Study for the evaluation of the EMA fee system

Final report

SANTE/2016/B5/021

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List of acronyms

Acronym	Description
AD	Scientific staff
ADUFA	Animal Drug User Fee Act
AEMPS	Spanish Agency for Medicines and Medical Devices
AGDUFA	Animal Generic Drug User Fee Act
AGES MEA	Austrian Medicines and Medical Devices Agency
AMR	Antimicrobial resistance
ANMV	French Agency for Veterinary Medicinal Products
AST	Non-scientific/administrative staff
ATMP	Advanced Therapy Medicinal Products
BfArM	Federal Institute for Drugs and Medical Devices (Germany)
BsUFA	Biosimilar User Fee Act
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
DDPS	Detailed Description of the Pharmacovigilance System
DG SANTE	Directorate General for Health and Food Safety
EASA	European Aviation Safety Agency
ECHA	European Chemicals Agency
EEA	European Economic Area
EFPIA	European Federation of Pharmaceutical Industries and Associations
EFTA	European Free Trade Association
EMA	European Medicines Agency
EMA MB	EMA Management Board
EMEA	European Medicines Evaluation Agency (now the EMA)
EU	European Union
EUIPO	European Union Intellectual Property Office
FD&C Act	Federal Food, Drug, and Cosmetic Act
FDA	U.S. Food and Drug Administration
GCP	Good clinical practice
GDUFA	Generic Drug User Fee Act
GMP	Good manufacturing practice
GVP	Good pharmacovigilance practices
HMA	Heads of Medicines Agencies
HMPC	Committee on Herbal Medicinal Products
HPRA	Health Products Regulatory Authority (Ireland)
HTA	Health technology assessment
ICH	International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICMRA	International Coalition of Medicines Regulatory Authorities
ISSG	Commission Inter-Service Steering Group
IT	Information technology
MA	Marketing authorisation
MAH	Marketing authorisation holder
MBDG	EMA Management Board Data Gathering
MDUFA	Medical Device User Fee Act
MRL	Maximum residue limit
MUMS	Minor-use-minor-species
NAP	Nationally authorised product
NCA	National Competent Authority
OHIM	European Intellectual Property Office

Acronym	Description
PAES	Post-authorisation efficacy study
PAM	Post-authorisation measure
PASS	Post-authorisation safety study
PDCO	Paediatric Committee
PDUFA	Prescription Drug User Fee Act
PhV	Pharmacovigilance
PIP	Paediatric investigation plan
PMF	Plasma Master File
PO	Purchase order
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic safety update report
PSUSA	Periodic safety update report (PSUR) single assessment
R&D	Research and development
SME	Small and medium-sized enterprise

Glossary of terms

Term	Definition
Additional activities	Both EMA and NCAs undertake additional activities, which are not categorised as procedural activities or time spent in committees and working groups, as defined in the NCA survey[1] (Questions 17-19). For EMA, these activities were provided as a separate list.[2] For NCAs, costs of these activities are calculated as a residual cost in the model.
Administrative staff	The definition used in the EMA Management Board Data Gathering (MBDG) exercise (EMA, 2017 Annex III[3]) is applied in the NCA survey, data provided by EMA and model. Administrative staff is defined as 'staff other than scientific/technical providing direct administrative support to procedures'. The same definition is applied to committee, working group and additional EMA-related activities.
Average incentive rate	The average discount rate applied to the full or theoretical industry fee for a given activity. It depends on the nature of the product and the industry organisation (e.g. whether it is an SME) making the application, among other things and is assumed to be fixed for the typical year.
Committee and working group activities	Time spent in and preparing for EMA committee and working group meetings.
Cost-based	In a cost-based system fees reflect the average cost of undertaking a procedure for an activity. In this study, cost-based is defined as cost-based in aggregate, not at the individual organisation level.
Cost per hour of EMA activities	The cost per hour of EMA activities is calculated based on the annual costs divided by the annual hours worked for each staff type. Overheads and non-staff costs are allocated to the annual costs for two different staff types (scientific and administrative staff).
EMA budget	The EMA budget consists of fee revenue from industry; EU and EEA budget contributions; EMA costs; payments EMA makes to NCAs for procedural activities (NCA remuneration) and reimbursements to NCAs for working group and committee-related travel and subsistence costs.
EMA costs	Costs to EMA for all the activities they undertake, which include the activities EMA undertakes as an organisation and reimbursement of NCAs for travel and subsistence costs. EMA also makes payments to NCAs for the procedural activities they undertake; these are not considered to be EMA costs, but rather enter the revenue model as a reduction in the EMA share of fee income from industry.
EMA fee income	EMA fee income is fee revenue from industry minus the NCA remuneration.
EMA revenue	EMA revenue consists of the fee revenue from industry and EU and EEA budget contributions minus NCA remuneration.

[1] The NCA survey is included as Appendix 5 to the Final Report.

[2] Data provided by EMA is available in spreadsheet form as an electronic supplement.

[3] Annex III only provides an example of how the definition applies to scientific advice and protocol assistance activities. Time spent by scientific and administrative staff was recorded for all activities covered in the MBDG exercise.

Term	Definition
EMA-related activities	These are all the cost-generating activities undertaken by NCAs that are reported in the NCA survey.
EU and EEA budget contributions	In the model, the actual EU and EEA budget contributions are used in the baseline and synthetic baseline. An additional term, denoted 'other income', is calculated in the synthetic baseline model. It corresponds to income from administrative operations, such as sale of publications and organisation of seminars, and is calculated as the EMA fee income plus EU and EEA budget contributions minus EMA costs. For scenarios where the EU budget contributions are used as a funding mechanism, additional EU budget contributions are calculated.
Procedural activities with NCA involvement	These comprise a specific number of procedural activities for which data were gathered during the MBDG exercise agreed with EMA and HMA and which formed the basis for two questions listed in Questions 17 and 18 in the NCA survey.
Fee revenue from industry	This is the total amount received from industry by EMA for services undertaken and annual fees. It depends on the number of procedures invoiced and the average incentive rate applied for each activity. The fee revenue further depends on the number of centrally authorised products (CAPs) and nationally authorised products (NAPs) holding a valid marketing authorisation (MA). The fee revenue received from the annual CAP fee and annual pharmacovigilance (PhV) fee depend respectively on the number of CAP and NAP MAs.
Fee rule	Determines the full fees paid by industry for the services they receive. Incentives are not part of the fee rule. EMA income depends on the fee rules and the incentives that are applied.
Procedural activities without NCA involvement	These are a set of activities undertaken by EMA without NCA involvement and for which fees are charged to industry.
Fixed inputs	These comprise the number and type of procedures, average incentive rates and times taken to undertake activities. They have been determined for a 'typical year' and remain constant in the model calculations. They are independent of the fee and NCA remuneration rules.
Full fee	The full fee is the average fee paid under a given fee rule per procedure of a given activity over the reporting year, prior to the application of incentives. Full fees were obtained from data provided by EMA.
NCA budget	The NCA budget covers EMA-related activities only and consists of NCA costs and NCA remuneration. Other sources of costs or income not related to EMA activities are not included.
NCA costs	Costs to NCAs to undertake EMA-related activities. Costs from other activities that NCAs undertake are not included.
NCA income	Income that NCAs receive from EMA for the EMA-related activities they undertake. NCA income from other sources is not included.

Term	Definition
NCA reimbursement	NCA reimbursement consists of travel costs and substance allowances paid to experts travelling to London to take part in committees and working groups. Under the existing fee system such travel costs are reimbursed by the EMA under the relevant rules. They are included in the EMA costs only. Additional travel and subsistence costs for member state experts have been declared by NCAs in the survey and are taken into account in the cost calculation.
NCA remuneration	Payments NCAs receive from EMA for undertaking EMA-related activities.
NCA remuneration rule	This rule determines the payments NCAs receive from EMA for undertaking EMA-related activities. EMA fee income depends in part on the remuneration rule as that determines the payments they make to NCAs. NCA income depends on the remuneration rule.
NCA roles	Committee rapporteur, committee co-rapporteur, peer reviewer or member of a multi-national assessment team. Rapporteur could also encompass a coordinator or inspector role depending on the type of activity involved.
Non-EMA activities	These are activities undertaken by NCAs that contribute to their total costs but are not EMA-related and not included in the NCA survey.
Other income	This is an additional term calculated in the baseline and synthetic baseline to balance the EMA budget. It corresponds to income from administrative operations, such as sale of publications and organisation of seminars.
Overhead costs	Overhead costs: e.g. depreciation, information technology (IT), administration. These costs cannot be directly allocated to an activity as is salary or other non-staff costs. Overheads are allocated to salary costs in the model according to a specified rule based on staff time.
Procedure	The term 'procedure' is used by the study team, for the purposes of the report, as instances of the activities listed in Questions 17 and 18 of the NCA survey and the procedural activities without NCA involvement listed by EMA. It is acknowledged that there are a wider range of activities not included in our definition for which procedures may be undertaken. In the study, unit fees are defined per procedure. Several procedural roles may be associated with a single procedure.
Procedural activities with NCA involvement	These comprise a specific set of procedural activities listed in Questions 17 and 18 of the NCA survey.

Term	Definition
Procedural role	The term 'procedural role' is used by the study team to refer to each instance that an NCA undertakes a particular activity in a given role for which data were reported in the NCA survey. There are three classifications of roles that correspond to the data requested in Q17 and Q18 of the NCA survey. These are: • Rapporteur or equivalent lead role (column 1) • Co-rapporteur or equivalent support (column 2) • Other role that is required for completion of a procedure (column 3). Other roles include PRAC rapporteur and co-rapporteur and peer-reviewer, as well as members of multi-national teams. For example, NCA X could report carrying out a co-rapporteur procedural role ten times for the activity 'type II variation – level I'.
Purchase orders	Purchase orders (POs) are a commitment for future payment to NCAs by EMA. Under the existing fee system, one purchase order is sent out for each rapporteur, co-rapporteur or equivalent remunerable role undertaken by NCAs for a given procedure. POs do not cover non-remunerated roles, such as peer review.
Scaling factor	In the synthetic baseline it is assumed that the 29 respondent NCAs in the model undertake all the invoiced procedural activities reported by EMA. To achieve this, each procedural role reported by an NCA for a given procedural activity is multiplied by a scaling factor so that the total number of rapporteur and co-rapporteur roles is equal to the number of POs reported by EMA. This scaling factor is equal to the ratio of the total number of purchase orders reported by EMA to the total sum of the number of rapporteur and co-rapporteur roles or equivalent remunerable roles reported in the NCA survey by the 29 respondent NCAs included in the model.
Scientific staff	The definition used in the EMA Management Board Data Gathering (MBDG) exercise (EMA, 2017 Annex III[4]) is applied in the NCA survey, data provided by EMA and model. Scientific staff is defined as 'Scientifically qualified staff acting as co-ordinator, quality, safety, efficacy assessor, peer reviewer, QA, External Expert, SA officer, EPL/Specialist, Secretariat and Regulatory and in addition legal support.'
Staff salary costs/hour	These are costs before overheads and direct (non-staff) costs are added.

[4] Annex III only provides an example of how the definition applies to scientific advice and protocol assistance activities. Time spent by scientific and administrative staff was recorded for all activities covered in the MBDG exercise.

Term	Definition
Synthetic baseline	A 'synthetic baseline' is used to determine NCA costs and EMA costs excluding NCA remuneration. The synthetic baseline relies on assumptions about a common set of activities for both EMA and NCAs. That is, for procedural activities involving NCAs, the number of procedural activities that EMA undertakes in a typical year is the same as the number of activities undertaken by NCAs at EMA's request. Both the fee revenue and NCA remuneration are then based on this number of activities. For procedural-activities involving EMA only, the number of invoiced procedures is the same as the number of procedures undertaken by EMA.
Theoretical fees	The full fee per activity under a cost-based fee system.
Types of cost generating activities undertaken by EMA	Three types: (i) costs for the scientific and administrative work they undertake as part of procedural activities they provide which also involve NCAs; (ii) costs for the scientific and administrative work they undertake as part of procedural activities they provide which do not involve NCAs; (iii) costs for additional activities they undertake.
Types of cost generating activities undertaken by NCAs	Three types for EMA related activities only: (i) costs for the scientific and administrative work they undertake as part of procedural activities for EMA; (ii) costs associated with committees and working groups excluding costs associated with rapporteur, co-rapporteur and equivalent remunerable roles; and (iii) costs for additional activities they undertake.
Typical year	The typical year is based on data from the reporting years for NCAs and EMA and the MBDG sample year. In this year it is assumed that, for procedural activities involving NCAs or carried out by EMA only, the number of invoiced procedures is the same as the number of procedures undertaken. Data for all other activities remains the same as in the baseline year. The typical year is used in the synthetic baseline.
Unitary fee	This is the fee per procedure for a given activity.

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1. INTRODUCTION TO THE STUDY

The European Union (EU) provides for a centralised procedure that enables medicinal products for human and veterinary use to undergo a single EU-wide assessment and marketing authorisation that is valid throughout the European Economic Area (EEA) (28 EU Member States and Iceland, Liechtenstein and Norway) (Regulation (EC) No 726/2004). The European Medicines Agency (EMA)[5] was established under Council Regulation (EEC) No 2309/93 as a decentralised EU Agency with a role in the evaluation and supervision of centrally authorised medicines and pharmacovigilance of all medicinal products in the EU (Regulation (EU) No 1235/2010, Commission Implementing Regulation (EU) No 520/2012). National Competent Authorities (NCAs) in the Member States work together with the EMA to carry out assessments aimed at granting, maintaining and monitoring EU marketing authorisations and other services related to medicinal products for human and veterinary use including pharmacovigilance activities for medicines for human use at EU level. The EMA fee and NCA remuneration system was established to provide a sound financial basis for these activities under Council Regulation (EC) No 297/95 on general fees payable to the EMA[6], and Regulation (EU) No 658/2014 on fees payable for the conduct of pharmacovigilance activities.

This is a study of the EMA fee and NCA remuneration system and its relationship to the underlying costs associated with the services provided. The study assesses the strengths and weaknesses of the 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 fee system avoids unnecessary administrative burden on fee-payers. It addresses these questions with reference to the fee system's relevance, effectiveness, efficiency, coherence and sustainability. This analysis provides a basis from which to consider the need for reform of the EMA fee and NCA remuneration system, and to consider which elements of the fee system might be specifically targeted for reform.

This is the final report for the 'Study for the evaluation of the European Medicines Agency fee system'. The study was commissioned by the Directorate General for Health and Food Safety (DG SANTE) and is being delivered by RAND Europe.

1.1. Background

Council Regulation (EEC) No 2309/93 indicated the need to establish a European agency for the evaluation of medicinal products, to help harmonise authorisations of national medicinal regulatory bodies in European Economic Community (EEC) Member States as well as enable centralised authorisation procedures for medicinal products for human and veterinary use across the EEC. This agency should provide scientific advice gained in close collaboration with Member States' agencies, in order to undertake centralised authorisations and supervision of medicinal products. As outlined in Article 57 of Council Regulation (EEC) No 2309/93, the Agency should be funded by contributions from the Community and fees paid by industry for obtaining and maintaining marketing authorisations and providing other authorisation-related services.

The European Agency for the Evaluation of Medicinal Products (EMEA) was formally established in 1995. In the same year, Council Regulation (EC) No 297/95 was adopted, which defines the services provided by the EMEA and related fees payable to the Agency for undertaking authorisation procedures. Since then, the regulation has been

[5] The EMA was named European Agency for the Evaluation of Medicinal Products in Council Regulation (EEC) No 2309/93. Regulation (EC) No 726/2004 replaced Regulation (EEC) No 2309/93 in March 2004, which included the renaming as European Medicines Agency.

[6] Along with a set of implementing rules (EMA/MB/57356/2018).

substantially amended three times, most recently in November 2005. The regulation was accompanied by rules for the implementation of the regulation (most recently EMA 2017d), which define the structure of the fees payable to the Agency, rules for fee exemptions and reductions as well as rules for remuneration paid to national authorisation bodies undertaking the requested services. Since its establishment in 1995, the EMA's areas of responsibility have significantly expanded; its underlying legislation was correspondingly amended several times and accompanied by additional legislation, including Directive 2001/82/EC and Directive 2001/83/EC on the Community codes relating to human and veterinary medicinal products; and Regulation (EC) No 726/2004 on authorisation and supervision procedures of medicinal products for human and veterinary use. Regulation (EC) No 726/2004 also stipulated the renaming of the EMEA to the European Medicines Agency (EMA). Following the need to revise the legislation for pharmacovigilance activities, Directive 2010/84/EU, Regulation (EU) No 1235/2010 and Commission Implementing Regulation (EU) No 520/2012 were adopted in 2010 and 2012, amending existing legislation as regards pharmacovigilance. The new pharmacovigilance legislation was completed by Regulation (EU) No 658/2014 on fees payable for pharmacovigilance activities in 2014.

1.1.1. General context

The EMA is the central organisation of the European medicines regulatory network, which also includes the European Commission and human and veterinary medicines NCAs in 31 EU and EEA Member States. Scientific experts from the NCAs are represented in seven EMA scientific committees as well as in working parties and other groups. The main aim of the network is to ensure that safe, effective and high-quality medicines are authorised in the EEA and guarantee adequate information about medicinal products (EMA n.d.-b).

In order to place a medicinal product for human or animal use on the European market, producers either need to have their product authorised by the competent authority of a Member State through a national procedure, through a decentralised or mutual recognition procedure via the Heads of Medicines Agencies (HMA) (HMA 2015, HMA n.d.), or through a centralised procedure via the EMA.

Under a national procedure, new medicinal products are authorised by the NCA for its Member State's territory only, while under a decentralised procedure, products are authorised in several Member States in parallel. A mutual recognition procedure enables authorisation of a medicinal product in one or more additional Member States based on an already existing authorisation in one Member State.

Under a centralised procedure, applicants submit one application for a marketing authorisation to be valid in all EEA Member States. The application is reviewed by the relevant scientific committee, which provides a scientific opinion on whether the product should be authorised. In more complex cases, more than one committee can be involved in the application review, in which case the main scientific committee reports back to the European Commission (EMEA 2007a). The committee(s)'s opinion is submitted to the European Commission, which then takes a decision on whether or not to grant the authorisation.

The responsible committee appoints one of its members as a rapporteur to coordinate the scientific assessment of a medicinal product (Article 62(1) of Regulation (EC) No 726/2004). The committee may also engage another NCA to act as a co-rapporteur. The scientific assessment is led by the rapporteur and co-rapporteur. The assessment and a scientific opinion are prepared by the relevant scientific committee(s) which are composed of representatives appointed by each Member State (Article 62 of Regulation (EC) No 726/2004). Moreover, Recital 25 of Regulation (EC) 726/2004 provides that committees may delegate tasks to working parties, which are open to external scientific experts. The EMA is responsible for technical, scientific and administrative support for its

committees and the working parties, coordinates activities between them and performs other activities as defined in Council Regulation (EC) No 297/95.

1.1.2. The EMA fee system

Applicants (e.g. pharmaceutical companies) aiming to place a medicinal product for human or veterinary use on the European market pay fees for the assessment of their medicinal products, which are defined in the implementing rules to Council Regulation (EC) No 297/95 (EMA 2017d). In addition, the EMA collects fees for changes to marketing authorisations, annual fees for already authorised products as well as fees for other services, for instance referrals, scientific advice, inspections or pharmacovigilance activities. Fees paid by industry constitute the majority of the EMA's budget; in 2016, 88 per cent of the budget was derived from fees, and in 2017, 86 per cent of the budget was derived from fees (EMA 2017b).[7]

The EMA may grant partial or total fee exemptions under exceptional circumstances or in cases of public or animal health threats on a case-by-case basis. Micro-sized enterprises and small and medium-sized enterprises (SMEs) (as defined in Commission Regulation (EC) No 2049/2005), and in specific cases academic sector applicants (EMA 2016d), are also eligible for fee exemptions and reductions. In addition, partial or total fee reductions are offered for specific products: medicinal products for paediatric use (Regulation (EC) No 1901/2006, Regulation (EC) No 1902/2006), and designated orphan medicinal products (Regulation (EC) No 141/2000, EMA 2014d) (EMA 2014f). In addition, there are procedural activities for which no fees are foreseen under the current legislation, such as orphan designation, paediatric investigation plan (PIP), PIP waiver, PIP compliance check, and veterinary medicinal products indicated for minor-use-minor-species (MUMS).

Most activities involving EMA and NCAs are common to both human and veterinary activities, for example, 'scientific advice' activities including initial and follow-up scientific advice. Fees paid to EMA for scientific advice and line extensions vary depending on the level of advice. A second large group of activities relate to marketing authorisations. The fee system distinguishes between applications, extensions, variations, and renewals of marketing authorisations. The fees vary depending on the category of activity (human or veterinary) and, for initial applications, also the type of medicine (e.g. new active substances, generics, or biosimilars). Finally, fees are charged for inspections, whether the site inspected is inside or outside the European Union. Fees are normally charged before the start of a procedure, but there are fee deferrals for SMEs.

EMA also undertakes activities that do not involve NCAs. These are mainly minor variations to authorised products that have minimal or no impact on the product's quality, safety or efficacy and do not require approval before implementation (type IA variations), notifications of parallel distribution and transfers of marketing authorisations between different companies.

In addition to fees generated from procedural activities, there are two types of annual fees: annual fees for centrally authorised products (CAPs) for human and veterinary use and annual pharmacovigilance fees for nationally authorised products (NAPs) for human use. Annual fees for CAPs are charged on the anniversary date of the marketing authorisation (MA) and annual fees for pharmacovigilance (PhV) are charged on a yearly basis for all MAs.

[7] The modelling exercise undertaken for this study uses the 2016 figures.

1.1.3. NCA remuneration

The EMA is required to remunerate NCAs acting as rapporteurs or co-rapporteurs for their scientific assessment work as stated in Article 62(3) of Regulation (EC) No 726/2004. NCAs receive a share of the fees collected by EMA from industry. The share is set according to the implementing rules for Council Regulation (EC) No 297/95 and, for pharmacovigilance activities, Regulation (EU) No 658/2014.

For services covered under Council Regulation (EC) No 297/95, NCA rapporteurs and co-rapporteurs receive 50 per cent of the fees (i.e. 25 per cent each when a rapporteur and co-rapporteur are assigned). NCA remuneration for these services is based on the full fees regardless of any fee incentives applied (e.g. fee reductions or exemptions for SMEs or specific medicinal products). EMA receives the remaining fee share once incentives have been applied and NCAs have been remunerated. For pharmacovigilance services, NCA remuneration is specified in Regulation (EU) No 658/2014 and is reduced proportionally when reductions or exemptions have been applied. NCAs do not receive any remuneration for procedures where no fee is foreseen (e.g. orphan designation, MUMS and PIPs).

