee system is still relevant in relation to the need originally identified to provide a sound financial basis to EMA for its operation, including remunerating NCAs, but does not fully respond to some of the current needs:**

In particular, the funding model based both on fee income paid by industry applicants and EU contributions is considered relevant. The fee system is also relevant regarding the need to remunerate NCAs for undertaking EMA-related activities, although the fee charged and remuneration provided are not cost-based across all activities. The current fee system overall meets the originally identified need to provide lower fees for activities for veterinary medicinal products due to their specificities; however, there are indications that such lower fees are not aligned with the cost and complexity of services provided. Alignment was also found between the original requirement to offer incentives to respond to public or animal health threats and the current fee system.

The need to minimise the administrative burden is still relevant but not fully met by the current system. The introduction of various cross-cutting and sectorial pieces of legislation and the separate pharmacovigilance fee legislation, made the overall system complex and heavy to implement. Furthermore, the current fee system is not fully relevant in its capacity to respond and adapt to the increasing complexity of the activities undertaken stemming from advances in science.

➤ **The fee system has elements of internal and external incoherence that need to be addressed in order to support the functioning of the regulatory system in future:**

Whilst being overall internally coherent with the Implementing Rules, the Fee Regulation has elements of incoherence with the Pharmacovigilance Fee Regulation and the recently revised Founding Regulation, specifically with Article 67(3) detailing the sources of revenue for the EMA.

Furthermore, considering that, as already noted, the fee system is not cost-based at the level of specific activities, internal coherence with the requirement that ‘the calculation of the amount of fees charged by the Agency must be based on the principle of the service actually provided’ may be improved at the level of procedures.

From an external coherence point of view, the fee system is coherent with sectorial and cross-cutting legislation, with the exception of the Paediatric Regulation where there are some elements of incoherence in terms of providing remuneration to NCAs experts for their scientific support.

Furthermore, the system is not aligned with the new provisions introduced by the recent VMP Regulation. That regulation foresees changes to regulatory procedures for which there may not be fees. In addition, the VMP Regulation broadens the scope of veterinary medicinal products eligible for the centralised procedure. This may affect EMA income and NCA remuneration as well as their costs related to veterinary activities. The relationship of the VMP Regulation with the current fee system therefore needs to be analysed. Such analysis was however outside of the scope of this evaluation and will be conducted separately.

If not addressed, these issues might impact in future EMA’s ability to meet its costs, including to provide an adequate cost-based remuneration to NCAs for their EMA activities.

# **Annex 1: Procedural information**

## **1. LEAD DG, DeCIDE PLANNING/CWP REFERENCES**

DG SANTE, Decide 2015/SANTE/683

## **2. ORGANISATION AND TIMING**

The evaluation project started in December 2016. The Inter-services steering group (ISSG) was composed of the following DGs: SANTE, RTD, SG, LS, BUDG, GROW. For the follow-up of the external study supporting the evaluation, the group met once in 2016 (kick-off) and twice in 2018 (interim and final report). This Staff Working Document was endorsed by the ISSG on 13 August 2019.

A written consultation with NCAs was held from April to May 2017 notably to collect cost data on involvement in EMA activities. Eight interviews with EMA representatives were conducted face-to-face at EMA headquarters in London during two day-long sessions (23 and 27 March 2017).

## **3. EXCEPTIONS TO THE BETTER REGULATION GUIDELINES**

The evaluation criterion ‘EU added value’ was considered not relevant for this evaluation; the EMA is a European decentralised Agency established under Union legislation (Regulation (EC) No 726/2004) and hence the decision on its funding and charging of fees is to be taken at the EU level. Only the Union can act to enable the Agency to charge fees.

The assessment of effectiveness was based on the extent to which the objectives of the fee system have been achieved, i.e. allowing the EMA to perform its tasks and to remunerate NCAs adequately, being fair and transparent, being flexible and supporting SMEs. In this case, effectiveness is closely tied to efficiency and these criteria are therefore considered together. An efficiency assessment should consider the relationship between the resources used by an intervention and the changes generated by the intervention as well as the costs and benefits of the EU intervention as they accrue to different stakeholders. Efficiency has thus been assessed by examining the relationship between costs and fees for the activities covered by the EMA.

## **4. CONSULTATION OF THE RSB (IF APPLICABLE)**

N/A

## **5. EVIDENCE, SOURCES AND QUALITY**

The evaluation was supported by an external study performed by RAND Europe. This study used the outcome of a data gathering by the EMA Management Board (MBDG) on time data for EMA procedures. A validation of that data was performed by the contractor.

Further, the study included targeted consultations with EMA and NCAs on their costs. In the case of EMA, unitary cost data supplied by EMA was applied to the procedural activities and separate cost data was supplied by EMA on groups of crosscutting activities. In the case of NCAs, only the part of their overall costs dedicated to contributing to EMA activities was considered. The overall yearly costs of NCAs to contribute to EMA were declared by NCAs and the part of that cost dedicated to procedures and to preparing and attending EMA committees and working groups (outside being rapporteur and co-rapporteur) was calculated based on time data from the MBDG and data on yearly frequency of procedures provided both by EMA and NCAs. The difference between the total cost declared by NCAs and these two categories of costs was considered to be the costs for 'additional activities' of NCAs in relation to EMA. These additional activities and their associated costs were not further studied in the evaluation.



## Annex 2: List of EU/EEA NCAs

Name of agency	State	Area of responsibility: human (H) or veterinary (V) health	Responded to survey: Y/N	Interview: Y/N
<b>Austrian Medicines and Medical Devices Agency (AGES MEA) – Austrian Federal Office for Safety in Health Care (BASG)</b>	Austria	H + V	Y	Y
<b>Federal Agency for Medicines and Health Products (FAMHP)</b>	Belgium	H + V	Y	N
<b>Bulgarian Drug Agency (BDA)</b>	Bulgaria	H	N	N
<b>Bulgarian Food Safety Agency (BFSA)</b>	Bulgaria	V	N	N
<b>Agency for Medicinal Products and Medical Devices (HALMED)</b>	Croatia	H	Y	N
<b>Ministry of Agriculture – Veterinary and food safety directorate</b>	Croatia	V	N	N
<b>Ministry of Health – Pharmaceutical Services</b>	Cyprus	H	N	N
<b>Ministry of Agriculture, Natural Resources and Environment - Veterinary Services</b>	Cyprus	V	N	N
<b>State Institute for Drug Control (SÚKL)</b>	Czech Republic	H	Y	Y
<b>Institute for State Control of Veterinary Biologicals and Medicines (USKVBL)</b>	Czech Republic	V	N	N
<b>Danish Medicines Agency (DKMA)</b>	Denmark	H + V	Y	N
<b>State Agency of Medicines (Ravimiamet)</b>	Estonia	H + V	Y	N
<b>Finnish Medicines Agency (Fimea)</b>	Finland	H + V	Y	N
<b>National Agency for the Safety of Medicine and Health Products (ANSM)</b>	France	H	N	N
<b>French Agency for Food, Environmental and Occupational Health &amp; Safety (ANSES) - French Agency for Veterinary Medicinal Products (ANMV)</b>	France	V	Y	Y
<b>Federal Institute for Drugs and Medical Devices (BfArM)</b>	Germany	H	Y	Y

Name of agency	State	Area of responsibility: human (H) or veterinary (V) health	Responded to survey: Y/N	Interview: Y/N
<b>Paul Ehrlich Institute (PEI)</b>	Germany	H + V	Y	Y
<b>Federal Office of Consumer Protection and Food Safety (BVL)</b>	Germany	V	Y	N
<b>National Organization for Medicines (EOF)</b>	Greece	H + V	Y	N
<b>National Institute of Pharmacy and Nutrition (OGÉYI)</b>	Hungary	H	Y	Y
<b>Directorate of Veterinary Medicinal Products</b>	Hungary	V	N	N
<b>Icelandic Medicines Agency (IMA)</b>	Iceland	H + V	N	N
<b>Health Products Regulatory Authority (HPRA)</b>	Ireland	H + V	Y	Y
<b>Department of Agriculture, Food and the Marine</b>	Ireland	V	N	N
<b>Italian Medicines Agency (AIFA)</b>	Italy	H	Y	N
<b>Ministry of Health – Directorate General for Animal Health and Veterinary Medicines</b>	Italy	V	Y	N
<b>Food and Veterinary Service (PVD)</b>	Latvia	V	Y	N
<b>State Agency of Medicines (ZVA)</b>	Latvia	H	Y	N
<b>Office of Health</b>	Liechtenstein	H + V	N	N
<b>State Medicines Control Agency (VVKT)</b>	Lithuania	H	Y	N
<b>State Food and Veterinary Service (VVT)</b>	Lithuania	V	N	N
<b>National Food and Veterinary Risk Assessment Institute (NMVRVI)</b>	Lithuania	V	Y	N
<b>Ministry of Health (MS)</b>	Luxembourg	H + V	N	N
<b>Medicines Authority</b>	Malta	H	Y	N
<b>Veterinary Medicines Section within the Veterinary and Phytosanitary Regulation Division</b>	Malta	V	N	N
<b>Medicines Evaluation Board (MEB)</b>	Netherlands	H + V	Y	Y
<b>Healthcare Inspectorate</b>	Netherlands	H + V	N*	N

Name of agency	State	Area of responsibility: human (H) or veterinary (V) health	Responded to survey: Y/N	Interview: Y/N
<b>Norwegian Medicines Agency (NOMA)</b>	Norway	H + V	Y	N
<b>Office for Registration of medicinal Products, Medical Devices and Biocidal products</b>	Poland	H + V	N	N
<b>Chief Pharmaceutical Inspectorate</b>	Poland	H + V	N	N
<b>National Authority of Medicines and Health Products (Infarmed)</b>	Portugal	H	N	N
<b>National Authority for Animal Health (DGAV)</b>	Portugal	V	N	N
<b>National Medicines Agency (ANM)</b>	Romania	H	N	N
<b>Institute for Control of Biological Products and Veterinary Medicines (ICBMV)</b>	Romania	V	N	N
<b>State Institute for Drug Control (SÚKL)</b>	Slovakia	H	Y	N
<b>Institute for State Control of Veterinary Biologicals and Medicaments (UŠKVBL)</b>	Slovakia	V	N	N
<b>Agency for Medicinal Products and Medical Devices of the Republic of Slovenia (JAZMP)</b>	Slovenia	H + V	Y	N
<b>Spanish Agency for Medicines and Medical Devices / Spanish Agency for Medicines and Health Products (AEMPS)</b>	Spain	H + V	Y	Y
<b>Medical Products Agency (MPA)</b>	Sweden	H + V	Y	N
<b>Veterinary Medicines Directorate (VMD)</b>	United Kingdom	V	Y	N
<b>Medicines and Healthcare Products Regulatory Agency (MHRA)</b>	United Kingdom	H	Y	Y

\* In their response to the survey, the Medicines Evaluation Board in the Netherlands also included data for the Healthcare Inspectorate after having consulted with them.

## **Annex 3: The authorisation and monitoring of medicines in the EU**

### **1. THE MEDICINES REGULATORY NETWORK OF EMA, NCAs AND EC**

A medicinal product for human or veterinary use may only be placed on the market in the European Union (EU) when a marketing authorisation has been issued either by a competent authority of a Member State for its own territory (national procedure) or when an authorisation has been granted by the European Commission for the entire Union (centralised procedure). In addition, once a medicinal product has been authorised and placed on the market, its safety profile continues to be monitored throughout its entire lifespan (pharmacovigilance).

The system for regulating medicines in the EU is based on a closely-coordinated regulatory network of the European Medicines Agency (EMA) and National Competent Authorities (NCAs) in the European Economic Area (EEA) Member States working together with the European Commission. The main aim of the work undertaken by the network is to ensure that safe, effective and high-quality medicines are authorised in the EEA and to guarantee regulatory, scientific and technical information about medicinal products is available to patients, consumers and healthcare professionals.<sup>152</sup> In addition, the various actors within the network undertake a wide range of (regulatory) activities to facilitate the development of new, innovative products, to enable timely patient access to new medicines and to promote innovation and development of new medicines by micro, small and medium-sized enterprises (SMEs). Examples of such activities are the provision of scientific advice, the PRiority MEDicines (PRIME) scheme<sup>153</sup> and the provision of regulatory and administrative assistance to SMEs.

The **EMA** (or ‘the Agency’) is a decentralised agency of the EU, which was established in 1995 as the European Agency for the Evaluation of Medicinal Products (EMEA). The Agency is responsible for coordinating the existing scientific resources put at its disposal by the Member States for the evaluation, supervision and pharmacovigilance of medicinal products. It operates at the centre of the regulatory network, coordinating and supporting on a technical, scientific and administrative level interactions between over fifty NCAs for medicinal products for human and/or veterinary use. These include national medicines regulatory agencies and inspectorates (see Annex 2).

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<sup>152</sup> Articles 57 and 80 of Regulation (EC) No 726/2004, the Founding Regulation of the EMA.

<sup>153</sup> The voluntary scheme PRIME was launched by the EMA to provide early and proactive support for the development of medicines that target an unmet medical need in order to optimise development plans and, as such, the generation of robust data on the safety and efficacy of medicines, and in order to enable accelerated assessment so that medicines reach patients earlier. For more information, see EMA’s ‘Enhanced early dialogue to facilitate accelerated assessment of PRiority MEDicines (PRIME) ([EMA/CHMP/57760/2015, Rev. 1](#))

The EMA is headed by an Executive Director, who is responsible for all operational matters, staffing issues and drawing up the annual work programme.<sup>154</sup> The Executive Director is supported by a Secretariat, which provides technical, scientific and administrative support for EMA's scientific committees and technical and administrative support for the coordination group<sup>155</sup>. It also ensures appropriate coordination between the different committees and between the coordination group and the committees.<sup>156</sup> The EMA Management Board is the supervisory body of the EMA, consisting of 36 members appointed to act in the public interest.<sup>157</sup> The members are representatives of each Member State, the Commission, the European Parliament and patients', doctors' and veterinarians' organisations. It sets the Agency's budget, approves the annual work programme and is responsible for ensuring that the Agency works effectively and cooperates successfully with partner organisations both within and outside the EU. The Management Board also takes decisions on the rules and amounts for NCA remuneration in relation to services covered by the Fee Regulation (Council Regulation (EC) No 297/95) as well as on the general criteria of fee incentives granted by the Executive Director in exceptional circumstances and for imperative reasons of public or animal health (see Annexes 5 - 7 for more information on fees payable to the EMA, NCA remuneration and fee incentives).<sup>158</sup>

The EMA has seven scientific committees, established by Union legislation, which are responsible for the scientific work of the Agency. These committees are: the Committee for Medicinal Products for Human Use (CHMP), the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee for Medicinal Products for Veterinary Use (CVMP), the Committee for Orphan Medicinal Products (COMP), the Committee on Herbal Medicinal Products (HMPC), the Committee for Advanced Therapies (CAT), and the Paediatric Committee (PDCO). Each committee is composed of representatives appointed by each Member State. Additional members are appointed by the EMA for CHMP, CVMP and HMPC and by the Commission for PRAC, COMP, CAT and

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<sup>154</sup> Articles 56(1)(g) and 64 of Regulation (EC) No 726/2004

<sup>155</sup> The coordination groups for human medicinal products (CMDh) and veterinary medicinal products (CMDv) were set up for the examination of any questions relating to nationally authorised medicinal products, specifically related to disagreements on the grounds of potential serious risks to public health between Member States on pending initial marketing authorisation and variation procedures. The tasks also include certain pharmacovigilance activities related to nationally authorised products.

<sup>156</sup> Article 56(1)(f) of Regulation (EC) No 726/2004

<sup>157</sup> Article 63(2) of Regulation (EC) No 726/2004 provides that Members of the Management Board, members of the committees, rapporteurs and experts 'shall undertake to act in the public interest and in an independent manner'. Article 65 further stipulates that the Management Board shall consist of one representative of each Member State, two representatives of the Commission and two representatives of the European Parliament. In addition, two representatives of patients' organisations, one representative of doctors' organisations and one representative of veterinarians' organisations shall be appointed by the Council in consultation with the European Parliament on the basis of a list drawn up by the Commission.

<sup>158</sup> Articles 65, 66 and 67 of Regulation (EC) No 726/2004 ; Articles 9 and 11(2) of Regulation (EC) No 297/95

PDCO.<sup>159</sup> The primary role of the committees is to evaluate applications for a marketing authorisation submitted through the centralised procedure. These evaluations provide the basis for the authorisation of medicines in the EU granted by the **European Commission**.<sup>160</sup> In addition, the Agency has numerous working parties, scientific advisory groups and other associated groups, which may be consulted by the committees on scientific issues relating to their particular field of expertise.<sup>161</sup> In addition to their primary role, the committees and working parties, together, contribute to the development of medicines and medicine regulation, by providing scientific advice to companies researching and developing new medicines, by preparing scientific guidelines and regulatory guidance to help companies prepare marketing authorisation applications, and by contributing to the harmonisation of regulatory requirements both in the EU and internationally.<sup>162</sup>

**Member States** supply the experts for the Agency's scientific committees, working parties and other expert groups. The vast majority of these experts come from **NCAs** in the Member States. These Member State experts are either nominated by the Member State itself or by the EMA. NCAs within the medicines regulatory network cooperate between themselves within the Heads of Medicines Agencies (HMA).<sup>163</sup>

The **European Commission** takes Union-wide binding decisions on the granting, varying or withdrawal of marketing authorisations based on scientific opinions provided by the Agency's scientific committees.

## **2. THE CENTRALISED PROCEDURE, NATIONAL PROCEDURES AND INSPECTIONS**

### **The centralised procedure**

The scope of the centralised procedure is defined in Article 3 and the Annex of Regulation (EC) No 726/2004<sup>164</sup>, the Founding Regulation of the EMA. Medicinal

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<sup>159</sup> Depending on the committee, these additional members may be representatives from patients' associations or healthcare professionals and/or independent scientific experts from Member States appointed to provide additional expertise in a particular scientific area.

<sup>160</sup> See Articles 56(1), 61 and 61a of Regulation (EC) No 726/2004, Article 4 of Regulation (EC) no 141/2000 ('the Orphan Regulation'), Articles 20 and 21 of Regulation (EC) No 1394/2007 ('the ATMP Regulation') and Chapter 2 of Regulation (EC) No 1901/2006 ('the Paediatric Regulation').

<sup>161</sup> In accordance with Articles 56(2) and 56(3) of Regulation (EC) No 726/2004, EMA's committees may establish standing and temporary working parties which they may consult on scientific issues and for providing scientific advice to undertakings as well as scientific advisory groups in connection with the evaluation of specific types of medicinal products or treatments.

<sup>162</sup> For more information, see the individual work plans of the committees as published on EMA's website under 'Committees' ([www.ema.europa.eu](http://www.ema.europa.eu)).

<sup>163</sup> More information on the HMA can be found on the [HMA website](#) (added link valid in May 2019).

<sup>164</sup> Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency: OJ L 136, 30.4.2004, p. 1–33

products falling within the defined scope of that Annex cannot be placed on the market unless a Union marketing authorisation has been granted (mandatory scope). In addition, any medicinal product not appearing in the Annex but falling within the scope of Articles 3(2) and 3(3) are eligible for the centralised procedure (non-mandatory scope).<sup>165</sup>

Under a centralised procedure, applicants submit a single application for a marketing authorisation. The application is reviewed by the relevant scientific committee of the EMA, which provides a scientific opinion on whether the product should be authorised. The committee's opinion is submitted to the European Commission, which then takes a decision on whether or not to grant the authorisation. This authorisation will be valid throughout the EU/EEA. Often, more than one committee is involved in the application review, in which case the main scientific committee reports back to the European Commission.

The responsible scientific committee appoints one of its members as rapporteur<sup>166</sup> to conduct the scientific assessment of a medicinal product. Depending on the type of regulatory procedure, the committee may also appoint another member from a different Member State to act as co-rapporteur. The scientific assessment is led by the rapporteur and co-rapporteur.<sup>167</sup> Further, for particular regulatory procedures, a third committee member from yet another Member State is appointed as CHMP/CVMP peer-reviewer that focusses on the quality of the list of questions compiled by the rapporteurs.<sup>168</sup> Committee members not appointed an official role as (co-)rapporteur or peer-reviewer may provide comments on the assessment of the (co-)rapporteur prior to discussion of the application in the relevant committee(s), in order to form a motivated opinion addressing

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<sup>165</sup> In accordance with Article 3(1) and the Annex of Regulation (EC) No 726/2004, medicinal products that need to be authorised by the Union are: (1) Medicinal products developed by means of one of the following biotechnological processes: recombinant DNA technology, controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells, hybridoma and monoclonal antibody methods; (2) Medicinal products for veterinary use intended primarily for use as performance enhancers in order to promote the growth of treated animals or to increase yields from treated animals; (3) Medicinal products for human use containing a new active substance which, on the date of entry into force of Regulation (EC) No 726/2004, was not authorised in the Union, for which the therapeutic indication is the treatment of any of the following diseases: acquired immune deficiency syndrome, cancer, neurodegenerative disorder, diabetes, autoimmune diseases and other immune dysfunctions, viral diseases; (4) Medicinal products that are designated as orphan medicinal products pursuant to Regulation (EC) No 141/2000. In addition, Article 3(2) and 3(3) provide that the centralised procedure is optional for: (i) Medicinal products containing a new active substance which, on the date of entry into force of this Regulation, was not authorised in the EU; (ii) Medicinal products that constitute a significant benefit, scientific or technical innovation or that are in the interests of patients or animal health at Union level; (iii) Generic medicinal products of a centrally authorised reference medicinal product.

<sup>166</sup> Depending on the type of regulatory activity, the rapporteur role could also encompass a coordinator or lead inspector role.

<sup>167</sup> Article 62(1) of Regulation (EC) No 726/2004

<sup>168</sup> Peer-reviewers are appointed for initial marketing authorisations and line extensions for human and veterinary medicinal products as well as for maximum residue limit applications and Article 34/35/45 referrals for veterinary medicinal products. In addition, in some cases a peer-reviewer may also be appointed for scientific advice/protocol assistance procedures for medicines for human use and Type II clinical variations for veterinary medicines. The role of peer-reviewer is not established by EU legislation.

potential weaknesses of the rapporteur's(s') assessment.<sup>169</sup> However, this is not common practice for all regulatory procedures, and per procedure usually only a small number of committee members provide such comments. The assessment and scientific opinion are discussed in and adopted by the relevant scientific committee(s).

Recently, a new concept on Member State cooperation has been introduced allowing the option of an assessment team to be formed from different NCAs. This multinational assessment team (MNAT) concept was formalised in the beginning of 2015 upon agreement of the Executive Director of the EMA. Its aim is to maximise the use of available resources and expertise within the network and to facilitate participation of NCAs in assessments allowing for expertise to be built up, while maintaining the high quality scientific work of the scientific committee. The current scope of the MNAT concept includes (co-)rapporteurships for the assessment of initial applications, scientific advice procedures, extensions of indication, and extensions of the marketing authorisation for human and veterinary medicines as well as the evaluation of maximum residue limit (MRL) applications and the addition of non-food target species for veterinary medicinal products.<sup>170</sup>

### **National procedures**

As indicated further above, the scope of the centralised procedure is defined in Article 3 and the Annex of the Founding Regulation. Medicinal products that are not eligible for the centralised procedure in accordance with this Annex can only be placed on the EU market upon authorisation by the competent authority of a Member State either through a purely national procedure or through a decentralised or mutual recognition procedure<sup>171</sup> under Directive 2001/83/EC<sup>172</sup> and Directive 2001/82/EC<sup>173</sup> for medicinal products for, respectively, human and veterinary use. Under a purely national procedure, new medicinal products are authorised by the NCA for its Member State's territory only, while under a decentralised procedure (DCP), products are authorised in several Member States in parallel. A mutual recognition procedure (MRP) enables authorisation of a medicinal product in one or more additional Member States based on an already existing

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<sup>169</sup> Member States not acting as rapporteur, co-rapporteur or peer-reviewer may provide comments on the assessments conducted by the rapporteur(s) prior to discussion in the relevant scientific committee(s). A timeslot for providing these comments is factored into the timetables of the different regulatory procedures. Providing comments is not an activity established by EU legislation.

<sup>170</sup> For more information on the centralised procedure, including the MNAT concept, please refer to the following EMA documents: '[Multinational assessment concept: The next phase – Broadening the concept to the post-authorisation phase \(EMA/619544/2016\)](#)' and '[Multinational assessment teams: guide for rapporteurs and coordinators \(EMA/486654/2016\)](#)'.