Rapporteur and co-rapporteur NCAs are also paid 30 per cent (i.e. 15 per cent each) of the CAP annual fees collected for services underlying Council Regulation (EC) No 297/95. The NCA fee share of the annual fees is due a month following the authorisation of the sales order to the marketing authorisation holder (created on the anniversary of the Commission decision on the marketing authorisation). Annual fees collected for pharmacovigilance services, by contrast, are only for IT maintenance and literature monitoring (Regulation (EU) No 658/2014, Article 7), and are retained in full by the EMA with none being passed on to NCAs. Rapporteur and co-rapporteur NCAs should receive their remuneration once they have fulfilled their obligations, as outlined in Article 4 of the cooperation agreement between EMA and NCAs (EMA 2016c, 3). Similarly, Article 9(3) of Regulation (EU) No 658/2014 on fees payable for pharmacovigilance activities states that remuneration will be provided after the final assessment report for a recommendation has been delivered. In the case of post-authorisation safety studies, remuneration is provided in two instalments. In the case of fee deferrals for SMEs, if an initial marketing authorisation ends negatively and no fee is charged, NCAs are not remunerated for their work.

1.1.4. EU and EEA budget contributions and other activities undertaken in the EMA fee and NCA remuneration system

Fees represent the majority of the EMA revenue (88 per cent in 2016), but EMA also receives EU and EEA budget contributions to balance costs and revenues so that EMA can carry out both procedural activities and other tasks. EU and EEA contributions are adjusted annually in order to address increases or decreases in fee income. This is done within a maximum amount defined within the seven-year EU budget framework. Contributions include both a general subsidy and a ring-fenced subsidy to be used exclusively to address the fee exemptions provided for orphan designated medicines. EMA reported to the study team that the amount usually covers all or most of the cost. Any shortages to the subsidy appropriation established in the initial budget are handled via transfers from the general EU contribution budget line to the special contribution for Orphan Medicinal Products line.

In addition to the procedural activities described in section 1.1.2, EMA and NCAs also undertake additional non-procedural activities. For EMA and NCAs, this includes particularly the development of databases and telematics activities, and development of guidelines. EMA and NCAs are also engaged, among other things, in public health activities, international cooperation, and post-authorisation activities that are not directly linked to marketing authorisations. EMA and NCAs are involved in committees, working

parties and other groups, and they undertake peer reviews. These and other activities undertaken by EMA and NCAs support the functioning of the regulatory system, including the operation of procedures, and in some cases are linked to legislative changes that have occurred since the fee and remuneration system was established.

1.1.5. The rationale for this study

Council Regulation (EC) No 297/95 states that fees charged to industry 'must be based on the principle of the service actually provided' (Council Regulation (EC) No 297/95, 2). Similarly, Regulation (EU) No 658/2014 on fees payable for pharmacovigilance activities states that the fees 'should be transparent, fair and proportionate to the work carried out', whereas any changes to fees levied by the EMA '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' (Regulation (EU) No 658/2014, L 189/113).

When the EMA fee system was originally established, it was not built on a direct cost-based approach but rather a system of graduated fees with a relatively low fee and/or no fee applied for development activities and a higher fee applied for both initial and post-authorisation procedures. This was based on a Marketing Authorisation Holder's ability to pay once marketed products began to generate a return on investment. In addition benefit-in-kind outcomes and consequential cost savings for Member States were also considered as key drivers when the centralised procedure and EMA was set up in 1995.

As outlined in the cooperation agreement between EMA and NCAs, NCAs should be paid for their services as determined in a remuneration scheme; the remuneration for each activity should be based on workload estimations multiplied by a fixed flat hourly cost (EMA 2016c). However, previous analyses of the EMA and its fee system[8] have shown that NCAs' costs are not aligned with the remuneration for the activities they provide, partly because they undertake activities that are not remunerated. The European Court of Auditors has commented on the imbalance of remuneration and costs to NCAs, noting that there is 'the need to introduce a system of remuneration for services provided by Member State authorities based on their real costs' (European Court of Auditors 2012, C 388/117).

This study has been commissioned to gather data and model the fee and remuneration system as it currently exists to determine whether and to what extent collected fees are aligned with costs to EMA and NCAs to undertake the required work.

1.1.6. Scope of the study

This study examines whether the fee and remuneration system is economically sound, fair, proportionate and as simple as possible for all stakeholders. Following Council Regulation (EC) No 297/95 and Regulation (EU) No 658/2014, the analysis is based on an assessment of the underlying costs of the regulatory system and thus on costing models and includes information gained through consultation with EMA and NCA representatives as well as wider stakeholders.

In line with the Better Regulation Guidelines of the European Commission, this study covers the following four criteria and associated high level study questions:

[8] For example, see the costing exercise in 2008–2009 of the EMA Management Board (EMA MB) (EMEA 2009a) and the evaluation of the EMA in 2010 (Ernst & Young 2010).

- **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?
- **Relevance**: To what degree does the fee system fulfil the need to fund the relevant legislative tasks of EMA, including the remuneration of NCAs?
- **Coherence**: To what degree is the EMA fee system coherent, internally and externally?
- **Sustainability**: To what degree is the current fee system of EMA sustainable?

The criterion of EU added value was not evaluated, as it is only possible to assess the EMA fee system at EU level (in relation to the tasks assigned to the EMA by the legislation) and not in relation to what might have occurred without the EU intervention.

Based on the four criteria, this study addresses 12 questions (Table 1). A detailed assessment matrix for this study is presented in Appendix 1.

1.2. Methodology

This study applied a mixed-methods approach, both quantitative and qualitative, in order to address the questions set out in Table 1. This section of the final report provides a summary of the overall approach, the specific methods applied, data sources used, approach to data validation, and limitations. A detailed description of the modelling methodology is presented in a separate methodology note which accompanies this report.

1.2.1. Overall approach to the study

The EMA fee and remuneration system study is composed of the following tasks:

- Data gathering through desk research and consultation.
- Validating time data provided by the EMA Management Board Data Gathering (MBDG) exercise.
- Developing a costing methodology for the fee system.[9]
- Developing a financial model for the fee system.
- Comparing the current fees and remuneration levels to actual costs
- Identifying gaps between cost based fees/remuneration and the current fee system.
- An open public consultation exercise to gather feedback on the findings.

Taken together, the results of these tasks enable the study team to answer the study questions posed in the Terms of Reference to assess the relevance, effectiveness and efficiency, coherence and sustainability of the fee system.

[9] Throughout this report we use the term 'fee system' to refer to both the fees charged by the EMA to industry and the remuneration of NCAs by the EMA for the work that the NCAs do as part of the European medicines regulatory network.

Table 1: Study questions

Criterion	Question	Section in the report
Effectiveness and efficiency	Q1. To what extent do the fees charged correspond with EMA costs?	Section 2.1
	Q2. To what extent does the current financial model allow the EMA to effectively perform the activities in its remit?	Section 2.2
	Q3. To what extent does the current financial model allow the EMA to remunerate the NCAs adequately for the activities they perform?	Section 2.3
	Q4. To what extent is a balance struck between a fee and remuneration system based on actual costs and simplicity of the fee system?	Section 2.4
	Q5. To what extent does the fee system enable needs to be met in exceptional circumstances or under particular priorities/imperatives?	Section 2.5
	Q6. To what extent are SMEs and micro-sized enterprises supported through effective incentives and reductions in their costs to use the centralised system?	Section 2.6
Relevance	Q7. 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?	Section 3.1
	Q8. Is the fee system relevant in terms of current needs?	Section 3.2
Coherence	Q9. To what extent is the fee system coherent internally?	Section 4.1
	Q10. To what extent is the fee system coherent with Member State fee systems?	Section 4.2
	Q11. To what extent is the fee system coherent at EU level with other EU policies?	Section 4.3
Sustainability	Q12. To what extent does the current financial model ensure the financial stability of the EMA including its ability to remunerate NCAs?	Section 5.1

1.2.2. Desk research

Objective: Review existing information sources available on the EMA fee and NCA remuneration system, including time and cost data related to the regulatory system. Identify fee system approaches used by selected EU agencies and third countries for comparison.

Approach:

- Review of information sources available on the EMA fee and NCA remuneration system (including legislative documents, EMA annual reports and budgets, European Court of Auditors reports, final report of an evaluation of the EMA in 2010, EU policies and other relevant documents) (see Appendix 2 for a list of the relevant documents and data sources for this study).
- Review of data collected by the data gathering initiative of the EMA Management Board (MBDG exercise), covering time data for the EMA and NCAs over the period

January 2016 to March 2017 (see Appendix 3 for a summary of the available time data).
- Review of cost data for the EMA, covering the year 2016.
- Review of NCA cost data collected through a survey (see subsection 1.2.3); and
- Desk research on fee-based approaches in other EU agencies (European Chemicals Agency (ECHA), European Union Intellectual Property Office (EUIPO) and the European Aviation Safety Agency (EASA) as well as the fee system of the U.S. Food and Drug Administration (FDA). The selection of these agencies was made in consultation with DG SANTE.

Limitations:

- The identification of legislation, policies and other documents to be reviewed for this study did not follow a systematic search protocol. Instead, it focused on documents identified by the study team in consultation with DG SANTE and EMA. Some of the documents were also provided or suggested by interviewees.
- Reviews and comparisons of other agencies' fee and remuneration approaches were mainly based on desk research and to a minor extent, information about the U.S. FDA shared by EMA, NCAs and wider stakeholder representatives consulted for this study.
- Time data from the MBDG exercise was the main source of time data used in the study. It included a selected set of procedures covering the majority of existing procedures over a specific time period and did not cover all of the activities that EMA and NCAs undertake.
- Limitations related to the data used in the modelling exercise are described in sections 1.2.4 and 1.2.5.

1.2.3. Consultation

Stakeholder mapping

Objective: Identify the relevant stakeholder groups, their involvement in the regulatory system and the influence they exert on the fee system to assess the potential impact of changes to the fee system and differences across groups. Use the mapping results to design an effective data collection approach and identify key informants representing the relevant stakeholder groups.

Approach: The study team conducted the stakeholder mapping using a three-step approach:

1. **Stakeholder identification** in collaboration with DG SANTE and EMA representatives.
2. **Characterisation and categorisation** of stakeholders according to their expected levels of interest and influence in the subject of the study to identify the best approach to consulting with stakeholders for the study.
3. **Identification of representatives and their preferred contact channels** to allow the study team to determine sets of target groups and to adapt its engagement approach/data collection methods.

The stakeholder mapping is presented in Appendix 4.

Limitation:

- All NCAs were contacted and EMA representatives consulted cover all EMA departments considered relevant to the fee and remuneration system. Two Member States, Poland and the Netherlands, have separate inspectorates. For the Healthcare Inspectorate in the Netherlands, survey responses were included with the NCA survey responses of the Medicines Evaluation Board and incorporated in the modelling exercise. Poland was not included in the modelling exercise as the Polish Office for Registration of Medicinal Products, Medical Devices and Biocidal Products did not respond to the survey. However, the list of wider stakeholders identified in this mapping exercise cannot be considered as comprehensive and representative of their groups. This list is limited to a selection of companies, associations and representative groups. This selection does not cover the overall population of companies, associations and representative groups relevant to the EMA, but is intended to cover the different interests affected by the EMA fee and remuneration system.

In-depth interviews with EMA representatives

Objective: Elicit the views of EMA on the relevance, efficiency, effectiveness, coherence and sustainability of the EMA fee system. Gather information on data gaps identified and contextual factors that are not documented to develop a description of the fee system.

Approach: The study team conducted in-depth interviews with representatives from the EMA as well as follow-up by telephone and email to supplement provided cost and time data. Interviews examined:

- The different forms of collaboration between EMA and NCAs.
- Wider contextual factors affecting the EMA fee and NCA remuneration system.
- The viability of the fee and remuneration system and the potential need for a dispute settlement procedure for fees.
- Services and costs that are not currently covered by the fee system.

Interviewees were identified in consultation with EMA; interviews were conducted with:

- The EMA Executive Director and Deputy Executive Director.
- Representatives from divisions responsible for stakeholders and communication; administration, legal and audit; and information management.
- Senior managers from operational divisions: Human Medicines Research and Development (R&D), Human Medicines Evaluation, Inspections and Pharmacovigilance, and Veterinary Medicines.

The interviews followed a customised set of semi-structured protocols. Topic guides containing the questions and introductory information about the study were sent to EMA in advance of the interviews. The eight interviews were conducted face-to-face at EMA headquarters in London during two day-long sessions (23 and 27 March 2017). Interviews were audio recorded and fully transcribed.

Limitation:

- Interviews covered a broad range of areas and often interviewees discussed topics in broad terms. The study team prompted interviewees to provide specific

examples where possible, but interviewees tended to provide high-level information, which may have an impact on the quality and comprehensiveness of the data collected. To mitigate this limitation, the study team has checked quantifiable information provided against legislation and other documents as well as against the time data collected through the EMA MBDG initiative and cost data provided to the study team by EMA and NCAs. Furthermore, a three-stage validation exercise was undertaken with EMA to review and confirm the data provided. Ongoing exchanges with EMA via email and teleconferences were also undertaken to support the validation exercise in order to clarify and confirm the information provided throughout the study.

Survey of NCAs

Objective: Collect data from NCAs about the costs they incur from undertaking EMA-related activities, including corresponding overheads. Elicit the views of NCAs on the relevance, efficiency, effectiveness, coherence and sustainability of the EMA fee and NCA remuneration system.

Approach: The NCA survey was designed to collect data on NCA costs to complement and add to the time data collected through the EMA MBDG initiative. The survey gathered information regarding:

- NCAs' levels of engagement with the EMA and the activities they are involved in.
- National-level contextual factors affecting NCA engagement with the EMA.
- The portion of NCA total costs that are related to EMA activities and the portion that is related to non-EMA activities, and the total costs for overheads that support both of these categories of activity.
- EMA-related activities and costs that are not covered by the EMA remuneration system.
- The coherence and sustainability of the fee and remuneration system.

NCA cost data is self-reported and the study team has had to assume that the data reported is accurate and complete. A three-stage validation exercise was undertaken with NCAs to review and confirm the data provided – through two rounds of review of the factual summary reports summarising the NCA inputs to the study and review of the interim report and methodology note for the study. Ongoing exchanges with NCAs via email and teleconferences were also undertaken to support the validation exercise in order to clarify and confirm the information provided throughout the study. NCA data were triangulated against data provided by EMA and information obtained through desk research.

The study team used RAND Europe's in-house online survey tool Select Survey for the survey. Beyond the specific questions, respondents were invited to submit any additional information they deemed necessary, including through attachments. The survey ended with three open questions on strengths and weaknesses of the EMA fee and remuneration system and provided space for final comments.

Altogether 47 NCAs (both human and veterinary NCAs) were invited to contribute to the survey, based on a contact list provided by the HMA. It was open for eight weeks, from 4 April to 30 May 2017. In total, 30 of 47 NCAs completed the survey, representing 23 Member States and 95 per cent of all EMA activities in the reporting period (2016 calendar year, except the UK which reported from April 2015 to March 2016).

Appendix 5 presents the questions asked in the survey. Table 24 and Figure 23 in Appendix 8 provide a summary of the responses received.

Limitations:

- When interpreting the survey results, and in particular answers provided to the open questions, responses received cannot be understood as representative of the views of all NCAs.
- The review of the responses received to the open questions showed that 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 Quantitative data on costs and participation in specific EMA-related activities was individual to each NCA.

In-depth interviews with NCAs

Objective: Discuss in depth the views of a subset of NCAs on the relevance, efficiency, effectiveness, coherence and sustainability of the EMA fee and NCA remuneration system to complement and contextualise the information received in the survey.

Approach: The study team conducted in-depth interviews with representatives from ten selected NCAs to enrich the analysis by providing detail on any gaps identified, exploring NCAs' views on the relevance, efficiency, effectiveness, coherence and sustainability of the EMA fee and NCA remuneration system. The interviews also supported the data validation undertaken by the study team.

The selection was made in coordination with the European Commission Inter-Services Steering Group (ISSG) and through consultation with the HMA Management Board and EMA. They include NCAs undertaking EMA-requested activities from human and veterinary sectors as well as those with different levels of costs associated with their activities, types and levels of involvement with the EMA, and geographical distribution in the EU, covering NCAs in Northern and Southern Europe as well as newer and older Member States in Eastern and Western Europe.

Based on that assessment, NCAs from the following countries were selected across human medicines and veterinary medicines:

- **Focus of the in-depth interview on human medicines:** Austria, the Czech Republic, Germany (two agencies), Hungary, the Netherlands, Spain and the United Kingdom.
- **Focus of the in-depth interview on veterinary medicines:** France and Ireland.

The interviews were based on a semi-structured interview protocol. They were conducted either face-to-face or by telephone and lasted between 45 minutes and two hours each. All but one of the NCA interviews involved 4–6 representatives from each NCA; the remaining NCA interview was conducted with one representative from the NCA who had collected information from colleagues in advance of the interview. All but one interview were audio recorded for the purposes of accurate notetaking (one NCA did not consent to audio recording). Detailed notes were taken during all of the interviews.

Limitation:

- Interviews covered a broad range of areas and often interviewees discussed topics in broad terms. The study team prompted interviewees to provide specific examples where possible, but interviewees tended to provide high-level information, which may have an impact on the quality and comprehensiveness of the data collected. To mitigate this limitation, the study team has checked quantifiable information provided against legislation and other documents as well as against the time data collected through the EMA MBDG initiative and cost data provided to the study team by EMA and NCAs. Furthermore, a three-stage validation exercise was undertaken with NCAs to review and confirm the data provided. Ongoing exchanges with NCAs via email and teleconferences were also undertaken to support the validation exercise in order to clarify and confirm the information provided throughout the study.

Survey of wider stakeholders

Objective: Elicit the views of stakeholders on the relevance, efficiency, effectiveness, coherence and sustainability of the EMA fee and NCA remuneration system and to complement the information gathered from other sources.

Approach: The study team conducted a survey covering European-level industry, research, healthcare, patient, consumer and other relevant associations and representative groups. The groups that were contacted were identified through the stakeholder mapping described above. Appendix 4 provides the organisations identified in the mapping exercise.

The study team used RAND Europe's in-house online survey tool Select Survey for the survey. Beyond specific closed questions, respondents were invited to submit comments on their responses, including through attachments.

The survey was open for eight weeks, from 5 May to 30 June 2017. In total, 40 complete responses were received.

The final survey questions are presented in Appendix 6. Table 25, Table 26 and Figure 24 in Appendix 8 provide a summary of the responses received to the wider stakeholder survey.

Limitations:

- Responses received to the survey cannot be understood as representative of the views of any particular group of stakeholders. Given the relatively small number of respondents (n=40), generalisations cannot be made.
- In this report, some results of the survey are presented by stakeholder group to highlight differences in reported views. As the number of respondents was low, the findings need to be interpreted with caution. We included the number of respondents per stakeholder group where possible.
- Any information provided was based on self-reported values, including data on the size classifications, areas of responsibility and geographic distribution of responding organisations.

Open public consultation

Objective: Elicit information, views and concerns of all groups having an interest in the EMA fee system and its implementation, including the remuneration to NCAs. In particular, it sought to gather input from groups having experience with the fee and remuneration system on its effectiveness and efficiency, relevance, coherence and sustainability.

Approach: An open public consultation was undertaken to complement the data collected from the targeted consultations described above. It was hosted by the European Commission's website for open public consultations[10] using an online survey format to elicit the views of stakeholders engaged and/or interested in the topic.

The study team developed a questionnaire, which relied predominantly on a set of closed questions, but also incorporated a small number of open questions. Beyond replying to the questions, respondents were invited to submit a document supporting their questions as an attachment.

The consultation was open for 13 weeks, from 2 May to 2 August 2018. In total, 51 responses were received.

The final survey questions are presented in Appendix 7. Table 27, Table 28 and Table 29 provide a summary of the responses received to the open public consultation.

Limitations:

- Responses to the public consultation cannot be understood as representative of the views of any particular population or stakeholder group. Given the relatively small number of respondents (n=51), generalisations cannot be made.
- In this report, OPC results are presented by stakeholder group to highlight differences in reported views. As the number of respondents was low, the findings need to be interpreted with caution. We included the number of respondents per stakeholder group where possible.
- Any information provided is based on self-reported values, including data on demographic profiles.
- The review of the submissions received to a question on final comments to the survey showed that 12 of 27 respondents submitted the same verbatim (or almost verbatim) response. This limitation was considered and highlighted in the analysis of the results as well as in the discussion of the results in this report.

1.2.4. Validation of time data

Objective: Validate the time data collected by the EMA MBDG initiative for use in the estimation of costs incurred by EMA and NCAs in undertaking EMA-related activities. Check and verify the data provided to the study team by EMA and by NCAs through the NCA survey. The validation process was used to identify which, if any, data should be excluded from the cost estimates to be undertaken in this study.

Approach: Data validation was undertaken on the inputs to the model. This included the time data from the MBDG exercise, data provided by EMA, and data provided by NCAs in the survey. Costs per procedure calculated in the model depend on the costs per

[10] European Commission, Consultations: https://ec.europa.eu/info/consultations_en

hour that are based on data provided by EMA and NCAs and the time taken to undertake procedures. A single cost per hour was calculated for each staff type in an organisation. The time to undertake an activity is the most important determinant of the relative cost of different activities and the data validation focused on the MBDG data. Data checking steps were also undertaken for the data provided by EMA and in the NCA survey, including through an extensive validation process described above.

The validation process first established a clear rule for characterising a data point as an outlier (i.e. more than two standard deviations from the mean) and then assessed whether the outlier could be explained in terms of the behaviour of an organisation relative to other organisations or the particular procedure of interest. Data were considered for exclusion if they were outliers and there was no explanation for the value in terms of the complexity of the procedure or in the reporting behaviour of an organisation. There is no reason to expect that EMA would spend a similar amount of scientific or administrative time on an activity compared to NCAs or that, for activities where NCAs spend more time EMA would correspondingly spend more (or less) time. Outliers were tabulated by activity. The allocation of time spent on activities by scientific and administrative staff, and for NCAs on all rapporteur, co-rapporteur and equivalent and 'other'[11] roles, was compared across organisations and activities, where there was sufficient data. The findings were also compared to a previous cost exercise undertaken in 2009 (EMEA 2009a). Differences were found but these differences could be explained by differences in the reporting, the calculation methods, changes in existing legislation and introduction of new legislation or differences in the average complexity of procedures undertaken.

As well as determining outliers, the data validation process identified patterns in NCA reported values for different roles and staff types. The main verification of the EMA data was to check that EMA fee income and costs calculated by the revenue and cost models match the fee income and costs reported by EMA. A detailed validation methodology is included as part of the methodology note explaining the modelling exercise undertaken for this study. The methodology note is a standalone document accompanying this final report.

Limitations:

- For veterinary medicines, data samples were small. This is to be expected, given the small volume of activities undertaken relative to human medicines during the period of the MBDG exercise. The small 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.
- The validation process identified differences between organisations in the data they reported but it could not identify the causes of the differences. Differences could be explained by differences in the reporting, the calculation methods, changes in existing legislation and introduction of new legislation or differences in the average complexity of procedures undertaken. These differences could not be isolated for the purposes of the study.
- As well as determining outliers, the data validation process identified trends in NCAs' reported time spent on activities for different roles and staff types. However, these trends are not a reason to exclude data as they may reflect the real behaviour of a particular organisation. For example, an NCA may consistently

[11] Other roles included PRAC rapporteur and co-rapporteur and peer-reviewer, depending on the activities in question.

use more administrative time and less scientific time than the average across all activities.

1.2.5. Costing methodology and financial modelling

Objective: Calculate EMA and NCA costs for each category of EMA services and activities, including those for which no fee is currently charged. Calculate costs to individual NCAs of procedural activities, time spent in committees and working groups and additional EMA-related activities. Test scenarios based on different assumptions about the distribution of costs.

Approach: The modelling approach consists of two parts. A cost model was developed by the study team using an activity based costing methodology to allocate overheads to salary costs. Cost data from EMA and the NCA survey, and time data from the MBDG exercise were used to calculate costs of EMA-related work undertaken at activity level. Costs were divided into three types for NCAs: costs of EMA-requested, procedural activities;[12] costs of participation in EMA working groups and committees; and costs of additional EMA-related activities. For EMA, costs were divided into procedural activities, with and without NCA involvement and additional activities. EMA committee time was allocated across the relevant procedural activities. A full list of the activities considered in the modelling exercise is contained in Appendix 9. A full list of additional activities provided by NCAs in the survey is provided in Appendix 10.

The second part is a revenue model that calculates the income that NCAs' receive from EMA for the EMA-related activities they undertake, and how this is allocated across NCAs, and the share of total revenue that EMA retains (EMA fee income). EMA fee income consists of the fee revenue it receives from industry less NCA income. The fees paid by the pharmaceutical industry enter the model as the fee revenue that is received by EMA. Two rules were applied in the fee model to specify NCA remuneration and industry fees.

In addition to revenue from its share of industry fee income, EMA receives EU and EEA budget contributions. In the model, the actual EU and EEA budget contributions are used in the baseline and synthetic baseline. An additional term, denoted 'other income', was calculated as the difference between the EMA costs and revenues from fees and EU budget contributions. It corresponds to income from administrative operations, such as sale of publications and organisation of seminars..

For NCAs, the cost and revenue modelling only covers EMA-related activities and all other NCA activities were excluded.

In addition to the remuneration and fee rules, incentives and reductions are applied by the EMA to some industry fees. The industry fees per procedure before any incentives are applied to them are referred to as the unitary full fees and are presented in a fee grid for each of the activities considered in the cost model. The fee grid provides the full unitary fees in Euro for individual activities, covering both human and veterinary medicines, including the fees under the current financial model and average cost based fees for the scenarios described in this report. The fee grid is provided as a separate document.

In order to use the model to compare different theoretical fee system scenarios in a consistent manner, the study team had to make assumptions and, in particular, develop a synthetic baseline to represent a 'typical' year, for which the incentive rates and

[12] Some procedural activities are undertaken by EMA only.

numbers of procedures are fixed. This is the synthetic baseline year **and all the results presented in the following sections refer to the synthetic baseline**. Changes to the number of procedures and incentive rates for a given activity will have an impact on the cost and fee calculations. Costs depend directly on the number and type of procedures and fees paid by industry, and the EMA share of fee income depends on the number and type of procedures and the incentives and reductions applied. To take account of these effects without needing to test many combinations of incentives and numbers of procedures for different activities, we used average costs per procedure, unitary fees per procedure and full fees before incentives or reductions for some of the analysis of specific activities.

In the synthetic baseline the EU and EEA budget contribution balancing term was adjusted so as to balance the EMA budget. In the scenarios tested with the model, the EU budget contribution is one of the mechanisms used to make the EMA budget balance under different cost-based fee and remuneration rules. Hence, in these scenarios, EU and EEA budget contributions are calculated numbers and differ from the reported EU and EEA budget contributions.

The modelling process followed a number of stages:

1. The baseline costs and fees for EMA and NCAs under the current financial model were calculated using data provided by these organisations for a one year period. The fee rule and remuneration rule were determined by existing legislation (see section 1.2.2).
2. For modelling purposes, a synthetic annual baseline was developed so that in the model the volume of procedural activities for which industry pays a fee is equal to the activities that were undertaken by EMA and NCAs in the same year. For activities for which no fee is paid by industry, the total number of completed procedures reported by EMA was used. The average percentage level of incentive per activity was assumed to be the same as the baseline. This approach enabled fees and costs to be directly compared with one another and the impact of scenario tests to be clearly evaluated. The industry fee and NCA remuneration rules from the current financial model were applied. However, because, in the synthetic baseline, the number of procedures for each activity used for both cost and fee revenue calculations is the number of procedures for which industry pays a fee, the activity based fee shares and EMA income balancing term contributions differ slightly from the baseline values. EU and EEA budget contributions are assumed to be the same as in the baseline.
3. For each procedural activity, a unitary cost for NCAs was determined as a weighted average from the total costs for NCAs undertaking procedures for the activity in the synthetic baseline divided by the total number of procedures undertaken for the activity.
4. Scenario tests were carried out to model the potential for aligning the costs as closely as possible with the fee revenue and compared to the synthetic baseline costs.

A stand-alone methodology note detailing the costing methodology, including the sources of the cost information, and the financial modelling is provided with this final report. The financial modelling does not replicate costs and fees reported in NCA and EMA accounts. It uses reported data from EMA and NCAs with an activity based costing approach and fee implementing rules to estimate costs and fees.

Limitations:

- Time data from the MBDG exercise was the main source of time data used in the modelling. It included a selected set of procedures covering the majority of existing procedures over a specific time period but did not cover all of the activities that EMA and NCAs undertake. Average values from the MBDG data were used across all NCAs. For some activities where there was wide variation in the times reported, the costs to individual NCAs may not fully reflect the complexity of the work undertaken.
- For all NCAs, the costs per hour for scientific staff and administrative staff working on EMA related activities is assumed to be the same as the organisational average for each staff type. If for any given NCA, the staff costs for EMA-related activities are higher than the staff costs for other NCA activities, the corresponding cost per hour would be higher than the value used in the modelling.
- The study team requested data from NCAs and EMA on their costs for all the EMA-related activities they undertake. For procedural activities, the number of procedures undertaken was requested for a wider set of activities than those covered by the MBDG exercise; as a result there is not a one-to-one correspondence between the time data collected in the MBDG exercise and the cost data collected by the study team for all activities. For some activities time data have been obtained from other sources. However, there are costs that are not included in the model because time data was not available.
- The number of procedures undertaken as rapporteur/lead and co-rapporteur/support roles was reported by NCAs. These include activities for which NCAs were not remunerated. Information on numbers of procedures and purchase orders was provided by EMA.[13] NCAs also reported the number of other roles for procedural activities that are not remunerated under the current fee system. These could not be matched to information available from EMA. A constraint based approach was used to reduce the impact of over-reporting of these numbers in the analysis (explained in the costing methodology note). Over-reporting of other roles could lead to procedural costs being too high. Under-reporting could lead to procedural costs being too low.
- Information on unit fees was derived from data provided by EMA only. For some activities this was provided at a more aggregate level than requested, combining activities of the same type which had a common unitary fee under the current financial model. For example, aggregated fee data was provided for initial marketing authorisations for new active substances, known active substances and fixed combination products. However, more granular data was required because these activities may not take the same time to complete and therefore have different costs. The same unit fee was applied at the disaggregate level. The role of different industry sectors, such as SMEs, is accounted for through the average incentives applied to the full unit fees but a detailed analysis of industry sectors is not possible.
- NCAs reported their involvement in working groups and committees and additional EMA-related activities in questions 19 and 20 of the NCA survey,

[13] Information on unremunerated activities for which no purchase order data were available could be provided by EMA for any potential future analysis. In this study NCA survey data only were used.

respectively. A variety of responses were provided; these included costs, time taken, number of activities, or a list of activities, which could not be verified using data from other sources.[14] In order to maintain a consistent approach across all NCAs, data from the MBDG exercise was used to calculate time spent in working groups and committees. Additional activities were determined as a remainder term in the baseline. Additional activities therefore contain any EMA-related costs reported by NCAs that are not captured by procedural activities and committees and working groups. Under or over-reporting of other procedural roles could result in these additional costs being too high or too low, respectively.

- Data from one respondent NCA was excluded from the modelling as it did not report any EMA-related activities. This does not affect the model outcomes.

1.2.6. Analysis and synthesis

Objective: To assess the judgement criteria identified in the study framework and formulate answers to the study questions regarding the extent to which the EMA fee and NCA remuneration system is effective, efficient, coherent, relevant, and sustainable.

Approach: The framework presented in Appendix 1 was used to guide the assessment of judgement criteria. The data collection tasks 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 study questions.

The study team used different sources to validate and triangulate the findings. Triangulating the findings from each data source contributed to the weight of evidence. While for some research questions, the conclusions are more tentative, on the whole the research team believes that the study presents a coherent and robust set of answers to the study questions.

Limitations:

- Data for veterinary activities in the MBDG exercise were based on small samples with a large degree of variation across the reported values for some activities.

As explained above, there are several noteworthy limitations to the study methods. In reporting on the collected evidence, the study team has made those caveats and limitations explicit. In drawing conclusions, the report has been cautious not to over-interpret the evidence.

[14] Further analysis of the reported additional activities will be undertaken separately from the current study.

2. ASSESSMENT OF EFFECTIVENESS AND EFFICIENCY

According to the EU Better Regulation Guidelines, the assessment of effectiveness should consider how successful an EU intervention has been in achieving or progressing towards its objectives. This includes identifying factors driving or hindering progress and how they are linked (or not) to the EU intervention. For this study, the assessment of effectiveness is based on the extent to which the objectives of the fee system have been achieved in relation to the general needs of the fee system. This includes an assessment of the extent to which the fee system: allows the EMA to perform its tasks, allows the EMA to remunerate NCAs adequately to perform their tasks, is fair and transparent, is flexible to take into account exceptional circumstances, and supports SMEs.

In this study, effectiveness is closely tied to efficiency and so these criteria are 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 is assessed by examining the relationship between costs and fees for the activities covered by the EMA.

This chapter reports on the findings with regard to the study questions referring to effectiveness and efficiency. Table 2 provides an overview of those questions and their respective section in this report.

Table 2: Study questions referring to effectiveness and efficiency

Study question	Section in the report
Q1. To what extent do the fees charged correspond with EMA and NCA costs?	Section 2.1
Q2. To what extent does the current financial model allow the EMA to effectively perform the activities in its remit?	Section 2.2
Q3. To what extent does the current financial model allow the EMA to remunerate the NCAs adequately for the activities they perform?	Section 2.3
Q4. To what extent is a balance struck between a fee and remuneration system based on actual costs and simplicity of the fee system?	Section 2.4
Q5. To what extent does the fee system enable needs to be met in exceptional circumstances or under particular priorities/imperatives?	Section 2.5
Q6. To what extent are SMEs and micro-sized enterprises supported through effective reductions in their costs to use the centralised system?	Section 2.6

2.1. Correspondence between the fees charged and EMA costs

This section provides answers to the study question relating to the extent to which the fees charged correspond with costs to the EMA, and to NCAs for EMA-related activities. The question is addressed in two parts by looking at: (A) the alignment of fees charged with the services performed (section 2.1A); and an assessment of whether (B) total fees earned enable the EMA to meet its costs, taking into consideration the availability of EU and EEA contributions, and whether the remuneration paid to NCAs allows them to meet the costs of EMA-related activities (section 2.1B). The costs, fees and number of procedures used in the results reported in this section **all refer to the synthetic baseline**.[15] They do not aim to reproduce costs and fees reported in EMA and NCA

[15] The synthetic baseline is explained in section 1 and the methodology note accompanying this document.

accounts but are estimated values based on data provided by EMA and NCAs using an activity based costing approach and the current fee implementing rules.

Overall, the analysis of correspondence between the fees charged and EMA and NCA costs shows that 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. Equally, the total remuneration provided to NCAs covers the aggregate costs of the procedural activities that they undertake, as well as in aggregate their involvement in working groups and committees; however, alignment with individual NCAs varies.

The total fees are not, however, sufficient to cover all of EMA's activities. The additional EU and EEA budget contributions in effect finance additional activities that EMA undertakes.[16,17] For NCAs, the total value of remuneration they receive from EMA does not cover all of the additional EMA-related activities that they report undertaking in addition to procedural activities and time spent in working groups and committees.[18]

This study tested cost-based scenarios as part of a benchmarking exercise. Using an approach that applies average cost based fees[19] for procedural activities undertaken by EMA would help to balance unitary full fees against costs, but EMA income would need to be increased as compared to current revenue to balance its costs. The scenarios tested different fee mechanisms to achieve this as the fee mechanism used would have an impact on EU and EEA budget contributions or industry fees. Average cost-based fees would cover procedural costs for NCAs overall, but not for all individual NCAs.

More specifically, key findings relating to the correspondence between fees charged and costs incurred are as follows:

F1. The total EMA share of industry fees from procedural activities (excluding annual fees) for both human and veterinary medicines (€103.7 million/year) exceeds its costs for these activities (€81.6 million/year).

The total NCA share of fees from procedural activities (excluding annual fees) for both human and veterinary medicines (€92.1 million/year) exceeds their aggregate costs for these activities (€87.3 million/year). These costs are within 5 per cent of the fees.

However, in addition to procedural activities, both EMA and NCAs incur costs for activities that are not directly linked to procedural fees. Consequently the apparent aggregate excess in fees to EMA and remuneration paid to NCAs does not imply overcharging at aggregate level. Furthermore, at the level of individual NCAs (as opposed to all NCAs in aggregate), some NCAs are able to meet their costs for procedural activities while others are not.

[16] Some of the additional EMA-related activities partially encompass procedural activities.

[17] The study did not specifically assess whether special EU contributions for orphan medicinal and paediatric medicinal products are sufficient to compensate fee exemptions for orphan designation and paediatric medicine activities. Article 7.2 of Regulation (EC) No 141/2000 and Article 48 of Regulation (EC) No 1901/2006 require that the contributions are sufficient for this purpose but the data available for this study was not sufficient to undertake this assessment.

[18] A minority of procedural activities were not recorded through the MBDG exercise or Question 17 and Question 18 of the NCA survey, but rather through Question 20. Moreover, NCAs may not have reported all 'other' procedural roles in Question 17 and Question 18 so that these were included as additional activities in the model.

[19] Average cost based fees are full fees charged to industry that reflect the average combined costs to EMA and NCAs.

F2. The EMA share of fees for procedural activities (excluding annual fees) for human medicines (€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).

F3. The total remuneration received by NCAs for undertaking procedural activities for human 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 per cent 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.

F4. At a more granular level, the picture becomes more complex. There are many different procedural activities, some of which are charged full fees, some of which have reductions applied, some of which have the fees waived, and some of which are exempted from fees. Incentives and exemptions result in activities for which costs cannot be covered (fully or at all) by fees and so fees charged for other procedural activities and annual fees fund these costs, both for EMA and for NCAs.

In particular, costs are not covered for EMA or NCAs for initial marketing authorisations, although they are currently associated with the highest 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 the activity. Type II variations are the most notable example of this; fees for these activities well exceed costs both for EMA and NCAs.

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

F5. Under the current financial model fees are not always shared between EMA and NCAs in proportion to their costs. Scenarios that tested an average cost-based approach show that this approach would result in NCAs receiving less remuneration for some activities and more for others.

A. Overall, the fees charged for procedural activities broadly cover the costs for these activities for EMA and, in aggregate, for NCAs.

The assessment of alignment between fees charged and services provided was performed primarily through the quantitative assessment of the current financial model. The assessment focused mainly, though not exclusively, on procedural activities covered by the MBDG report.[20] Alignment was assessed in two ways. Firstly, for both EMA and NCAs,[21] 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 3). Secondly, the average costs and fees were compared for individual activities, activity by activity.

[20] The role of annual fees and non-procedure-based activities, including costs related to cross-cutting and horizontal activities such as working groups and committees is discussed separately later in this section.

[21] The NCA share of fee income in this case is the reimbursement for procedural activities they receive from EMA.

The assessment of total fees indicates that the EMA fee share for procedural activities (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 for which they receive no fee income.

The total remuneration received by NCAs for undertaking procedure-based 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 were overpaid, however, as they undertake additional activities for EMA for which they currently receive no remuneration.

Table 3: Total annual costs and remuneration for procedural activities for the current financial model over one synthetic year (€million/year)

		Current financial model		
		Human medicines	Veterinary medicines	Total
EMA	Cost of procedures[a]	74.9	6.7	81.6
	Share of industry fees from procedural activities[a]	100.3	3.4	103.7
NCA	Cost of procedures	83.1	4.2	87.3
	Remuneration from procedural activities	89.2	2.8	92.1

[a] These values exclude NCA remuneration. Procedural-activities include all activities listed in Question 17 and Question 18 of the NCA survey. EMA reported combined cost and fee information for inspections for human and veterinary medicines. In the synthetic baseline, these were allocated to human and veterinary medicines in proportion to the procedures reported by NCAs.

The distribution of fees and related costs for human and veterinary medicines were then considered separately. Table 3 shows that for EMA, the total costs incurred for all procedural activities for human medicines (€74.9 million/year) are covered by the EMA share of industry fees for those activities (€100.3 million/year). The total costs of procedural activities for veterinary medicines (€6.7 million/year) are not covered by the EMA share of industry fees for these activities (€3.4 million/year).

The total cost of procedural activities for human medicines undertaken by NCAs (€83.1 million/year) is covered by the remuneration they receive from EMA (€89.2 million/year). NCA costs for each procedural activity considered here include other roles[22] that are not remunerated under the current financial model, as well as the remunerated roles.[23] They also include procedural activities for which NCAs are not remunerated for any roles they undertake. At the level of individual NCAs, the total costs of procedural activities for human medicines are covered by the remuneration they receive for these activities. Five out of 24 NCAs that undertake human medicines activities do not cover costs i from EMA remuneration. These NCAs have a high workload of procedural activities. However, when remuneration from annual fees is included, there are three NCAs do not cover their costs from a combination of EMA remuneration for

[22] Calculations for other roles are based on numbers reported by NCAs, constrained so that the number of other roles per procedure is not excessive. Costs thereby not included in this category are added to the additional costs reported by NCAs. The approach is discussed in detail in the Methodology Note.

[23] This assessment does not include costs associated with more general activities that are EMA-related, but not specifically part of a procedural activity – these costs are discussed later in this section (see Figure 12 and associated analysis).

procedural activities and annual fees. In these cases, the costs for non-remunerated roles are a high proportion of the total procedural activity costs.

Seventeen of the 30 NCAs that provided data for this study reported undertaking procedures for veterinary medicines; 12 of these had costs for veterinary procedures that exceeded the remuneration they received. Overall costs of veterinary procedures for these 17 NCAs (€4.2 million/year) are almost 50 per cent higher than the fee share[24] (€2.8 million/year).[25] Overall, the evidence indicates that total fees for procedural activities for veterinary medicines are insufficient to cover total costs for procedural activities.

At the level of individual activities, the assessment of the current financial model indicates that the specific fees charged do not align with the costs identified by the EMA and the NCAs for undertaking these activities.

Fees were compared to costs for EMA and NCAs at the level of individual activities.[26] Fee income over a single year was first compared to yearly costs by activity and then unitary fees per procedure were compared with average costs per procedure. The impact of incentives was also considered.

For some activities, fees charged in a single year under the current financial model are greater than costs and for others they are lower. Figure 1 compares the total combined costs to EMA and NCAs over a one-year period for a set of activities, with the full fees that would be paid by industry if no incentives were applied. Incentives mainly reduce the EMA's share of fee income rather than the NCAs' share, as NCA remuneration is predominantly based on the full fees before incentives are applied. However, eight NCA interviewees explained that they do not receive full remuneration for some activities (e.g. activities for orphan designated or paediatric medicines such as scientific advice, assessments, PIPs, activities for SMEs), and that it is often not clear how much remuneration they will receive at the time they take on an activity.

A subset of procedural activities was used to illustrate the main results, which together represent the main activities in terms of fee generation and costs.[27] In particular, Figure

[24] These costs were calculated using average time data from the MBDG exercise. Data for veterinary activities in the MBDG exercise were based on small samples with a large degree of variation across the reported values for some activities. A decrease of 5 per cent in the average time taken would mean that fees balanced costs.

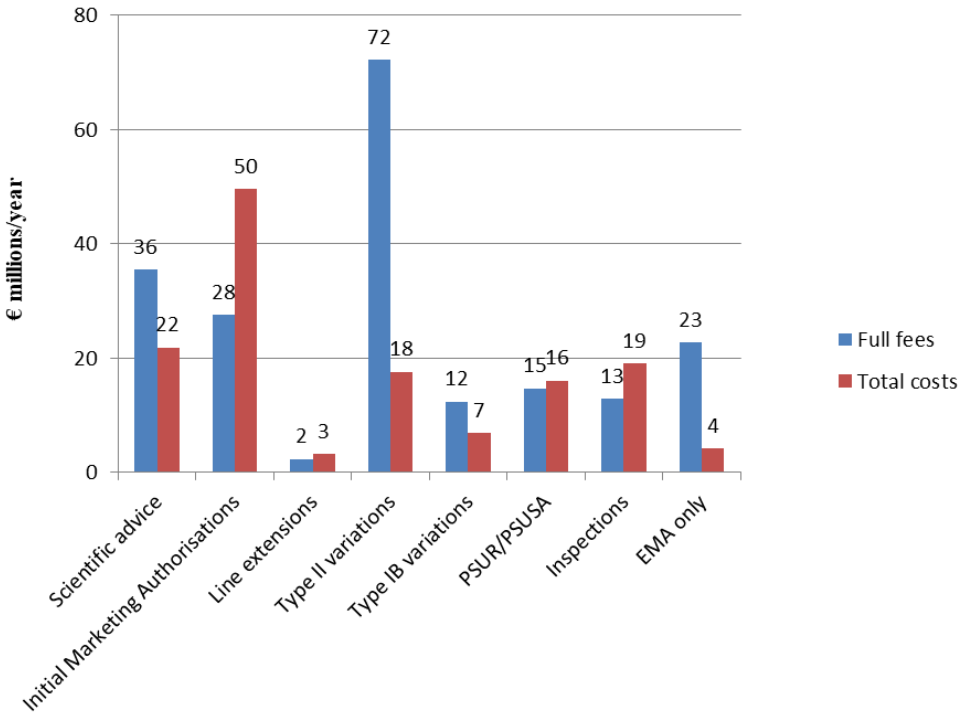
[25] It is not possible to completely separate activities related to human and veterinary medicine as EMA reported combined cost and fee information for inspections. This means that the costs and remuneration for inspections related to veterinary medicines are included in the costs for human medicines and not in the costs for veterinary medicines. For individual NCAs that undertake veterinary activities only, inspection costs and remuneration are accounted for, but they are categorised as human medicines-related costs and remuneration.