<sup>171</sup> Medicinal products authorised via the strictly national procedure, MRP or DCP are referred to in this document as nationally authorised products (NAPs).

<sup>172</sup> Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use: OJ L 311, 28.11.2001, p. 67–128

<sup>173</sup> Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products: OJ L 311, 28.11.2001, p. 1–66. This Directive will be repealed once the new Veterinary Medicinal Products Regulation (Regulation (EU) 2019/6) starts to apply (January 2022).



national authorisation in one Member State. For MRP and DCP, the assessment of the application is conducted by one Member State, which is acknowledged by the other concerned Member States.<sup>174</sup>

The role of the EMA in these national procedures is to provide technical and administrative support to the coordination groups for medicines for human and veterinary use of the Member States' authorities (CMDh and CMDv).<sup>175</sup> In addition, in case of disagreement between Member States on the assessment of a national application, the Agency, through its scientific committees, provides a scientific opinion on the topic at issue.<sup>176</sup> Further, the EMA has a role in assessing, through its committees, issues related to the post-authorisation safety monitoring of nationally authorised medicines (pharmacovigilance) when also one or more centrally authorised products are affected by that same procedure.<sup>177</sup>

### **Inspections**

All organisations, inside and outside the EU, involved in the development, marketing, manufacture and distribution of medicines for human and veterinary use are responsible for ensuring that they comply with all relevant standards set out in EU legislation and guidelines on pharmaceuticals.<sup>178</sup> Compliance with these standards is verified via inspections. The EMA is responsible for the coordination of inspections at Union level.<sup>179</sup> The responsibility of carrying out such inspections rests with the NCAs. The reporting national inspectorate is the leading inspectorate that takes the responsibility for organising, planning and reporting the inspection(s), acting as the main communication point between the inspection team and the Agency and, where applicable, writing and co-signing the integrated inspection report which summarises the critical and major findings of the inspection of several sites.<sup>180</sup>

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<sup>174</sup> For more information on national procedures, please refer to the HMA website ([www.hma.eu](http://www.hma.eu)) link valid in May 2019).

<sup>175</sup> Article 56(1)(f) of Regulation (EC) No 726/2004

<sup>176</sup> Articles 5(3) and 30(3) of Regulation (EC) No 726/2004

<sup>177</sup> Articles 57(1)(c) and 61a(6) of Regulation (EC) No 726/2004

<sup>178</sup> The relevant standards are Good Laboratory Practice (GLP), Good Clinical Practice (GCP), Good Manufacturing Practice (GMP), Good Pharmacovigilance Practice (GVP), and Good Distribution Practice (GDP). They define a set of rules and criteria for a quality system applicable to, respectively, the conduct of non-clinical and environmental studies, the conduct of clinical studies, manufacturing processes, the monitoring of medicine safety, and the supply chain of medicines.

<sup>179</sup> Article 57(1)(i) of Regulation (EC) No 726/2004

<sup>180</sup> Articles 8(2), 19(3), 33(2) and 44(3) of Regulation (EC) no 726/2004

## Annex 4: Legal and other provisions governing the EMA fee system and Union budget contributions

### 1. Current situation

The EMA charges fees to undertakings for obtaining and maintaining Union marketing authorisations and for other services provided by EMA and for certain pharmacovigilance services provided by the coordination group. The EMA also receives balancing EU and EEA budget contributions. Fee revenues and Union contributions currently provide the main financial basis for the work carried out by the EMA. Other sources of income constituting EMA's revenue are Union grants and charges (see further below). NCAs receive remuneration from the EMA, calculated as a share of the fees charged, for the scientific evaluations they carry out at Union level. The European Commission is part of the EU regulatory network of EMA and NCAs but its network-related activities are not covered by the EMA fee system.

The EMA fee system is established by EU legislation. The main legislative and non-legislative provisions governing EMA's fee system are laid down in:

- **The EMA Founding Regulation:** Regulation (EC) No 726/2004, which provides the sources of income constituting EMA's revenue (see further above) and which lays down that NCAs should be remunerated in accordance with a scale of fees established by the EMA Management Board;
- **The main Fee Regulation and its Implementing Rules:** Council Regulation (EC) No 297/95<sup>181</sup>, and its Implementing Rules<sup>182</sup>, which together provide the rules and amounts for fees charged to undertakings and for remuneration paid to NCAs for obtaining and maintaining Union marketing authorisations and for other services provided for centrally authorised medicines for human and veterinary use;
- **The Pharmacovigilance Fee Regulation:** Regulation (EU) No 658/2014<sup>183</sup>, which provides the rules and amounts for fees charged to industry and remuneration paid to NCAs for pharmacovigilance activities conducted at Union level for nationally and centrally authorised medicines for human use;
- **The SME Regulation:** Council Regulation (EC) No 2049/2005<sup>184</sup>, which provides the rules for and levels of fee incentives (partial and full fee waivers and

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<sup>181</sup> Council Regulation (EC) No 297/95 of 10 February 1995 on fees payable to the European Agency for the evaluation of medicinal products: OJ L 35, 15.2.1995, p. 1–5

<sup>182</sup> Rules for the implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures: [EMA/MB/57356/2018](#)

<sup>183</sup> Regulation (EU) No 658/2014 of the European Parliament and of the Council of 15 May 2014 on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use: OJ L 189, 27.6.2014, p. 112–127

<sup>184</sup> Council Regulation (EC) No 2049/2005 of 15 December 2005 laying down, pursuant to Regulation (EC) No 726/2004 of the European Parliament and of the Council, rules regarding the payment of fees

deferrals) for applicants fulfilling the definition of a micro, small or medium-sized enterprise (SME) as defined in Commission Recommendation 2003/361/EC<sup>185</sup>.

In addition, several pieces of sectorial legislation impact the fees charged to applicants, i.e. the Paediatric Regulation (Regulation (EC) No 1901/2006)<sup>186</sup>, the Orphan Regulation (Regulation (EC) No 141/2000)<sup>187</sup>, and the Advanced Therapy Medicinal Products (ATMPs) Regulation (Regulation (EC) No 1394/2007)<sup>188</sup>, which provide for fee incentives (partial and full fee waivers and deferrals) and activities exempted from fees for certain types of medicinal products. These sectorial legislative acts are not part of the EMA fee system. However, as they impact on fees charged and EMA and NCAs' income through fees, they are also listed here. To complete the list, decisions taken by the Executive Director of the EMA on fee incentives are included as well. These decisions can be amended, revoked or added at any point in time, changing the applicable types and levels of fee incentives and, thereby, the EMA fee system. More specifically:

**1) Provisions in Regulation (EC) No 726/2004** of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency ('the EMA Founding Regulation')<sup>189</sup>:

The EMA Founding Regulation lays down Union procedures for the authorisation, supervision and pharmacovigilance of medicinal products for human and veterinary use and indicates the need to establish a European Agency.<sup>190</sup>

Article 67(3) of this regulation provides that the revenue of the EMA shall consist of: (1) a contribution from the Union, (2) a contribution from third countries (EEA Member States) participating in the work of the Agency with which the Union has concluded international agreements for this purpose, (3) fees paid by undertakings (i) for obtaining and maintaining marketing authorisations and for other services provided by the Agency

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to, and the receipt of administrative assistance from, the European Medicines Agency by micro, small and medium-sized enterprises: OJ L 329, 16.12.2005, p. 4–7

<sup>185</sup> Commission Recommendation of 6 May 2003 concerning the definition of micro, small and medium-sized enterprises (2003/361/EC): OJ L 124, 20.5.2003, p. 36–41

<sup>186</sup> Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004: OJ L 378, 27.12.2006, p. 1–19

<sup>187</sup> Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products: OJ L 18, 22.1.2000, p. 1–5

<sup>188</sup> Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004: OJ L 324, 10.12.2007, p. 121–137

<sup>189</sup> OJ L 136, 30.4.2004, p. 1–33

<sup>190</sup> Regulation (EC) No 726/2004 repealed the 'EMEA Founding Regulation', Council Regulation (EEC) No 2309/93 (OJ L 214, 24.8.1993, p. 1–21). This Council Regulation provided in its Article 57 that the Agency should be funded by Union contributions and industry fees charged for obtaining and maintaining marketing authorisations.

in accordance with this Regulation or Regulation (EU) 2019/6<sup>191</sup> as well as (ii) for services provided by the coordination group as regards the fulfilment of its pharmacovigilance tasks<sup>192</sup>, (4) charges for other services provided by the EMA, and (5) Union funding in the form of grants for participation in research and assistance projects.

Article 67(3) further provides that the European Parliament and the Council ('the budgetary authority') shall re-examine, when necessary, the level of the Union contribution on the basis of an evaluation of needs and by taking account of the level of fees.

More specifically on fees, Articles 6(1) and 31(1)<sup>193</sup> of this regulation require that for human and veterinary medicinal products, respectively, any application for authorisation shall be accompanied by a fee payable to the Agency for evaluating the application. Article 67(4) provides that the Agency can charge fees to marketing authorisation holders for performing pharmacovigilance activities, provided that the independence of the Agency is strictly guaranteed. In accordance with Article 70(1), the level and structure of fees referred to in Article 67(3) shall be established by the Council on Commission proposal, once the latter has consulted pharmaceutical industry.

With regard to SMEs, Article 70(2) states that provisions shall be adopted by the Commission establishing the circumstances in which such companies may pay reduced fees, defer fee payment or receive administrative assistance.

On NCA remuneration, Article 62(3) provides that remuneration shall be paid for services provided by rapporteurs or experts in accordance with a scale of fees to be included in the financial arrangements established by the Management Board, and that the provisions of such services shall be governed by a written contract between the Agency and the rapporteur's or expert's employer.

Article 86a stipulates that, by 2019, the Commission should review the regulatory framework for fees payable to the Agency and put forward, as appropriate, legislative proposals with a view to update that framework. When reviewing the regulatory framework for fees payable to the Agency, the Commission should pay attention to potential risks related to the fluctuations in the fee revenue of the Agency.

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<sup>191</sup> Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC.

<sup>192</sup> These concern the following tasks in accordance with Directive 2001/83/EC and where only NAPs are involved: (1) determination of the harmonised frequency for submission of PSURs (Art. 107c), (2) appointment of the Member State responsible for the assessment of a PSUSA (Art. 107e), (3) decision on the maintenance, variation, suspension or revocation of a marketing authorisation following a PSUSA report from PRAC recommending action (Art. 107g), (4) decision on the maintenance, variation, suspension, revocation or refusal of the renewal of a marketing authorisation following a recommendation of the PRAC (Art. 107k) and agreement on the variation, suspension or revocation of a marketing authorisation following a PRAC recommendation on the outcome of a PASS (Art. 107q).

<sup>193</sup> Previously, Articles 6(3) and 28(3) of Council Regulation (EEC) No 2309/93.

**2) Council Regulation (EC) No 297/95** of 10 February 1995 on fees payable to the European Agency for the evaluation of Medicinal Products ('the Fee Regulation')<sup>194</sup> and its **Implementing Rules** adopted by the EMA Management Board<sup>195</sup>:

In the same year the EMA was established, the Fee Regulation was adopted, which lays down fees payable to the Agency for obtaining and maintaining Union marketing authorisations for medicinal products for human and veterinary use and for other services provided by the Agency. Since then, the Fee Regulation has been amended several times, mostly to adjust the fee levels in relation to the inflation rate. However, the number and types of fees charged were also changed twice, most recently in November 2005. In accordance with its Article 11 the Fee Regulation is accompanied by rules for implementation.

The Fee Regulation specifies in its Articles 3 – 8 the type of pre- and post-authorisation procedures for which fees shall be levied.<sup>196</sup> In addition, Articles 3(6) and 5(6) provide that an annual fee is to be charged for each marketing authorisation for a medicinal product for human or veterinary use. With regard to the level of the fees, the Fee Regulation stipulates in its recitals that the fees charged should be based on the service actually provided and that they should not be a determining factor for the applicant for an authorisation where there is a choice between the centralised and the national procedure.

In accordance with Article 9, in exceptional circumstances and for imperative reasons of public or animal health, fee reductions may be granted on a case-by-case basis by the Executive Director after consulting the competent scientific committee. This legal text specifically refers to orphan and compassionate use medicinal products, to veterinary products for diseases affecting minor animal species, or to an extension of an existing Maximum Residue Limit (MRL) to additional animal species. Further, Article 10 provides that deferral of payment is applicable to medicines to be used in a human pandemic situation until such situation is duly recognised by the World Health Organization (WHO) or the EU.

Recital 13 of the Fee Regulation further provides that a general reduction of fees payable for veterinary activities is justified considering that the market for veterinary medicines differs from that of medicines for human use. In accordance with this recital, procedural fees payable for veterinary activities are generally set in legislation at 50% of the level of

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<sup>194</sup> OJ L 35, 15.2.1995, p. 1–5

<sup>195</sup> Rules for the implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures ([EMA/MB/909612/2019](#))

<sup>196</sup> Fees shall be charged for the authorisation to market a medicinal product, for the extension, amendment, renewal or transfer of an existing marketing authorisation, for inspections within or outside the Union, for referral procedures, and for scientific advice for medicinal products for human and veterinary use. Further, fees shall be levied for the establishment of MRLs for veterinary medicines, for administrative services, and for scientific services including the evaluation of traditional herbal medicinal products, compassionate use opinions, consultation procedures for ancillary substances incorporated in medical devices and evaluation of plasma and vaccine antigen master files (PMF and VAMF).

fees for activities for human medicines, whereas those for annual fees are set at about one third of those for human medicinal products.

In accordance with Article 11 of the Fee Regulation, Implementing Rules are adopted by the EMA Management Board, following a favourable opinion from the European Commission. The Implementing Rules define at detailed level the structure of the fees payable to the Agency, rules for fee exemptions and reductions as well as rules for remuneration paid to NCAs for the provision of scientific services at EU level. The specific rules on the allocation of part of the resources deriving from annual fees levied under the Fee Regulation are set in Annex V and VI of the Implementing Rules.

Finally, Article 12 of the Fee Regulation specifies that the Commission shall review the fees annually by reference to the inflation rate as published in the Official Journal of the European Union and update them.

**3) Regulation (EU) No 658/2014** of the European Parliament and of the Council of 15 May 2014 on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use ('the Pharmacovigilance Fee Regulation')<sup>197</sup>:

Directive 2010/84/EU, Regulation (EU) No 1235/2010 and Commission Implementing Regulation (EU) No 520/2012 were adopted in 2010 and 2012, amending the existing legislative framework as regards pharmacovigilance. In 2014, the new pharmacovigilance legislation was complemented by the Pharmacovigilance Fee Regulation. The Pharmacovigilance Fee Regulation lays down the rules for the application of fees for pharmacovigilance activities relating to medicines for human use authorised in the Union under Regulation (EC) No 726/2004 (centrally authorised products (CAPs)) and Directive 2001/83/EC (nationally authorised products (NAPs)). Given that the 2010 pharmacovigilance legislation provides for a greater role for the EMA in the area of pharmacovigilance in general, i.e. irrespective of whether a medicinal product has been authorised via a Union procedure or a national procedure, the EMA was for the first time able to charge fees also for NAPs. Contrary to the main Fee Regulation, the Pharmacovigilance Fee Regulation is not accompanied by implementing rules, and all fee, incentive and remuneration levels are laid down in the legislation.

The Pharmacovigilance Fee Regulation stipulates that fees shall be levied for both CAPs and NAPs for the assessment of periodic safety update reports (PSURs), post-authorisation safety studies (PASS) and referrals initiated as a result of the evaluation of pharmacovigilance data. In addition, an annual fee for pharmacovigilance activities relating to IT systems and monitoring of selected medical literature shall be charged for NAPs but not CAPs. The Pharmacovigilance Fee Regulation also governs the rules for applying fee incentives (reduction or waiver of the full fee). With regard to the level of fees, it stipulates in Recital 6 that fees should be set at a level that avoids a deficit or a significant accumulation of surplus and that, therefore, they should be based on an

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<sup>197</sup> OJ L 189 27.6.2014, p. 112–127

evaluation of the Agency's and NCAs workload and related costs. Recital 7 provides that the fees should be transparent, fair and proportionate to the work carried out. In regards the structure of the fees, Recital 5 states that this should be as simple as possible to apply in order to minimise the related administrative burden.

Recital 8 further specifies that this regulation should only regulate fees which are to be levied by the Agency, whereas the competence to decide on possible fees levied by the NCAs should remain with the Member States, including in relation to signal detection tasks. MAHs should not be charged twice for the same pharmacovigilance activity; Member States should therefore not levy fees for the activities which are covered by this Regulation.

The regulation also provides that NCAs shall be remunerated when acting as rapporteur or co-rapporteur for fee-generating pharmacovigilance services, and that this remuneration shall be reduced proportionally when reductions or exemptions of fees have been applied. NCAs do not receive a share in the pharmacovigilance annual fee.

In regards incentives, reduced fees are set for SMEs, in line with the policy of the Union to support such enterprises.

Finally, Article 15(5) specifies that the amounts set out in the annex should be monitored annually by reference to the inflation rate, measured by means of the European Index of Consumer process published by Eurostat.

**4) Provisions in Commission Regulation (EC) No 2049/2005 of 15 December 2005 laying down, pursuant to Regulation (EC) No 726/2004 of the European Parliament and of the Council, rules regarding the payment of fees to, and the receipt of administrative assistance from, the European Medicines Agency by micro, small and medium-sized enterprises ('the SME Regulation')**<sup>198</sup>:

This Regulation establishes the circumstances under which, by derogation from the relevant provisions of the Fee Regulation, micro, small and medium-sized enterprises may pay reduced fees, defer payment of fees, or receive administrative assistance when submitting applications under the centralised procedures. More specifically, as provided for in Articles 5 to 8 of the SME Regulation, such enterprises can benefit from: fee deferrals for marketing authorisation applications and inspections; fee exemptions in case the marketing authorisation procedures ends negatively in case scientific advice was sought prior to the application; fee reductions in case of scientific advice, inspections, scientific services, administrative services, and MRLs.

The SME Regulation further provides in its Article 9 that where the applicant could, in respect of the same fee, also benefit from other reductions provided for in Union legislation, the provisions which are the most favourable to the applicant shall apply; cumulative fee reductions for a given fee and a given applicant shall not be allowed.

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<sup>198</sup> OJ L 329, 16.12.2005, p. 4–7, and OJ L 321M, 21.11.2006, p. 371–374



The SME Regulation also contains other provisions for the support of SMEs that are not fee-related, but those fall outside of the scope of the EMA fee system, and this evaluation, and are therefore not mentioned here.

5) Provisions in **Regulation (EC) No 141/2000** of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products ('the Orphan Regulation')<sup>199</sup>:

The purpose of the Orphan Regulation is to lay down a Union procedure for the designation of medicinal products as orphan medicinal products and to provide incentives for the research, development and placing on the market of designated orphan medicinal products.

Recital 7 provides that, in order to facilitate the granting or the maintenance of a Union authorisation, fees should be waived at least in part. The procedures to which fee incentives apply and the level of the incentive are not specified in the Orphan Regulation but determined via an Executive Director's decision, in accordance with Article 9 of the Fee Regulation. Further, Article 7(2) provides that a special contribution from the Union, distinct from the one established by the Founding Regulation, shall be allocated annually to the Agency. This specific orphan contribution shall be exclusively used to partially or fully waive industry fees related to orphan designated products, and any surplus occurring in a given year is to be carried forward and deducted from the special contribution for the following year.

6) Provisions in **Regulation (EC) No 1901/2006** of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004 ('the Paediatric Regulation')<sup>200</sup>:

This Regulation lays down rules concerning the development of paediatric medicinal products, without subjecting the paediatric population to unnecessary clinical trials. It stipulates in its Article 47(1) that a reduced fee shall be fixed for applications for paediatric use marketing authorisation. Additionally, in accordance with Article 47(3), assessments of new paediatric investigation plans (PIPs), PIP waivers, PIP deferrals and compliance with an agreed PIP should be free of charge. Further, Article 48 provides that the Union contribution provided for by the Founding Regulation shall cover the work of the Paediatric Committee and the Agency, including scientific support provided by experts, the assessment of PIPs, fee waivers for scientific advice, and information and transparency measures, including the database of paediatric studies and the network.

This regulation does not provide any further provisions on the level of fee incentives to paediatric medicines. These have been adopted by the Management Board in the Implementing Rules of the Fee Regulation.

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<sup>199</sup> OJ L 18, 22.1.2000, p. 1–5

<sup>200</sup> OJ L 378, 27.12.2006, p. 1–19



**7) Provisions in Regulation (EC) No 1394/2007** of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004 ('the advanced therapy medicinal products or ATMP Regulation')<sup>201</sup>:

The advanced therapy medicinal products (ATMP) Regulation lays down specific rules concerning the authorisation, supervision and pharmacovigilance of ATMPs. Article 16(2) of this Regulation stipulates the level of fee reductions applicable to scientific advice for ATMPs, providing a higher incentive rate for SMEs (90%) than for non-SMEs (65%). In addition, Article 19 provides for a 50% reduction of the fee for initial marketing authorisations, and for post-authorisation activities the first year after authorisation, if the applicant is a hospital or SME and can prove that there is a particular public health interest in the Community in the ATMP concerned. Further, Article 29 stipulates that no fee for an initial Union marketing authorisation application shall be levied on ATMPs that were already legally on the Union market in accordance with national or Community legislation on 30 December 2008.

**8) Decisions of the Executive Director of the EMA on incentives** related to PRIME (EMA/63484/2016), orphan medicinal products (EMA/317270/2014) and MUMS/limited market (EMA/308411/2014-Rev1)<sup>202</sup>:

The Executive Director has taken the following additional decisions on the application of incentives:

On PRiority MEDicines (PRIME) products: Fee waivers for scientific advice requests on medicinal products falling under the PRIME scheme shall be introduced for SMEs and applicants from academia/the academic sector.

On orphan medicinal products: A sponsor of an orphan medicinal product shall be eligible to a total or partial fee reduction once the decision on orphan medicinal product designation has been granted to that sponsor by the European Commission.

On minor use minor species (MUMS)/limited market: Financial incentives include partial and full fee waivers for scientific advice, maximum residue limit applications and marketing authorisation applications for MUMS/limited market medicinal products indicated in food producing species where no alternative product is authorised.

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<sup>201</sup> OJ L 324, 10.12.2007, p. 121–137

<sup>202</sup> Decision of the Executive Director on fee reductions for scientific advice requests on PRIME products for SMEs and applicants from the academic sector (EMA/63484/2016); Executive Director's decision on fee reductions for designated orphan medicinal products (EMA/317270/2014) ; Revised policy for classification and incentives for veterinary medicinal products indicated for minor use minor species (MUMS)/limited market (EMA/308411/2014-Rev.1)

## 2. Evolution of the EMA fee system

### 2.1. EM(E)A Founding Regulation

The Agency was established by Council Regulation (EEC) No 2309/93<sup>203</sup> as the European Agency for the Evaluation of Medicinal Products, also the European Medicines Evaluation Agency (EMEA), in order to harmonise the work of existing NCAs for medicinal products fulfilling the criteria listed in the Annex of that regulation<sup>204</sup>. The EMEA became fully operational in February 1995, the same month the main Fee Regulation was adopted (see under section 2.2 of this Annex).

Council Regulation (EEC) No 2309/93 ('the EMEA Founding Regulation') provided in its Articles 6 and 28 that applications for Union marketing authorisations for, respectively, human and veterinary medicines should be accompanied by a fee payable to the Agency for the examination of the application. Article 57(1) established that the Agency's revenue should consist of a Union contribution and fees paid by undertakings for obtaining and maintaining a Union marketing authorisation and for other services provided by the Agency. Article 58 provided that the structure and amount of these fees shall be established by the Council on a proposal from the Commission, following consultation with pharmaceutical industry. Finally, Article 53(3) stated that the provision of services by rapporteurs or experts shall be remunerated in accordance with a fixed scale of fees to be included in the financial arrangements established by the Management Board.