[26] In the modelling exercise, fees and costs were both calculated for the same number of procedures for a given activity in order to compare the alignment of fees and costs. However, different numbers of procedures are undertaken for different activities. For example, the model includes 581 scientific advice procedures and 113 initial marketing authorisations. Over a single year, the total fees received for each activity depends on the number of procedures undertaken and the fee per procedure, which is referred to as the unitary fee. Total fees received also depend on incentives – the fee reductions applied to the unitary fee for an activity for some industry sectors.

[27] The full set of procedural activities was agreed with HMA and EMA and was based on the current legislative fee basis and expected incentive level and time taken to complete an activity. Fees and costs for some of these activities were calculated at a more detailed level in the modelling exercise, namely for scientific advice, initial marketing authorisations, line extensions, type II variations, and inspections. For example, six types of scientific advice activity were included in the model – scientific advice and protocol assistance, levels I, II and III and scientific advice and protocol assistance follow-up levels I, II and III. These have been aggregated into one activity in the results provided here. The average costs and fees per procedure for all the activities analysed in the modelling exercise, including the details by sub-category, are presented in the fee grid provided separately with this report.

1 shows that the yearly full fees are much greater than the costs for type II variations (fees: €72 million/year, costs: €18 million/year) but much smaller than the costs for initial marketing authorisations (fees: €27.5 million/year, costs: €50 million/year).[28] Broadly, fees are also greater than costs for: EMA-only activities (that is, activities that NCAs do not contribute to); type IB variations (for which NCAs are not remunerated at all); and scientific advice. Fees and costs are broadly aligned for inspections; periodic safety update report (PSUR) and PSUR single assessment (PSUSA) activities; and line extensions (i.e. fees are within 20 per cent of costs).

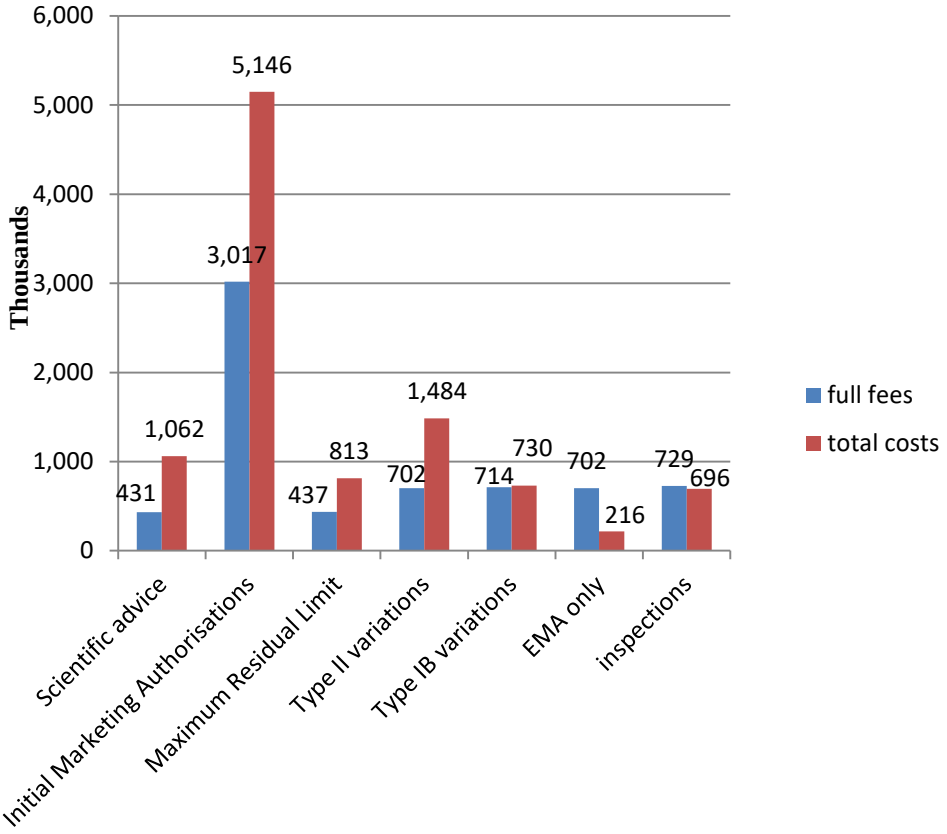
Figure 1: Comparison of total costs and fees for EMA and NCAs over one synthetic year before incentives have been applied under the current financial model – human medicines only



A similar comparison is made for veterinary medicines in Figure 2. In this case full fees are much smaller than costs for initial marketing authorisations (fees: €3 million/year, costs: €5.1 million/year), and also for scientific advice (fees: €431,000/year, costs: €1.1 million/year) and type II variations (fees: €702,000 /year, costs: €1.5 million/year). Full fees are broadly in line with costs for type IB variations (fees: €714,000/year, costs: €730,000/year) and inspections (fees: €729,000/year, costs: €696,000/year).

[28] This is also the case for the fees and costs per procedure. The ratio between the yearly fee revenue and costs is the same as the ratio between fee revenue and costs per procedure.

Figure 2: Comparison of total costs and fees for EMA and NCAs over one synthetic year before incentives have been applied under the current financial model – veterinary medicines only



The total fees charged to industry over one year are less than the full fees shown in Figure 1 and Figure 2 because of incentives. The average incentive applied differs between activities. The reduction in full fee income due to incentives is compared to the total fees charged in Figure 3 for human medicines and Figure 4 for veterinary medicines. For human medicines, incentives had the largest effect on scientific advice (29 per cent incentive, €10.4 million/year reduction in potential fee income) and initial marketing authorisations (12 per cent incentive, €10.4 million/year reduction in potential fee income).

Relatively, incentives for veterinary medicines are generally larger than for human medicines. The largest effects are again seen for scientific advice (42 per cent incentive, €182,000/year reduction in potential fee income) and initial marketing authorisations (17 per cent incentive, €255,000/year reduction in potential fee income) and also for maximum residual limit applications (44 per cent incentive, €194,000/year reduction in potential fee income).

Figure 3: Comparison of the shares of incentives and total fees charged over one synthetic year under the current financial model – human medicines only

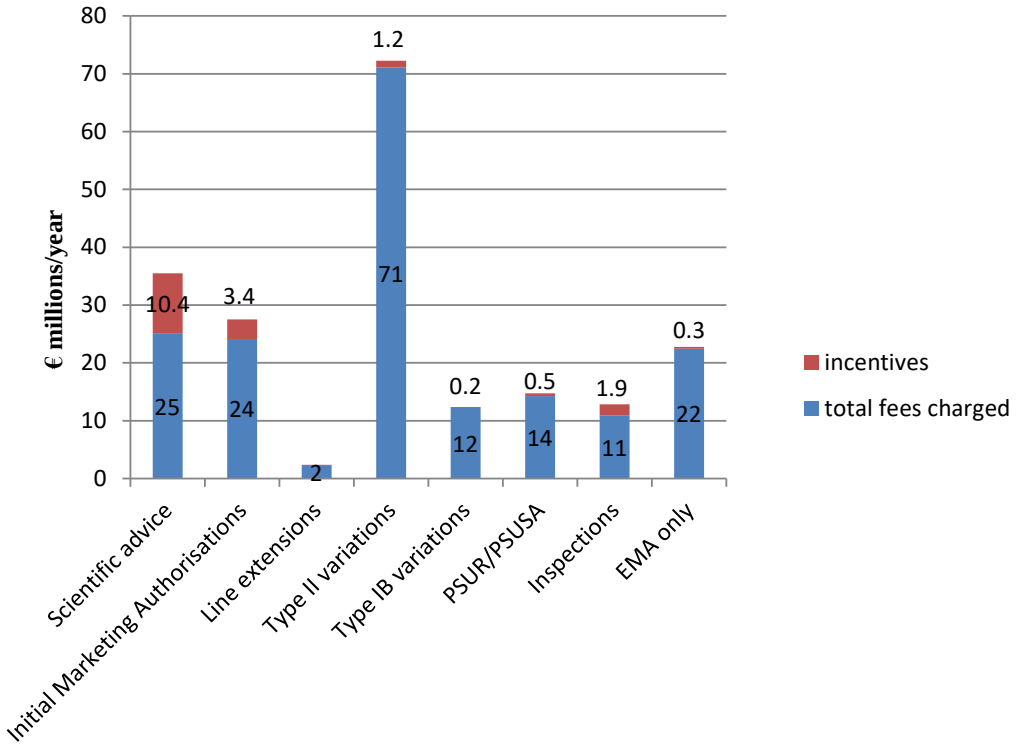


Figure 4: Comparison of the shares of incentives and total fees charged over one synthetic year under the current financial model – veterinary medicines only

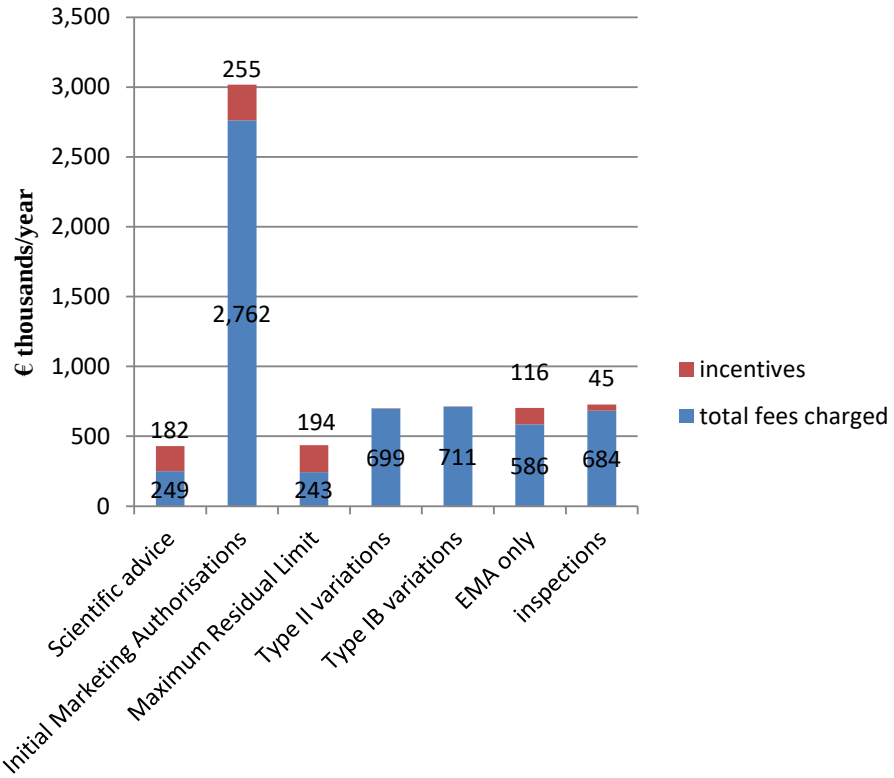
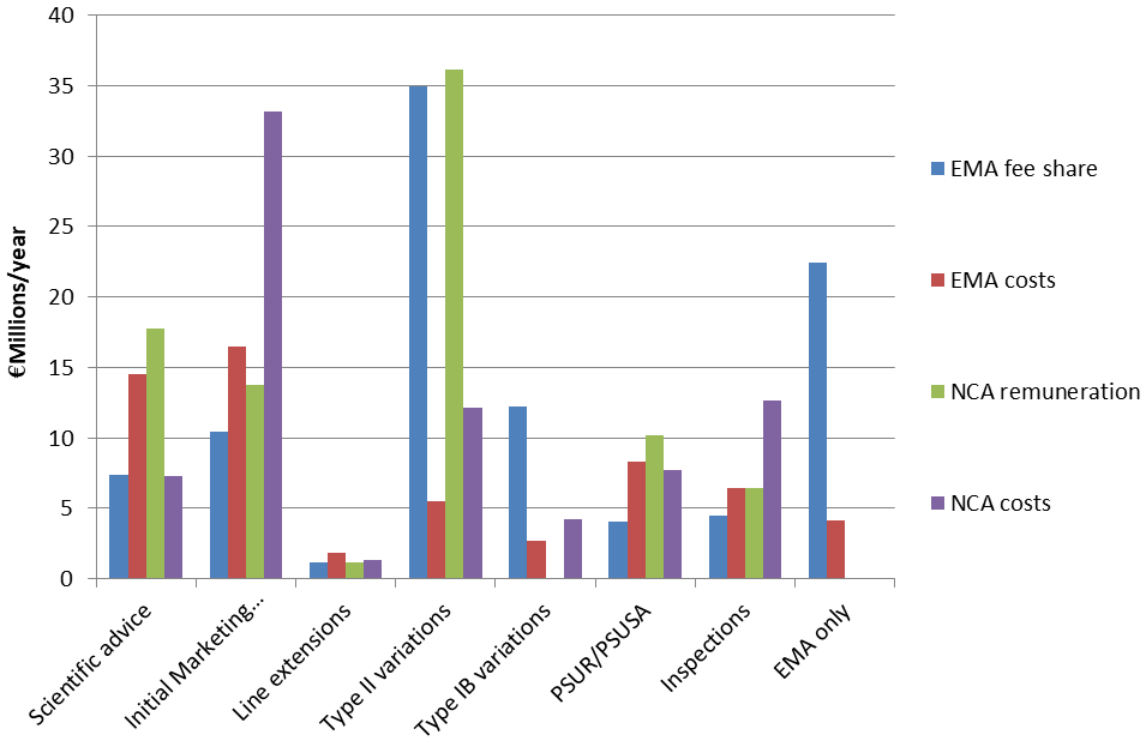


Figure 5 shows how the fees and costs are allocated across EMA and NCAs. Here, the fees are net of incentives and represent the fees received in the synthetic baseline year. In general under the current financial model, NCA remuneration is based on the full fees, while the EMA fee share comprises the remaining fees once incentives have been applied and NCAs have been paid (except for pharmacovigilance activities, for which NCA remuneration is net of incentives).

For initial marketing authorisations, costs exceed the share of fee income for both NCAs (costs: €33.5 million/year, remuneration: €13.8 million/year) and EMA (costs: €16.5 million/year, fee income: €10.4 million/year). This effect is also seen at the disaggregate level across the eight types of initial marketing authorisations. The largest differential between costs and remuneration are seen for new active substances, known active substances and biosimilars, and the smallest for generics. The losses incurred by NCAs at this initial stage are expected to be recovered in the longer term through annual fees and fees for type II variations. NCA remuneration from annual fees amounts to €21.1 million/year, which approximately offsets the difference between costs and remuneration for NCAs at the aggregate level. However, if the initial marketing authorisation ends negatively, the marketing authorisation is withdrawn or the product becomes dormant, individual NCAs may not recover their costs. It was not possible to estimate the order of magnitude of this effect.

In contrast, for type II variations, the share of fee income exceeds costs. For NCAs, costs were €12.5 million/year and remuneration was €36 million/year. For EMA, costs were €5.5 million/year and fee income was €35 million/year. For scientific advice and protocol assistance, where the average incentive is almost 50 per cent, EMA costs again exceed its fee share (costs: €14.6 million/year, fee income: €7.4 million/year). However, for the activities that EMA undertakes without NCA involvement, fees are significantly higher than costs (costs: €4.2 million/year, fee income: €22.5 million/year).

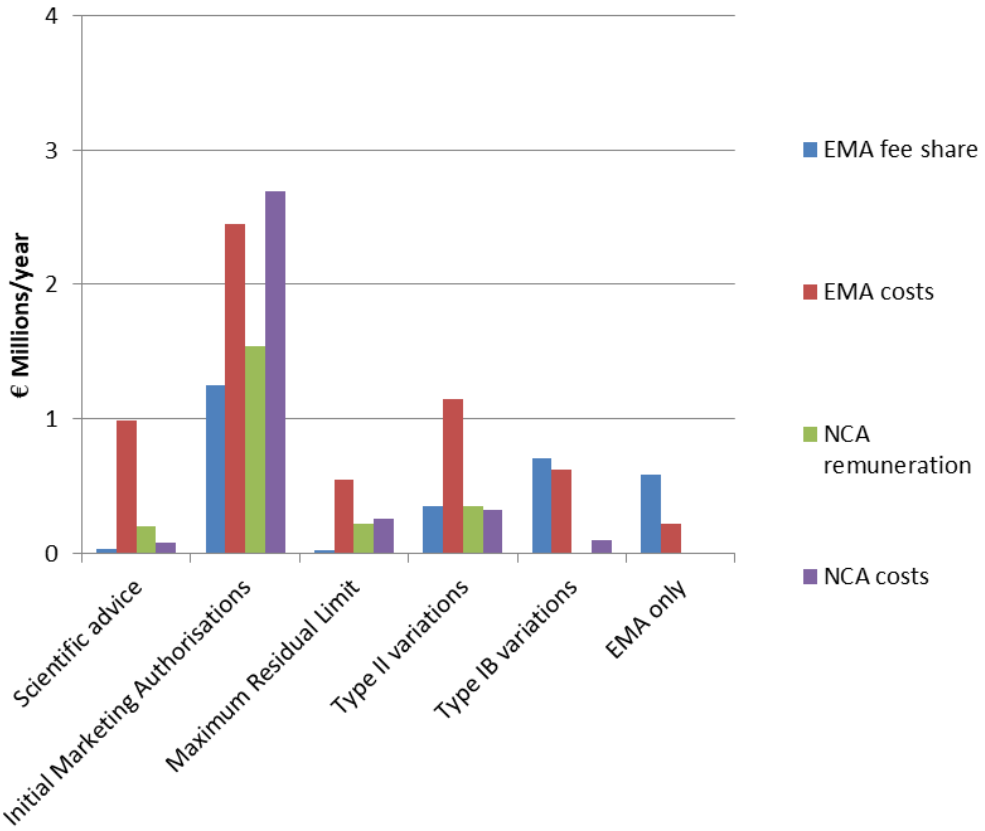
Figure 5: EMA and NCA shares of costs and fees over one synthetic year after incentives have been applied under the current financial model – human medicines[29]



A similar comparison is shown for veterinary medicines in Figure 6. The results are broadly in line with those for human medicines. The low EMA fee share for scientific advice occurs as a result of a 50 per cent average reduction being applied to the full fee. However, unlike for human medicines, type II variations for veterinary medicines do not generate high EMA and NCA fee shares relative to the costs incurred. Indeed the EMA fee share is only 30 per cent of its costs.

[29] Inspections were reported separately by NCAs for veterinary medicines and human medicines. They were combined in the EMA data reporting. In the synthetic baseline, these were allocated to human and veterinary medicines for EMA in proportion to the procedures reported by NCAs.

Figure 6: EMA and NCA shares of costs and fees revenue/income over one synthetic year with incentives applied under the current financial model – veterinary medicines



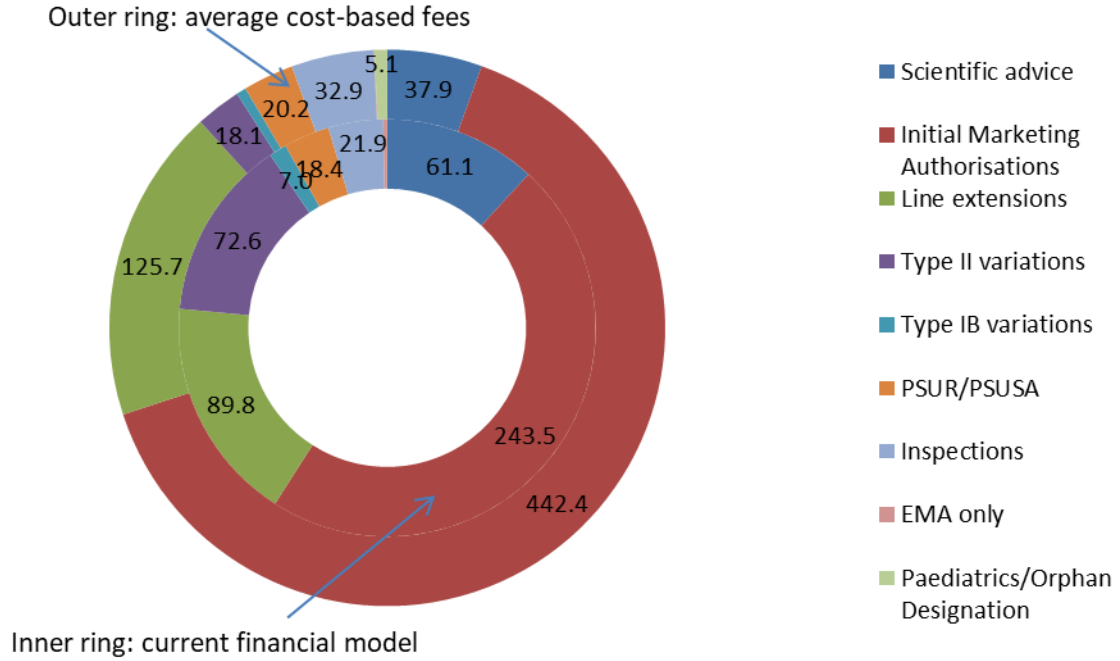
This study tested different approaches and modelled the results to assess the activity category-level differences between fees and costs, while maintaining the incentives and exemptions that are currently provided for in legislation. One approach that was tested in this study was to align the full fees EMA charges industry with the corresponding average costs and to remunerate NCAs for the average cost of their work. As a test of this principle, the study team compared the current fees for procedural activities to the average costs of the same activities, that is, to the total average cost per procedure for EMA and NCAs.[30] This comparison was undertaken for all procedural activities for which costs were available.

NCA costs vary across individual NCAs, with the consequence that some NCAs receive fees that cover their costs, while others experience a shortfall (see Section B below). This situation remains 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.

[30] Average costs for NCAs comprise the costs of all roles required for the completion of a procedure of a given procedural activity; in the terminology of the modelling exercise, average costs include costs of rapporteur/lead roles, co-rapporteur/support roles and other roles reported in Question 17 and Question 18 of the NCA survey. For a given activity, average cost is calculated as the sum of the costs of these roles for all NCAs undertaking roles divided by the number of procedures. Hence the average is 'weighted' by the number of roles undertaken and hourly costs of each NCA but not by the time taken as all NCAs are assumed to take the same average time for any role.