Regulation (EEC) No 2309/93 was repealed by Regulation (EC) No 726/2004, changing the name of the Agency to European Medicines Agency (EMA). Both the initial EMEA Founding Regulation and the new EMA Founding Regulation were amended several times extending the tasks of the Agency. In addition, with the entry into force of Regulation (EC) No 726/2004 in April 2004 more types of products became eligible for a Union marketing authorisation.<sup>205</sup>

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<sup>203</sup> Council Regulation (EEC) No 2309/93 of 22 July 1993 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products: OJ L 214, 24.8.1993, p. 1–21

<sup>204</sup> Council Regulation (EEC) No 2309/93 provided that the following medicines may only be placed on the market if a Community marketing authorisation had been granted in accordance with the regulation: (1) medicinal products developed by means of recombinant DNA technology, by means of controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells, or by means of hybridoma and monoclonal antibody methods, and (2) veterinary medicinal products intended primarily for use as performance enhancers in order to promote the growth of treated animals or to increase yields from treated animals.

<sup>205</sup> When entering into force in 2004, Regulation (EC) No 726/2004 (the EMA Founding Regulation) added to the existing scope of the Union marketing authorisation the following medicinal products: (1) human medicines containing a new active substance not yet authorised in the EU and indicated for treatment of AIDS, cancer, neurodegenerative disorder, diabetes, auto-immune diseases and other immune dysfunctions, and viral diseases; (2) orphan designated products. In addition, following the adoption of Regulation (EC) No 1394/2007 (the ATMP Regulation), the EMA Founding Regulation was amended to also include ATMPs.

The provisions in the EMA Founding Regulation related to the EMA fee system were adjusted twice. New 2010 pharmacovigilance legislation (see also under section 2.2 of this Annex) amended Article 67(3) of the Founding Regulation by adding that EMA's revenue should also consist of fees charged to undertakings for certain pharmacovigilance-related activities provided by the coordination group.<sup>206</sup> A recent amendment of the same Article 67(3) clarified that EMA's revenue consists of: (1) a contribution from the Union, (2) a contribution from third countries (EEA Member States) participating in the work of the Agency with which the Union has concluded international agreements for this purpose, (3) fees paid by undertakings (i) for obtaining and maintaining Union marketing authorisations for human and veterinary medicines and for other services provided by the Agency and (ii) for services provided by the coordination group as regards the fulfilment of its pharmacovigilance tasks, (4) charges for other services provided by the Agency, and (5) Union funding in the form of grants for participation in research and assistance projects.<sup>207</sup>

## 2.2. Fee Regulation and its Implementing Rules

In accordance with the provisions laid down in Articles 57(1) and 58 of the original EMEA Founding Regulation (see further above), Council Regulation (EC) No 297/95 ('the Fee Regulation') was adopted setting fees for human and veterinary medicines for the services provided by the Agency as described in Council Regulation (EEC) No 2309/93. When entering into force, the Fee Regulation provided that fees were payable to the Agency for applications for: an initial marketing authorisation; inspection; variation to or renewal, extension or transfer of an existing marketing authorisation; referral (arbitration); maximum residue limit (MRL) (veterinary medicines only). For initial marketing authorisations, reduced basic fees applied to applications for medicinal products which did not require a full dossier<sup>208</sup>. For veterinary vaccines, reduced fees applied to applications for and extension of a marketing authorisation. Altogether, the Fee Regulation recognised a total of 23 different basic fees ranging from ECU<sup>209</sup> 5,000 to

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<sup>206</sup> See Article 1(18)(a) of Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products. Via this article, Article 67(3) was amended to: 'The Agency's revenue shall consist of a contribution from the Union and fees paid by undertakings for obtaining and maintaining Union marketing authorisations and for other services provided by the Agency, or by the coordination group as regards the fulfilment of its tasks in accordance with Articles 107c, 107e, 107g, 107k and 107q of Directive 2001/83/EC.' (emphasis added)

<sup>207</sup> Amendment introduced by Regulation (EU) 2019/5: OJ L 4, 7.1.2019, p. 24–42

<sup>208</sup> More specifically, reduced fees applied to applications submitted in accordance with Article 4(8)(a) or (b) of Council Directive 65/65/EEC on the approximation of provisions laid down by law, regulation or administrative action relating to proprietary medicinal products (OJ 22, 9.2.1965, p. 369–373). This article provided that for certain types of medicines the results of pharmacological tests, toxicological tests and clinical trials may be substituted for published references or data.

<sup>209</sup> The European Currency Unit (ECU) was the official monetary unit of the European Communities. It was an artificial, electronic unit based on a basket of the national currencies of twelve EU Member States. The ECU was replaced by the euro on 1 January 1999 at the value of 1 EUR = 1 ECU.

ECU 140,000. Further, a supplementary fee could be charged for each additional strength or pharmaceutical form for applications of the same medicinal product, up to a certain ceiling specified in the Fee Regulation. This additional fee ranged from ECU 5,000 to ECU 20,000. The amounts for the different fees were determined based on the principle that they should not be a determining factor for the applicant for an authorisation where there is a choice between a centralised procedure and a national procedure<sup>210</sup>.

In accordance with Article 9 of the Fee Regulation the Management Board adopted Implementing Rules<sup>211</sup> laying down the due date for payable fees, the methods for payment, the consequences of belated payment or non-payment and any other measure needed to apply the Fee Regulation.

In its Article 7 the Fee Regulation also established that in exceptional circumstances and for imperative public or animal health reasons the Executive Director may grant on a case-by-case basis fee waivers and reductions for medicinal products with a limited number of applications. The general criteria of such incentives were to be determined by the Management Board. In accordance with this, the Management Board decided in December 1995 that fee waivers and reductions should only be available for orphan drugs for human use and comparable products for veterinary use, including the determination of certain MRLs of old products.<sup>212</sup> The Implementing Rules have been amended several times in regards the provision of partial or total fee reductions, changing levels for fee incentives and adding new ones. Some of these amendments were a direct consequence of changes in the Fee Regulation, as described above, or the adoption of relevant cross-cutting or sectorial legislation<sup>213</sup>. Others followed from budgetary decisions by the Management Board to ensure a balanced budget for the Agency.

Further, in accordance with Article 53(3) of the 1993 Founding Regulation (later repealed by Article 62(3) of Regulation (EC) No 726/2004) the Management Board decided in 1995 that 50% of the fees paid to the Agency would be allocated to the remuneration of NCAs for their scientific services (to be equally divided between the NCA of the rapporteur and co-rapporteur). It further agreed that direct payment to individuals should be excluded and that the financial relationship should instead be between the Agency and NCAs.<sup>214</sup> Total remuneration paid to NCAs in 1995 equalled ECU 3,6 million.<sup>215</sup>

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<sup>210</sup> See the recitals of the Fee Regulation.

<sup>211</sup> [EMA/MB/547356/2018](#)

<sup>212</sup> [First general report on the activities of the European Agency for the Evaluation of Medicinal Products of 1995, as adopted by the Management Board on 6 March 1996](#): page 13

<sup>213</sup> Note: also fee incentives fixed in type and level by such regulations and, hence, not decided on by the Management Board, are included in the Implementing Rules in order to create a complete overview for stakeholders.

<sup>214</sup> [First general report on the activities of the European Agency for the Evaluation of Medicinal Products of 1995, as adopted by the Management Board on 6 March 1996](#): page 14

<sup>215</sup> [Third general report on the activities of the European Agency for the Evaluation of Medicinal Products of 1997, as adopted by the Management Board on 3 December 1997](#): Annex 6

Since 1995, the Fee Regulation has been amended several times, mostly to adjust the fee levels in relation to the inflation rate. However, the structure of fees charged was also changed twice. The first amendment, which entered into force in January 1999, followed from a review in 1997 of the amounts and structure of the fees. It was concluded that although it was appropriate to maintain the general principles and overall structure of the fees as well as the main operational and procedural provisions, new fees needed to be established to cover all the services then provided by the Agency and to ensure coverage of costs connected with the supervision of authorised medicinal products. The amendments to the Fee Regulation concerned the addition of an annual fee for maintenance activities (e.g. development of central databases, safety monitoring), a fee for scientific advice and an administrative fee. The annual fee was set at ECU 20,000 and ECU 60,000 for respectively veterinary and human medicines. It was further specified that part of this fee would have to be allocated to NCAs in accordance with rules to be adopted by the Management Board<sup>216</sup>. In accordance with this, in February of 1999, the Management Board decided on a distribution of this fee whereby 30% is paid to the rapporteur and co-rapporteur (15% each) for the medicinal product concerned for the production of annual safety reports and other supervisory tasks<sup>217, 218</sup>. This decision was laid down in the Implementing Rules. Rules on NCA remuneration, both related to procedural and annual fees, included in the Implementing Rules have not changed since their introduction. The classification and levels of the administrative fees also needed to be specified by the Management Board and included in the Implementing Rules. However, the Fee Regulation specified that the amount of such fees may not exceed ECU 5,000.

The second amendment, which applied as of November 2005, was introduced to ensure cost coverage of new and changed tasks for EMA following changes in pharmaceutical legislation (the 1993 Founding Regulation was repealed by the 2004 Founding Regulation). Changes introduced in the Fee Regulation concerned the addition of a fee for scientific services and the replacement of a single fee for Type I variations by two separate fees for Type IA and Type IB variations.<sup>219</sup> In addition, it provided for inclusion of an indexation mechanism for automatically adjusting fees in relation to the inflation rate. In relation to fee incentives and reductions, the second amendment added that the Executive Director could also decide on waivers and reductions for orphan designated products, for medicines for MUMS, and for the addition of animal species in case of

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<sup>216</sup> Amended introduced by Council Regulation (EC) No 2743/98: OJ L 345, 19.12.1998, p. 3–8

<sup>217</sup> [Fifth general report on the activities of the European Agency for the Evaluation of Medicinal Products of 1999, as adopted by the Management Board on 1 December 1999](#): page 19

<sup>218</sup> Amending Council Regulation (EC) No 2743/98 provided in its recitals that '[w]hereas an annual fee must be introduced to ensure coverage of the costs connected with the supervision of authorised medicinal products; whereas a given part of this fee will have to be allocated to the competent national authorities required under the terms of Regulation (EEC) No 2309/93 to supervise the market on behalf of the Community; whereas, moreover, the rules for distribution amongst those authorities will have to be adopted by the Agency's Management Board in accordance with the procedure laid down in this Regulation'.

<sup>219</sup> Amendment introduced by Council Regulation (EC) No 1905/2005: OJ L 304, 23.11.2005, p. 1–9

determination of MRLs. In addition, the provision of reduced fees for veterinary vaccines was replaced by reduced fees for immunological veterinary medicines.

The amendments also gave additional flexibility to the Management Board and to the Executive Director of the EMA to adapt certain basic fee levels, under clearly-defined circumstances, to the particular situation of the application and the related product. The circumstances were to be included in the Implementing Rules.

The abovementioned changes led to a stark increase in the number of basic (full and reduced) fees applied through the fee system. Both amendments also changed the level of fees included in the Fee Regulation. Further, over the years the fee levels were increased in relation to the inflation rate.

### **2.3. Pharmacovigilance Fee Regulation**

In 2010 new pharmacovigilance legislation was adopted for medicines for human use authorised via the national or central procedure.<sup>220</sup> This legislation, which started to apply as of July 2012, brought significant changes in the safety monitoring of nationally and centrally authorised medicines for human use in the EU by introducing new and amended pharmacovigilance activities and by establishing a new EMA Committee, the Pharmacovigilance Risk Assessment Committee (PRAC). In regards to fees it provided that the EMA should be empowered to charge fees for pharmacovigilance activities to MAHs as well as fees in return for performing the activities of the coordination group within the Union system of pharmacovigilance. It also stipulated that rapporteurs within the coordination group should, in turn, be paid by the EMA. These provisions were adopted to facilitate adequate funding of pharmacovigilance activities and, thereby, to ensure the protection of public health. In accordance with these provisions, Regulation (EU) No 658/2014 ('the Pharmacovigilance Fee Regulation') was adopted, setting fees for pharmacovigilance activities at Union level in respect of medicines for human use.

It introduced fees for the assessment of periodic safety update reports (PSUR/PSUSA), post-authorisation safety studies (PASS) and pharmacovigilance referrals. The applicable fees were set at €19,500 for PSUR/PSUSA, €43,000 for PASS and €179,000 for referrals. The latter could be increased by €38,000 per each additional active substance or combination of active substances as of the third active substance or combination of substances, with a ceiling of €295,400.

An additional annual fee was established to finance EMA's pharmacovigilance activities relating to IT systems. This fee only applies to nationally authorised products, since for centrally authorised products these activities are already covered by the annual fee charged under the Fee Regulation. The amount payable for each market authorisation

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<sup>220</sup> Directive 2010/84/EU and Regulation (EU) 1235/2010 amended existing pharmacovigilance provisions in Directive 2001/83/EC and Regulation (EC) No 726/2004. This legislation was accompanied by Commission Implementing Regulation (EU) No 520/2012 on the performance of pharmacovigilance activities.

holder was set to depend on the number of ‘chargeable units’<sup>221</sup>, with a basic fee of €67 charged per chargeable unit.

The fees set out in this Regulation were based on an evaluation of the Agency’s estimations and forecasts as regards its workload and related costs, and on the basis of an evaluation of the costs of the work carried out by the NCAs.<sup>222</sup>

This regulation, unlike the main Fee Regulation, also establishes the level of remuneration to NCAs for their services provided. It further stipulates that where a fee reduction of exemption applies, NCA remuneration is reduced proportionally. This unlike fee reductions provided under the Fee Regulation or sectorial legislation, which do not affect NCA remuneration but only EMA fee income.

Unlike the Fee Regulation, the Pharmacovigilance Fee Regulation is not accompanied by implementing rules. Therefore, all provisions related to the type and level of basic fees, reduction of basic fees and NCA remuneration are laid down in (the Annex of) the regulation itself.

Since its adoption, the Pharmacovigilance Fee Regulation has been amended only to adjust fee levels to the inflation rate.

## **2.4. SME Regulation**

The EMA Founding Regulation specifies in Article 70(2) that, in order to reduce the costs for SMEs, provisions should be adopted to allow for a reduction of fees or deferral of the payment of fees. Following this provision, Commission Regulation (EC) No 2049/2005 (‘the SME Regulation’) was adopted, which entered into force in December 2005.<sup>223</sup> Experience gained since the Agency started operating showed that the main financial and administrative entry hurdles for SMEs are the various steps involved in pre-authorisation procedures, such as the seeking of scientific advice, the submission of the marketing authorisation application, and the undergoing of inspections. Provisions laid down in the SME Regulation are therefore focused on these aspects. In regards to fees, this regulation specifies both the services of EMA that should be incentivised for SMEs, the condition(s) under which the incentive is applicable and the level of the incentive (e.g. 90% of the full fee).

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<sup>221</sup> The chargeable unit was set to define, for the purposes of the Pharmacovigilance Fee Regulation, a marketing authorisation due to the lack of a harmonised definition across the EU. It is defined as a unique combination of the following dataset derived from information on all medicines authorised in the EU held by the Agency: (1) name of the medicinal product, as defined in point 20 of Article 1 of Directive 2001/83/EC; (2) marketing authorisation holder; (3) Member State in which the marketing authorisation is valid; (4) active substance or a combination of active substances; (5) pharmaceutical form.

<sup>222</sup> See Recital 6 of the Pharmacovigilance Fee Regulation

<sup>223</sup> Commission Regulation (EC) No 2049/2005 of 15 December 2005 laying down, pursuant to Regulation (EC) No 726/2005 of the European Parliament and of the Council, rules regarding the payment of fees to, and the receipt of administrative assistance from, the European Medicines Agency by micro, small and medium-sized enterprises: OJ L 329, 16.12.2005, p. 4–7

## 2.5. Sectorial legislation

Several pieces of sectorial legislation were adopted since the establishment of the EMA that impact its fee system in relation to fee incentives and the funding thereof as well as (the number of) non-fee-generating activities.

In the year 2000, Regulation (EC) No 141/2000 (the ‘Orphan Regulation’) entered into force.<sup>224</sup> It established the Committee for Orphan Medicinal Products (COMP) and introduced applications for orphan designation as new Union procedure. Its objective was to reduce costs for pharmaceutical industry of developing and bringing to the market of medicines for the treatment of rare diseases (orphan medicines) to ensure that patients suffering from such conditions receive the same quality of treatment as other patients. This regulation stipulates that in order to facilitate the granting or the possibility of obtaining a Union authorisation, fees should be waived at least in part. For this purpose, a specific Union orphan contribution was introduced to compensate the EMA for loss in revenue occasioned by partial or full fee waivers provided in relation to orphan designated products. This orphan contribution is distinct from the general Union contribution provided for in Article 67(3) of the Founding Regulation. The Orphan Regulation stipulates that any surplus occurring in a given year shall be carried forward and deducted from the orphan contribution for the following year.

In December 2006, Regulation (EC) No 1901/2006 (‘the Paediatric Regulation’)<sup>225</sup> was adopted with the aim to facilitate the development and accessibility of medicines for children as market forces so far had proven insufficient to stimulate adequate research into, and the development and authorisation of, medicinal products for the paediatric population. This regulation established the Paediatric Committee (PDCO) and introduced new Union procedures, i.e. applications for paediatric use marketing authorisation (PUMA) and paediatric investigation plan (PIP). In regards fees, it provides in its Articles 26 and 47 that scientific advice to sponsors developing medicines intended for use in children as well as procedures in relation to PIPs (i.e. new PIP, PIP waiver, PIP deferral, PIP compliance) should be free of charge. In regards to funding of the work of the PDCO, this regulation further stipulates that the general Union contribution provided for in Article 67(3) of the EMA Founding Regulation should cover the work of the PDCO, including scientific support provided by experts, and of the Agency resulting from the implementation of the Paediatric Regulation, including PIP assessments, scientific advice and any fee waivers provided for in that regulation.

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<sup>224</sup> Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products: OJ L 18, 22.1.2000, p. 1–5

<sup>225</sup> Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004: OJ L 378, 27.12.2006, p. 1–19



Finally, also in the year 2007, Regulation (EC) No 1394/2007 (the ‘ATMP Regulation’)<sup>226</sup> entered into force. It established the Committee for Advanced Therapies (CAT) and introduced recommendations of ATMP classification as new Union procedure. In its Recital 23 this regulation provides that the fee for scientific advice should be kept at a minimal level for SMEs, and should also be reduced for other applicants. In addition, Article 19 stipulates that the fee for marketing authorisation applications should be reduced by 50% for SMEs and hospitals for products with particular public health interests. This reduction should also apply to post-authorisation activities in the first year after the grant of the marketing authorisation.

It should be noted that, unlike with the 2010 pharmacovigilance legislation, the introduction of new EMA activities by above mentioned sectorial legislation was not followed by an amendment of the main Fee Regulation or the adoption of a separate, dedicated fee regulation. Further, none of the provisions in this sectorial legislation related to Union subsidies and fees were changed since their entry into force.

## **2.6. Decisions of the Executive Director**

As specified further above, the Fee Regulation provides that the Executive Director, after consultation of the competent Committee, may grant in exceptional circumstances and for imperative reasons of public or animal health waivers and fee reductions. It further stipulates that the Executive Director could also decide on waivers and reductions for orphan designated products, medicines for MUMS, and the addition of animal species in case of determination of MRLs. In accordance with these provisions, the following Decisions of the Executive Director were adopted defining the levels of fee incentives referred to in relevant legislation and adding new (temporary) fee incentives:

### No longer in force:

- *Decision of the EMA Executive Director on a 1-year initiative for fee reductions for notifications of parallel distribution (EMA/275221/20147: first published July 2017, last updated April 2018):* This Decision provided for fee incentives for parallel distribution in languages for which the population size is of such a size (i.e. less than 2 million) that the applicable full fee level might be an obstacle for parallel distribution in those languages. The duration of this initiative expired on 14 July 2018.

### Still in force:

- *Executive Director’s decision on fee reductions for orphan medicinal products (EMA/317270/2014: first published in February 2011, last updated in 2015):* This Decision specifies the type of services related to orphan designated products to which fee incentives should apply and the level of the applicable fee reductions. For instance, it specifies that for marketing authorisation applications SME’s should

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<sup>226</sup> Regulation (EC) No 1394/2007 of the European Parliament and of the Council of 13 November 2007 on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004: OJ L 324, 10.12.2007, p. 121–137

receive a 100% reduction of the full fee, whereas non-SMEs should be eligible for a 10% fee reduction.

- *Revised policy for classification and incentives for veterinary medicinal products indicated for MUMS/limited market (EMA/308411/2014: first published in September 2014, last updated in December 2018):* This Policy provides that financial incentives for MUMS/limited market medicines include free scientific advice and fee reductions for applications for establishing MRLs for minor species, fee waivers for applications for extensions of existing MRLs to include minor species and also fee reductions for submission of marketing authorisation applications under the centralised procedure. It further stipulates that only products indicated for food producing species are considered eligible for fee incentives where no alternative product is authorised.
- *Decision of the EMA Executive Director on fee reductions for scientific advice on PRIME products for SMEs and applicants from the academic sector (EMA/63484/2016: published in June 2016):* In March of 2016, the EMA launched the PRIority MEDicines (PRIME) scheme, providing early and enhanced scientific and regulatory support to medicines that have the potential to significantly address patients' unmet medicinal need. It offers fee waivers for scientific advice for SMEs and applicants from the academic sector.<sup>227</sup>

Decisions of the Executive Director can be amended, revoked or added at any point in time, changing the applicable types and levels of fee incentives and, thereby, the EMA fee system.

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<sup>227</sup> Mentioned Decisions of the Executive Director can be found [here](#) (link valid in April 2019).

## **Annex 5: Description of the EMA fee system and Union subsidies**

### **1. Fees charged to undertakings and NCA remuneration<sup>228</sup>**

EMA charges fees to MAHs and applicants for the services provided by EMA and the coordination group and remunerates NCAs for their contribution, in accordance with rules laid down by the Fee Regulation (Council Regulation (EC) No 297/95) and its Implementing Rules, as well with of the Pharmacovigilance Fee Regulation (Regulation (EU) No 658/2014). Several crosscutting and sectorial pieces of Union legislation provide for fee waivers and reductions.

#### Procedural fees

In accordance with the Fee Regulation and its Implementing Rules, the EMA charges fees per service or activity for the assessment of applications for a marketing authorisation under the centralised procedure, for post-authorisation changes to central marketing authorisations, as well as for other services such as referrals, scientific advice and inspections. Pharmacovigilance activities for both centrally and nationally authorised medicines for human use conducted at EMA level are also financed by fees, as laid down in the Pharmacovigilance Fee Regulation. For the purpose of this Staff Working Document, these one-off ‘per-service’ fees are referenced as ‘procedural’ fees.

The above mentioned procedures involve assessments conducted by NCAs. The EMA also levies procedural fees for activities that do not involve NCAs. These are minor variations to authorised products that have minimal or no impact on the product’s quality, safety or efficacy and do not require approval prior implementation (Type IA variations), notifications of parallel distribution, transfers of marketing authorisations between different companies, and the issuing of certificates.

For many types of procedural activities, the legislation does not set a single fee amount but instead a fee range. For certain activities<sup>229</sup>, the amount of the fee charged varies with the type of the application (e.g., the complexity of the underlying data to be evaluated). Further, amounts charged may be increased with an additional fee in case the application covers more than one pharmaceutical strength/potency, form or presentation. In addition, for initial marketing authorisations, the type of medicinal product/dossier (e.g., a full dossier vs an abridged application; a generic vs a biosimilar application) also determines the level of the total fee amount charged. Finally, even though most procedural activities are common to both human and veterinary medicines (similar data requirements, procedural steps and duration of the procedure), fees charged for the latter are set at a

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<sup>228</sup> Fee amounts quoted are those valid in April 2019.

<sup>229</sup> Scientific advice, extension of marketing authorisations, Type II variations, inspections, herbal medicinal products, ATMP certification, consultation procedures, Plasma Master File (PMF) and Vaccine Antigen Master File (VAMF) certification.

lower level than those charged for human medicines. In practice, procedural fees charged for veterinary medicinal products are 50% of those charged for human medicinal products.

For inspections, only a single fee amount is set, regardless of the geographical location of the site inspected (i.e. inside or outside the EU).

Not taking into consideration the additional fees, the above results in **around 90 different basic procedural fees** for medicinal products for human and veterinary use ranging from €3,200 to €297,800. A few examples of basic fees levied by the EMA are presented in the Table below. For the full list of fees, see Annex 6.

**Table 1: Examples of basic fees charged for procedural activities**

Procedural activity	Fees charged	
	Human medicinal products	Veterinary medicinal products (non-immunological)
Scientific advice (initial request)	Depending on the type of underlying data, the basic fee ranges from <b>€43,700 to €87,600</b>	Depending on the type of underlying data, the basic fee ranges from <b>€14,400 to €43,700</b>
Initial marketing authorisation	Depending on the type of application, the basic fee ranges from <b>€113,300 to €291,800</b>	Depending on the type of application, the basic fee ranges from <b>€72,600 to €146,100</b>
Variation requiring substantial assessment (Type II variation)	Depending on the type of underlying data, the basic fee ranges from <b>€22,000 to €87,600</b>	Depending on the type of underlying data, the basic fee ranges from to <b>€11,000 to €43,700</b>
Referral (Art. 30(1) and 31 of Dir. 2001/83/EC and Art. 34(1) and 35 of Dir. 2001/82/EC)	If triggered by the MAH: <b>€72,600</b>	If triggered by the MAH: <b>€43,700</b>
Inspection	For each inspection inside or outside the EU, the basic fee is <b>€22,000</b>	For each inspection inside or outside the EU, the basic fee is <b>€22,000</b>

Procedural fees are paid before the start of the procedure, within 45 days of the date of the notification of administrative validation, unless a fee deferral applies (see further down). In case of inspections, however, the relevant fee is payable within 45 days from the date on which the inspection is carried out.<sup>230</sup>

### Annual fees

The EMA levies annual fees to marketing authorisation holders for maintenance services related to existing marketing authorisations, in accordance with the Fee Regulation and the Pharmacovigilance Fee Regulation. Two types of annual fees are charged: an annual fee per authorisation for centrally authorised products (CAPs) for human and veterinary use and an annual pharmacovigilance fee for nationally authorised products (NAPs) for human use.

CAP annual fees are charged in accordance with the Fee Regulation. They fund the Agency's activities of pharmacovigilance and inspection staff costs (30% of the total

<sup>230</sup> Council Regulation (EC) No 297/95, and its Implementing Rules, and Regulation (EU) No 658/2014.

fee), sampling and testing of centralised products under the EDQM<sup>231</sup>-EMA scientific agreement and programme<sup>232</sup> (up to 10% of the total fee) and special activities<sup>233</sup> determined by the Management Board in consultation with the scientific committees (30% of the total fee). The remaining 30% of the CAP annual fee is to be divided between rapporteur and co-rapporteur for scientific evaluation services provided at EMA request, e.g. annual product reports and specific reporting for pharmacovigilance, and for other activities carried out by the relevant Member State under their Union obligations. The fee system defines six levels of CAP annual fees: three for human medicinal products and three for veterinary medicines. The fee amount charged per authorised product depends on the type of dossier supporting that product (i.e. full dossier, biosimilar or abridged dossier), where the fees charged for veterinary products are set at 33% of the CAP annual fee for human medicinal products.

Pharmacovigilance annual fees are charged in accordance with Pharmacovigilance Fee Regulation for pharmacovigilance activities of the EMA relating to information technology (in particular maintenance of the EudraVigilance database<sup>234</sup>) and the monitoring of selected medical literature. Pharmacovigilance annual fees are only charged for NAPs as CAPs already pay the aforementioned CAP annual fee for the maintenance of their authorisations, which includes pharmacovigilance activities. For pharmacovigilance annual fees the amount payable for each MAH depends on the

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<sup>231</sup> The European Directorate for the Quality of Medicines & Healthcare (EDQM) is responsible for supporting the basic human right of access to good quality medicines and health care in Europe. The EDQM protects public health by enabling the development, supporting the implementation and monitoring the application of quality standards for safe medicines and their safe use, which are recognised as a scientific benchmark world-wide. For more information, see [the EDQM website](http://www.edqm.eu) (www.edqm.eu) (link valid in April 2019).

<sup>232</sup> Since CAPs are authorised throughout the Union, a coordinated EU approach to controlling their quality is required. A contract governing an annual CAP Sampling & Testing Programme was signed by the EMA and EDQM. The EMA is the sponsor of the programme and has overall responsibility for it, whereas the EDQM coordinates the sampling and testing operations. EDQM duties include reporting the results and, if required, proposing follow-up actions, to the EMA (<https://www.edqm.eu/en/CAP-programme-613.html> and <https://www.ema.europa.eu/partners-networks/international-activities/multilateral-organisations-initiatives/european-directorate-quality-medicines-healthcare-edqm-council-europe>) (links valid in April 2019).

<sup>233</sup> Special activities comprise, among others, specific type of meetings, bringing additional expertise, special evaluation activities, certain fee exemptions related to human and veterinary medicines and MRLs, training for EU assessors, and access to adequate information or safety data (e.g. databases). See Annex VI of the [Implementing Rules](#) for Council Regulation (EC) No 297/95.

<sup>234</sup> Article 24 of Regulation (EC) No 726/2004.

number of ‘chargeable units’<sup>235</sup>, with a basic fee of €69 set per single unit. The EMA retains 100% of the pharmacovigilance annual fee.<sup>236</sup>

**Table 2: Annual fees**

Procedural activity	Fees charged	
	Human medicinal products	Veterinary medicinal products (non-immunological)
CAP annual fee	Depending on the type of product, the fee ranges from <b>€26,000 to €104,600</b>	Depending on the type of product, the fee ranges from <b>€8,600 to €35,000</b>
Pharmacovigilance annual fee	<b>€69</b> per chargeable unit <sup>237</sup>	N/A

CAP annual fees shall be paid within 45 days of the first and each subsequent anniversary date of the marketing authorisation, whereas pharmacovigilance annual fees are charged annually for all marketing authorisations. The annual fees relate to the preceding year.<sup>238</sup>

### Administrative fees

Administrative fees apply for administrative services (1) where documents or certificates are issued outside the framework of services covered by ‘procedural fees’, (2) where an application is rejected following the conclusion of the administrative validation of the related dossier, (3) where the information required in the case of parallel distribution has to be checked, and (4) where worksharing arrangements are applicable to variations.

A total of 13 different administrative basic fees apply for medicines for human and veterinary use, ranging from €290 to €7,290. In addition, where the activity concerns the provision of certificates, additional fees are charged for each additional set of certificate issued.

### Rules for setting the fee levels

The fees in the Fee Regulation were set on the basis that they should not be a determining factor for the applicant to follow the national or centralised procedure for obtaining a marketing authorisation. The fees set out in the Pharmacovigilance Fee Regulation were

<sup>235</sup> The chargeable unit was set to define, for the purposes of the Pharmacovigilance Fee Regulation, a marketing authorisation due to the lack of a harmonised definition thereof across the EU. It is defined as a unique combination of the following dataset derived from information on all medicines authorised in the EU held by the Agency: (1) name of the medicinal product, as defined in point 20 of Article 1 of Directive 2001/83/EC; (2) marketing authorisation holder; (3) Member State in which the marketing authorisation is valid; (4) active substance or a combination of active substances; (5) pharmaceutical form.

<sup>236</sup> Fee amounts quoted are those valid in April 2019.

<sup>237</sup> In accordance with Article 2(1) of Regulation (EU) No 658/2014 a ‘chargeable unit’ means a unit defined by a unique combination of the following dataset: (a) name of the medicinal product, (b) marketing authorisation holder, (c) the Member State in which the marketing authorisation is valid, (d) active substance or a combination of active substances, and (e) pharmaceutical form.

<sup>238</sup> Council Regulation (EC) No 297/95, and its Implementing Rules, and Regulation (EU) No 658/2014.

based on an evaluation of the Agency's estimations and forecasts as regards its workload and related costs, and on the basis of an evaluation of the costs of the work carried out by the NCAs.

#### Rules for increase of fee levels

In accordance with Article 12 of the main Fee Regulation and Article 15(5) of the Pharmacovigilance Fee Regulation, any review of the fees shall be based on a (transparent and independent) evaluation of the Agency's costs and on the basis of the related costs of the services provided by the NCAs. In addition, fees are reviewed annually by the Commission by reference to the inflation rate and updated as required.

#### Fee incentives, fee deferrals and non-fee generating activities

To incentivise the development and bringing to the market of certain medicines or by certain applicants, incentives (fee reductions and full waivers) are applied to some of the above mentioned fees. The grounds for fee reductions and waivers are laid down in a number of legislative acts, i.e. the Founding Regulation, the Fee Regulation and its Implementing Rules, the SME Regulation, the Pharmacovigilance Fee Regulation, the Paediatric Regulation, the Orphan Regulation, and the ATMP Regulation.

More specifically, EU legislation has introduced **fee incentives** for paediatric and orphan medicinal products, ATMPs and veterinary medicinal products for MUMS/limited market. Fee reductions and exemptions also exist for companies that fulfil the definition of a micro-sized enterprise or SME as set out in Commission Recommendation 2003/361/EC<sup>239,240</sup>. In addition, EMA grants fee reductions and exemptions for applicants from the academic sector in the case of scientific advice procedures for PRIME products<sup>241</sup>.

Further, there are certain procedural activities for which **no fee** is foreseen under the current legislation. For medicinal products for human use these concern: the evaluation of orphan designations (initial assessment and reassessments at the time of the marketing authorisation application); paediatric investigation plans (PIPs); PIP waivers; PIP modifications, PIP deferrals; PIP compliance checks; scientific advice procedures for medicinal products for paediatric use<sup>242</sup>; non-pharmacovigilance referrals initiated by a

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<sup>239</sup> C(2003) 1422

<sup>240</sup> The European Commission is currently evaluating the SME definition for a possible revision (ref. Ares(2017)2868537). For more information, see [http://ec.europa.eu/growth/smes/business-friendly-environment/sme-definition\\_en](http://ec.europa.eu/growth/smes/business-friendly-environment/sme-definition_en)

<sup>241</sup> In 2016, the EMA launched the PRIority MEdicines (PRIME) scheme to support developers of medicinal products that may offer a major therapeutic advantage over existing treatments or may benefit patients without treatment options. This scheme also provides fee incentives for scientific advice requests for PRIME products from micro-sized enterprises and SMEs as well as academic sector applicants.

<sup>242</sup> However, fees are set for scientific advice procedures for paediatric medicinal products that are also an orphan designated product or an ATMP.

Member State or the European Commission<sup>243</sup>; ATMP classification. Non-fee generating procedures for veterinary medicinal products under the currently applicable legislation are: MUMS/limited market applications; referrals that are not triggered by the MAH<sup>244</sup>; pharmacovigilance procedures such as Periodic Safety Update Reports (PSURs), Surveillance/Signal detection, Adverse Event Reporting (AER), Rapid Alerts (RA), Non-Urgent Information (NUI) and Incident Management Plan (IMP)<sup>245</sup>.

Where an applicant could, in respect of the same fee, benefit from more than one category of fee reduction or incentive the provisions which are the most favourable to the applicant apply.

**Fee deferrals** exist for applications for medicinal products to be used in a human pandemic situation and for SMEs. In case of SMEs, the payment of fees for their application for an initial marketing authorisation and for inspections is deferred until notification of the final decision on the marketing authorisation or until withdrawal of the application. In addition, if an initial marketing authorisation procedure ends negatively for a product for which scientific advice was sought, no fee is charged to the SME.

Examples of the effect of fee incentives on EMA's share of fees and NCA remuneration are included in Table 3 in Section 2.3.3 below.

#### Remuneration of NCAs

The EMA remunerates NCAs for the provision of services by rapporteurs or experts (Article 62(3) of Regulation (EC) 726/2004), i.e. for scientific assessments conducted by rapporteurs and co-rapporteurs appointed by the relevant EMA scientific committees. The details of this financial compensation are laid down in the Implementing Rules of the Fee Regulation and in the Pharmacovigilance Fee Regulation.

The rules for financial compensation of NCAs under the existing fee system are as follows:

- The EMA Management Board and the CHMP/CVMP have agreed on the principle of excluding direct payments to individuals. Instead, financial compensation occurs via the NCAs;
- For non-pharmacovigilance fee-generating procedural activities, the rapporteur together with, where applicable, the co-rapporteur receive 50% (25% each) of the full

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<sup>243</sup> For non-pharmacovigilance referrals, a fee amount is foreseen only when the referral is initiated by the applicant or the MAH. Non-pharmacovigilance referrals concern procedures in accordance with Articles 29(4), 30 and 31 of Directive 2001/83/EC, Article 13 of Regulation (EC) No 1234/2008 and Article 5(3) of Regulation (EC) 726/2004.

<sup>244</sup> Referrals for veterinary medicinal products are procedures in accordance with Articles 33(4), 34 and 35 of Directive 2001/82/EC, Article 13 of Regulation (EC) No 1234/2008 and Article 45 of Regulation (EC) No 726/2004.

<sup>245</sup> Pharmacovigilance procedures for veterinary products will change with the new Veterinary Medicinal Products Regulation (Regulation (EU) 2019/6).



fee (i.e. fee reductions do not affect the amount received by NCAs which is based on the full fee).

- For pharmacovigilance fee-generating activities, rapporteurs are remunerated a fixed amount, which in case of incentives is reduced in proportion to the incentive rate applied to the full fee.
- Non-remunerated roles include peer-reviewer<sup>246</sup> and Pharmacovigilance Risk Assessment Committee (PRAC) (co-)rapporteur for non-pharmacovigilance procedures. In addition, for services for which no fee is currently set in legislation, EMA does not charge a fee and NCAs acting as rapporteur or co-rapporteur do not receive remuneration. Similarly, in the case of fee deferrals for SMEs, if an initial marketing authorisation procedure ends negatively for a product for which scientific advice was received, no fee is charged by the EMA and NCAs are not remunerated for their assessment work. Finally, NCAs receive no remuneration for assessment work related to Type IB variations<sup>247</sup>;
- The rapporteur and co-rapporteur together receive 30% (15% each) of the CAP annual fee for scientific evaluation services at the request of EMA (e.g. annual product reports and specific reporting for pharmacovigilance and safety reports) and other activities carried out by Member States under their EU obligations;
- The pharmacovigilance annual fee is fully retained by EMA;
- NCAs do not receive remuneration for their involvement in committees and working parties;
- Payments made are divided equally between the NCAs of the rapporteur and co-rapporteur. Where no co-rapporteur has been appointed, the rapporteur receives the full remuneration due to NCAs;
- Where multi-national teams (MNATs) have been established, the percentage share of the remuneration is decided by the NCAs involved;
- For inspections, the remuneration to the NCAs is divided by  $n+1$ , where 'n' is the number of inspectorates participating in a site inspection. The additional ('+1') fee portion is allocated to the reporting inspector, via payment to the inspector's authority, in addition to the part of the fee that the inspectorate receives for participating in the site inspection;
- NCAs of the committee members acting as rapporteur or co-rapporteur receive their remuneration for procedural activities once they have fulfilled their obligations (i.e. after submission of the final assessment report for an EMA committee recommendation). The NCA share of the CAP annual fee is due a month following the authorisation of the sales order to the MAH (created on the anniversary of the Commission decision on the marketing authorisation);

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<sup>246</sup> This role is not expressly foreseen in legislation. This role was introduced to ensure high-quality standards of scientific evaluation of the rapporteurs. Appointment of a peer-reviewer is foreseen in EMA's Rules of procedure for its different scientific committees and other relevant documents related to the operation, roles and responsibilities of the several committees.

<sup>247</sup> EMA has categorised Type IB variations into three separate groups: (1) not requiring NCA involvement (EMA-only procedure), (2) requiring NCA review of EMA assessment and (3) requiring NCA assessment.

Table 3 below presents examples of full fees, EMA's net share of those full fees and remuneration amounts paid to NCAs.

**Table 3: Examples of EMA's share of fees and NCA remuneration**

Procedural activity or annual fee	Full fee (before incentives)	EMA's share of fee	NCA remuneration
<b>Human medicinal products</b>			
Scientific advice	Depending on the type of underlying data, the basic fee ranges from <b>€43,700 to €87,600</b>	From <b>€21,850 to €43,800</b> (50% of the full fee)	From <b>€21,850 to €43,800</b> (50% of the full fee, to be equally split between rap and co-rap)
Initial marketing authorisation for orphan medicines	Depending on the type of application, the basic fee ranges from <b>€113,300 to €291,800</b>	From <b>€45,320 to €116,720</b> (orphan medicines receive 10% reduction of the full fee) <sup>248</sup>	From <b>€56,650 to €145,900</b> (50% of the full fee, to be equally split between rap and co-rap)
PSUR/PSUSA	<b>€20,110</b>	<b>€6,590</b>	<b>€13,520</b> (to be equally split between rap and co-rap)
Orphan designation	No fee set in legislation	<b>€0</b>	<b>€0</b>
CAP annual fee	Depending on the type of product, the fee ranges from <b>€26,000 to €104,600</b>	From <b>€18,200 to €73,220</b> (70% of the full fee)	From <b>€7,800 to €31,380</b> (30% of the full fee, to be equally split between rap and co-rap)
Pharmacovigilance annual fee	<b>€69</b> per chargeable unit	<b>€69</b> per chargeable unit	<b>€0</b>
<b>Veterinary medicinal products</b>			
Scientific advice for MUMS/limited market	Depending on the type of underlying data, the basic fee ranges from <b>€14,400 to €43,700</b>	<b>€0</b> <sup>249</sup> (MUMS/limited market medicines receive 100% reduction of the full fee)	From <b>€7,200 to €21,850</b> (50% of the full fee, to be equally split between rap and co-rap)
Initial marketing authorisation	Depending on the type of application, the basic fee ranges from <b>€72,600 to €146,100</b>	From <b>€36,300 to €73,050</b> (50% of the full fee)	From <b>€36,300 to €73,050</b> (50% of the full fee, to be equally split between rap and co-rap)
PSUR	No fee set in legislation	<b>€0</b>	<b>€0</b>
CAP annual fee	Depending on the type of product, the fee ranges from <b>€8,600 to €35,000</b>	From <b>€6,020 to €24,500</b> (70% of the full fee)	From <b>€2,580 to €10,500</b> (30% of the full fee, to be equally split between rap and co-rap)

Fees charged by NCAs via national fee systems and other sources of funding are not within the scope of this evaluation.

<sup>248</sup> NCA remuneration is based on the full fee before incentives are applied to this full fee. Therefore: EMA's share of fees = {full fee} – {10% of full fee} – {NCA remuneration}. This means that in case a 10% reduction of the full fee applies, EMA's share of fees is lower than the total remuneration amount paid to rapporteur and co-rapporteur.

<sup>249</sup> NCA remuneration is based on the full fee before incentives are applied to this full fee. Therefore: EMA's share of fees = {full fee} – {100% of full fee} – {NCA remuneration}.

## **2. EU and EEU budget contributions**

In accordance with Regulation (EC) No 726/2004 (Founding Regulation) and Regulation (EC) No 141/2000 (Orphan Regulation), the EMA receives EU budget contributions, in addition to fees charged to pharmaceutical companies. Contributions include a general contribution and a special orphan contribution to be used exclusively to address the fee incentives provided for orphan designated medicinal products. The level of the orphan contribution is determined based on the loss in revenue EMA incurs due to those incentives. The general budget contribution is adjusted annually in order to address increases or decreases in fee income, thus balancing EMA's costs and revenues. The adjustment is done within a maximum amount defined within the seven-year EU budget framework. The EU/EEA contributions should in principle balance the fluctuations of the fee revenue of EMA and finance the applicable fee incentives and waivers, i.e. costs not covered by fee revenue. In addition, Regulation (EC) No 1901/2006 (Paediatric Regulation) stipulates that the general contribution should cover the work of the PDCO, including scientific support provided by experts, and of the activities of the Agency resulting from implementation of the Paediatric Regulation, such as the assessment of PIPs, scientific advice and any fee waivers provided for in that regulation.<sup>250</sup>

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<sup>250</sup> Article 48 of the Paediatric Regulation.

## Annex 6: Fee amounts and NCA remuneration levels (as valid in April 2019)

The information below is in accordance with Council Regulation (EC) No 297/95 ('the Fee Regulation') and its Implementing Rules, Regulation (EU) No 658/2014 ('the Pharmacovigilance Fee Regulation'), and the two explanatory notes of EMA on these regulations.<sup>251</sup> Unless stated otherwise, the fees presented in the table concern the basic fees. It should be noted that fees are reviewed annually by reference to the inflation rate and amended as appropriate.<sup>252</sup> The fee amounts mentioned below are those valid in April 2019.

A 'copy' means an additional presentation of the same strength/potency and pharmaceutical form, submitted at the same time as the initial authorisation or extension application.

Activity	Fee (per presentation of a medicinal product unless specified otherwise)	NCA remuneration	Notes
<b>HUMAN MEDICINAL PRODUCTS</b>			
<b>Scientific advice: initial request</b>	Level I: € <b>43700</b> Level II: € <b>65700</b> Level III: € <b>87600</b>	<b>50%</b> of the full fee for rapporteur (Rap) and co-rapporteur (Co-Rap) (to be divided equally), regardless of incentives applied	Level I: quality / safety / bioequivalence (BE) study for generics Level II: clinical / quality + safety / quality + BE study for generics Level II: quality + safety + clinical / quality + clinical / safety + clinical / qualification advice
<b>Scientific advice: initial request for a paediatric-only product</b>	€ <b>0</b>	€ <b>0</b>	Product is not also an orphan and/or ATMP
<b>Scientific advice: follow-up request</b>	Level I: € <b>22000</b> Level II: € <b>33000</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided)	Level I: quality / safety / BE study for generics

<sup>251</sup> In order of mention: Council Regulation (EC) No 297/95 of 10 February 1995 on fees payable to the European Agency for the Evaluation of Medicinal Products (OJ L 35, 15.2.1995, p. 1–5); Rules for the implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures (EMA/MB/909612/2019); Regulation (EU) No 658/2014 of the European Parliament and of the Council of 15 May 2014 on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use (OJ L 189, 27.6.2014, p. 112–127); Explanatory note on general fees payable to the European Medicines Agency (EMA/909567/2019); Explanatory note on pharmacovigilance fees payable to the European Medicines Agency (EMA/580301/2018)

<sup>252</sup> In accordance with Article 12 of Council Regulation (EC) No 297/95 and Article 15(5) of Regulation (EU) No 658/2014.