Figure 7 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 7 represents the distribution of fees in Euro per procedure under the current financial model.[31] The outer ring represents what fees per procedure would look like when modelling the principle of average cost pricing.

Figure 7: Comparison of unitary full fees for human medicine procedural activities for current financial model and when modelling average cost-based fees (€ thousand/procedure)



The fees for initial marketing authorisations are by the far the highest fee in both cases and the fee would be even higher than it is under the current financial model using average cost pricing as current fees do not fully reflect the cost of these procedures (€442,400/procedure when modelling average cost pricing compared with €243,500/procedure under the current financial model).[32] Type II variations have high fees under the current financial model for human medicines but the model shows that these would be 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;[33] these are PIPs, exemptions and compliance checks for paediatrics and orphan designation. However these activities incur costs. The corresponding average cost-based fees modelled for these activities are 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.

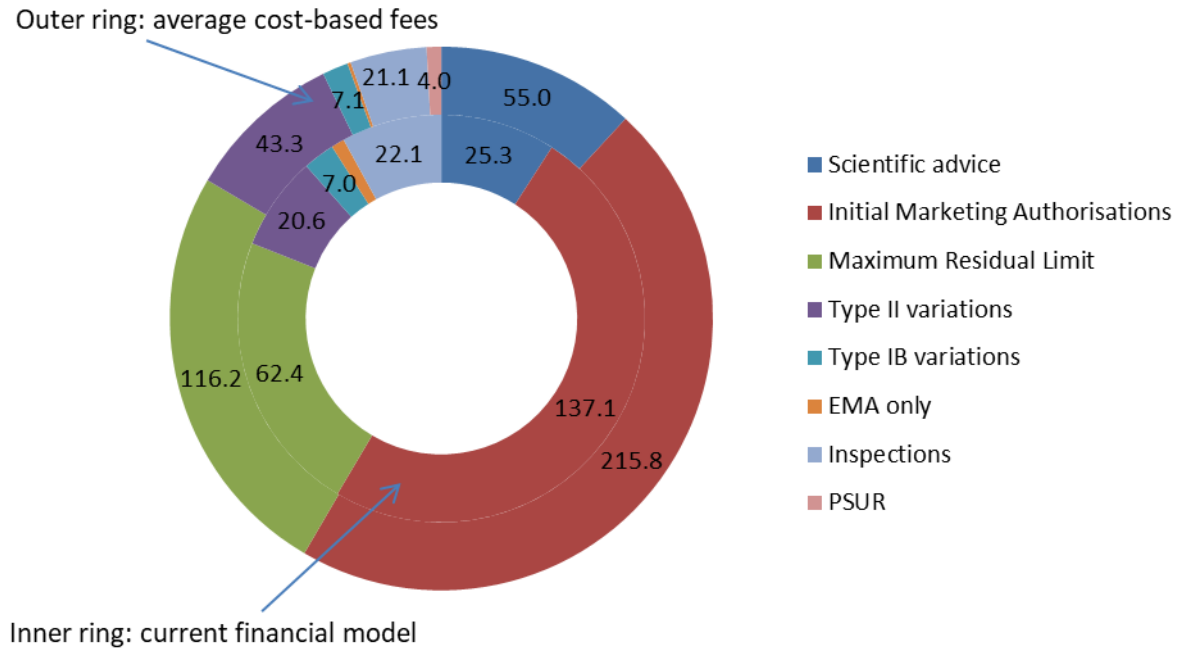
[31] Under the current financial model, unitary full fees are determined by legislation (see section 1.1.2). For this study, the values used are averages based on full fee revenue provided by EMA.

[32] These numbers have been rounded to the nearest €5,000. They are also based on data provided by EMA that takes into account variable fee components that depend on pharmaceutical strength and form.

[33] These are limited to the agreed list of activities included in Question 17 of the NCA survey.

The same fee comparison is presented in Figure 8 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.[34]

Figure 8: Comparison of unitary full fees for veterinary medicine procedural activities for current financial model and when modelling average cost-based fees (€ thousand/procedure)



While activities undertaken by EMA only, for both human and veterinary medicines, have low fees per activity relative to other activity categories, they are high volume activities and therefore make an important contribution to fee income (Figure 5 and Figure 6). These fees would be lower under average cost based fees: €300/procedure under average cost pricing compared with €1,640/procedure under the current financial model, for human medicines and €790/procedure under average cost pricing compared with €2,570/procedure under the current financial model, for veterinary medicines.

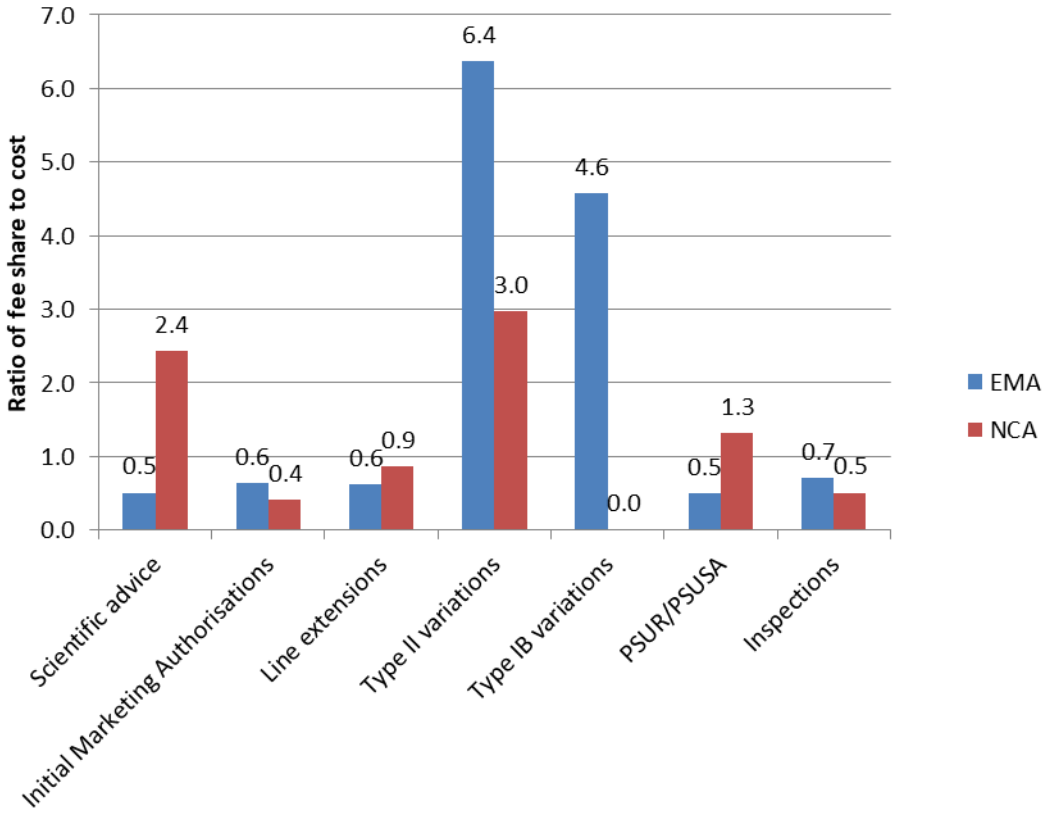
For other activities (inspections and type IB variations for veterinary medicines), the fees remain approximately the same under the current fee systems and when they are modelled based on average costs. This indicates that the fees are aligned with the overall costs to EMA and NCAs of undertaking the respective activities.

However, under the current financial model fees are not always shared between EMA and NCAs in proportion to their respective share of the total costs of the corresponding activities for both human and veterinary medicines. For non-pharmacovigilance

[34] For NCAs, PSURs were reported in Q18 of the NCA survey. Data on PSURs relating to veterinary medicines for EMA were not reported separately and are counted in the costs of additional activities. The average cost based fee component included here for EMA has been calculated using the number of procedures reported by NCAs. It is not included in the model calculations.

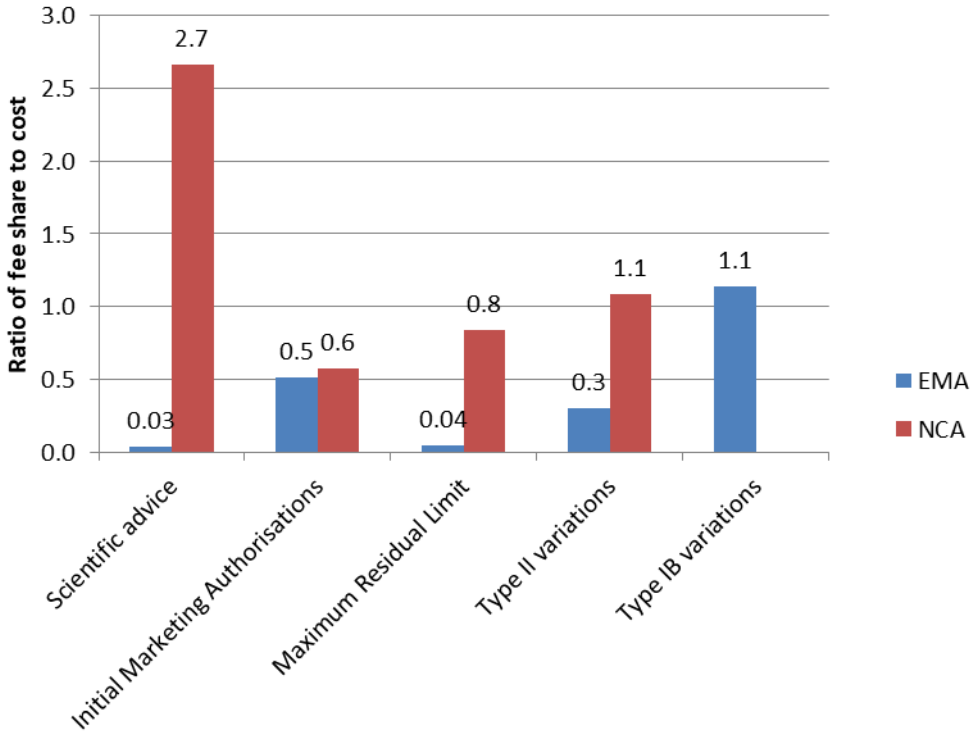
procedural activities for which EMA and NCAs receive a share of fee income, the allocation of fees between EMA and NCAs under the existing fee system is based on a 50/50 fixed percentage split of the total fees. However, the NCA share is based on the full fee income before any incentives are applied. EMA remunerates the NCAs this amount and retains the remainder of the total fees charged after incentives are applied. The 50 per cent NCA share is split equally between rapporteur/lead and co-rapporteur/support roles. The exceptions are pharmacovigilance activities for human medicinal products – PASS, PSUR, PSUSA and referrals – for which NCAs are remunerated a fixed amount, which is scaled according to the incentives applied (for veterinary medicines, no fee is charged by EMA and NCAs are not remunerated). The ratios of fee share to cost for EMA and remuneration to cost for NCAs in total for the main set of activities are shown in Figure 9 and Figure 10. Under the current financial system, the fee share for EMA is net of incentives, whereas, with the exception of pharmacovigilance activities for human medicines, the NCA remuneration is based on full fees before incentives are applied. Thus, for example, for provision of scientific advice on human medicines, EMA currently receives 50 per cent of its costs, whereas NCAs are remunerated more than double the costs they incur in contributing to providing scientific advice.[35]

Figure 9: Ratio of fee share to cost for EMA and NCA remuneration to cost over one synthetic year for human medicine procedural activities – current financial model



[35] The incentive rate for scientific advice partly reflects the proportion of procedures undertaken for paediatric products that are not an ATMP or orphan product and for which there are no fees under the current financial system.

Figure 10: Ratio of fee share to cost for EMA and NCA remuneration to cost over one synthetic year for veterinary medicine procedural activities – current financial model



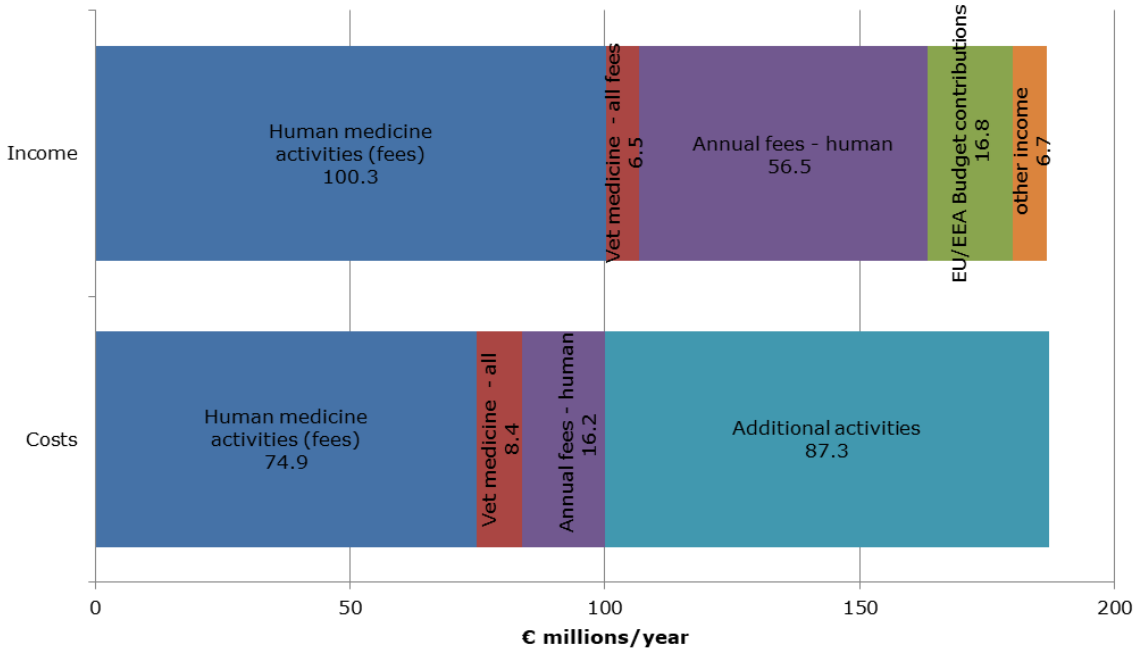
Under the current financial system, the fee share for EMA is net of incentives, whereas, with the exception of pharmacovigilance activities for human medicines, NCA remuneration is based on full fees before incentives are applied. If the fee share for EMA and NCAs was equal to their respective share of the costs, for a given activity, the ratio of fee share to cost share would be one. Figure 9 and Figure 10 show that the ratio of fees to costs is different for EMA and NCAs for most activities. This means that, for procedural activities such as PSUR/PSUSAs, where overall fees are approximately equal to total EMA and NCA costs, these fees are nevertheless not shared between EMA and NCAs in proportion to their respective shares of those costs. Fee shares are approximately proportionate to costs for initial marketing authorisations for both human and veterinary medicines (0.6 for EMA and 0.5 for NCAs) but these fee shares only reflect roughly half the actual costs. This again indicates that the fees for initial marketing authorisations are much lower than the corresponding costs.

B. Modelling the principle of average cost-based fees, whereby NCA activities that are not currently remunerated are covered at cost, and there are no incentives applied, implies that, by definition, the EMA and NCAs (in respect of their EMA-related work) would break even. However, unremunerated activities and incentives and exemptions create a shortfall in revenue. This study further explored approaches that could address this shortfall.

The total fees retained by EMA after NCA remuneration under the current financial model are not sufficient to cover its costs without EU and EEA budget contributions. EMA incurs costs both for procedural activities and for the additional activities that it undertakes. After remunerating NCAs, EMA retains a share of the total

fees from industry for the procedural activities and the estimates from the modelling exercise show that these fees are not sufficient for EMA to cover the costs of its procedural activities, considering human and veterinary medicines together (Table 3). Industry is also charged two types of annual fees under the current financial model in addition to the fees for procedural activities presented in Table 3: CAP annual fees for human and veterinary medicines and annual pharmacovigilance fees for nationally authorised human medicines only. EMA retains 70 per cent of the CAP annual fee income and pays 30 per cent to eligible NCAs.[36] EMA retains all of the pharmacovigilance annual fee income in compliance with Regulation (EU) No 658/2014. There are costs to EMA associated with the administration of these annual fees (€16.2 million)[37] and both types are subject to incentives, but, after taking this into account, there is still sufficient fee income that the annual fees can be used by EMA to cover the costs of some additional EMA-related activities (Figure 11).

Figure 11: EMA income (fee revenue and EU/EEA budget contributions) and costs over one synthetic year under the current financial model (€millions/year)



Note: EMA fee income is equal to total fee income net of incentives and NCA remuneration. The depiction used in this figure makes the EMA share of fee income clear. The EMA budget could be presented with total fee income net of incentives in the income bar and NCA remuneration as a cost. The EMA share of fee income would not be immediately apparent in that case. * Appendix 10 contains the list of additional activities undertaken by EMA.

EMA income (fee revenue, 'other income' and EU/EEA budget contributions) and costs for one year are shown in Figure 11. Fees for procedural activities exceed the costs associated with procedural activities for human and veterinary medicines for EMA; the fees for human medicines partially finance the veterinary activities. Annual fees more than cover the costs to EMA of administering them and are used in part to finance

[36] This is linked to initial marketing authorisations. The allocation of these fees in the modelling exercise relied on purchase order data provided by EMA.

[37] Data provided by EMA is available in spreadsheet form as an electronic supplement

additional activities undertaken by EMA (Appendix 10). The EMA fee share from industry (for human and veterinary, procedure related fees and annual fees) is not, however, sufficient to fully finance the additional activities that EMA undertakes. The EU/EEA budget contributions are the balancing terms that are required to enable EMA to break even.

EU and EEA budget contributions are used to balance EMA costs and revenues so that EMA can carry out tasks related to procedural activities and additional activities, including additional activities that directly contribute to procedures. In the modelling exercise, the EU and EEA budget contributions are fixed at the 2016 level of €16.8 million. [38] An additional term, denoted 'other income' of €6.7 million per year, was calculated to balance the EMA budget.[39] The combined total of EU and EEA budget contributions and 'other income' of €23.5 million is still well below the €40 million officially allowed for under the Commission programming of human and financial resources for the EMA provided for in Commission Communication COM(2013) 519.

Costs of procedural activities depend on the number and type of procedures undertaken in a given year. EMA fee income depends on the number and type of procedures, the number of products currently registered, and the average incentives and reductions applied. Incentives and exemptions reduced EMA fee revenue by over €20 million in the synthetic baseline year.[40]

As was shown in section 2.1A, fees and costs for procedural activities are not aligned at the activity level. Fees for initial marketing authorisations, for example, are not sufficient to cover costs (Figure 5). This means that if the volume of initial marketing authorisation procedures were to increase, then the EMA budget would not balance without a reduction in the additional activities undertaken or an increase in EU and EEA budget contributions or fee revenue from other procedural activities. By contrast, for type II variations, the fees exceed the costs of those procedures, so if the volume of type II variations were to increase, then the EU/EEA budget contribution or fee income from other procedural activities needed for the EMA to break even would be reduced.

Any differences in the average incentive rates applied because of the types of applicants or types of products involved would have a further impact on EMA fee income, potentially resulting in less income for EMA where the average incentives applied are higher. Hence, changes to these parameters in a given year could affect the ability of EMA to carry out additional, non-procedural activities, or would require changes in the EU/EEA budget contribution.

Incentives and exemptions would also have an impact on EMA fee income under the principle of average cost pricing. If unitary fees before incentives are assumed to equal average costs, then the costs of procedural activities would be recovered for EMA only if full fees were applied without incentives. When incentives are applied, these costs are no longer completely covered and would need to be paid for in some other way, such as by an increased EU/EEA budget contribution.

[38] The actual EU and EEA budget contributions in 2016 of €16.8 million consisted of €2 million general subsidy, €12.8 million ring-fenced orphan designation subsidy and €2 million outturn from previous years.

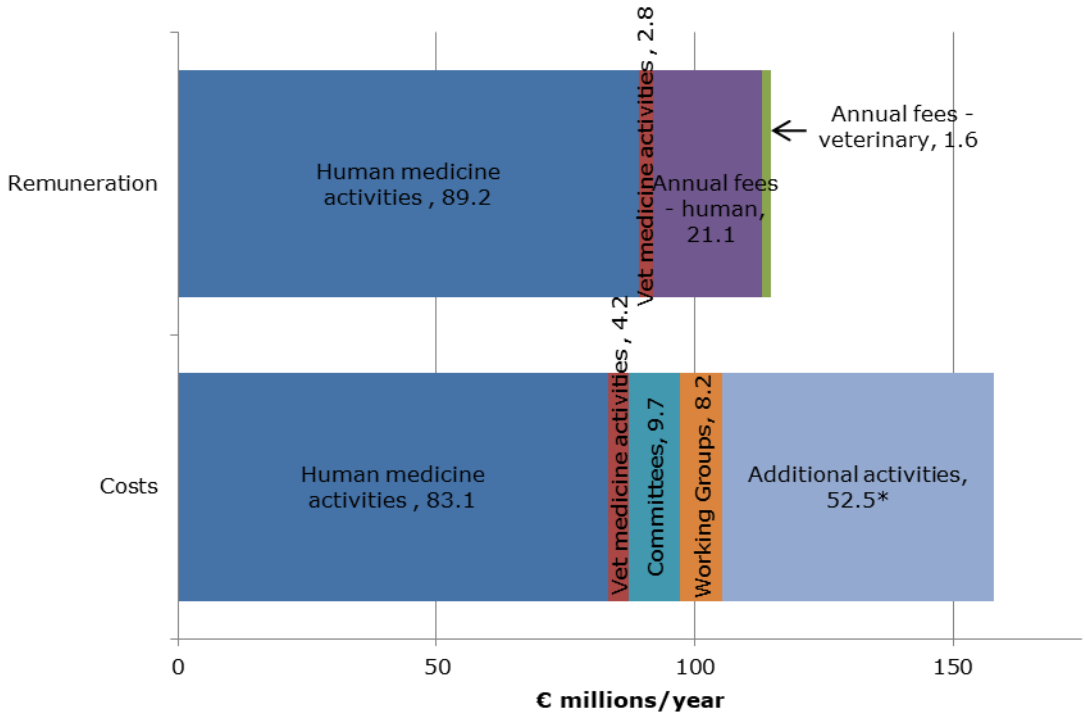
[39] This term corresponds to income from administrative operations, such as sale of publications and organisation of seminars.

[40] Fees are currently waived for the paediatrics, orphan designation and MUMS activities listed in Question 17 and Question 18 of the NCA survey and included in the modelling exercise. Paediatrics, orphan designation and MUMS activities together account for an additional €10 million/year of costs. Fee incentives for other procedural activities and annual fees reduce EMA income by roughly €30 million/year under both the current financial model and when modelling average cost pricing. For scientific advice, these incentives also reflect the proportion of procedures undertaken for paediatric products that are not ATMPs or orphan products and for which there are no fees or NCA remuneration under the current system.