	Level III: <b>€43700</b>	equally), regardless of incentives applied	Level II: clinical / quality + safety / quality + BE study for generics  Level II: quality + safety + clinical / quality + clinical / safety + clinical / qualification advice
<b>Scientific advice: follow-up request for a paediatric-only product</b>	€0	€0	Product is not also an orphan and/or ATMP
<b>Orphan designation: initial assessment</b>	€0	€0	
<b>Orphan designation: reassessment</b>	€0	€0	
<b>PIP application</b>	€0	€0	
<b>PIP waiver</b>	€0	€0	
<b>PIP deferral</b>	€0	€0	
<b>PIP modification</b>	€0	€0	
<b>PIP compliance check</b>	€0	€0	
<b>Initial marketing authorisation application (MAA): full dossier</b>	Basic fee: <b>€291800</b> Each additional strength/form: <b>+€29300</b> Copy: <b>+€7300</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Basic fee covers a single strength/potency associated with one pharmaceutical form and one presentation  Copy fee covers one presentation
<b>Initial MAA: biosimilar (Art. 10(4) of Dir. 2001/83/EC<sup>253</sup>)</b>	Basic fee: <b>€188700</b> Each additional strength/form: <b>+€11300</b> Copy: <b>+€7300</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Basic fee covers a single strength/potency associated with one pharmaceutical form and one presentation  Copy fee covers one presentation
<b>Initial MAA: Generic, informed consent, hybrid (Art. 10(1), 10(c) and 10(3) of Dir. 2001/83/EC)</b>	Basic fee: <b>€113300</b> Each additional strength/form: <b>+€11300</b> Copy: <b>+€7300</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Basic fee covers a single strength/potency associated with one pharmaceutical form and one presentation  Copy fee covers one presentation
<b>Extension of marketing</b>	Basic fee – Level I:	<b>50%</b> of the full fee for Rap and Co-Rap	Basic fee covers a single strength/potency

<sup>253</sup> Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (OJ L 311, 28.11.2001, p. 67–128)

<b>authorisation *</b>	<p><b>€87600</b></p> <p>Basic fee – Level II: <b>€65700</b></p> <p>Each additional strength/form: <b>+€22000</b></p> <p>Copy: <b>+€7300</b></p>	(to be divided equally), regardless of incentives applied	<p>associated with one pharmaceutical form and one presentation</p> <p>Level I: supported by non-clinical and/or clinical data</p> <p>Level II: quality extension for which no clinical or non-clinical data are submitted or no cross-references to previously submitted clinical or non-clinical data are made (bioequivalence data are clinical data, biowaivers are not clinical data)</p> <p>Copy fee covers one presentation</p>
<b>Extension of marketing authorisation for use in paediatric population *</b>	<p>Basic fee – Level III: <b>€87600</b></p> <p>Each additional strength/form: <b>+€22000</b></p> <p>Copy: <b>+€7300</b></p>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	<p>Basic fee covers a single strength/potency associated with one pharmaceutical form and one presentation</p> <p>Copy fee covers one presentation</p>
<b>Type IA variation *</b>	<b>€3200</b>	N/A: NCAs are not involved in this activity	
<b>Type IB variation *</b>	<b>€7300</b>	<b>€0</b>	Depending on the underlying data, certain Type IB variations are fully processed by EMA without Rap involvement, whereas for others the Rap is consulted by EMA or Rap is asked to perform the assessment
<b>Type II variation *</b>	<p>Level I: <b>€87600</b></p> <p>Level II: <b>€65700</b></p> <p>Level III: <b>€22000</b></p>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	<p>Level I: major variation affecting quality, safety and/or efficacy</p> <p>Level II: quality variation without clinical or non-clinical data</p> <p>Level III: for each of the third and subsequent Type II variation in a grouped variation or worksharing</p>
<b>New paediatric indication *</b>	<b>€87600</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Basic fee applies to each new indication

<b>Renewal</b>	<b>€14400</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Basic fee covers a single strength/potency associated with one pharmaceutical form and one presentation
<b>Inspection</b>	Level I: <b>€22000</b> (For inspections outside the EU travel expenses shall be charged extra on the basis of actual costs) Level II: <b>€11000</b> Level III: <b>€11000</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Level I: for each inspection inside or outside the EU Level II: for each consecutive distinct PFM inspection performed in conjunction with an inspection that attracts the Level I fee Level III: for each inspection cancelled due to withdrawal of the application or changes to manufacturing arrangements
<b>Transfer of marketing authorisation</b>	<b>€7300</b>	N/A: NCAs are not involved in this activity	Basic fee covers all presentations of the medicinal product
<b>Non-pharmacovigilance referral initiated by MAH (Art. 30 and 31 of Dir. 2001/83/EC)</b>	<b>€72600</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	If more than one applicant/MAH is concerned, they pay a single fee.
<b>Non-pharmacovigilance referral initiated by MS or EC (Art. 29(4), 30, 31 and 35 of Dir. 2001/83/EC, Art. 13 of Reg. 1234/2008<sup>254</sup>, Art. 5(3) of Reg. 726/2004<sup>255</sup>)</b>	<b>€0</b>	<b>€0</b>	
<b>Pharmacovigilance referral (Art. 31(1)(2<sup>nd</sup> sub), 31(2) and 107i-k of Dir. 2001/83/EC, Art. 20(8) of Reg. 726/2004)</b>	<u>Full fee:</u> <b>€184600</b> for 1 or 2 active substances and/or combination of active substances if $\geq 2$ MAHs are involved <b>+€40020</b> per active substance for referrals for more than 2 active substances, up to a	For 1 or 2 active substances: <b>€119333</b> For 3 active substances: <b>€145200</b> For 4 active substances: <b>€171066</b> For $\geq 5$ active substances: <b>€196933</b>	

<sup>254</sup> Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisation for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, p. 7–24)

<sup>255</sup> Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136, 30.4.2004, p. 1–33)

	<p>max. of <b>€304660</b></p> <p><u>Reduced fee:</u></p> <p><b>€123067</b> for 1 active substance or 1 combination of active substances if 1 MAH is involved</p>	<p>To be shared by Rap and Co-Rap, to be reduced proportionally if fee incentives apply.</p> <p>Where 3 or more active substances are included: the Rap receives an additional <b>€1000</b> for 3 active substances / <b>€2000</b> for 4 active substances / <b>€3000</b> for <math>\geq 5</math> active substances, which will be paid from the fee and remuneration share attributed to the EMA and Co-Rap, each of which shall contribute the same amount.</p>	
<b>PSUR/PSUSA</b>	<b>€20110</b>	<b>€13100</b> to be shared by Rap and Co-Rap, to be reduced proportionally if fee incentives apply	
<b>PASS</b>	<b>€44340</b> ( <b>€17740</b> for assessment draft protocol and <b>€26600</b> for assessment final study report)	<b>€18200</b> ( <b>€7280</b> for protocol assessment and <b>€10920</b> for final report assessment) to be shared by Rap and Co-Rap, to be reduced proportionally if fee incentives apply	
<b>Scientific services: scientific opinions pursuant Art. 58 of Reg. 726/2004</b>	<p>The basic and additional fees specified above apply by analogy for a scientific opinion for the evaluation of medicinal products for human use intended exclusively for markets outside the European Union. Likewise, the inspection fees above apply by analogy to any inspection undertaken for the purpose of assessment prior to an opinion.</p> <p>Fees for post-opinion services and annual fees are charged according to the</p>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	



	<p>corresponding fees for centrally authorised products. Therefore the fees specified above apply by analogy.</p> <p>The fee incentives for SMEs apply to scientific services. However, fee deferrals and conditional fee exemptions do not apply to services in relation to scientific opinions pursuant to Article 58 of Regulation (EC) No 726/2004.</p>		
<b>Scientific services: compassionate use</b>	€146100	50% of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	For any opinion on medicinal products for compassionate use
<b>Scientific services: evaluation of herbal medicinal products</b>	<p>Level I: €22000</p> <p>Level II: €14400</p>	50% of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	<p>Level I: for requests for scientific support and advice by the HMPC on multiple areas related to traditional herbal medicinal products</p> <p>Level II: for requests for scientific support and advice by the HMPC on single areas related to traditional herbal medicinal products, for example quality or safety or long-standing use</p>
<b>Scientific services: certification of quality and non-clinical data for ATMPs developed by micro-sized companies and SMEs</b>	<p>Level I: €65700</p> <p>Level II: €43700</p> <p>The above fees are subject to the fee reduction for scientific services applicable to SMEs.</p>	50% of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	<p>Level I: application related to quality and non-clinical data</p> <p>Level II: application related to quality data</p>
<b>Consultation on ancillary substances including blood derivatives: initial request</b>	<p>Level I: €87600</p> <p>Level II: €65700</p> <p>Level III: €43700</p>	50% of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	<p>Level I: substance new to the EMA</p> <p>Level II: known ancillary blood derivative from known source</p> <p>Level III: known ancillary substance from a known source</p>

<p><b>Consultation on ancillary substances including blood derivatives: follow-up request</b></p>	<p>In case of further consultation requested by notified body: <b>€22000</b></p> <p>Amendment to documentation equivalent to an extension: <b>€43700</b></p> <p>Major amendment to documentation equivalent to a Type II variation: <b>€43700</b></p> <p>Two or more amendments (grouped) where at least one is equivalent to a Type II variation or an extension: <b>€43700</b></p> <p>Minor amendment to documentation equivalent to a Type IB variation: <b>€7300</b></p> <p>Minor amendment to documentation equivalent to a Type IA variation: <b>€3200</b></p>	<p><b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied</p>	
<p><b>Initial certification plasma master file (PMF): not submitted simultaneously with a new marketing authorisation application</b></p>	<p>Level I: <b>€72600</b></p> <p>Level II: <b>€65700</b></p> <p>Level III: <b>€22000</b></p>	<p><b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied</p>	<p>Level I: where the data have not been previously evaluated</p> <p>Level II: changes to data previously evaluated</p> <p>Level III: previously evaluated data without changes</p>
<p><b>Initial certification PMF: submitted simultaneously with a new marketing authorisation application</b></p>	<p><b>€7300</b></p>	<p><b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied</p>	
<p><b>Variation to certified PMF</b></p>	<p>Type II variation (single): <b>€65700</b></p> <p>Grouped variation where at least one is Type II: <b>€65700</b></p> <p>Type IB variation: <b>€7300</b></p> <p>Type IA variation: <b>€3200</b></p>	<p><b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied</p>	
<p><b>Annual re-certification</b></p>	<p>Documentation includes variations</p>	<p><b>50%</b> of the full fee for Rap and Co-Rap</p>	

<p><b>of PMF</b></p>	<p>where at least one is Type II: <b>€65700</b></p> <p>Documentation includes no Type II variations: <b>€14400</b> (fee increased by applicable fee for each Type IB or IA included in the documentation up to a max. of <b>€65700</b>)</p>	<p>(to be divided equally), regardless of incentives applied</p>	
<p><b>Initial certification vaccine antigen master file (VAMF): not submitted simultaneously with a new marketing authorisation application</b></p>	<p>Data not previously evaluated: <b>€72600</b></p> <p>Changes to data previously evaluated: <b>€65700</b></p> <p>Previously evaluated data without changes: <b>€22000</b></p> <p>+<b>€7300</b> for each VAMF application submitted simultaneously for antigens from the same group, up to a max. of <b>€87600</b></p>	<p><b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied</p>	
<p><b>Initial certification VAMF: submitted simultaneously with a new marketing authorisation application</b></p>	<p><b>€7300</b></p> <p>+<b>€7300</b> for each VAMF application submitted simultaneously for antigens from the same group, up to a max. of <b>€87600</b></p>	<p><b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied</p>	
<p><b>Variation to certified VAMF</b></p>	<p>Type II variation (single): <b>€65700</b></p> <p>Two or more grouped variations where at least one is Type II: <b>€65700</b></p> <p>+<b>€7300</b> for each VAMF application submitted simultaneously for antigens from the same group, up to a max. of <b>€87600</b></p> <p>Type IB variation: <b>€7300</b></p> <p>+<b>€7300</b> for each VAMF application submitted simultaneously for</p>	<p><b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied</p>	

	antigens from the same group, up to a max. of <b>€43700</b> Type IA variation: <b>€3200</b> + <b>€3200</b> for each VAMF application submitted simultaneously for antigens from the same group, up to a max. of <b>€22000</b>		
<b>CAP annual fee (maintenance of marketing authorisation)</b>	Level I: <b>€104600</b> Level II: <b>€52400</b> Level III: <b>€26000</b>	<b>30%</b> for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Basic fee covers all presentations of a medicinal product Level I: full dossier Level II: biosimilar Level III: generic, hybrid or informed consent
<b>Pharmacovigilance annual fee (IT and literature monitoring) for NAPs</b>	<b>€69</b>	<b>€0</b>	Fee covers one chargeable unit
<b>VETERINARY MEDICINAL PRODUCTS</b>			
<b>Scientific advice: initial request</b>	Level I: <b>€43700</b> Level II: <b>€22000</b> Level III: <b>€14400</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Level I: quality + safety + clinical / quality + clinical / safety + clinical / qualification advice Level II: clinical / quality + safety / quality + bioequivalence (BE) study for generics Level III: quality / safety / BE study for generics
<b>Scientific advice: follow-up request</b>	Level I: <b>€22000</b> Level II: <b>€14400</b> Level III: <b>€11000</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Level I: quality + safety + clinical / quality + clinical / safety + clinical / qualification advice Level II: clinical / quality + safety / quality + BE study for generics Level III: quality / safety / BE study for generics
<b>Scientific advice in relation to products classified by CVMP</b>	<b>€11000</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	For assessing compliance of a proposed data package with relevant guidelines on data requirements for veterinary medicinal products intended for

			MUMS
<b>Initial marketing authorisation application (MAA): full dossier</b>	<p>Basic fee: <b>€146100</b></p> <p>Each additional strength/form: <b>+€14400</b></p> <p>Copy: <b>+€7300</b></p>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	<p>Basic fee covers a single strength/potency associated with one pharmaceutical form and one presentation</p> <p>Copy fee covers one presentation</p> <p>The number of target species applied does not impact the fee</p>
<b>Initial MAA: biosimilar (Art. 13(4) of Dir. 2001/82/EC)</b>	<p>Basic fee: <b>€123300</b></p> <p>Each additional strength/form including one presentation: <b>+€14400</b></p> <p>Copy: <b>+€7300</b></p>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	<p>Basic fee covers a single strength/potency associated with one pharmaceutical form and one presentation</p> <p>Copy fee covers one presentation</p> <p>The number of target species applied does not impact the fee</p>
<b>Initial MAA: Generic, informed consent, hybrid (Art. 13(1), 13(c) and 13(3) of Dir. 2001/82/EC<sup>256</sup>)</b>	<p>Basic fee: <b>€72600</b></p> <p>Each additional strength/form including one presentation: <b>+€14400</b></p> <p>Copy: <b>+€7300</b></p>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	<p>Basic fee covers a single strength/potency associated with one pharmaceutical form and one presentation</p> <p>Copy fee covers one presentation</p> <p>The number of target species applied does not impact the fee</p>
<b>Initial MAA: immunologicals</b>	<p><u>Full fee:</u></p> <p>Basic fee: <b>€72600</b></p> <p>Each additional strength/form: <b>+€7300</b></p> <p>Copy: <b>+€7300</b></p> <p>For each multi-strain additional presentation of the same application: <b>+€7300</b> up to a maximum of <b>€146100</b></p> <p><u>Reduced fee:</u></p> <p>Basic fee: <b>€36500</b></p> <p>Each additional strength/form</p>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	<p>Basic fee covers a single strength/potency associated with one pharmaceutical form and one presentation</p> <p>Copy fee covers one presentation</p> <p>The number of target species applied does not impact the fee</p>

<sup>256</sup> Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products (OJ L 311, 28.11.2001, p. 1–66)

	including one presentation: +€7300 Each additional strength/form: +€7300		
<b>MUMS/limited market</b>	€0	€0	NCA's are rarely involved in this activity.
<b>Extension of marketing authorisation *</b>	Basic fee – Level I: €36500 Basic fee – Level II: €33000 Basic fee – Level III: €9100 Each additional strength/form including one presentation: +€9100 Copy: +€7300	50% of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Basic fee covers a single strength/potency associated with one pharmaceutical form and one presentation Copy fee covers one presentation The number of target species applied does not impact the fee Level I: supported by non-clinical and/or clinical data Level II: quality extension for which no clinical or non-clinical data are submitted or no cross-references to previously submitted clinical or non-clinical data are made (BE data are clinical data, biowaivers are not clinical data) Level III: as Level II but for immunologicals
<b>Type IA variation *</b>	€3200	N/A: NCA's are not involved in this activity	
<b>Type IB variation *</b>	€7300	€0	Depending on the underlying data, certain Type IB variations are fully processed by EMA without rapporteur involvement, whereas for others the rapporteur is consulted by EMA or the rapporteur is asked to perform the assessment
<b>Type II variation *</b>	Level I: €43700 Level II: €33000 Level III: €11000 Level IV: €7300	50% of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Level I: major variation affecting quality, safety and/or efficacy Level II: quality variation without clinical or non-clinical data Level III: for each of the

			third and subsequent type II variation in a grouped variation or worksharing  Level IV: for each variation for immunologicals
<b>Renewal</b>	<b>€7300</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Basic fee covers a single strength associated with a pharmaceutical form
<b>Inspection</b>	Level I: <b>€22000</b> (For inspections outside the EU travel expenses shall be charged extra on the basis of actual costs) Level II: <b>€11000</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Level I: inspections inside or outside the EU Level II: each inspection cancelled due to withdrawal of the application or changes to the manufacturing arrangements
<b>Transfer of marketing authorisation</b>	<b>€7300</b>	N/A: NCAs are not involved in this activity	Basic fee covers all presentations of a medicinal product
<b>Referral initiated by MAH (Art. 34(1) and 35 of Dir. 2001/82/EC)</b>	<b>€43700</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	
<b>Referral initiated by a MS or EC (Art. 33, 34, 35, 45, 39 and 78 of Dir. 2001/82/EC)</b>	<b>€0</b>	<b>€0</b>	
<b>MRL</b>	Initial MRL: <b>€72600</b> Modification or extension of existing MRL: <b>€22000</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	MRL fees are deducted from the fees for initial MAAs/extension applications up to a total of no more than 50% of the fee to which it applies
<b>Scientific services: any scientific advice/opinion not covered by Art. 3 – 7 or Art. 8(1) of Reg. 297/95<sup>257</sup></b>	Level I: <b>€146100</b> Level II: <b>€36500</b> Level III: <b>€7300</b>	<b>50%</b> of the full fee for Rap and Co-Rap (to be divided equally), regardless of incentives applied	Level I: veterinary products Level II: e.g. VAMF Level III: variations to VAMF
<b>CAP annual fee (maintenance of marketing authorisation)</b>	Level I: <b>35000</b> Level II: <b>17300</b>	<b>30%</b> for Rap and Co-Rap (to be divided equally), regardless of	Basic fee covers all presentations of a medicinal product

<sup>257</sup> These concern services not related to an application for marketing authorisation, extension, variation, renewal, inspection, transfer of marketing authorisation, referral, MRL and scientific advice as well as those not related to services covered by the annual fee.

	Level III: <b>8600</b>	incentives applied	Level I: full dossier Level II: biosimilar Level III: generic, hybrid or informed consent
<b>PSUR</b>	€0	€0	
<b>Surveillance/signal detection</b>	€0	€0	
<b>Adverse event reporting</b>	€0	€0	
<b>Rapid alert</b>	€0	€0	
<b>Non-urgent information and incident management plan</b>	€0	€0	
<b>ADMINISTRATIVE FEES</b>			
<b>Negative validation</b>	<b>€3170</b> Applies to all negative validations. In case of grouping/worksharing, this fee shall only apply if all variations/extensions in the application are invalid	N/A: NCAs are not involved in this activity	
<b>Issuing certificates</b>	Standard procedure: <b>€300</b>  +€150 for each additional set of certificates  Urgent procedure: <b>€900</b>  +€450 for each additional set of certificates	N/A: NCAs are not involved in this activity	
<b>Withdrawal request for certificates</b>	<b>€300</b>	N/A: NCAs are not involved in this activity	If request for withdrawal follows confirmation of start of procedure
<b>Parallel distribution notification</b>	Initial notification: <b>€3170</b>  Annual update notification, manual check: <b>€610</b>  Annual update notification, automated check: <b>€290</b>  Notification of bulk	N/A: NCAs are not involved in this activity	Bulk change is a change that affects all notifications of a parallel distributor (e.g. change of address or repackager)



	<p>changes: <b>€3170</b></p> <p>Notification of changes, manual check: <b>€610</b></p> <p>Notification of changes, automated check: <b>€290</b></p>		
<b>Worksharing</b>	<p>For each variation in a single worksharing:</p> <p>Type II variation for human medicines: <b>€7290</b></p> <p>Type II variation for veterinary medicines: <b>€3620</b></p> <p>Type II variation for human medicines, applications on usage patent grounds: <b>€4130</b></p> <p>Type II variation for human medicines, applications on usage patent grounds: <b>€4200</b></p> <p>Type IB variation: <b>€1210</b></p> <p>Type IA variation: <b>€610</b></p> <p>The above fees are only charged if the full variation fee is applicable</p>	N/A: NCAs are not involved in this activity	<p>Fees are payable for each positively validated variation in the worksharing procedure</p> <p>Fees for applications on usage patent grounds are applicable as long as the concerned marketing authorisation is affected by usage patent(s) pertaining to indication(s) and/or dosage form(s)</p>

\* In case of grouping or worksharing of extension or variation applications the following applies:

- (1) The applicable fee is payable for each individual extension or variation grouped in a single notification or application or for each individual variation to one authorisation of the same MAH included in the worksharing application.
- (2) The applicable level I and II basic fees for Type II variations are payable for the 1st and 2nd Type II variation respectively when both levels of fees apply to variations in the same grouped application/worksharing procedure.
- (3) Consequential variations in a grouping are similarly charged the applicable fees as specified in the table.
- (4) In the case of grouping of the same Type IA variation(s) of several marketing authorisations of the same holder, the basic fee is payable for each Type IA variation and each marketing authorisation in the grouping.
- (5) Where any extension/variation in a grouping are found invalid, the applicable fees is payable for each positively validated extension/variation.
- (6) For worksharing procedures including both NAPs and CAPs, a fee is only payable to the EMA for CAPs.

## Annex 7: Fee incentives (as valid in April 2019)<sup>258</sup>

The tables below list the fee incentives (partial and total waivers, deferral of payment) applied by the EMA to different types of activities. Where an applicant could, in respect of the same fee, benefit from more than one category of fee reduction or incentive (e.g. ATMP, SME, orphan medicine) the provisions which are the most favourable to the applicant apply.

**Table 1: Fee incentives for SMEs**

Unless specified otherwise, the information in this table applies to micro, small and medium-sized enterprises. Fee incentives (type of incentives and incentive level) for SMEs are laid down in Article 7 and 8 of the SME Regulation (Commission Regulation (EC) No 2049/2005) and the Pharmacovigilance Fee Regulation (Regulation (EU) No 658/2014). Additional fee incentives for SMEs were adopted by the Management Board and included in the Implementing Rules of the Fee Regulation (Council Regulation (EC) No 297/95). These concern:

Type of procedure	Fee incentives for SMEs
<b>Scientific advice / Protocol assistance (initial and follow-up request)</b>	<ul style="list-style-type: none"> <li>• <b>90%</b> reduction to the total applicable fee for non-orphan medicinal products</li> <li>• <b>100%</b> reduction to the total applicable fee for designated orphan medicinal products*</li> <li>• <b>100%</b> reduction to the total applicable fee for products eligible to the PRIME scheme<sup>259</sup></li> </ul>
<b>Inspections (pre-authorisation)</b>	<ul style="list-style-type: none"> <li>• Deferral of total applicable fee</li> <li>• <b>90%</b> reduction to the total applicable fee for non-orphan medicinal products</li> <li>• <b>100%</b> reduction to the total applicable fee for designated orphan medicinal products*</li> </ul>
<b>Inspections (post-authorisation)</b>	<ul style="list-style-type: none"> <li>• <b>90%</b> reduction to the total applicable fee*</li> </ul>
<b>Applications for a marketing authorisation</b>	<ul style="list-style-type: none"> <li>• Deferral of total applicable fee</li> <li>• Conditional fee exemption (unsuccessful application for a marketing authorisation for a medicine for which scientific advice was given by the Agency)</li> </ul>
<b>Scientific services (e.g. certification, Article 58 procedures)</b>	<ul style="list-style-type: none"> <li>• <b>90%</b> reduction to the total applicable fee for non-orphan medicinal products</li> <li>• <b>100%</b> reduction to the total applicable fee for designated orphan medicinal products*</li> </ul>
<b>Establishment, extension or modification of maximum</b>	<ul style="list-style-type: none"> <li>• <b>90%</b> reduction to the total applicable fee</li> </ul>

<sup>258</sup> The fee incentives presented in this Annex can also be found in the Explanatory note on general fees payable to the European Medicines Agency ([EMA/9095647/2019](#)), the Explanatory note on pharmacovigilance fees payable to the European Medicines Agency ([EMA/580301/2018](#)), the Decision of the Executive Director on fee reductions for scientific advice requests on PRIME products for SMEs and applicants from the academic sector ([EMA/63484/2016](#)), and the Executive Director's decision on fee reductions for designated orphan medicinal products ([EMA/317270/2014](#)).

<sup>259</sup> The fee reduction is restricted to the development in the indication for which eligibility to the PRIME scheme was accepted.

<b>residue limits (MRL) for a veterinary medicinal product</b>	
<b>Administrative services (excluding parallel distribution)</b>	<ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee</li> </ul>
<b>Post-authorisation activities<sup>260</sup></b>	<ul style="list-style-type: none"> <li>• Micro-sized enterprises: <b>100%</b> reduction to the total applicable fee</li> <li>• Small and medium-sized enterprises: <b>40%</b> reduction to the total applicable fee</li> <li>• <b>100%</b> reduction to the total applicable fee for designated orphan products during the first year after marketing authorisation*</li> </ul>
<b>Pharmacovigilance activities<sup>261</sup></b>	<ul style="list-style-type: none"> <li>• Micro-sized enterprises: <b>100%</b> reduction to the total applicable fee</li> <li>• Small and medium-sized enterprises: <b>40%</b> reduction to the applicable fee or share of fee</li> </ul>

\* See also Table 2

**Table 2: Fee incentives for designated orphan medicinal products**

The Orphan Regulation (Regulation (EC) No 141/2000) provides in its recitals that fees for orphan designated products should be waived at least in part. The type and level of fee incentives is determined by the EMA Management Board and laid down in the Implementing Rules of the Fee Regulation. These concern:

Type of procedure	Fee incentives for orphan designated products
<b>Protocol assistance (initial and follow-up request)</b>	Non-SME applicants: <ul style="list-style-type: none"> <li>• Non-paediatric-related: <b>75%</b> reduction to the total applicable fee</li> <li>• Paediatric-related: <b>100%</b> reduction to the total applicable fee</li> </ul>
	SME applicants: <ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee*</li> </ul>
<b>Inspections (pre-authorisation)</b>	SME and non-SME applicants: <ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee*</li> </ul>
<b>Inspections (post-authorisation)</b>	SME applicants: <ul style="list-style-type: none"> <li>• <b>90%</b> reduction to the total applicable fee*</li> </ul>
<b>Applications for a marketing authorisation</b>	Non-SME applicants: <ul style="list-style-type: none"> <li>• <b>10%</b> reduction to the total applicable fee</li> </ul>
	SME applicants: <ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee*</li> </ul>
<b>Scientific services<sup>262</sup></b>	SME applicants: <ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee*</li> </ul>
<b>Post-authorisation activities<sup>263</sup></b>	SME applicants:

<sup>260</sup> Post-authorisation activities are defined as: extension of a marketing authorisation; type IA, type IB or type II variation; renewal of a marketing authorisation; transfer of a marketing authorisation to a second micro, small or medium-sized enterprise; annual fee; referral procedure laid down in Article 30(1) or the first sub-paragraph of Article 31(1) of Directive 2001/83/EC initiated by the marketing authorisation holder.

<sup>261</sup> Pharmacovigilance activities are defined as PSURs, PASS, pharmacovigilance-related referrals and the pharmacovigilance annual fee for human medicinal products. The fee incentives for pharmacovigilance activities applicable to SMEs are laid down in Articles 4(5), 5(4), 6(6) and 7(3) of Regulation (EU) No 658/2014.

<sup>262</sup> Fee reductions for scientific services and post-authorisation inspections are not funded by the special contribution from the European Union for designated orphan medicinal products but are provided for by Article 7 of Regulation (EC) No 2049/2005 on SMEs.

	<ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee during the first year after marketing authorisation*</li> </ul>
<b>Pharmacovigilance activities</b>	N/A <sup>264</sup>

\* See also Table 1

**Table 3: Fee incentives for multiple applications on usage patent grounds**

The following reduced fees apply for multiple applications on usage patent grounds. These fee reductions 3 are applicable for as long as the concerned marketing authorisation is affected by usage patent(s) pertaining to indication(s) and/or dosage form(s). Unless specified otherwise, the information in this table applies to both human and veterinary medicines.

Type of procedure	Fee incentives for multiple applications on usage patent grounds
<b>Applications for a marketing authorisation</b>	Second and each subsequent multiple generic and hybrid application <sup>265</sup> : <ul style="list-style-type: none"> <li>• Human medicines: <b>€21,700</b></li> <li>• Veterinary medicines: <b>€14,400</b></li> </ul> Second and each subsequent multiple biosimilar application <sup>266</sup> : <ul style="list-style-type: none"> <li>• Human medicines: <b>€36,200</b></li> <li>• Veterinary medicines: <b>€26,000</b></li> </ul> Additional strengths, pharmaceutical forms and presentations submitted at the same time as the aforementioned applications: <ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee</li> </ul>
<b>Extension of a marketing authorisation</b>	Basic fee: <ul style="list-style-type: none"> <li>• For human medicines: <b>€20,800</b></li> <li>• For veterinary medicines: <b>€7,290</b></li> </ul> Additional strengths, pharmaceutical forms and presentations submitted at the same time as the aforementioned applications: <ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee</li> </ul>
<b>Type IA variation<sup>267</sup></b>	<ul style="list-style-type: none"> <li>• <b>€610</b></li> </ul>
<b>Administrative fees for Worksharing procedure</b>	<ul style="list-style-type: none"> <li>• Type II variations: <b>€2,100</b></li> <li>• Type IB variations: <b>€1,210</b></li> <li>• Type IA variations: <b>€610</b></li> </ul>

<sup>263</sup> Post-authorisation activities are defined in the same way as for Table 1 – Fee incentives for SMEs.

<sup>264</sup> Pharmacovigilance fees, specified in Regulation (EU) No 658/2014, apply to centrally and nationally authorised products (CAPs and NAPs) whereas Regulation (EC) No 141/2000 on orphan medicinal products applies to CAPs only.

<sup>265</sup> For human medicines, these concern applications under Articles 10(1) and 10(3) of Directive 2001/83/EC. For veterinary medicines, these concern applications under Articles 13(1) and 13(3) of Directive 2001/82/EC.

<sup>266</sup> For human medicines, these concern applications under Article 10(4) of Directive 2001/83/EC. For veterinary medicines, these concern applications under Article 13(4) of Directive 2001/82/EC.

<sup>267</sup> This fee shall only apply in the case of grouping of the same type-IA variations to the terms of multiple marketing authorisations on usage patent grounds owned by the same holder (as defined in Article 7(2)(a) of Commission Regulation (EC) No 1234/2008). The applicable fee shall be payable for each individual Type IA variation relating to the second and each of the subsequent multiple marketing authorisations in the grouping.

<b>Renewal</b>	Basic fee: <ul style="list-style-type: none"> <li>• For human medicines: <b>€2,800</b></li> <li>• For veterinary medicines: <b>€1,210</b></li> </ul> Additional strengths, pharmaceutical forms and presentations submitted at the same time as the aforementioned applications: <ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee</li> </ul>
<b>Annual fee for generics and hybrids</b>	<ul style="list-style-type: none"> <li>• For human medicines: <b>€5,000</b></li> <li>• For veterinary medicines: <b>€1,740</b></li> </ul>
<b>Annual fee for biosimilars</b>	<ul style="list-style-type: none"> <li>• For human medicines: <b>€10,000</b></li> <li>• For veterinary medicines: <b>€3,620</b></li> </ul>

**Table 4: Fee incentives for paediatric medicines**

Article 47(1) of the Paediatric Regulation (Regulation (EC) No 1901/2006) provides that a reduced fee should be fixed for the examination of the application and maintenance of the marketing authorisation. In its recitals, it also refers to fee waivers for scientific advice. In accordance with this, the EMA Management Board has adopted the following fee incentives in the Implementing Rules of the Fee Regulation.

Type of procedure	Fee incentives for paediatric medicines
<b>Applications for a paediatric use marketing authorisation (PUMA)<sup>268</sup></b>	<ul style="list-style-type: none"> <li>• <b>50%</b> reduction to the total applicable fee</li> </ul>
<b>Inspection (pre-authorisation) for PUMA</b>	
<b>During the first year after grant of a PUMA:</b> <ul style="list-style-type: none"> <li>• extension of the PUMA</li> <li>• type IA, IB and II variations</li> <li>• annual fee</li> <li>• inspection (post-authorisation)</li> </ul>	
<b>Scientific advice on the development of a medicinal product for the paediatric population<sup>269</sup></b>	<ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee</li> </ul>

In addition to the partial and total fee exemptions shown above, there are several procedures that are free of charge, in accordance with Article 47(3) of the Paediatric Regulation. These concern the assessment of applications for a paediatric investigation plan (PIP), PIP waiver and PIP deferral as well as the assessment of compliance with an agreed PIP.

**Table 5: Fee incentives for advanced therapy medicinal products (ATMPs)**

Fee incentives (type of incentives and incentive level) for ATMPs are laid down in Article 16(2) of the ATMP Regulation (Regulation (EC) No 1394/2007). These concern:

<sup>268</sup> PUMAs concern medicines submitted under Article 30 of Regulation (EC) No 1901/2006 on medicinal products for paediatric use.

<sup>269</sup> These concern medicinal products for the paediatric population as laid down in Regulation (EC) No 1901/2006 on medicinal products for paediatric use.

Type of procedure	Fee incentives for ATMPs
<b>Scientific advice</b>	Non-SME applicants: <ul style="list-style-type: none"> <li>• <b>65%</b> reduction to the total applicable fee</li> </ul> SME applicants: <ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee</li> </ul>

**Table 6: Fee incentives related to pandemic core dossier (including informed consent) for ‘non-recognised’ strain**

The following incentives apply within the framework of the submission of a core dossier for a pandemic influenza vaccines and the follow-up submission of a pandemic variation<sup>270</sup>, as described in the ‘Guideline on dossier structure and contents for pandemic influenza vaccine marketing authorisation application’<sup>271</sup>. These exemptions apply until the Type II pandemic variation, submitted once the human pandemic situation is duly recognised, has been authorised by the European Union but, in any case, do not apply after the five-year period from the date of administrative validation of the marketing authorisation application for the core dossier has elapsed.

Type of procedure	Fee incentives for pandemic core dossiers
<b>Scientific advice</b>	<ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee</li> </ul>
<b>Post-authorisation activities including Type IA, IB and II variations (but excluding Type II pandemic variation) and annual fee</b>	
<b>Negative validation of a Type IB or II variation (but excluding Type II pandemic variation)</b>	

**Table 7: Fee incentives for products for minor uses and minor species (MUMS)/limited markets**

The fee incentives below apply for as long as the veterinary product concerned remains classified by the CVMP as (1) MUMS/limited market and (2) eligible for fee incentives.

Type of procedure	Fee incentives for MUMS/limited markets
<b>Scientific advice</b>	<ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee</li> </ul>
<b>Administrative fee for negative validation</b>	<ul style="list-style-type: none"> <li>• <b>100%</b> reduction to the total applicable fee</li> </ul>
<b>Applications for a marketing authorisation</b>	<ul style="list-style-type: none"> <li>• <b>50%</b> reduction to the total applicable fee</li> </ul>

<sup>270</sup> A special urgent variation procedure is foreseen in Article 21 of Commission Regulation (EC) No 1234/2008 (‘the Variation Regulation’) for pandemic situations. This article provides that where a pandemic human influenza situation is duly recognised by the WHO or the Union, the competent authority (Commission for CAPs) may exceptionally and temporarily accept a variation to the terms of a marketing authorisation for a human influenza vaccine, where certain non-clinical or clinical data are missing.

<sup>271</sup> [EMA/CPMP/VEG/44717/03](https://www.ema.europa.eu/en/documents/variation/emea_cpmp_veg_44717_03_en.pdf)

Extension of existing maximum residue limit (MRL) to relevant minor species for which no data are required and therefore no assessment is performed	<ul style="list-style-type: none"> <li>• 100% reduction to the total applicable fee</li> </ul>
Establishment or extension of maximum residue limit (MRL) for a veterinary medicinal product requiring an assessment of data	<ul style="list-style-type: none"> <li>• 50% reduction to the total applicable fee</li> </ul>
Extension of a marketing authorisation for a MUMS/limited market product to add: <ul style="list-style-type: none"> <li>• another species of food producing animal</li> <li>• another indication classified as MUMS</li> </ul>	<ul style="list-style-type: none"> <li>• 50% reduction to the total applicable fee</li> </ul>
Annual fee for a product authorised exclusively for indications classified by the CVMP as MUMS/limited market	<ul style="list-style-type: none"> <li>• 75% reduction to the total applicable fee</li> </ul>

**Table 8: Fee incentives for pharmacovigilance-related variations to veterinary marketing authorisations**

Type of procedure	Fee incentives for MUMS/limited markets
Type IA variation related to changes to an existing pharmacovigilance system <sup>272</sup>	<ul style="list-style-type: none"> <li>• 100% reduction to the total applicable fee</li> </ul>
Type IA variation relating to a change in the frequency and/or date of submission of a PSUR <sup>273</sup>	

**Table 9: Fee incentives for veterinary vaccines against certain epizootic diseases**

The following fee incentives apply to veterinary vaccines (1) which are indicated against bluetongue, pandemic avian influenza, foot and mouth disease and classical swine fever, (2) which is authorised under normal circumstances and (3) which has not been marketed within the EU/EEA at any time during the totality of the period covered by the fee.

Type of procedure	Fee incentives for veterinary vaccines against epizootic diseases
Renewal	<ul style="list-style-type: none"> <li>• 100% reduction to the total applicable fee</li> </ul>
Annual fee	

**Table 10: Fee incentives applicable to PRIME products**

The fee reduction is restricted to the development in the indication for which eligibility to the PRIME scheme was accepted.

Type of procedure	Fee incentives for PRIME products
Scientific advice	<ul style="list-style-type: none"> <li>• 100% reduction to the total applicable fee, in the case of SMEs and applicants from the academic sector</li> </ul>

<sup>272</sup> Variation no. C.I.9 in the [Variation Guidelines](#) of Commission Regulation (EC) No 1234/2008.

<sup>273</sup> Variation no. C.II.8 in the [Variation Guidelines](#) of Commission Regulation (EC) No 1234/2008.



Applicants from the academic sector must be established in the EEA and fulfil the definition of public or private higher education establishments awarding academic degrees, public or private non-profit research organisations whose primary mission is to pursue research, or international European interest organisations as set out in Commission Regulation (EU) No 1290/2013<sup>274</sup>.

Applicants should not be financed or managed by private profit organisations in the pharmaceutical sector, nor should have they concluded any operating agreements with such organisations concerning their sponsorship or participation to the specific research project for which a fee exemption is sought for scientific advice under the PRIME scheme.

**Table 11: Fee incentives for generics, well-established use, authorised herbal and authorised homeopathic medicines<sup>275</sup>**

Type of fee	Fee incentives for generics, well-established use, authorised herbal and authorised homeopathic medicines
<b>Pharmacovigilance annual fee</b>	<ul style="list-style-type: none"> <li>• <b>20%</b> reduction to the total applicable fee</li> </ul>

<sup>274</sup> Regulation (EU) No 1290/2013 of the European Parliament and of the Council of 11 December 2013 laying down the rules for participation and dissemination in "Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020)" and repealing Regulation (EC) No 1906/2006 Text with EEA relevance: OJ L 347, 20.12.2013, p. 81–103

<sup>275</sup> In accordance with Article 7(4) of Regulation (EU) No 658/2014, the annual fee should be reduced for medicines approved under Article 10(1) or 10a of Directive 2001/83/EC (respectively generic and well-established use medicines), as well as for authorised herbal medicines and authorised homeopathic medicines.



## Annex 8: Methods and analytical models

### 1. Introduction

A quantitative modelling was undertaken as part of the evaluation study supporting the evaluation of the current fee system. The model was designed to:

- Assess the extent to which the fee and remuneration levels under the current financial model correspond to the costs of the European Medicines Agency (EMA) and the National Competent Authorities' (NCAs') contribution to EMA activities;
- For that purpose, generate and test the impact of theoretical cost-based fee systems on the EMA financial model, including the EU/EEA budget contributions, NCA remuneration and industry fees.

The model first determined the cost to EMA and NCAs of undertaking EMA-related activities. Fees and remuneration levels under the current system were then calculated. These were compared to EMA and NCA calculated costs (i.e. the extent to which the current fee system is cost-based). Then, by changing the model parameters, different theoretical cost-based scenarios were tested as a benchmark to the current figures.

### 2. Evaluation questions

The evaluation assesses the strengths and weaknesses of the EMA fee system to show the extent to which fees and remuneration are founded on a sound economic basis, whether they are fair and proportionate, and whether the system avoids unnecessary administrative burden on fee-payers. In line with the Commission's Better Regulation Guidelines<sup>276</sup>, the assessment is based on the examination of the following criteria and associated high-level evaluation questions:

1. **Effectiveness and efficiency:** To what degree is the financial model of fees charged by EMA to industry at large sustainable and fair, including the remuneration paid by EMA to NCAs?
2. **Relevance:** To what degree does the fee system fulfil the need to fund the relevant legislative tasks of EMA, including the remuneration of NCAs?
3. **Coherence:** To what degree is the EMA fee system coherent, internally and externally?

The criterion of **EU added value** was not evaluated. Although there are implicit benefits for Member States of being part of the centralised regulatory system, Regulation (EC) No 726/2004, which governs this system, is not within scope of this evaluation. In addition,

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<sup>276</sup> For more information, please see [https://ec.europa.eu/info/law/law-making-process/planning-and-proposing-law/better-regulation-why-and-how/better-regulation-guidelines-and-toolbox\\_en](https://ec.europa.eu/info/law/law-making-process/planning-and-proposing-law/better-regulation-why-and-how/better-regulation-guidelines-and-toolbox_en)

the criterion of EU added value is not considered applicable to the fee system itself, since a fee system for an EU agency like the EMA can only be set by EU legislation.

The main questions were supported by several sub-questions, which are outlined in the table below.

<b>Effectiveness and efficiency</b>	
Q1	To what extent do the fees charged correspond with EMA and NCA costs?
Q2	To what extent does the current financial model allow the EMA to effectively perform the activities in its remit?
Q3	To what extent does the current financial model allow the EMA to remunerate the NCAs adequately for the activities they perform?
Q4	To what extent is a balance struck between a fee and remuneration system based on actual costs and simplicity of the system?
Q5	To what extent does the system enable needs to be met in exceptional circumstances or under particular priorities/Imperatives?
Q6	To what extent are SMEs and micro-sized enterprises supported through effective reductions in their costs to use the system?
Q7	To what extent does the current financial model ensure financial stability of the EMA including its ability to remunerate NCAs?
<b>Relevance</b>	
Q8	To what extent does the fee system address the problems and needs originally identified to fund the relevant legislative tasks of the EMA, including NCA remuneration?
Q9	Is the fee system relevant in terms of current needs?
<b>Coherence</b>	
Q10	To what extent is the fee system coherent internally?
Q11	To what extent is the fee system coherent with Member State fee systems?
Q12	To what extent is the fee system coherent at EU level with other EU policies?

A detailed assessment matrix is presented in Appendix 1 of RAND’s Final Report on the study for the evaluation of the EMA fee system. This matrix was used to guide the assessment of judgement criteria. The data collection tasks listed in Section 4.1 targeted the sets of indicators for each of the judgement criteria. Information collected under each approach was aggregated and analysed separately to identify the main findings emerging from each. The results were then drawn together to allow for a synthesis of findings for each judgement criterion across all of the evaluation questions.

### **3. Consultation questions**

The contractor performed extensive targeted consultations with EMA and NCAs. Other stakeholders, in particular industry, were consulted via an online survey. In addition, an online public consultation (OPC) was held.

The targeted consultations consisted of: in-depth interviews with representatives from the EMA; a survey targeted at all NCAs within the EU/EEA regulatory network; an in-depth interview with representatives from a selection of NCAs<sup>277</sup>; and a survey for a wider stakeholder group of associations for industry, researchers and healthcare professionals. Selected NCAs represent both the human and veterinary sector, exhibit different levels of EMA engagement and are located in different parts of the EU.

The objective of the targeted consultations and the online public consultation was to elicit the views of stakeholders and interested EU citizens on the relevance, efficiency, effectiveness, coherence and sustainability of the EMA fee system. In addition, the survey of NCAs was also designed to collect data from NCAs on their costs incurred from undertaking EMA-related activities, including corresponding overhead costs, as well as on their level of engagement with the EMA.

## **4. Model overview**

### **4.1. Modelling approach, inputs and outputs**

The objective of the modelling exercise was to calculate costs and income of EMA and NCAs, both in aggregate and at the individual NCA level, for different categories of EMA-related services, with the aim to gain understanding of how well the existing fee system reflects the costs of the activities undertaken. These categories are:

1. For EMA and NCAs: Fee- and non-fee-generating procedural activities;
2. For NCAs: Non-procedural time spent in meetings of EMA committees and working parties and on the preparation for those meetings. (For the EMA, time spent in and on committees is mostly procedure-related and was therefore allocated across the relevant procedural activities);
3. For EMA and NCAs: Additional activities not covered under category 1 or 2.

The model calculated costs incurred by EMA and NCAs on EMA-related services and an EMA income from industry fees and Union budget contributions as well as NCA income from EMA remuneration.<sup>278</sup>

The following data were used as model inputs:

- Time data (workload):  
Over the period of December 2015 – March 2017 EMA’s MBDG Steering Group collected time data for EMA and NCAs for two type of activities:
  - Fee- and non-fee-generating procedural activities<sup>279</sup>.

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<sup>277</sup> Selection was based on level of involvement in EMA activities and taking into account geographical diversity of NCAs.

<sup>278</sup> NCA income other than remuneration paid by the EMA, e.g. fees received via national fee systems and contributions from national budgets, is outside of the scope of this evaluation and, hence, was not used for the modelling exercise.

- Non-procedural time spent in meetings of EMA committees and working parties and on the preparation for those meetings.<sup>280</sup>
- Cost data:  
The contractor collected from EMA (directly) and NCAs (via the survey and direct follow-up) the following cost data incurred during a one-year period (2016): total costs per NCA for EMA- and non-EMA-related work; NCA total staff and non-staff costs (further split between EMA-related and non-EMA-related work); NCA total overhead costs (further attributed to staff and non-staff costs); EMA total overhead and total staff costs; EMAs costs for EMA's additional activities.
- Frequency of procedure-related activities:  
The number of activities completed by EMA in the reporting year was based on the number of invoiced procedures<sup>281</sup>. NCAs were asked to provide for a list of procedure-related activities the number of times they completed each of those activities within the reporting year as rapporteur, co-rapporteur or 'other, including multi-national teams'. Where an NCA indicated that it had no data available or that, for certain activity types, it had only data in aggregate<sup>282</sup>, purchase order data provided by the EMA were used to determine their involvement per activity type<sup>283</sup>. For procedural activities where NCAs do not receive remuneration (i.e. non-fee-generating activities and non-remunerated roles for fee-generating activities) the number of procedures per year was determined solely on the basis of NCAs' responses to the survey. With a few exceptions, the survey list was aligned with the list of activities for which time data were gathered as part of the MBDG exercise, see Annex 9.
- Additional activities:  
NCAs were asked to report additional activities not covered by the aforementioned survey list which they considered to be EMA-related and for which they incurred costs in the reporting year. The respective cost of these additional activities was calculated as an output, based on the total cost declared by NCAs as EMA-related (see below). EMA also provided a list with additional activities, including the costs incurred per activity. The list of these additional activities reported respectively by EMA is provided in Section 5. The list of additional activities declared by NCAs

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<sup>279</sup> For the full list of activities for which time data were collected, see Annex 9.

<sup>280</sup> For the MBDG exercise a common data collection method was applied across the regulatory network. Participation was voluntary but widely publicised. Data were gathered on the vast majority of fee- and non-fee-generating activities and committee/working party time. Activities not covered by the MBDG exercise relate to cross-cutting areas where there are no individual procedures. These are discussed under 'additional activities' which are different for EMA and for NCAs.

<sup>281</sup> Invoices are sent to payers prior to the start of each procedure, presenting the fee due for that procedure.

<sup>282</sup> This was the case for procedures for which different fee and complexity levels exists, i.e. scientific advice, initial marketing authorisations, line extensions and Type II variations. Some NCAs were only able to provide the total number of each of these procedures, but had no data available on the portion of the different levels (Level I, II or III) per type of procedural activity.

<sup>283</sup> For each fee-generating procedure involving NCAs, EMA sends out purchase orders (POs) to the NCAs acting as rapporteur or co-rapporteur as a commitment for future remuneration. POs are not sent for unremunerated roles (e.g. peer-review) and procedures (e.g. PIP).

requires further analysis, which was not within scope of this evaluation, and has therefore not been included in this document. However, a few examples of reported activities are given in Section 5.

The model integrated (with some simplification) the rules for fees (including incentives) charged to industry and remuneration paid to NCAs that pertain under the current fee system.

#### Outputs of the baseline model:

The modelling process followed a series of steps to calculate the different components of the costs and revenues for the existing fee system and for theoretical cost-based scenarios.

The first step was to calculate the actual baseline costs and shares of fee income for EMA and NCAs. The baseline year is the year for which data were reported by EMA and NCAs (2016). The model uses data from three sources:

- The NCA survey conducted by the study team;
- The Management Board Data Gathering (MBDG) exercise carried out by the EMA Management Board; and
- Information on EMA costs and revenues provided by EMA.

These sources provide information on the number of procedural activities that were undertaken by EMA and the NCAs and the estimated time taken to carry them out (per type of procedure). Cost and revenue data are also provided separately. The activities include both fee- and non-fee-generating procedural activities. A validation of the time data from the MBDG data was undertaken before it was used in the model (see further below in this Annex).

In the baseline, data reported by EMA and NCAs for the baseline year and the validated time data were used in the model to calculate costs and fees. Costs were calculated using an activity based approach. Fees and NCA remuneration were calculated using the fee and remuneration rules that pertain under the current fee system.

The baseline model provides a verification of the modelling approach in which the costs calculated for EMA could be compared with the actual costs EMA reported, and the total calculated fee remuneration for NCAs could be compared with the NCA remuneration reported by EMA. Secondly, the baseline model serves to calculate the EMA-related costs of additional activities reported by NCAs, i.e. the total cost of EMA-related activities declared by the NCAs less the calculated cost for procedures less the calculated cost for non-procedural time spent in EMA committees and working parties. (The additional NCA activities are discussed in more detail in Section 4.2 on the limitations and robustness of the findings). The actual 2016 EU and EEA budget contributions are used as fixed inputs in the model in the baseline.