Under the current fee system, payments to NCAs for procedural activities and annual fees finance NCA costs for working groups, committees and some additional activities for both human and veterinary medicines. For NCAs in total, combined remuneration received under the current financial model for procedural activities for human and veterinary medicines is more than sufficient to cover the total costs of these procedural activities (Table 3). Eligible NCAs additionally receive 30 per cent of the full CAP annual fee income (i.e. before incentives are applied),[41] which can be used to partially finance other EMA-related activities (Table 16) undertaken by NCAs (Figure 12).

NCAs participate in EMA committee meetings and working groups in addition to specific EMA-requested, procedural activities. In the survey undertaken by the study team, NCAs also reported additional EMA-related activities, beyond attending committee meetings and working groups (Appendix 3, Table 16).

Figure 12: Total NCA remuneration and costs over one synthetic year under the current financial model (€millions/year)



* Appendix 10 contains a categorisation of additional activities reported by NCAs.

The overall costs and remuneration for EMA-related activities for NCAs in total are shown in Figure 12. The remuneration received for procedural activities and related annual fees funds the costs of committees and working groups and partially funds additional activities. However, (in our synthetic baseline) there remains a shortfall of around €43 million per year across all NCAs taken together, so that not all the costs of the additional EMA-related activities NCAs report are covered.

Some of these additional activities are procedural activities that were not included in the modelling exercise or were not reported in Question 17 and Question 18 of the NCA

[41] Eligibility is linked to reimbursed roles undertaken for initial marketing authorisations by NCAs. The NCA share is allocated equally between rapporteurs and co-rapporteurs.

survey but which NCAs are legally obliged to undertake. There may also be activities that should have been included in Question 17 and Question 18 but were not reported there by NCAs (and were instead reported as additional activities). A list of additional activities reported by NCAs in Question 20 of the NCA survey is provided in Appendix 10.[42]

A comparison of individual NCAs to the 'average' NCA also provides an indication of how well remuneration enables NCAs to cover their costs of EMA-related activities.[43] First, considering remuneration for procedural activities only, excluding annual fees, on average, the remuneration an NCA receives under the current financial model covers the costs of undertaking procedural activities, including those that are not currently remunerated. However, at individual NCA level, 10 of 29 NCAs that provided cost information for this study do not cover their costs for procedural activities with the remuneration they receive. When remuneration from annual fees is also included, only 5 NCAs do not cover procedural activity costs.

Human and veterinary medicines are considered separately at the activity level and there are 24 NCAs that undertake human medicine activities and 18 that undertake veterinary medicine activities. For only 5 of the 24 NCAs that undertake human medicine activities, procedural remuneration is not sufficient to cover the corresponding procedural costs of these activities. For 12 of the 18 NCAs that undertake veterinary medicine activities, procedural remuneration is not sufficient to cover the corresponding procedural costs of these activities.

NCAs can be further divided into three types: NCAs that undertake human medicine activities only (11 survey respondents), NCAs that undertake both human and veterinary medicine activities (13 survey respondents) and NCAs that undertake veterinary medicine activities only (5 survey respondents). Fees from human medicine activities are able to partially cover the costs of veterinary medicine activities for some NCAs that undertake both types of activities. The modelling shows that annual fees and procedural remuneration are sufficient to cover costs for almost all NCAs that undertake both human and veterinary medicine procedures. NCAs that undertake activities for veterinary medicines only are unable to partly finance veterinary procedures from remuneration for procedural activities for human medicines. Two of the five veterinary NCAs are unable to cover their procedural activity costs when annual fees are included. Two of the 11 NCAs that undertake human medicine activities only are also unable to cover their costs. When committees and working groups as well as other EMA-related activities are taken into account, the model calculations show that the 'average' NCA runs a deficit of -€1.5 million and none of the NCAs in the survey that undertake veterinary medicine activities only cover their committee and working group costs. At individual NCA level, all EMA-related costs are covered for 5 out of 29 NCAs but not for the other 24. These five NCAs cover both human and veterinary medicines.

Figure 13 compares costs and remuneration for individual NCAs. The horizontal axis shows how much remuneration an NCA receives for procedural activities compared to the costs of these. This includes remuneration from annual fees, the purpose of which is to provide additional income to NCAs undertaking initial marketing authorisations. The vertical axis shows the costs of non-procedural activities (working groups and committees and additional EMA-related activities). The figure shows a wide variation in both the fees and costs for procedural activities, and the additional costs across NCAs.

[42] The list of additional activities reported by NCAs in Question 20 of the NCA survey is also provided in the Methodology note.

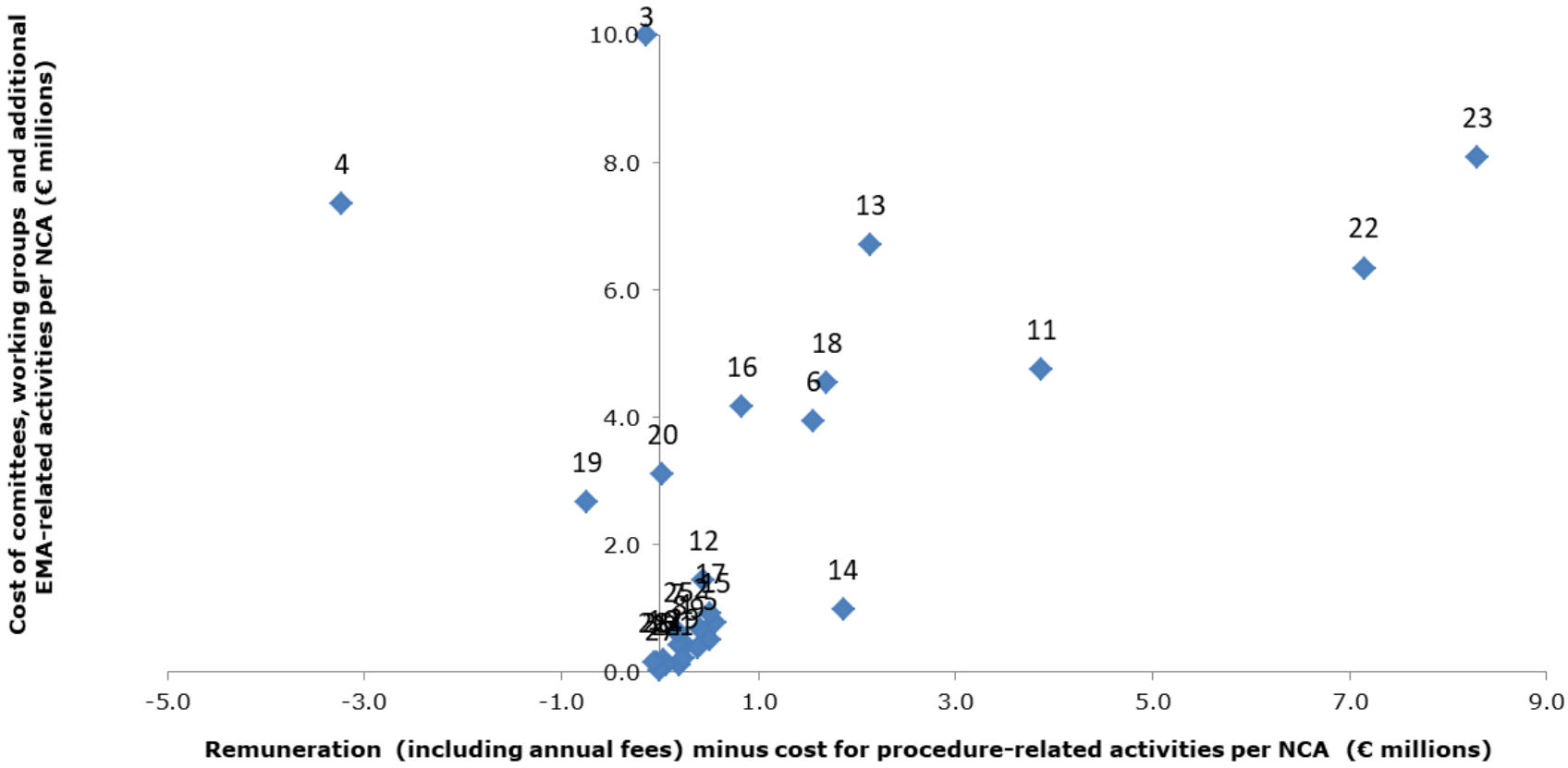
[43] The 'average' NCA is a weighted average over all procedural activities and all NCAs. For each procedural-activity, a separate weighted average is calculated.

Individual NCAs undertake different numbers of procedures for different activities and the remuneration for these activities differs from the costs involved. Hence, an NCA with high costs for procedural activities does not always have a high level of remuneration These NCAs may also have high costs for non-procedural activities (committees, working groups and additional activities); these NCAs are shown close to the vertical axis in Figure 13. For some NCAs, costs exceed remuneration. The NCAs that receive the highest level of remuneration for procedural activities also have high additional costs (top right of Figure 13). In some cases, the unremunerated work can be funded by fee-related remuneration from EMA, 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.

A caveat is that some additional costs may include procedural activities that were not included in the NCA survey or were not reported as such. Additionally, some NCAs stated that they have high costs of additional, unremunerated activities, and others less so. It is difficult to assess the impact of this on the individual NCAs. Additional costs would be reduced but remuneration would not necessarily increase if these costs were associated with unremunerated roles. Further, it is important to note the relationship between procedural and additional activity costs in the model. The additional activity costs are calculated as the difference between the reported NCA costs including overheads and the calculated procedural, committee and working group costs. Under or overestimation of procedural costs would result in the over or underestimation of additional activity costs. For an individual NCA, this could arise because they spend more (or less) time than the NCA average that is used in the model to complete a procedure for a given activity. For example, an NCA could undertake more complex procedures.[44] Although the effect of this is expected to be small at the aggregate level, it may have an impact on the results for individual NCAs. The procedural costs would also be underestimated (and the additional activity costs overestimated) if the average cost per hour of scientific staff working on EMA-related activities is greater than the organisational average for scientific staff used in the model.

[44] For example, the NCA average for type II variations (level I) includes clinical, clinical indicator and safety procedures that, on average, take different times to complete. This level of detail cannot be distinguished in the modelling.

Figure 13: Comparison of remuneration and costs for procedural activities with costs of unremunerated additional activities for individual NCAs in the synthetic baseline year



Note: NCAs are numbered in the figure only to provide a reference to Figure 13; the numbers do not have any other significance in the analysis.

In the synthetic baseline, in order to compare fees with cost, it was assumed that the 29 respondent NCAs undertook all the invoiced procedures. This is equivalent to the additional procedures for an activity being undertaken at (weighted) average cost. However, this will overestimate the costs and remuneration for individual NCAs compared to their actual reported values.

The costs and remuneration for NCAs determined in the modelling exercise are based on a fixed number of procedures for each activity type and for each NCA. As was shown in section 2.1A, remuneration and costs across all NCAs for procedural activities are not aligned at the activity level. As different NCAs undertake different procedural activities, changes in the volume of procedures for some activities could affect some NCAs more than others. Remuneration for initial marketing authorisations, for example, is not sufficient to cover costs (Figure 5). If the volume of initial marketing authorisation procedures were to increase, those NCAs undertaking most of these procedures would see costs increase more than remuneration reducing their ability to cover procedural activity costs. The opposite would be seen for NCAs undertaking procedures for type II variations, if the volume of these were to increase, as remuneration exceeds costs in this case. The procedural activity costs for NCAs are based on a fixed NCA average time taken for each activity type. More complex procedures would take longer to process, raising the average time taken and, consequently, the procedural costs.

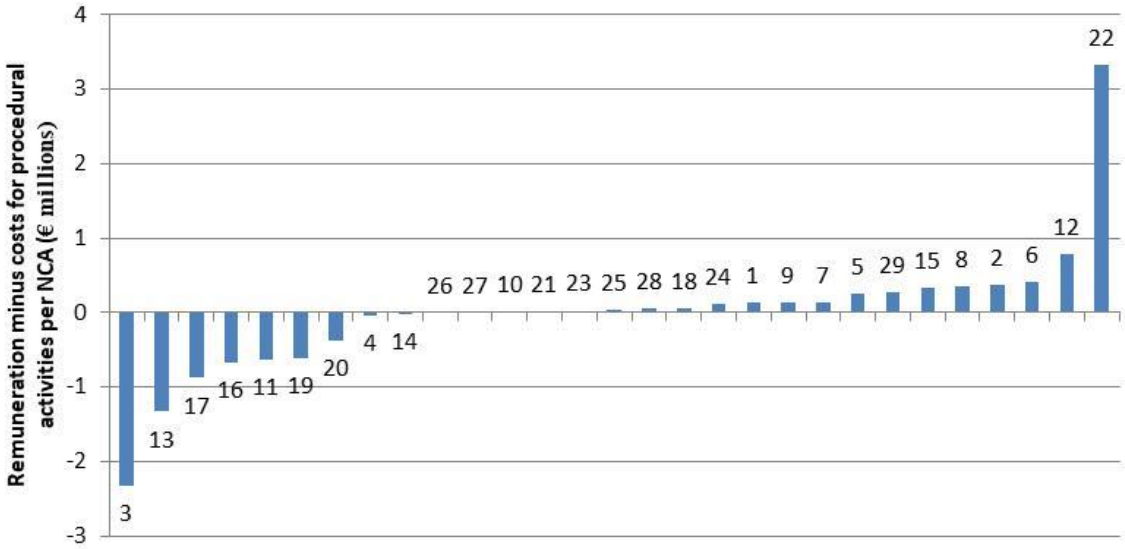
NCAs that undertake procedures for pharmacovigilance activities are also affected by incentives. These are fixed in the model. Future changes in incentives would also change NCA remuneration under the current fee system.

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. Modelling average-cost based fees for procedural activities and remuneration for NCAs at average cost implies that, for NCAs in total, remuneration would by definition be equal to total costs. This holds because, for NCAs, the average cost is effectively a weighted average, which is calculated as the total cost over all procedures for a given activity divided by the number of procedures. Total costs include the cost of all procedural roles and the allocation of remuneration across NCAs depends on the roles they undertook and the average cost of those roles. But any individual NCA might be left with a financial surplus or deficit depending on whether their individual costs are below or above the average cost across all NCAs. For 19 of 29 individual NCAs from whom the study team received cost data, modelling average cost-based remuneration covers costs for procedural activities. This is illustrated in Figure 14. Each bar on the horizontal axis represents the cost recovery for one NCA. Negative values on the vertical axis indicate costs are not recovered, and positive values indicate that they are recovered.

The 10 NCAs for which modelling average cost-based remuneration does not cover costs have the highest costs per hour for scientific staff, are amongst the NCAs with the highest costs per hour for administrative staff and some of the highest procedural activity costs.[45] For those NCAs with lower than average procedural activity costs, modelling average cost-based remuneration enables some funding of non-procedural activities (committees, working groups and additional activities). Such possibility of funding would generally be much less than under the current financial model because fees would be much more closely aligned with costs at the procedural activity level when modelling average cost-based remuneration. However, this does depend on how the cost of individual NCAs compare to the weighted average. The modelling exercise indicates that 11 of the 21 NCAs would also cover costs of time spent in committees and working groups and two NCAs cover all their costs when modelling average-cost based remuneration alone.

[45] The results presented in the report are based on average time taken (across all NCAs in total) for each activity from the MBDG exercise, so that in our model NCAs differ in costs based on hourly costs only and not on the number of hours taken per procedure. Greater variations in costs per activity between NCAs are introduced when times per procedure specific to each NCA from the MBDG exercise are used.

Figure 14: Distribution of remuneration for procedural activities minus costs for individual NCAs when modelling average cost based remuneration

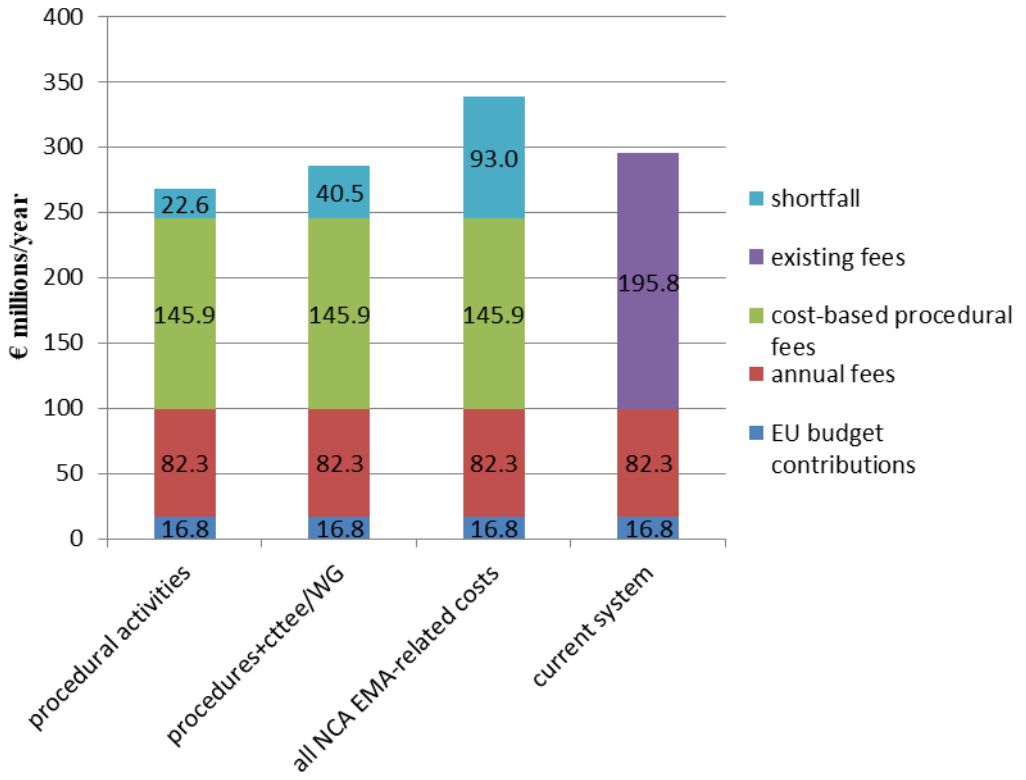


Note: NCAs are numbered in the figure only to provide a reference to Figure 13; the numbers do not have any other significance in the analysis

When modelling average cost-based fees with incentives for procedures and average cost-based remuneration for NCAs, EMA income needs to be increased to balance its costs. The mechanism used to achieve this would have an impact on EU and EEA budget contributions and/or industry fees. Modelling fees and NCA remuneration based on average costs also has implications for EMA, the EU and EEA budget contributions and industry. In the model, full unitary fees for procedural activities are equal to the average cost to EMA plus the weighted average cost to NCAs of undertaking a procedure for that activity. EMA and NCA committee time that is allocated to procedural activities is already included in these costs.[46] Incentives are then applied to these fees. NCA remuneration depends on average costs only and would therefore not be affected by fee incentives. However, EMA fee income in the modelling exercise is calculated as the remainder from the total actual fee income once NCA remuneration has been paid. For activities where incentives are applied to full fees, EMA receives less than its average cost, leading to a shortfall in its budget, for which a funding mechanism would be needed if current spending on additional activities was maintained and 'other income' remains fixed. This shortfall is illustrated in Figure 15.

[46] This is understood as NCA committee time in a procedural role and all EMA committee time. See methodology note for more details.

Figure 15: The shortfall in EMA funding with average cost based fees for procedural activities with incentives when NCA costs are partially or fully remunerated



Note: 'Other income' has been omitted from this figure as it is assumed fixed at €6.7 million per year in all scenarios. It has been taken account of in the shortfall calculation.

Average cost-based fees and remuneration only apply to procedural activities, excluding annual fees. NCAs also report costs for committee and working group time and additional activities. Under the current fee system, these activities are partially funded by remuneration from procedural activities and annual fees for a number of NCAs. The modelling exercise under an average cost-based fee system shows that funding some or all of these activities would have a further impact on the EMA budget; as more costs are remunerated, a larger shortfall in EMA funding has to be addressed (Figure 15).

Scenarios were developed to illustrate the possible impacts on EMA, the EU and EEA budget contributions, and industry of average cost-based fees and remuneration when different levels of NCA remuneration are covered by different funding mechanisms. These are compared to the existing fee system. The NCA remuneration rules and the funding mechanisms (fee rules) examined in the scenarios are for illustrative purposes only as a benchmarking exercise for cost-based fees and remuneration.

First, the impact on the EMA share of fee income was considered for remunerating NCAs for their costs: for procedural activities only, based on average costs (scenario A); for procedural activities (average costs) and committees and working groups (costs based on time data from the MBDG exercise) (scenario B): and for all costs (i.e. costs of

procedural activities, working groups and committees and additional, EMA-related activities) (scenario C).[47]

Second, the impact on industry and EU and EEA budget contributions of different fee mechanisms for balancing EMA costs and revenues was considered if the EMA budget shortfall is addressed through: an additional EU and EEA budget contribution (scenario 1), an increase in the CAP annual fee[48] (scenario 2), or a general pro-rata increase in all fees for procedural activities (scenario 3). These scenarios are presented in Table 4 with the possible fee mechanisms listed in the far left column and the remuneration rules across the top row.

The main assumptions for the scenario analysis are:

- NCAs are remunerated at average cost for all procedural activities for which costs are available in the model. This includes pharmacovigilance activities. NCAs are also remunerated in the scenarios for activities where there are full fee waivers or exemptions under the current fee system and NCAs are not remunerated. The remuneration does not otherwise depend on the fee rule or funding mechanism and is not subject to incentives.
- For scenarios B and C where NCAs are additionally remunerated for committees and working groups, and additional EMA-related activities, respectively, this remuneration is not average-cost based. NCAs are each remunerated separately for these costs.
- Average cost-based full fees minus incentives are charged to industry. These fees are increased in scenario 3 where the funding mechanism is a general pro-rata increase across all procedural activities. Fees are also charged for activities subject to full waivers or exemptions under the current fee system. EMA retains the residual fee income once NCAs have been remunerated.
- Annual fee income is calculated as under the existing fee system except for scenario 2, where an increase in the CAP annual fee is the funding mechanism. For all scenarios, annual fee income (CAP and PhV) is retained by EMA and no share is ring-fenced for NCAs. NCAs do not directly incur costs for annual fees, although under the current fee system these are used to provide additional remuneration for initial marketing authorisations, as specified in the eligibility criteria. This additional remuneration is intended to cover activities related to marketing authorisations such as annual product reports and safety reports that are undertaken by NCAs at the request of EMA as part of their EU obligations. Under average cost-based remuneration, NCAs are remunerated at average cost for activities and no additional remuneration should be needed. However, costs for additional activities specifically related to marketing authorisations could not be estimated as part of the modelling exercise and the costs of these activities

[47] For working groups and committee costs, these are based on times reported in the MBDG exercise. The costs of additional, EMA-related activities are determined as the difference between the total reported EMA-related costs and the calculated procedure-based and working group and committee costs. In the scenarios, both these cost types are assumed to be remunerated for each NCA separately and not as an average over all NCAs. It is noted that insufficient data were available to identify the costs of individual, additional EMA-related activities, so an aggregate value based on reported costs was calculated for each NCA. More details of the approach and, the potential issues of misallocation of costs from procedural-activities to additional EMA-related activities are provided in the methodology note that accompanies this report.

[48] Income from PhV annual fees is fully retained by EMA under the current fee system for PhV related activities and this remains the case in the scenarios analysed here. The fees would need to be assessed separately.

are classified as part of the general category of additional EMA-related activities. In the scenarios, the remuneration of these additional activities is independent of the fee mechanism. Further, in the scenarios, the annual fee is used as a mechanism to increase the fee for a subset of industry (in contrast to the general pro-rata increase) as the annual fee only applies to organisations that have applied for marketing authorisations.

- EU and EEA budget contributions remain fixed at synthetic baseline values unless they are used as the funding mechanism (scenario 1).
- Numbers of procedures and incentive rates for procedural activities and all EMA and NCA activity costs are the same in the scenarios as in the synthetic baseline.

Table 4: Cost-based benchmark scenarios of different fee and remuneration mechanisms

NCA Remuneration / Funding mechanism[a]	Average cost-based remuneration for procedural activities only	Average cost-based remuneration for procedural activities and costs of committees and working groups	All NCA costs reimbursed (procedural, working groups and committees, and additional activities)
Remainder in EU and EEA budget (existing CAP and PhV annual fee)[b]	A1	A2	A3
Remainder in CAP annual fee (existing EU and EEA budget)	B1	B2	B3
Remainder spread proportionally across fees for procedural activities (existing EU and EEA budget contribution, existing CAP and PhV annual fee)	C1	C2	C3

[a] Average-cost based fees applied for procedural activities under all fee mechanisms.
[b] Existing CAP annual fee means that the existing full fee with incentives is charged to industry but EMA retains 100 per cent of the fee.

Fee shares and costs for one year were calculated for each of the nine combinations of fee rules (rows) and NCA remuneration rules (columns). In each case, full fees and NCA remuneration for procedural activities are based on average costs. For the working groups and committees and the additional EMA-related activities, average costs are not used and the scenarios assumed that each individual NCA will be directly remunerated for the actual costs incurred.[49] A detailed breakdown of the fees for all the scenarios is provided in the fee grids, which are provided separately with this report. The impact of average cost based remuneration on the total NCA budget is shown in Figure 16. The procedural activities are remunerated at average cost in all scenarios and hence cover

[49] Actual time spent on working groups and committees was available from the MBDG exercise. The contribution varies across NCAs as NCAs are involved in different working groups and reported different amounts of time in any given committee or working group, which also meet at different frequencies. It is not possible to construct a weighted average as there is no common unit of activity such as a procedure. Hence an average time for all NCAs was not considered appropriate. Insufficient data were available to identify the costs of individual, additional EMA-related activities, so an aggregate value based on reported costs was calculated for each NCA. More details are provided in the methodology note that accompanies this report.

the total cost to NCAs (although not necessarily the cost to individual NCAs as shown in Figure 13 and Figure 14). Other costs are only remunerated for the scenarios indicated. For scenarios 1 and 2, all NCA costs are therefore not covered by remuneration.

Figure 16: Impact of average-cost based fee and NCA remuneration benchmark scenarios on the overall NCA budget (€ millions/year)

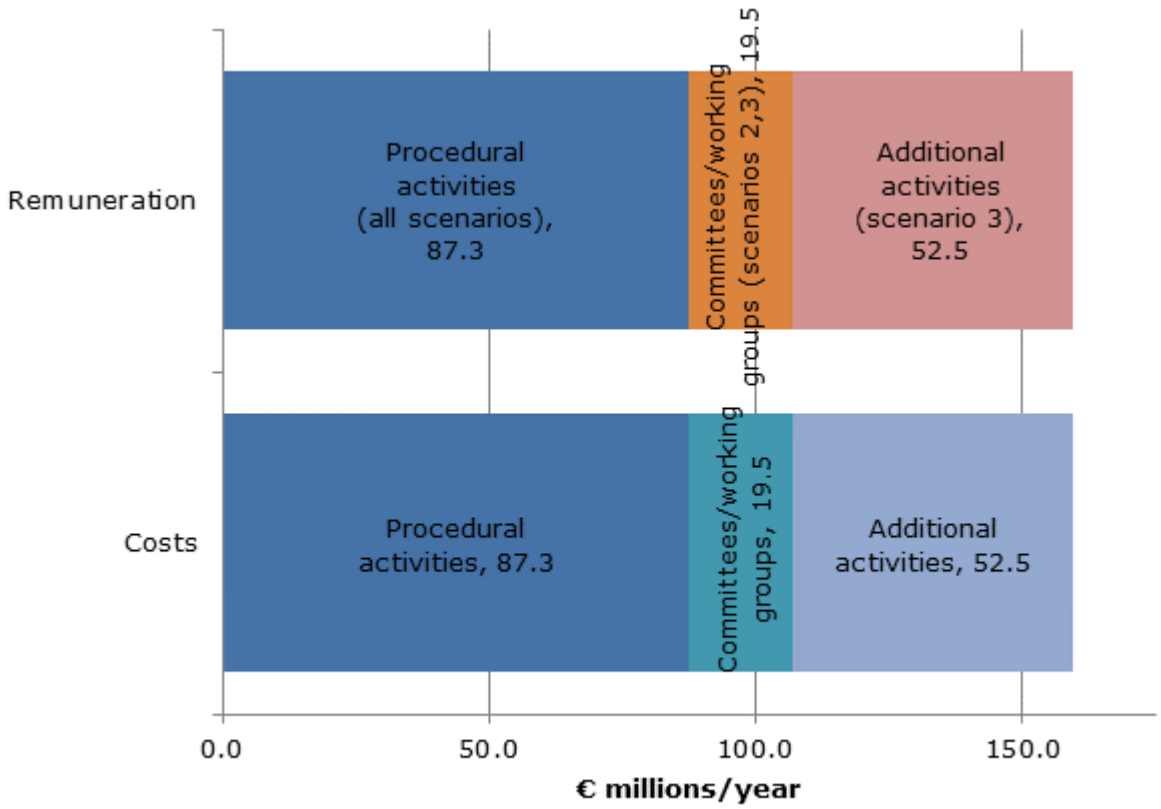


Table 5 shows the impact on the EMA budget when modelling average cost-based fees and NCA remuneration for procedural activities only. The shortfall (last row) is the amount that would be needed to balance the EMA budget under this fee system. This could be funded via an additional EU and EEA general budget contribution (scenario A1).

Table 5: Impact on EMA budget when modelling average cost based fees and remuneration under scenario A1 (€ million/year)

		Current financial model	Benchmark average cost-based fees and NCA remuneration for procedural activities only
Industry fees	**Total**	**278**	**228.1**
	Procedural activities	195.8	145.9
	Annual fees (CAP + PhV)	82.3	82.3
NCA remuneration	**Total**	**114.7**	**87.3**
	Procedural activities	92.1	87.3
	Annual fees (CAP)	22.6	0
EMA income	**Total**	**186.8**	**164.3**
	Procedural activities	103.7	58.5
	Annual fees (CAP + PhV)	59.6	82.3
	Existing EU/EEA contributions	16.8	16.8
	Other income	6.7	6.7
EMA costs		186.8	186.8
Budget shortfall		0	22.6

The total industry fees (€228.1 million/year) when modelling average cost-based fees for procedural activities only are less than under the current financial model (Table 5, column 3), as these now reflect average costs for procedural activities (totalling €145.9 million/year), augmented by current annual fees (€82.3 million/year). Average incentive rates have been applied to these industry fees at the activity level to determine the total. The impact on different industry sectors will depend on the average costs of the activities for which they incur fees and the incentives they receive. These sector effects are beyond the scope of this study.

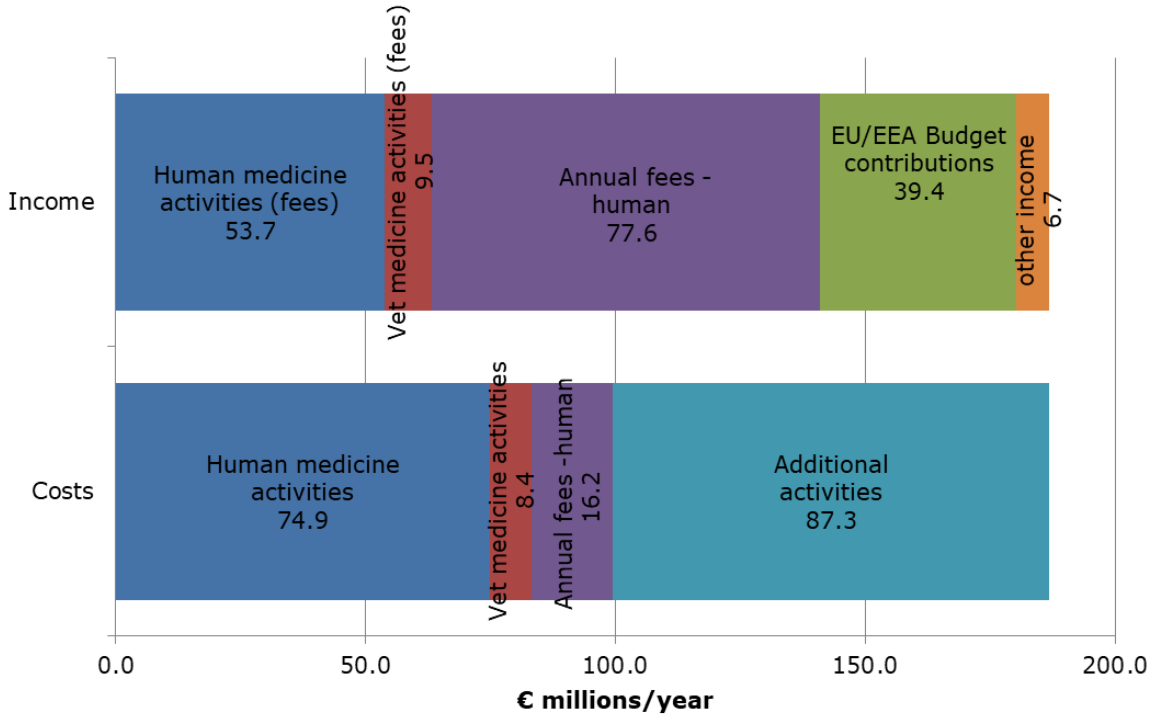
Although EMA retains all of the annual fees, its share of procedural fees (€58.5 million/year) is much lower in the modelling results (scenario A1) because full fees are linked to both average costs and incentives. The share of fee income retained by EMA is therefore also smaller at €140.8 million/year (including both procedural activities at €58.5 million/year and annual fees at €82.3 million/year) compared with €164.3 million/year (including procedural fees at €103.7 million/year and annual fees at €59.6 million/year). This fee income is not sufficient for the EMA budget to balance, given the existing EU and EEA budget contributions. The budget shortfall is €22.6 million/year.

The industry fees, NCA remuneration and EMA income under the average-cost based fee system also reflect the additional fees for work activities subject to fee waivers or exemptions under the current fee system and for which NCAs are currently not remunerated. The industry fees for the paediatric and orphan designation activities included in the modelling amount to €4.8 million/year and €3.1 million/year respectively. These fees cover relevant committee time for EMA staff for these activities and EMA meeting costs as these are included in the average cost calculations for EMA. They do not cover PDCO and COMP committee time for NCAs as these are included in the committee and working group costs for NCAs and not in the activity costs.

The scenarios tested using the EU and EEA budget contributions as a funding mechanism for this shortfall to balance EMA costs (scenario A1, where the current CAP annual fee is unchanged). The total EU and EEA budget contribution would then be €39.4 million/year

(an increase of €22.6 million/year over the existing contributions of €16.8 million/year). The impact of average cost based fees and remuneration on the EMA budget is also illustrated in Figure 17. In this case human and veterinary activities have been separated out. In comparison with the existing budget (Figure 11), costs are unchanged, income from procedural activities has gone down but income from annual fees has increased and the EU and EEA budget contribution have also increased to rebalance the EMA budget.

Figure 17: Impact of average cost-based fee and NCA remuneration benchmark scenario A1 on the overall EMA budget (€ millions/year)



EMA income would also need to increase by €22.6 million/year to cover its costs when modelling average cost-based remuneration if a different fee mechanism were used: the study tested an increase in the CAP annual fee (scenario B1) or a proportionate increase in average cost pricing for all fees for procedural activities (scenario C1). For all of these scenarios, NCA remuneration and EMA costs remain constant, as does 'other income', as these are not affected by the funding mechanism used. The share of income from the EU and EEA budget contributions (scenario A1) and from industry (scenarios B1 and C1) under the different fee mechanisms is illustrated in Figure 18.

If the additional income was raised by an increase in the CAP annual fee (scenario B1) or a proportionate increase in average cost pricing for all procedural activities (scenario C1), the total fee burden to industry would be slightly less (€250.7 million/year) than under the current fee system (€278 million/year) but slightly more than if the income was raised from EU and EEA budget contributions (€228.1 million/year). However, the fees would be distributed differently across industry stakeholders. For scenario B1, the annual fee would increase by almost 30 per cent, from the total current level of €82.3 million/year to €104.8 million/year. For scenario C1, a mark-up of 15 per cent would be applied to the average-cost based fees, increasing these in total from €145.9 million/year (scenarios A1 and B1) to €168.4 million/year. The EU and EEA budget contributions remain at the existing level of €16.8 million/year when the fees to industry are used as the funding mechanisms to balance the EMA budget (scenarios B1 and C1). The costs to EMA in Figure 17 would remain unchanged under these scenarios but the

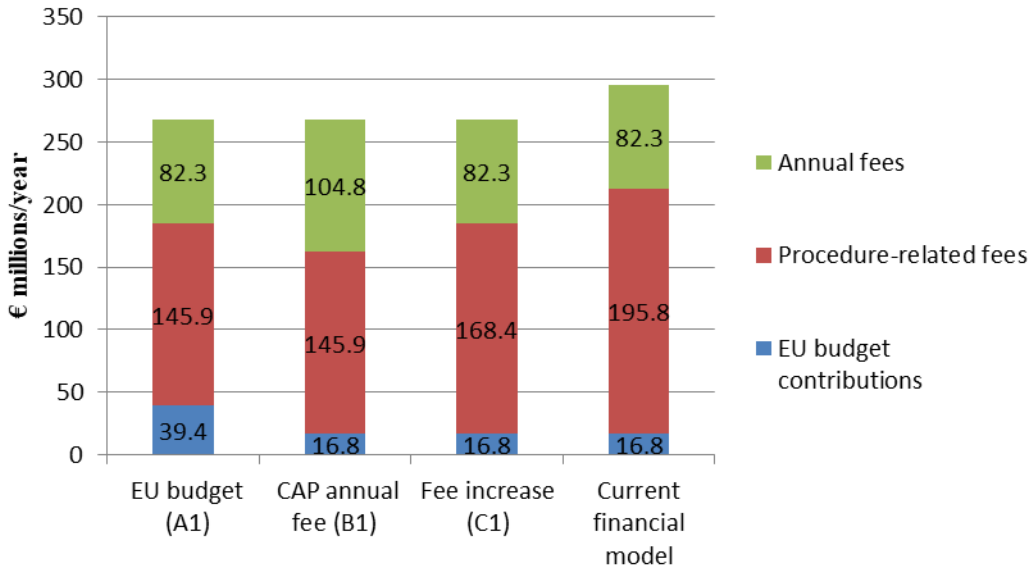
allocation of income between procedural and annual fees and EU and EEA budget contributions would change according to the funding mechanism used.

Table 6: Industry fee allocation for benchmark scenarios B and C

		Average cost-based remuneration for procedural activities only (scenario 1)	Average cost-based remuneration for procedural activities and costs of committees and working groups (scenario 2)	All NCA costs reimbursed (procedural, working groups and committees, and additional activities) (scenario 3)
Additional fee income required to balance EMA budget		22.6	40.5	93.0
Total fees from industry		**250.7**	**268.7**	**321.1**
Remainder in CAP annual fee (existing EU and EEA budget) (scenario B)	Procedural fees	145.9	145.9	145.9
	Annual fees	104.8	122.8	175.3
Remainder spread proportionally across fees (existing EU and EEA budget contribution, existing annual fee) (scenario C)	Procedural fees	168.4	186.4	238.9
	Annual fees	82.3	82.3	82.3

Note: The Pharmacovigilance annual fee is the same as under the existing fee system in all scenarios.

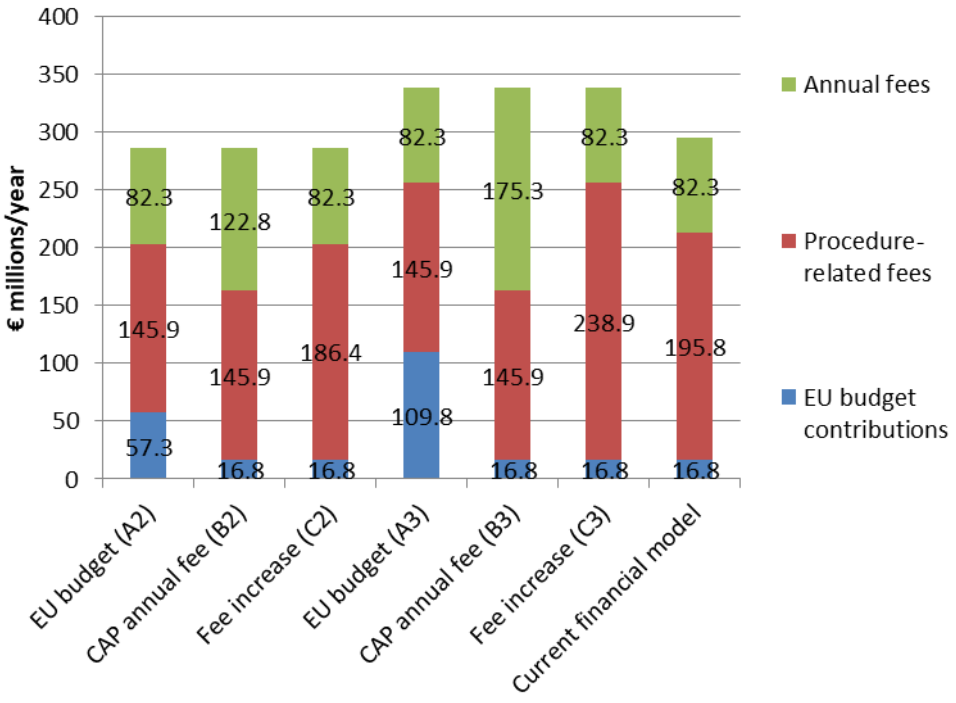
Figure 18: Relative contributions to total yearly EMA income for cost-based benchmark scenario 1 (€ millions/year)



Note: 'Other income' has been omitted from this figure as it is assumed fixed at €6.7 million per year in all scenarios.

If cost-based remuneration was also provided to NCAs for working groups and committees and additional, EMA-related activities, the EMA budget shortfall would increase and accordingly, the additional EU and EEA budget contribution or fee revenue required would also increase. The additional income needed to cover costs of working groups and committees, and additional activities (Figure 19) further increases the EU and EEA budget contributions required under scenario A by €40.5 million/year (scenario A2) and €93 million/year (scenario A3) on top of the existing contributions of €16.8 million/year. The same amount of additional income, €40.5 million/year and €93 million/year respectively, would also be needed in each case whether the mechanism was to increase the CAP annual fees (scenarios B2 and B3) or a proportionate increase in fees for procedural activities (scenarios C2 and C3). This is shown in Table 6 (row 2). However, the burden of the additional fee income would then fall on industry rather than on the EU/EEA and, potentially on different sectors of industry, depending on whether the fee mechanism was CAP annual fees or fees for procedural activities. This is shown in Table 6. It is important to note that the EMA share of fee income remains fixed at the level calculated for scenarios B1 and C1 (€163.3 million/year) for both types of industry fee mechanisms (although the €163.3 million/year is allocated differently across procedural and annual fees for the two fee mechanisms). The additional fees charged in scenarios B2 and C2 compared with scenarios B1 and C1 are used only to remunerate NCAs for the costs of committees and working groups. The additional fees charged in scenarios B3 and C3 are used only to remunerate NCAs for the costs of committees, working groups and additional activities. Although the remuneration may be administered by EMA, it is not considered as a cost to EMA in the modelling exercise under the existing fee system or in the scenarios. The impacts for both the EU and industry are presented in Figure 19.

Figure 19: Relative contributions to total yearly EMA income and NCA remuneration for cost based benchmark scenarios 2 and 3 (€ millions/synthetic year)



Note: 'Other income' has been omitted from this figure as it is assumed fixed at €6.7 million per year in all scenarios.

The modelling exercise calculated that if NCAs were also remunerated for their individual costs for working groups and committees and the additional remuneration was paid for by industry fees rather than from additional EU and EEA contributions, the amount of industry fees would increase to €268.7 million per year. Recompensing NCAs for all costs of EMA-related tasks would cost industry €321.1 million per year, an increase of 12 per cent over the current fee level (Table 6). Under the current financial model, NCAs partially co-finance EMA-related activities that are not covered by the remuneration they receive from fees for procedural activities and annual fees (Figure 12).

Figure 19 shows that the total EMA and NCA income under the current financial model is greater than scenarios remunerating working groups and committees (A2, B2, C2) and smaller than scenarios remunerating all EMA-related activities (A3, B3, C3). Thus the current industry fees of €278.1 million per year (Table 5) enable some funding of non-procedural activities undertaken by NCAs in total, although the allocation of fees across activities is not cost based (section 2.1A) and not all individual NCAs are able to fund costs they incur in addition to costs for procedural activities they undertake.

2.2. Alignment between current financial model and activities of EMA staff

This section presents answers to the study question relating to the extent to which the current financial model allows the EMA to effectively perform the activities in its remit. The question is addressed by looking at: if (A) the financial model enables EMA staff to

perform tasks related to procedural activities within its remit; and if (B) the financial model enables EMA staff to perform additional (i.e. cross-cutting, horizontal and related) supporting activities within its remit.