The objective pursued with the model was to represent a 'typical' year for both EMA and NCAs in terms of services provided and activities undertaken. Therefore, the next step was to determine the fees and costs for a 'synthetic baseline' which is an adjusted baseline where the effect of differences in the way EMA and NCAs reported data was neutralised. The synthetic baseline was used to determine NCA costs as well as EMA costs (net of NCA remuneration) for a typical year. The current fee and remuneration rules were then applied to the synthetic baseline year to determine revenues (EMA share of fee income and NCA remuneration).

Based on the above, the following calculations were made for the reporting year (baseline):

- In the cost model: (i) EMA and NCA costs per procedural activity and total costs for procedural activities. For NCAs, this was done for each individual NCA as well as for NCAs in aggregate; (ii) Costs incurred by NCAs for participation in committees and working parties were calculated based on data gathered via the MBDG exercise<sup>284</sup>. These costs are further referred to as 'committee time'; (iii) Costs incurred by NCAs for additional activities were calculated as the total costs reported by NCAs incurred for EMA-related activities (with the overheads attributed) minus the calculated total costs for procedural activities and the calculated total costs for the time spent on participation in committees and working parties.
- In the revenue model: (i) EMA's total fee income (both in aggregate and per procedural activity) was determined by applying the fee rules of the current fee system to the number of times EMA completed a procedural activity in the reporting year. (Amounts for NCA remuneration, based on existing rules, were then deducted from this revenue to determine EMA's net share of fee income); (ii) NCA remuneration was calculated by applying the existing remuneration rules to the data on their level of engagement (frequency); (iii) The level of Union contributions received by EMA was based on the actual amount received in 2016; the 'other income' of EMA, i.e. income that EMA receives from administrative operations such as sale of publications and organisation of seminars (3.2 to 7.4% of EMA's budget between 2007 and 2017, see Section 5) was calculated as a residual.

From 'baseline' to 'synthetic' model (typical year):

In the baseline model, the yearly number of procedural activities undertaken by EMA involving NCAs and the number of procedural activities reported by NCAs did not fully match. The reason for this is that EMA's activity level was based on the number of *invoiced* procedural activities, whereas NCAs were provided data on procedures *completed* in the reporting year. As a result, EMA costs and fee income were based on a different data set than NCA costs and remuneration. Further, not all NCAs replied to the

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<sup>284</sup> These data included: (a) attendance time to all committees and working parties/groups when not actively discussing procedures for which members were acting as (co-)rapporteur (time for active discussions on their respective procedures was recorded under the procedure itself); (b) travelling time to / from the EMA from / to their respective NCAs; (c) preparation and debriefing time of members and for any additional support received by scientific and administrative staff in their own NCAs.

survey; 30 NCAs responded to the survey, and data from 29 of those 30 NCAs could be included in the baseline calculations. However, these 29 NCAs undertook 95% of the procedural activities conducted in the reporting year. In order to be able to compare fees, remuneration amounts and costs directly, a synthetic baseline was developed to represent a ‘typical year’. For this typical year, it was assumed that: (1) there is a common set of activities for both EMA and NCAs<sup>285</sup>, (2) the 29 responding NCAs undertake all procedural activities invoiced for the reporting year<sup>286</sup>, and (3) the average incentive rate applied to procedural and annual fees in 2016 is representative of a typical year<sup>287</sup>. Data for committee time, additional activities and Union contributions in the synthetic year did not change as compared to the baseline. Outputs of the synthetic baseline calculations were average costs for EMA and for NCAs for undertaking a particular procedural activity, EMA fee income, and NCA remuneration based on NCAs’ average costs. These costs and incomes were calculated for both individual types of procedural activities (unitary costs) and yearly totals over all procedural activities for EMA, for individual NCAs and for NCAs in aggregate. No average costs were calculated for NCA committee time and additional activities. Instead, total costs equal the sum of individual NCA costs for these activity types as calculated by the baseline model.

Theoretical fee levels used as benchmark to test the extent to which the current fee system is cost-based:

Finally, the contractor developed several cost-based benchmark scenarios, using data from the synthetic baseline, to assess the impact of a change in NCA remuneration level on the level of procedural fees, annual fees or Union contributions. In a cost-based system, fees charged for a particular activity reflect average costs incurred for undertaking that activity. Three different definitions of ‘cost-based system’ were tested by calculating the level of fees and Union contributions for three different remuneration scenarios: (i) where NCAs would be remunerated for procedural activities at average cost, (ii) where NCAs would be remunerated for procedural activities at average cost plus

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<sup>285</sup> This means that for procedural activities involving both EMA and NCAs, the number of activities undertaken by EMA equals the number of activities undertaken by NCAs at EMA’s request. Procedural activities involving only EMA equal the number of invoiced procedures.

<sup>286</sup> This was achieved by scaling up the number of activities undertaken by the responding 29 NCAs as rapporteur and co-rapporteur to match the number of procedures for which POs were sent by EMA in the reporting year. The same scaling factor was applied to the number of activities reported for non-remunerated roles (e.g. peer-reviewer).

<sup>287</sup> EMA provided the monetary value of incentives applied in 2016 based on the invoiced procedures for a given activity in that year. From this, the average incentive rate (in percentage) was calculated for a given activity. As explained in Section 2, the average incentive rate depends on the nature of the product, the type of procedural activity and the type of applicant. It was assumed that the combination of types of product, procedures and applicants observed in 2016 are representative for a typical year, allowing for the application of the same, single incentive rate calculated in the baseline to the synthetic baseline and the cost-based benchmark scenarios.

committee time in aggregate, and (iii) where NCAs would be remunerated for procedural activities at average cost plus committee time plus additional activities.<sup>288</sup>

The synthetic baseline calculations and benchmark scenarios allowed to draw conclusions on whether, and to what extent, fees charged for procedural activities reflect average costs incurred by EMA, NCAs in aggregate and individual NCAs, both at the level of individual procedural activities as for procedural activities in total. It further allowed to assess what the impact of different cost-based theoretical fee systems would be on EMA, NCAs and industry.

## **4.2. Verification and validation of time and cost data**

The contractor undertook an extensive data verification and validation exercise on the information collected via the MBDG exercise and as provided by NCAs and EMA in support of the contractor's study. The following steps were undertaken:

- The time data gathered through the MDBG exercise were validated in order to identify which data, if any, should be excluded from the cost estimates to be undertaken in the study. Outliers were characterised and assessed in terms of behaviour of an organisation relative to other organisations or the particular procedure of interest. Findings were compared across organisations and activities and to a previous pilot cost exercise carried out by EMA in 2009.<sup>289</sup>
- A three-stage verification and validation exercise was undertaken with EMA and NCAs to review and confirm the data they provided for the evaluation study. This exercise comprised two rounds of review of the factual summary reports summarising EMA and NCAs' inputs to the study and review of the interim report and methodology note. Any remaining uncertainties were clarified and confirmed via ongoing exchanges with EMA and NCAs via email and telephone.
- Data provided by NCAs via the survey were triangulated against data provided by EMA and information obtained through desk research.
- The main verification of EMA data was to check that EMA fee income and costs calculated via the modelling exercise match the fee income and costs reported by the EMA.

The main findings of the validation exercise are that time data outliers do not appear to be associated with particular activities, organisations, roles or staff types. Given the relatively short time period for data collection and the range of complexity in the procedures for which time was reported, there were insufficient grounds to exclude the outliers. Further, it was identified that the time reported by the same organisation for the same type of procedural activity may vary significantly. No evidence was however found

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<sup>288</sup> Average NCA costs for procedural activities used in the different scenarios were the average costs for NCAs in aggregate and not average costs per NCA.

<sup>289</sup> This pilot exercise aimed to assess the costs of assessment of centralised applications by NCAs: Minutes of the 65<sup>th</sup> meeting of the Management Board ([EMA/MB/806136/2009](#)), Agenda point 12.



that any NCA consistently reported a longer time to complete an activity as compared to other NCAs and, thus, it is likely that this variation in time reporting reflects a variation in the level of complexity for the same type of procedure (e.g. marketing authorisation applications).

### **4.3. Desk research**

The contractor performed an extensive desk research which consisted of the following components:

- A review of existing information sources on the EMA fee system (including legislation, EMA annual and budget reports, and European Court of Auditors reports);
- A review of both time data collected via the MBDG exercise as well as cost data from EMA and NCAs. These data were used as main input for the modelling;
- A review of fee systems used by other EU agencies (European Chemicals Agency (ECHA), European Union Intellectual Property Office (EUIPO), European Aviation Safety Agency (EASA)) and the U.S. Food and Drug Administration (FDA). This review was conducted to compare the EMA fee system with other fee-based approaches.

### **4.4. Analysis and synthesis of collected information**

The objective of this step was to assess the judgement criteria identified in the evaluation framework and to formulate answers to the evaluation questions regarding the extent to which the EMA fee system is effective, efficient, coherent, relevant and sustainable. The contractor used an extensive evaluation matrix to guide the assessment of judgement criteria.<sup>290</sup> Information collected and calculated via the desk research, targeted and open consultations and modelling exercise was aggregated and analysed separately to identify the main findings emerging from each of these approaches. The results were then drawn together to allow for a synthesis of findings for each judgement criterion across all of the evaluation questions in the matrix. Different sources were used to validate and triangulate the findings. Triangulating the findings from each data source contributed to the weight of evidence. Based on this, the study concluded that, while for some research questions the conclusions are more tentative, on the whole the study supporting the evaluation presents a coherent and robust set of answers to the evaluation questions.

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<sup>290</sup> RAND Europe, 2018, Study for the evaluation of the EMA fee system – Final report: Appendix 1

## Annex 9: List of activities included in the MBDG exercise and financial modelling

Activities	Included in the MBDG exercise	Time period for data collection	Activities included in the financial modelling
<b>Human medicinal products</b>			
	Scientific advice/Protocol assistance (initial request and follow-up request (Level I, II and III))	February – June 2015	Scientific advice/Protocol assistance (initial request and follow-up request (Level I, II and III))
	Initial marketing authorisations (new active substance, known active substance, fixed-dose combination, generic, hybrid, biosimilar, informed consent, well-established use (phase I, II and III))	January – September 2016	Initial marketing authorisations (new active substance, known active substance, fixed-dose combination, generic, hybrid, biosimilar, informed consent, well-established use)
	Line extensions (phase I, II and III)	January – September 2016	Line extensions (Level I, II and III)
	Type II variations (new clinical indication, clinical, clinical safety and quality)	January – September 2016	Type II variations (Level I, II and III)
	Type IB variations	July 2016	Type IB variations
	Type IA variations	July 2016	
	Renewals	January – September 2016	Renewals
	Transfer of marketing authorisation	January – October 2016	
	Pharmacovigilance Referrals	January – October 2016	Pharmacovigilance referrals (Art.31, Art.20, Art.107i)
	PSUR	January – October 2016	Periodic Safety Update Reports for CAPs (PSUR) Periodic Safety Update Reports for NAPs & CAP/NAP (PSUSA)
	PASS	January – October 2016	Post-AUTHORISATION Safety Studies (PASS)
	PIP (phase I and II)	March – September 2016	PIP (phase I and II)

	PIP modification	March – September 2016	
	PIP compliance check	March – September 2016	PIP compliance check
	Orphan designation (initial assessment and re-assessment)	March – September 2016	
	Non-Pharmacovigilance referrals (Art. 29(4), Art. 30, Art. 31, Art. 13, Art. 5(3))	March – September 2016	Referrals of disputes from decentralised and mutual recognition procedures (Art.29(4), Art.30, Art.31, Art.20)
	<b>Veterinary medicinal products</b>		
	Scientific Advice	July 2015 – April 2016	
	Maximum Residue Limits (MRL) (phase I, II and III)	January – November 2016	
	Initial Marketing Authorisations (new active substance, known active substance, generic (phase I, II and III))	January – November 2016	
	Line extensions (line-extension and line-extension + re-examination (phase I, II and III))	January – November 2016	
	Type II variations (quality/clinical, clinical, quality)	July 2015 – August 2016	
	Type IB variations	May – August 2016	
	Type IA variations	May – November 2016	
	Renewals	March – September 2016	
	Transfer of marketing authorisation	March – October 2016	
	Minor use/Minor species procedures (MUMS)	April – October 2016	
	PSUR	April – July 2016	
	Surveillance and signal detection	April – July 2016	
	Adverse event reporting (AER)	April – July 2016	

	Rapid alert (RA)/non-urgent information (NUI) with and without incident management plan (IMP)	April – July 2016	
	Referral procedures (Art. 34 and Art. 35 (phase I, II and III) and Art. 45 (total procedure))	March – August 2016	
<b>Inspections/Parallel Distribution &amp; Certificates (human and veterinary)</b>			
	Parallel distribution	February – October 2016	
	Issuing certificates	February – October 2016	
	GMP Inspections	February – October 2016	
	GCP Inspections (human only)	February – October 2016	
	Pharmacovigilance Inspections (human only)	February – October 2016	
	<b>Scientific committee activities</b> (CHMP, PRAC, CVMP, PDCO, CAT, HMPC, COMP)	September – October 2016	
	<b>Working party activities</b> (BWP, BSWP, SAWP, SWP, INRG, PKWP, RIWP, BPWP, MSWG, CNSWP, HCPWP, CVSWP, BMWP, PCWP, VWP, GEG, RDG, IDWP, ONCWP, GDG, HMPC QDG, EXCP DG, PGWP, RAD DG, GCG, EWP, AWP, PhVWP, IWP, ERAWP, ADVENT, SWP, QWP, QRD, JEG 3RS, GCP IWG, GMPDP IWG, PHV IWG, PAT)	April– July 2016	

## **Annex 10: Stakeholder consultation**

### **1. INTRODUCTION**

This synopsis report presents the results from the stakeholder consultations conducted for the ‘Study for the evaluation of the European Medicines Agency fee system’.

The objective of the consultation was to obtain information that should, together with other data provided by the European Medicines Agency (EMA) Management Board (Management Board Data Gathering Exercise, MBDG), enable the study team to examine the economic basis of the current fee and remuneration system and to identify assessment options and benchmarks to evaluate to what extent it is cost-based, fair, proportionate and not unduly complex. The consultation activities were related to the four main evaluation criteria that were used by the contractor: effectiveness and efficiency, relevance, coherence and sustainability.<sup>291</sup> The consultation activities were complemented by extensive desk research and review of documents and information resources relevant to the fee and remuneration system, a validation of time data provided by the EMA MBDG exercise and the development of a costing methodology and financial modelling for the fee and remuneration system.

This document covers the four main consultation activities conducted as part of the evaluation of the EMA fee and remuneration system based on the relevant legislation and implementing arrangements: (1) consultation with representatives of the EMA (in-depth interviews); (2) consultation with representatives of National Competent Authorities (NCAs) (survey of all NCAs and in-depth interviews with selected NCAs); (3) consultation with wider stakeholders (survey); and (4) online public consultation (survey).

### **2. CONSULTATION STRATEGY AND METHODOLOGY USED FOR THE CONSULTATION ACTIVITIES**

#### **2.1. Stakeholder mapping**

The study team conducted a stakeholder mapping exercise prior to the consultation activities to (1) identify relevant stakeholder groups: the EMA, NCAs and European-level industry, research, healthcare, patient, consumer, and other relevant associations and representative groups; (2) assess their involvement in, and the influence they exert on the fee system; and (3) determine the views in terms of potential changes to the fee system, and the differences in views across stakeholder groups.

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<sup>291</sup> In this Staff Working Document, the findings relevant to the contractor’s study criterion ‘sustainability’ have been incorporated under the evaluation criterions as used for this Commission evaluation (effectiveness and efficiency, relevance and coherence).

The stakeholder mapping exercise followed a three-step approach and considered both internal and external stakeholders:

1. **Stakeholder identification:** The study team consulted DG SANTE and EMA representatives on the list of stakeholders. The document review conducted during the inception phase was used to elaborate, extend and confirm the stakeholder mapping.
2. **Characterisation and categorisation:** Stakeholders were characterised according to their expected levels of interest and influence in the subject of the study, and categorised based on the estimated impact of EMA-related activities on each group, the influence the stakeholder may exert on the fee system, and the dependence (sensitivity) of the stakeholders on the fee system's outcomes and the actions of other stakeholders. The assessment was used to identify the best approach to consulting with stakeholders for the study.
3. **Identify representatives and their preferred contact channels:** The categories (and sub-categories) defined in the previous step provided the input for determining sets of target groups and allowed the study team to adapt its engagement approach/data collection methods, for example, the suitability of particular stakeholder groups for the targeted consultation or public consultation.

## **2.2. In-depth interviews with representatives of the EMA**

The study team conducted interviews with representatives of the EMA to obtain information on data gaps identified in the MBDG exercise and contextual factors that are not documented to develop a description of the current fee and remuneration system. Individual interviewees were identified in consultation with the EMA.

Overall, eight group interviews with two to six individuals each were conducted face-to-face at EMA headquarters in London, UK on 23 and 27 March 2017. Interviewees included the EMA Executive Director and Deputy Executive Director and representatives from several divisions: stakeholders and communication; administration, legal and audit; information management; Human Medicines Research and Development (R&D); Human Medicines Evaluation; Inspections and Pharmacovigilance; and Veterinary Medicines.

## **2.3. Survey of NCAs**

The objective of the NCA survey was to obtain information that should, together with other data provided by the EMA Management Board, enable the study team to examine the economic basis of the current fee and remuneration system. Beyond specific questions on time and cost data related to NCAs' activities for the EMA, respondents were invited to submit any additional comments and documents they deemed necessary. In addition, respondents could describe strengths and weaknesses of the current fee and remuneration system.

The survey was sent to representatives of all EU and EEA NCAs and was open for eight weeks, from 4 April to 30 May 2017. Overall, 30 of 47 NCAs (based on a list provided by the EMA) participated in the survey, representing 23 Member States and 95% of all NCAs EMA-related activities in the reporting period (2016).

#### **2.4. In-depth interviews with NCAs**

In-depth interviews with representatives of selected NCAs were undertaken to obtain detailed information on any gaps identified in the survey and allow the study team to explore NCAs' views. Coverage across all activities, and the geographic distribution of NCAs was considered to ensure representation from across the European regions. Interviews were conducted with representatives of the following ten NCAs:

- **Focus of the interviews on human medicines:** Austrian Medicines and Medical Devices Agency (Austria), State Institute for Drug Control (Czech Republic), Federal Institute for Drugs and Medical Devices (Germany), Paul-Ehrlich-Institut/Federal Institute for Vaccines and Biomedicines (Germany), National Institute of Pharmacy and Nutrition (Hungary), Medicines Evaluation Board (Netherlands) and Medicines and Healthcare Products Regulatory Agency (United Kingdom).
- **Focus of the interviews on veterinary medicines:** French Agency for Veterinary Medicinal Products (France) and Health Products Regulatory Authority (Ireland).

The interviews took place between 3 July and 29 August 2017.

#### **2.5. Survey of wider stakeholders**

The main objective of the survey of wider stakeholders (WS survey) was to elicit external stakeholders' views on the EMA fee and remuneration system. It addressed stakeholders covering European-level industry, research, healthcare, patient, consumer and other relevant associations and representative groups.

The survey was sent to 116 wider stakeholder representatives. It was open for eight weeks, from 5 May to 30 June 2017. A total of 44 responses were received, of which 40 were complete and not duplicates. Table 1 provides an overview of the respondents by organisation/institution type.

**Table 1: Breakdown of respondent types (n=40)**

Type of respondent	Contacted	Responses received
Pharmaceutical Industry (Large)	51	11
Pharmaceutical Industry (SME)		14
Industry organisation		3
Wholesalers association		1
Research organisation	20	7
Healthcare professional association	38	0
Public Health NGO		0
Patient association	7	1
Other/respondent type not provided	n/a	3
<b>Total</b>	<b>116</b>	<b>40</b>

**Notes:**

- *When identifying the stakeholders, the study team clustered some stakeholder types in larger groups: Pharmaceutical Industry (Large), Pharmaceutical Industry (SME), Industry organisation and Wholesalers association; healthcare professional associations and Public Health NGOs.*
- *Respondents were asked to self-identify the type of their organisation/institution. The clusters and identification of types made by the study team prior to sending the survey invitations thus do not necessarily match respondents' self-reported values.*

**2.6. Online public consultation**

The objective of the online public consultation (OPC) was to elicit information, views and concerns of all groups and individuals having an interest in the EMA fee system and its implementation, including the remuneration to NCAs. In particular, it sought to gather input from stakeholders having experience with the fee and remuneration system on its effectiveness and efficiency, relevance, coherence and sustainability.

The OPC was open for 13 weeks, from 2 May to 2 August 2018. A total of 51 responses to the OPC were received. An overview of the respondents by type is provided in Table 2.



**Table 2: Breakdown of respondent types (n=51)**

Type of respondent	Count
Representative of a company with direct relevance to the EMA (e.g. pharmaceutical company)	22
<i>Large enterprise (more than 250 employees)</i>	10
<i>Micro, small- or medium-sized enterprise (0–249 employees)</i>	12
Member of a research organisation/academic institution	9
Individual citizen in their personal capacity	6
Member of a representative organisation	5
Member of a non-governmental organisation (NGO)	3
Member of a Member State/EEA medicine regulation agency	2
Member of a central government or public authority at EU level	1
Member of a civil society organisation	1
Member of a think-tank/consultancy	1
Representative of a company with no direct relevance to the EMA	1
<b>Total</b>	<b>51</b>

Both the WS survey and the OPC asked respondents to provide their organisational affiliation. An analysis of the affiliations showed that representatives of only two organisations (both are large pharmaceutical companies) replied to both surveys.<sup>292</sup>

## 2.7. Presentation and interpretation of results

Questions asked in the surveys of NCAs and WS were optional; therefore the sample size (n) for each question varies. Multiple choice questions where only one option could be selected are reported as percentages in the analysis. Questions where multiple options could be selected are reported as response counts.

Although 30 of 47 NCAs responded to the survey of NCAs, the cross-analysis of the quantitative data showed that those 30 NCAs undertook 95% of all EMA activities in the reporting period. Findings related to cost and time data can thus be understood as representative of the overall group of NCAs. However, any other responses to the survey of NCAs, to the WS survey and to the OPC as well as information shared in the interviews cannot be understood as representative of views of any particular population or group of stakeholders. Information on the demographic profile of respondents is based

<sup>292</sup> In the OPC, indicating the organisational affiliation was optional; 26 respondents did not provide this information (nine representatives of research organisations; six individual citizens; three NGO representatives; two NCA representatives; two patient organisation representatives; one civil society organisation representative; one representative of a representative organisation; one representative of a central government or public authority at EU level; one representative of a think-tank/consultancy).

on self-reported values and the survey design did not allow for any verification of received data.

Stakeholder-specific findings from the WS survey and the OPC are included in this document; however, these stakeholder-specific results need to be interpreted with caution given the overall low number of respondents to both consultation activities (WS survey: 40 respondents; OPC: 51 respondents). In addition, 12 of 27 respondents who submitted final comments to the OPC provided the same verbatim (or almost verbatim) responses. Similarly, seven NCA survey respondents used the same verbatim (or slightly changed) replies to the three open questions on strengths and weaknesses of the EMA fee and remuneration system.

The results in the consultation activities cannot be regarded as the official position of the European Commission and its services and thus do not bind the Commission.

### 3. RESULTS OF THE CONSULTATION ACTIVITIES

This section presents the results of each of the consultation activities described above. Findings are presented for each of the four evaluation criteria used by the contractor (effectiveness and efficiency, relevance, coherence and sustainability), and structured along key themes addressed in the consultation activities. The results of the consultation activities were compared where applicable to show any similarities in views, interdependencies, consistencies or contradictions.

#### 3.1. Effectiveness and Efficiency

##### 3.1.1. Transparency

Overall, stakeholders considered the fee system to be clear and transparent. More than half of NCA survey respondents (19 of 30 NCAs in open-text responses), WS survey respondents WS survey (21 of 39 respondents) and OPC respondents (34 of 51 respondents) found the fee system to be transparent (Table 3).

**Table 3: WS survey and OPC: extent of agreement with statements related to the transparency of the fee and remuneration system<sup>293</sup>**

Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Do not know
WS survey: ‘Overall, the fees charged for different EMA services are transparent.’ (n=39)	0%	54%	31%	5%	0%	10%
OPC: ‘The operation of the EMA fee system is transparent.’ (n=51)	10%	57%	14%	2%	2%	16%

<sup>293</sup> Percentages in this table were rounded and may not sum up to 100%.

However, several NCA, wider stakeholder and OPC respondents highlighted their views of areas in need of more transparency, which include:

- The fee split between EMA and NCAs and which activities are reimbursed or not (11 NCA survey respondents and one patient organisation representative in the OPC).
- The timing of reimbursement to NCAs (mentioned by 11 NCA survey respondents)
- The breakdown of fees, i.e. the cost of an activity and to what extent each activity would be remunerated (mentioned by six NCA survey respondents) and how much each activity costs (mentioned by a representative of a large pharmaceutical company who responded to the WS survey).
- Fee exemptions and reductions (mentioned by three NCA survey respondents).
- How the EMA spends its share of the fees (mentioned by two NCA survey respondents).
- Time spent by NCAs on activities (mentioned by two company representatives in the OPC).
- Use of the annual fees (mentioned by a member of the European Federation of Pharmaceutical Industries and Associations (EFPIA) in the OPC).
- Why academic institutions have to pay the same for scientific advice as large pharmaceutical companies (mentioned by one academic respondent in the OPC).

EMA representatives did not report any transparency issues.

### **3.1.2. *Fairness of the fee system***

Overall, consulted stakeholders found the fee and remuneration system fair and felt that there is proportionality between the fees charged to industry and the services provided. However, they also highlighted areas where more fairness is needed.

EMA representatives discussed the fairness of the fee system when reflecting on possible changes to the current fee and remuneration system. For instance, they noted that more simplicity through, for example, introducing a flat fee could make the fee system more unfair to industry payers. NCA survey respondents directly referred to the perceived fairness of the current fee system: a majority of NCAs (63% or 19 NCAs) noted that the current fee system is fair when it comes to the fees charged to industry, given industry's access to the overall EU population of more than 510 million people. Several NCA and EMA interviewees also indicated that legislative changes such as the amended pharmacovigilance legislation made the fee system fairer.

Compared to NCA and EMA representatives, respondents to the WS survey and the OPC showed less satisfaction regarding the appropriateness of the level of fees charged by the EMA given the services they provide: 25% of respondents to the WS survey and 33% of OPC respondents agreed that the fees are appropriate, while 25% of WS survey respondents and 8% of OPC respondents disagreed or strongly disagreed (Table 4).

In the WS survey, disagreement was larger among SME respondents and those who identified as ‘other’ than large pharmaceutical companies, SMEs or research organisation representatives: 21% of SME respondents and 13% of ‘other’ respondents strongly disagreed that fees are appropriate (all stakeholder groups: 25%) and 21% of SME respondents and 38% of ‘other’ respondents disagreed (all stakeholder groups: 25%). Similarly, while 55% of representatives of large pharmaceutical companies and 29% of representatives of research organisations agreed with the statement, only 7% of SME respondents and 13% of ‘other’ respondents agreed.

Similar to the WS survey, representatives of companies with direct relevance to the EMA were more satisfied with the costs: 50% of this group agreed with the statement provided (no one strongly agreed), while none of the individual citizens responding to the consultation agreed or strongly disagreed, 22% of research organisation representatives strongly agreed or agreed, and 20% of representative organisations – an industry organisation representative – agreed (no one strongly agreed).

**Table 4: WS survey and OPC: extent of agreement with statements related to the appropriateness of fees charged and services provided<sup>294</sup>**

Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Do not know	Not applicable
WS survey: ‘Overall, the level of fees charged by the EMA is appropriate given the services they provide.’ (n=40)	0%	25%	25%	25%	13%	13%	n.a.
OPC: ‘The EMA fee system reflects the overall costs of the services charged for.’ (n=51)	2%	33%	28%	8%	0%	29%	n.a.
WS survey: ‘The fees for additional strengths or presentations are proportionate.’ (n=39)	0%	18%	49%	15%	5%	5%	8%

Fourteen respondents to the WS survey provided a follow-up comment on their answers outlining activities which they felt were not proportionately charged. Examples were given for variations (Type II, Type IA, Type IB) (mentioned by four large company representatives, an SME representative and a representative of EFPIA), inspections (mentioned by three large company representatives and a representative of EFPIA) and post-marketing authorisations (mentioned by two SME representatives and one large company representative), which are considered to be too expensive. Similarly, one OPC

<sup>294</sup> Percentages in this table were rounded and may not sum up to 100%.

respondent from a pharmaceutical company thought that post-approval fees are too high compared to mutual recognition procedures/decentralised procedures, and respondent from a research organisation thought that fees for scientific advice and annual fees (level 1) are too high. Two OPC respondents (a representative of a company with direct relevance to the EMA, and a representative of EFPIA) also indicated that fees for variations (grouped variations, type IA, type IB and type II variations) are not proportionate.

While NCA survey respondents found fees charged to industry fair, 83% of NCA survey respondents (25 NCAs) indicated dissatisfaction when it comes to the allocation of fees between EMA and NCAs. Consultees highlighted that the current fee system does not guarantee a balance between the fee share they receive and the actual costs of their activities, as the fee share for NCAs does not cover all EMA-related activities. EMA interviewees, by contrast, noted that they find the fee share in general fair.

Eight NCA survey respondents (27%) also commented that they do not find it fair that the EMA receives their share of the fee immediately after the payment is made while NCAs do not.

### ***3.1.3. Balance between a cost-based fee system and simplicity***

Overall, there is agreement among all consulted stakeholders that there is a general balance between a cost-reflective fee system and simplicity considering the size of the fee system, including the amount of different activities, each with their own fees and associated costs. A majority of respondents to the WS survey and the OPC agreed or strongly agreed (WS survey: 53%, OPC: 69%) that the fee system is simple and easy to understand (Table 5).

In the WS survey, agreement with the statement was lower among representatives of SMEs and research organisations compared to other stakeholder groups: 43% of SME respondents and 33% of research organisation respondents agreed (no one strongly agreed), while 73% of large pharmaceutical company representatives agreed or strongly agreed and 57% of 'other' respondents agreed (no one strongly agreed). Conversely, disagreement was higher among SME and research organisation representatives: 29% of SME respondents and 33% of research organisation respondents disagreed with the statement (no one strongly disagreed), compared to 19% of large pharmaceutical company respondents who disagreed (no one strongly disagreed). Similar to SME respondents, 29% of 'other' respondents disagreed or strongly disagreed with the statement.

Agreement with the statement provided in the OPC was higher among representatives of companies with direct relevance to the EMA and members of representative organisations: 86% of company representatives and 80% of representative organisation members strongly agreed or agreed (two patient organisation representatives and two industry organisation representatives). Conversely, individual citizens (33% disagreed) and 'other' stakeholder groups (29%) disagreed more often. By contrast, none of the

representatives of companies with direct relevance to the EMA, members of representative organisations and NCA respondents disagreed or strongly disagreed.

**Table 5: WS survey and OPC: extent of agreement with statements related to the simplicity of the fee system<sup>295</sup>**

Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Do not know	Not applicable
WS survey: ‘Overall, the fee system is straightforward and easy to understand.’ (n=38)	3%	50%	16%	24%	3%	5%	0%
OPC: ‘The EMA fee system rules are clear and easy to understand.’ (n=51)	10%	59%	6%	10%	0%	16%	n.a.

Most interviewed NCA representatives also indicated satisfaction with the simplicity of the fee system. Interviewed EMA representatives, by contrast, were less satisfied with the simplicity, noting that they find the fee system complex. As interviewees noted, this complexity is a result of several attempts to make the fee system more cost-based and fairer for payers and NCAs, for example through breaking down fees by activities.

Respondents to the WS survey indicated that they are in favour of a cost-based fee system: 44% of respondents agreed and 10% strongly agreed that fees should be based on the costs incurred by the EMA and NCAs delivering services (Table 6). The level of agreement was stronger among respondents from large pharmaceutical companies (73% (strong) agreement; no disagreement) compared to SME respondents (31% (strong) agreement, 31% (strong) disagreement).

<sup>295</sup> Percentages in this table were rounded and may not sum up to 100%.

**Table 6: WS survey: extent of agreement that fees should be based on the costs incurred by EMA and experts in delivering the services<sup>296</sup>**

Stakeholder group	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Do not know	Not applicable
All respondents (n=38)	11%	45%	26%	8%	5%	5%	0%
Large pharmaceutical companies (n=11)	9%	64%	27%	0%	0%	0%	0%
SMEs (n=13)	0%	31%	31%	15%	15%	8%	0%
Research organisations (n=6)	17%	33%	33%	17%	0%	0%	0%
Other (n=8)	25%	50%	13%	0%	0%	13%	0%

In a follow-up comment, a respondent from a large pharmaceutical company commented that a cost-based fee system could increase the fees and thus lead to more cost pressures which could hamper patients' access to affordable medicine. In addition, it was commented that only larger companies (as well as SMEs, if reductions continue to exist) might have the financial means to submit new applications and that companies that do not meet SME criteria could be excluded through higher fees.

#### **3.1.4. Satisfaction with NCAs' level of engagement**

Only NCA interviewees were asked about their satisfaction with their level of engagement in EMA-related activities. All interviewed NCAs but one indicated overall satisfaction. Nine of ten NCAs also noted that they would like to increase the number of remunerated activities in which they are involved in the future (e.g. rapporteurships, co-rapporteurships). Two interviewed NCAs noted that they do not want to increase unremunerated activities and would prefer to decrease their engagement in them in the future as they are not able to fully fund their costs with other remuneration provided by the EMA.

#### **3.1.5. Alignment of remuneration with actual costs/adequacy of remuneration**

The NCA survey as well as interviews with NCA and EMA representatives aimed to assess whether remuneration provided to NCAs is aligned with actual costs. All interviewed NCAs reported that the remuneration provided by the EMA enables them to cover the costs for fee-related activities in most cases, but not fully cover unremunerated activities. Nine of ten interviewed NCAs explained that they use their national budgets to cover remaining costs; one interviewed NCA stated it does not use its national budget as the national legislation does not allow doing so.

<sup>296</sup> Percentages in this table were rounded and may not sum up to 100%.

### 3.1.6. Fee arrangements for SMEs

The consultation activities showed mixed views regarding the appropriateness of incentives offered to SMEs. Overall, all consulted stakeholders highlighted the importance of waivers and reductions for SMEs, as such incentives enable stakeholders who otherwise might not be able to use the centralised system to do so. While dissatisfaction with SME arrangements were not observed by EMA and NCA representatives, only 21% of respondents to the WS survey agreed and 26% strongly disagreed or disagreed that SME support is appropriate. Stakeholders who identified their organisations as SMEs in the survey were less satisfied than the group of respondents as a whole: 54% disagreed or strongly disagreed with the statement provided (Table 7).

**Table 7: WS survey: extent of agreement that specific fee arrangements made for SMEs are appropriate<sup>297</sup>**

Stakeholder group	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Do not know	Not applicable
All respondents (n=39)	0%	21%	18%	10%	15%	18%	18%
Large pharmaceutical companies (n=11)	0%	9%	18%	0%	9%	27%	36%
SMEs (n=14)	0%	14%	29%	21%	29%	0%	7%
Research organisations (n=6)	0%	50%	0%	17%	0%	33%	0%
Other (n=8)	0%	25%	13%	0%	13%	25%	25%

### 3.1.7. Incentives for specific products

There was overall agreement among stakeholders that incentives for particular types of medical products (orphan medicines, veterinary medicines for MUMS, medicines for paediatric use, etc.) are important, and there was also overall satisfaction with the incentives. EMA interviewees noted that such incentives are a particular strength of the current fee and remuneration system, although one interviewee also noted that introducing an initial application fee for products eligible for fee reductions could ensure that NCAs and the EMA can better cover their costs. In the WS survey, 26% of respondents strongly agreed or agreed that fee incentives for specific products are appropriate, while 18% disagreed or strongly disagreed. Satisfaction with the special fee arrangements was higher among OPC respondents (45% strongly agreed) (Table 8).

In the WS survey, agreement with the statement was higher among research organisation representatives: 68% of them strongly agreed or agreed, while only 27% of large company representatives, 14% of SME representatives and 13% of ‘other’ respondents

<sup>297</sup> Percentages in this table were rounded and may not sum up to 100%.



agreed (no one of these groups strongly agreed). Strong disagreement with the statement was only indicated by SME respondents.

Representatives of companies with direct relevance to the EMA agreed more often with the statement provided in the OPC than other stakeholder groups: 64% of company respondents agreed (no one strongly agreed), compared to 44% of research organisation representatives, 17% of citizens, 0% of representative organisation members and 43% of ‘other’ stakeholders. Members of representative organisations showed the highest degree of dissatisfaction: 40% disagreed with the statement (one patient organisation and one industry organisation representative); the remaining 60% neither agreed nor disagreed (two industry organisation and one patient organisation representative).

**Table 8: WS survey and OPC: extent of agreement with statements related to the appropriateness of fee incentives and support<sup>298</sup>**

Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Do not know	Not applicable
WS survey: ‘The specific fee arrangements made for particular types of medicines (orphan medicines, veterinary medicines for MUMS, medicines for paediatric use, etc.) are appropriate.’ (n=39)	3%	23%	23%	19%	5%	15%	18%
OPC: ‘The EMA fee system rules provides adequate incentives and support (e.g. SMEs, orphan, paediatric, advanced therapy medicinal products, veterinary medicines for minor use/minor species, academia.’ (n=51)	6%	39%	18%	8%	8%	22%	n.a.

In follow-up comments, respondents to the WS survey and the OPC mentioned the following areas where additional incentives or more support would be needed:

- More incentives for academics/researchers (mentioned by three research organisation representatives in the OPC).

<sup>298</sup> Percentages in this table were rounded and may not sum up to 100%.

- Patients who are involved in EMA activities should receive compensation for the time invested and should be better supported (mentioned by two patient association representatives in the OPC).
- Financial incentives for MUMS should also apply to animals other than food-producing species (mentioned by one SME respondent to the WS survey).

## **3.2. Relevance**

### **3.2.1. *Dispute settlement procedure***

Stakeholders did not identify the need for a dispute settlement procedure between the EMA and industry. EMA representatives as well as respondents to the WS survey did not refer to any disputes between different stakeholder groups. While EMA interviewees agreed that payers sometimes have queries, it was clarified that issues raised are usually quickly solved. Only one respondent to the OPC, a member of an industry organisation, indicated that they had previously had the need for a dispute settlement procedure. The reason provided was that they think that the EMA is not always objective in the decision of the amount of fees charged. However, that respondent did not provide any suggestions for a dispute settlement procedure.

### **3.2.2. *Timeliness and relevance***

Seven respondents to the NCA survey (23%) directly referred to the timeliness and relevance of the current fee and remuneration system. In particular, they found that the fee legislation does not sufficiently reflect changes within the European regulatory network on medicines. They also indicated that the fee system does not reflect changes in the workload and activities of the EMA and NCAs. EMA interviewees noted that the fee legislation, and in particular Council Regulation (EC) No 297/95, does not take into account changes to the fee system since 2005 resulting from additional legislation.

Both EMA and NCA representatives highlighted that the fee system does not reflect the increasing complexity of activities (coordination and administration activities as well as NCAs' EMA-related activities such as authorisation procedures). Respondents to the WS survey did not refer to an increase in complexity.

### **3.2.3. *Comparison of the EMA fee system to other regions' fee systems***

Respondents to the WS survey and the OPC were asked to compare the EMA fee system to other regions' fee systems. Four WS survey respondents (two SME respondents, one research organisation representative and one large company representative) indicated that compared to other fee systems, the EMA fee system is transparent. While three respondents (two SME representatives and one research organisation representative) noted that the EMA fee system is broadly comparable to other fee systems, two respondents (one representative each of a large pharmaceutical company and an SME) indicated that comparisons would be difficult as the EU landscape includes so many

different agencies (as well as countries and languages) and is therefore more complex. Three respondents (one representative each of a large pharmaceutical company, of an SME and a research organisation) also stated that the fee system of the U.S. FDA is more straightforward and user-friendly.

OPC respondents were asked to compare the EMA fee system with the FDA, the Pharmaceuticals and Medicinal Devices Agency in Japan, Health Canada in Canada, and the Therapeutic Goods Administration in Australia. However, respondents showed little familiarity with the four fee systems: across the questions for each of the comparator fee systems, between 63 and 94% of respondents (i.e. between 32 and 48 respondents) indicated that they ‘Do not know’ which fee system compares better. Consequently, only very few respondents chose any of the other response options (for the majority of questions, each option was selected by only up to three respondents). EFPIA – a representative organisation of pharmaceutical industries and associations in Europe – indicated that they believe the EMA fee system is comparable to or performs better than other countries’ fee systems:

- The clarity of the rules of each fee system is comparable, but the U.S. FDA fee system rules were considered to be clearer and easier to understand than those of the EMA.
- The EMA fee system was seen as more transparent than the U.S. fee system, less transparent than the Australian fee system, and comparable to the Canadian and Japanese fee systems.
- The EMA fee system rules and those in the Australian, Canadian and Japanese fee system were seen as comparably easy to apply in practice, but the U.S. fee system rules were considered to be easier to apply in practice than those of the EMA.
- The EMA fee system was seen as more cost-based than the Canadian, Japanese and U.S. fee system, but as less cost-based than the Australian fee system.
- Fee incentives for specific products and stakeholder groups provided by the EMA were seen as more appropriate than similar incentives provided by the Australian, Canadian and Japanese fee system. The appropriateness of the fee incentives provided by the EMA and the U.S. were considered to be comparable.

### **3.3. Coherence**

#### ***3.3.1. Alignment of the fee system with EMA’s underlying legislative basis and regulations***

Interviewed NCA representatives did not identify any gaps in the fee and remuneration system when it comes to the underlying legislative basis and regulations. Similarly, none of the respondents to the WS survey reported issues of misalignment. EMA interviewees also generally found that the fee system and the legislation are aligned. However, some interviewees noted that since the regulation on general fees payable to the EMA (Council Regulation (EC) No 297/95) has not been amended since 2005, it does not reflect new

regulations that have been introduced since then (e.g. legislation related to paediatric medicinal products, advanced therapy medicinal products, SMEs). Some EMA representatives indicated that they would prefer an overall revision of all legislative documents and consolidating them into one coherent piece of legislation.

### 3.3.2. *Alignment of the fee system with the overall strategy of the EMA*

None of the consulted stakeholder groups referred to any gaps regarding the general strategy and objectives of the EMA and the current fee and remuneration system.

### 3.3.3. *Alignment with national-level fee systems*

Responses to the WS survey showed mixed results regarding an alignment of the EMA fee and remuneration system with the fee systems of national regulatory authorities in the EU. Amongst the respondents to this question, 23% agreed or strongly agreed with the statement, 33% disagreed or strongly disagreed and 26% chose the answer option ‘neutral’ (other: 13% ‘don’t know’, 5% ‘not applicable’). Agreement was particularly high among representatives of large pharmaceutical companies: 46% of this stakeholder group agreed with the statement (no one strongly agreed), while 14% of SME respondents agreed (no one strongly agreed), 33% of research organisation respondents strongly agreed or agreed, and none of the ‘other’ stakeholders strongly agreed or agreed (Table 9).

**Table 9: WS survey: extent of agreement that the EMA fee system is consistent with fees charged for similar services by national regulatory authorities in the EU<sup>299</sup>**

Stakeholder group	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Do not know	Not applicable
All respondents (n=39)	3%	21%	26%	26%	8%	13%	5%
Large pharmaceutical companies (n=11)	0%	46%	27%	18%	0%	9%	0%
SMEs (n=14)	0%	13%	29%	50%	0%	0%	7%
Research organisations (n=6)	17%	17%	17%	0%	17%	33%	0%
Other (n=8)	0%	0%	25%	13%	25%	25%	13%

Of the twelve respondents providing follow-up comments to their responses a majority indicated that fees charged by the EMA are higher than those charged by national authorities. NCA interviewees and survey respondents also noted that EMA fees are in general higher. However, considering the complexity of the EMA fee system as a result

<sup>299</sup> Percentages in this table were rounded and may not sum up to 100%.

of its size and scope (i.e. approval of a product in 31 countries), NCA representatives found the higher fees appropriate.

Two comments in the WS survey referred to the comparison of the fee systems as such, of which one stated that national fee systems are very heterogeneous, whereas the other respondent indicated that the EMA fee system is comparable to many other national fee systems. NCA interviewees also noted that their national fee systems differ from the EMA fee system (e.g. different types of fees, fewer fees, more cost-based fee systems, annual fees based on annual turnover); however, such differences do not interfere or hinder activities undertaken for the EMA.

EMA interviewees did not provide insights on the (perceived) alignment of national fee systems and the EMA fee system.

### **3.4. Sustainability**

#### ***3.4.1. Sustainability of the EMA fee and remuneration system***

EMA and NCA interviewees were asked whether they considered the current fee and remuneration system to be sustainable. Overall, EMA representatives showed satisfaction with the current fee and remuneration system and think it is sustainable as it has proven to be stable over the last 20 years. It has also allowed the EMA to carry out its activities and fulfil its obligations to industry and NCAs.

EMA interviewees particularly emphasised that flexible funding contributes to the fee system's sustainability. They also emphasised that the financial system of fees paid by industry in combination with general EU and EEA contributions contributes to the fee system's sustainability, as it ensures sufficient flexibility to undertake required activities regardless of fee fluctuations or in cases where fee reductions are granted.

In contrast to EMA interviewees, all interviewed NCAs indicated that they do not find the current fee system sustainable, particularly as it does not allow them to fully cover all of their costs related to EMA-related activities. Similarly, 83.3% of NCA survey respondents noted that the remuneration provided does not enable them to finance all EMA-related activities. NCA interviewees also find that the current fee system is not flexible enough to address changes related to the increasing complexity of procedures, which could endanger the fee system's sustainability.

Five respondents to the NCA survey (17%) directly indicated that the fee system lacks sustainability, particularly because of the current split of fees between the EMA and NCAs as well as the amount of unremunerated activities. While they are overall satisfied with the fee system's sustainability, EMA interviewees also find that unremunerated activities are a barrier to the fee system's sustainability. Some EMA interviewees observed an increase of unremunerated activities for both the EMA and NCAs over time which has led to an imbalance in the distribution of activities among Member States – some NCAs tend to not volunteer for unremunerated activities, and they are usually

undertaken by the same NCAs. As noted by an EMA interviewee in that respect, the multinational team assessments are important to establish more balance and ensure more sustainability. Six out of ten NCA interviewees also indicated that they appreciate the introduction of multinational team assessments; one interviewee directly noted that multinational team assessments improve the centralised system.

Another barrier to sustainability mentioned by EMA representatives relates to changes to legislation, which made the fee system fairer and more cost-based in some instances, but also made some activities less flexible (e.g. granting waivers and fee reductions after 30 calendar days from the date of the invoice for pharmacovigilance activities). Inflexibility resulting from legislative amendments was also pointed out by NCA interviewees. For instance, an interviewee noted that simplifications in the legislation do not reflect the actual complexity of activities and their related tasks.

The importance of fee incentives for SMEs as well as exemptions for specific medicinal products and procedures was highlighted in all consultation activities. Survey respondents and interviewees indicated that they are important elements of the current fee system, contribute to its sustainability and support the enhancement of innovation.

Only two respondents to the WS survey (both are representatives of large pharmaceutical companies) directly provided comments on the sustainability of the fee system. One consultee noted that the fee system should ensure sufficient resources (without further specifying what resources are meant) ‘to support high quality scientific assessment by highly qualified experts within competitive timeframes’. This would support public health and pharmaceutical innovation and thus contribute to the sustainability of the fee system. The second respondent indicated that an entirely cost-based fee system would endanger the sustainability of the fee system as well as independence from the interests of the industry.

### **3.5. Other issues addressed**

#### ***3.5.1. Activities not covered by the current fee system that could be covered in the future***

NCA survey respondents and NCA interviewees referred to activities that are currently not remunerated, but could be covered in the future: peer reviews, activities of committee and working party members (e.g. preparation work), development of guidelines, orphan designation assessments, herbal monographs as well as other activities that are not covered by the annual fee (e.g. assessments, pharmacovigilance, inspections, quality control, etc.). EMA interviewees mentioned services that are subject to fee incentives, which are currently not fully fee-financed. As noted in Section 3.1 of this Annex, an interviewee suggested introducing an initial application fee for such products, which could enable NCAs and the EMA to better cover incurred costs.