Overall, there is evidence that the current financial model enables the EMA to perform both procedural and additional activities. The budgetary principle of universality particularly contributes to the efficient financing and effective performance of EMA activities. More specifically, the findings relating to the ability of the current financial model to enable EMA activities to perform its activities are as follows:

- **F6.** The findings in section 2.1 show that the current financial model (including both fees from industry and EU and EEA budget contributions) allows EMA to undertake all of its procedural activities and provides for additional resources to undertake generic (cross-cutting and horizontal) tasks.
- **F7.** The EU budgetary principle of universality is considered to be an important factor that enables the EMA to effectively perform tasks within its remit.
- **F8.** There is no evidence that the EMA is hindered in its activities by the charging and remuneration arrangements.

A. The financial model enables EMA staff to effectively perform tasks within its remit for procedural activities.

The current financial model enables EMA staff to perform tasks for procedural activities effectively. 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 (section 2.1, Table 3). Total fees for procedural activities and annual fees are however sufficient to cover all costs for procedural activities (section 2.1, Figure 11). At the activity level, however, EMA fee income does not generally align with the costs of undertaking the activities for human medicines (section 2.1, Figure 5) and veterinary medicines (section 2.1, Figure 6).

The incentives applied to the full fees for an activity in a given year also have an impact on the ability of EMA to perform procedural activities. Under the current financial model, 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 in the modelled year, EMA recovers only a small part of its costs directly from the fees for scientific advice (section 2.1, Figure 5). 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.

EMA representatives are overall satisfied with the alignment of the current financial model and their activities, and this is borne out in the modelling exercise undertaken for this study. However, EMA representatives indicated that in some instances meeting the costs can be difficult. An example provided concerns the fees for initial marketing authorisations; these are regularly complex applications, which cannot be covered by the specific fee charged for this activity. The disparity between fees and costs for these activities is shown in section 2.1, Figure 5). However, when NCA remuneration from CAP annual fees (section 2.1, Figure 12) is added to the direct remuneration for initial marketing authorisations, costs are almost covered. This may not be the case for different sub-types of initial marketing authorisations but it was not possible to link annual fees to specific sub-types of initial marketing authorisations in the modelling exercise. In the case of marketing authorisations submitted through the centralised procedure, at least one scientific committee provides an evaluation. Depending on the type of product, it could be that several committees have to be consulted. Indeed, the

results of the cost modelling exercise show that total fees to EMA for initial marketing authorisations do not directly meet the costs of undertaking these activities.

NCA rapporteurs and co-rapporteurs receive remuneration totalling 50 per cent of the full fee for most procedural activities for which a fee is charged, although this remuneration may not reflect the cost to NCAs of undertaking these activities (section 2.1, Figure 5). This is not the case for pharmacovigilance activities for human medicines, where incentives are applied to NCA remuneration or for procedural activities where there are fee exemptions or waivers. EMA fee income, on the other hand is determined from actual fee income from industry net of incentives, once NCA remuneration has been paid. As the modelling exercise shows, EMA relies on additional income from annual fees and the EU and EEA budget contributions to address the shortfall.

The 2010 evaluation of the EMA indicated that the EU general budget is important to ensure financial balance of the EMA. As noted in the report, EU and EEA contributions are annually adapted, responding to increases or decreases of fee income. The annual revenue of the EMA in the years 2012 to 2016 shows that total revenue steadily increased over this five year period from €223 million in 2012 to €305 million in 2016. General budget contributions have been adapted to balance fluctuations in orphan medicines contributions and fee income (EMA 2017a, 80). Budget contributions have also been adapted to take account of exchange rate fluctuations in the pound and additional sources of EMA fee income, such as the rent rebate received by EMA in 2016.

EMA representatives reported increasing complexity of coordination activities. An example provided relates to the approval of new medicines in a field where already a high quantity of similar products have been approved. EMA staff and NCA rapporteurs have to consider the previously approved products as well as whether the approvals have been consistent over the years. EMA representatives raised the concern that the complexity of such coordination activities will increase even more in the future.

B. The financial model enables EMA staff to effectively perform additional (i.e. cross-cutting, horizontal and related) activities within the remit of the Agency.

The current financial model enables the EMA to undertake procedural activities as well as other tasks, and there is evidence that the current financial model enables the EMA to perform these additional tasks effectively. According to EMA representatives, one of the key pillars of the fee and remuneration system 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. As pointed out above, in the current model this is particularly important in the case of waived or reduced fees for SMEs and for specific types of products.

2.3. Alignment between EMA remuneration to NCAs and NCA activities at EMA level

This section summarises answers to the study question regarding the extent to which the current financial model allows the EMA to remunerate NCAs adequately for the activities they perform. The question is addressed by looking at: (A) the alignment of remuneration provided to NCAs with the actual costs to NCAs for the activities they perform; and (B) evidence of any issues regarding the current model's ability to adequately remunerate NCAs.

Overall, the study found that there is alignment between remuneration to NCAs and NCA procedural activities, and committee and working group activities, while it is insufficient to fund other unremunerated activities.

More specifically, key findings relating to the alignment between EMA remuneration to NCAs and NCA activities are as follows:

F9. Section 2.1 shows that total remuneration provided to NCAs is sufficient to cover all of their procedural activities, as well as committee and working group activities. It is not, however, sufficient to cover all of the additional activities that NCAs reported to be EMA-related.

F10. At individual NCA level, remuneration is also sufficient to cover the costs of procedural activities, as well as committee and working group activities, for some but not all NCAs.

F11. At the activity level, NCA remuneration is sufficient to cover the costs of some but not all activities.

A. Remuneration provided to NCAs does not align with the actual costs to NCAs for the activities they perform at EMA level.

Remuneration for NCAs in total exceeds the costs of undertaking procedural activities requested by EMA but does not cover the respective costs of all individual NCAs. At the activity level, fees are also not aligned with the actual costs to NCAs for the activities they perform. Under the current financial model, NCAs are not remunerated for all of the roles for which they incur costs in relation to procedure-based activities. For example, for initial marketing authorisations, while a rapporteur or co-rapporteur role is remunerated, a peer review or PRAC rapporteur role is not. The analysis shows that the total remuneration for procedural activities covered the total (remunerated and unremunerated) costs of procedural activities for NCAs (section 2.1, Figure 12). However, at the individual NCA level, 10 out of 29 NCAs that provided cost information for this study do not cover their costs for procedural activities with the remuneration they receive. When remuneration from annual fees is also included, only 5 NCAs do not cover procedural activity costs.

At the activity level, the remuneration does not reflect costs (section 2.1, Figure 5 and Figure 6) with the fees for some activities effectively funding the costs of others, including those such as paediatric investigation plans and orphan designation for which no remuneration is paid. Although individual NCAs do not undertake the same procedural activities, the funding works to some extent across NCAs as almost all cover their costs. When modelling average cost pricing, the total NCA remuneration for procedural activities would cover the weighted average costs of the procedural roles for these activities, assuming that the remuneration is not subject to reduction due to incentives. However, in the modelling exercise, 10 individual NCAs do not recoup their costs related to procedural activities (section 2.1, Figure 14).

The remuneration provided to NCAs partially funds other non-procedural activities at EMA level. NCA representatives take part in working groups and committees. NCAs also report additional EMA-related activities that they carry out. These activities are not currently directly remunerated. Remuneration received under the current financial model is sufficient to recompense NCAs in total for the costs of work they undertake for working groups and committees (section 2.1, Figure 12). The procedural and annual NCA remuneration also partially funds the additional EMA-related activities they report. However, 24 out of 29 NCAs do not cover their total declared costs, with an average shortfall of €1.5 million/year (section 2.1, Figure 12). Analysis of individual NCAs compared to the average of NCAs is provided in section 2.1, Figure 13.

When modelling average cost pricing, additional remuneration is needed to cover the costs for NCAs of working groups, committees and additional activities. The cost-based benchmark scenarios analysed in this report consider the possibility that this additional funding could be raised from three possible mechanisms: increases to the EU and EEA budget contributions, increases to annual fees, or increases to procedure-based fees (i.e. a mark-up applied to average cost) (or to some combination of these mechanisms). It is assumed that the costs of activities for which there are currently no fees (e.g. paediatrics) would also be covered in this way. These are discussed in section 2.1.

Similar to EMA, ECHA works with national competent authorities that conduct work as rapporteurs and co-rapporteurs of the agency's committees. Commission Regulation (EC) No 340/2008 indicates that a 'proportion of the fees and charges collected' should be paid to the respective NCAs. The regulation does not indicate the exact proportion or amount. However, it should be the 'maximum proportion of the fees and charges' (Commission Regulation (EC) No 340/2008, L 107/7), taking into account the workload of the activities allocated to the respective NCAs. The proportion should be determined by ECHA's Management Board following Article 27 of Council Regulation (EC, Euratom) No 1605/2002 of 25 June 2002 on the Financial Regulation, as well as 'following a favourable opinion from the Commission' (Regulation (EC) No 340/2008, L 107/13). Regulation 340/2008 neither suggests the proportion of the share, nor whether non-rapporteur and non-co-rapporteur NCAs will be remunerated. In the case of the EASA, Commission Regulation (EU) No 319/2014 on fees and charges levied by EASA states that Member States may undertake certification tasks for the agency and that they will be reimbursed for such; however, it does not indicate whether they follow a rapporteur/co-rapporteur approach similar to EMA and ECHA.

B. Additional evidence shows that the current model is not able to adequately remunerate NCAs.

EMA representatives acknowledged the difficulties the NCAs face due to a lack of remuneration for some activities. According to some EMA interviewees, cross-financing such activities would be reasonable, considering the complexity and the size of the regulatory system, number of NCAs and the size of the market. In addition, an EMA interviewee indicated that while some NCA activities might be insufficiently remunerated, other areas should enable NCAs to compensate for some activities. An EMA interviewee also highlighted that despite the lack of remuneration for some activities, Member States greatly benefit from the centralised system, as they have more products on their national markets without necessarily having participated in the procedures and thus save costs.

Interviewed NCA representatives generally agreed with EMA interviewees that the EMA network brings benefits to their national markets, such as access to products in their countries without undertaking national procedures. However, these acknowledged benefits could not be calculated for the purposes of this study. Seven NCA interviewees also explicitly acknowledged the importance of the network; for example, one interviewee emphasised that the work of the EMA and the network of NCAs 'is a great example of Europe working together', and another interviewee thinks that it 'is one of the most successful networks' at European level. NCA interviewees often reported that they are therefore highly committed to the EMA and the work they do as part of the network.

In addition, they emphasised that they find unremunerated activities important – particularly from a public health perspective – and they are willing to undertake these activities for this reason. However, while NCA interviewees consider unremunerated activities to be crucial elements of the network, two interviewees 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. These NCAs did not indicate the number or type of procedures they would give up, however.

All but one interviewed NCA use their national budgets to cover costs incurred for at least some unremunerated activities.[50] Five NCA interviewees noted that while they do not aim to decrease their EMA-related activities, they raised concerns that they would not be able to maintain their level of engagement in the long term if the remuneration were not aligned with costs to NCAs. The study was unable to quantify these long-term effects as no data were provided.

The cooperation agreement, which is signed by the EMA and each participating NCA states that the EMA is not required to cover any additional costs that may be incurred (Article 3(2)), but the costs outlined in Annex II of the agreement 'include all other expenditure that may be incurred by [the signing NCA] in performance of this Agreement' (EMA 2016c, Article 3(2)). In 'cases of force majeure', however, which include 'any unforeseeable and exceptional situation or event beyond the control of the parties' (EMA 2016c, Article 10(6)), the NCA does not have to cover the costs. The agreement only mentions one example for such cases of force majeure, 'acts of terrorism, which prevents either of [the NCAs] from performing any of their obligations under the Agreement' (EMA 2016c, Article 10(6)).

Three NCA survey respondents and three interviewees also reported that the remuneration system does not take into account different living costs and salaries across participating Member States. Instead, Member States undertaking EMA-related activities receive the same remuneration regardless of actual costs in their country. Interviewees thus consider the fee system to be unsustainable as NCAs in countries with higher living costs need to compensate for additional costs incurred with their national budgets. The NCAs with the highest costs tend to be those that also undertake the highest share of EMA-related activities.

Insufficient remuneration to NCAs was emphasised in the 2010 evaluation of the EMA; the authors noted that NCAs' engagement in unremunerated activities 'becomes all the more tricky [sic] that NCAs are facing an increasing lack of resources' (Ernst & Young 2010, 11). The European Court of Auditors also highlighted the imbalance of remuneration to NCAs and activities they undertake in its 2011 report. They noted that there is 'the need to introduce a system of remuneration for services provided by Member State authorities based on their real costs' (European Court of Auditors 2012, C 388/117). While similar comments have been made in previous audit reports, the following reports (years 2012 to 2015)[51] neither include any reference to inadequate remuneration of NCAs nor indicate that their 2011 comment was resolved.

2.4. Balance between a cost-based fee system and simplicity of the fee system

This section outlines answers to the study question relating to the balance between a fee and remuneration system based on actual costs and simplicity of the fee system. The question is addressed by looking at (A) evidence of satisfaction (or dissatisfaction) with the balance between costs and simplicity.

[50] The NCA indicating that they would not use their national budget to cross-finance EMA-related activities reported that the national legislation does not allow doing so.

[51] The audit report for the financial year 2016 has not been published at the time of preparing this report.

Overall, the study showed that there is a balance between a cost-based fee system and simplicity when considering its size and scope. Changes to legislation have improved this balance to some extent, but there is also evidence of increasing complexity resulting from legislative amendments. Both NCA and EMA representatives found the fee system generally transparent and that fees are overall proportionate. However, there are areas where more transparency and proportionality is needed.

More specifically, key findings relating to the balance between a cost-based fee system and simplicity of the fee system are as follows:

F12. Overall, changes in legislation (e.g. pharmacovigilance legislation in 2010/2012/2014, Clinical Trials Regulation in 2014) have contributed to improving the balance between a cost-based fee system and the fee system's simplicity. There is evidence that several procedures follow simpler and more structured processes as a result of amended legislation (e.g. PSURs).

F13. While in some cases changes in legislation better address the complexity of procedures (e.g. reflecting different products and related activities), they in turn increased the complexity with regard to implementing the procedures. In addition, in some cases legislative amendments made the fee system less flexible (e.g. the amended pharmacovigilance legislation does not allow fee reductions after 30 calendar days from the date of the invoice).

F14. Overall, the fee system is clear and transparent. However, there are some areas that need more clarity and transparency including fee breakdowns for industry and NCAs, the basis for each fee, and criteria for fee exemptions and reductions.

F15. Overall, the fee system is proportionate between the fees charged to industry and the services provided. However, there are specific areas within the fee system that are disproportionate, particularly at the level of fees charged for specific activities, where the costs in some cases are much higher than the fees and in others where the reverse is the case.

A. Overall, there is satisfaction with the current fee system's balance between costs and the fee system's simplicity.

As there are many different activities, each with their own fees and associated costs, there is a general balance to be struck between a fully cost-reflective fee system and a simple fee system. Eight interviewed NCA representatives reported that they find the fee system simple enough and that guidelines are clear and easy to follow. An interviewed NCA representative reported that the EMA fee system is simpler than many national fee systems. Similarly, wider stakeholders agreed that the fee system rules and guidelines are clear.

The survey of wider stakeholders showed that the majority of the respondents consider the fee system to be straightforward and easy to understand: overall, 52.6 per cent agreed or strongly agreed that the current fee system is simple, compared to 23.7 per cent who disagreed. The remaining 2.6 per cent strongly disagreed, 15.8 per cent were neutral about whether they find it straightforward or not, and 5.3 per cent indicated that they 'don't know'. Respondents from large pharmaceutical companies in particular found the fee system straightforward and easy to understand: 72.7 per cent agreed or strongly agreed, 9.1 per cent were neutral and 18.2 per cent disagreed. By contrast, 42.9 per cent of SME and 33.3 per cent of research organisation respondents agreed, while 28.6 per cent of SME and 33.3 per cent of research organisation respondents disagreed (28.6 per cent of SME respondents and 16.7 per cent of research organisation respondents were neutral, and 16.7 per cent of research organisation respondents indicated that they 'don't know').

The results of the open public consultation mirrored this result, indicating that the majority of the 51 respondents felt that the EMA fee system rules are clear and easy to understand (9.8 per cent strongly agreed and 58.8 per cent agreed), while only 5.9 per cent neither agreed nor disagreed, 9.8 per cent disagreed and no respondent strongly disagreed (the remaining 15.7 per cent indicated that they do not know). Agreement with the statement provided was particularly high among representatives of companies with direct relevance to the EMA and members of representative organisations: 86.4 per cent of company representatives and 80.0 per cent of representative organisation members strongly agreed or agreed (two patient organisation and two industry representative organisation respondents). None of the representatives of companies with direct relevance to the EMA, members of representative organisations and NCA respondents disagreed or strongly disagreed. By contrast, individual citizens (33.3 per cent disagreed) and 'other' stakeholder groups (28.6 per cent) disagreed more often.

The majority of open public consultation respondents also felt that the EMA fee system rules are easy to apply in practice: 5.9 per cent strongly agreed and 47.1 per cent agreed, while only 5.9 per cent disagreed, no respondent strongly disagreed and 21.6 per cent neither agreed nor disagreed (the remaining 19.6 per cent indicated that they do not know). Agreement with both statements was particularly high among representatives of companies with direct relevance to the EMA: 86.4 per cent strongly agreed or agreed that the EMA fee system rules are clear and easy to understand, and 81.8 per cent strongly agreed or disagreed that they are easy to apply in practice.

Compared to NCAs and wider stakeholders, EMA representatives indicated that the fee system is complex; one interviewee noted that lack of simplicity is a considerable weakness of the fee system. According to several EMA representatives, the complexity of the fee system is a result of the detailed breakdown of fees and the complexity of the activities themselves. An interviewee provided the example of fee incentives for SMEs and micro-sized enterprises, which were changed as part of an amendment to the Pharmacovigilance Directive and Regulation in 2010 (Directive 2010/84/EU, Regulation (EU) No 1235/2010) as well as the accompanying Commission Implementing Regulation No 520/2012 in 2012. Before the amendments, incentives were the same for all SMEs regardless of their size, whereas Regulation (EU) No 658/2014 on the fees for pharmacovigilance activities breaks down exemptions and reductions by company size (see also section 2.6). An EMA interviewee also noted that the new Clinical Trial Regulation of 2014 (Regulation (EU) No 536/2014) contributed to more fairness and balance between a cost-based fee system and simplicity.

These changes were introduced to make the fee system fairer. 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 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. Overall, EMA representatives indicated that there should be a balance between simplicity, fairness and proportionality and that all three should be taken into account in any changes to the fee system or legislation. In 2010, Ernst and Young also recommended a simplification of the fee system 'while keeping the fairness of fees as an important goal' (Ernst & Young 2010, 159).

Overall, there is agreement that previous amendments made regulations and implementing rules – and consequently fees charged to industry – fairer and more proportionate. Several interviewees (both NCA and EMA representatives) referred to the amended pharmacovigilance legislation and other legislative changes when discussing the simplicity of the fee system. An interviewee provided the example of the centralisation of periodic safety update reports (PSURs), which had led to more structured and simplified processes as well as to a better balance between a cost-based fee system and the fee system's simplicity. However, as already outlined above,

concerns were also raised that increased granularity defined in legislation makes the fee system more complex and also less flexible. For example, the amended pharmacovigilance legislation does not allow fee reductions after 30 calendar days from the date of the invoice (Regulation (EU) No 658/2014, L 189/117).

While some EMA services seem to have become simpler through legislative changes (e.g. centralisation of activities), some changes in legislation increased the complexity with regard to implementing the procedures. In general, NCA interviewees indicated that they are in favour of simplifying regulatory processes through changes in legislation. However, six NCA representatives observed that while such changes make the services simpler for industry they sometimes make NCAs' activities more complex. According to some interviewees, such increases in complexity are often not considered in the implementing rules to the Fee Regulation (Council Regulation (EC) No 297/95), for example, through increasing fees and changing the level of remuneration. In the case of centralisation of some activities, interviewees indicated that remuneration is not sufficient. An interviewee noted that 'it's not easy to put [former nationally authorised activities] all in the same basket and say they are covered by a single fee'. In some instances, such simplifications make procedures even more complicated, as they do not fully reflect all of the tasks related to the procedure or the increasing complexity of procedures. NCA interviewees commented that both the fees charged and the remuneration provided to NCAs should be better reflected in legislative changes (e.g. changed remuneration for more complex activities).

In general the study found that the fee system is transparent. NCAs, EMA, wider stakeholder representatives, and respondents to the open public consultation generally agreed that the fee system is transparent with respect to the legislation, implementing rules and explanatory notes. In the survey of NCAs, 63.3 per cent of the respondents agreed that the fees charged are transparent. Similarly, 53.8 per cent of respondents to the wider stakeholder survey agreed that the fees are transparent, 30.8 per cent felt neutral about the perceived transparency, 10.3 per cent indicated that they did not know and only 5.1 per cent disagreed. However, of those who agreed that the fees are transparent, most respondents are large pharmaceutical company representatives (72.3 per cent of all large pharmaceutical company respondents agreed), while the majority of SME representatives were neutral (57.1 per cent), and 28.6 per cent of SME consultees agreed.

The majority of respondents to the open public consultation also felt that the operation of the EMA fee system is transparent: 66.7 per cent of respondents strongly agreed or agreed with the statement provided on the transparency of the fee system, while only 4 per cent disagreed or strongly disagreed (13.7 per cent neither agreed nor disagreed, 15.7 per cent indicated that they do not know). Representatives of companies with direct relevance to the EMA found the fee system particularly transparent: 86.4 per cent strongly agreed or agreed, and the remaining respondents neither agreed nor disagreed or indicated that they do not know (9.1 per cent neither agreed nor disagreed, and 4.5 per cent (one respondent) indicated that they do not know).

The 2010 EMA evaluation (Ernst & Young 2010, 87) reported that industry asked for more transparency, particularly regarding the roles of EMA Secretariat units they work with. However, in the wider stakeholder survey conducted for the present study, only one respondent – a representative of a large pharmaceutical company – provided a follow-up comment indicating that there are some areas where full transparency to industry is not provided. Examples mentioned include lack of clarity on how fees are calculated and that fee invoices do not show the breakdown of fees. A respondent from an industry representative organisation to the open public consultation (representing companies producing homeopathic medicinal products), however, specifically noted that the EMA invoicing practice is transparent, timely and works well for their members.

In the open public consultation, several respondents also specifically referred to other areas where more transparency is needed: two representatives of companies with direct relevance to the EMA indicated lack of transparency regarding the time spent by NCAs, which makes it difficult for industry to assess whether the fees charged are proportionate to the services provided. A representative of a patient organisation noted that more information about the fee share between the EMA and NCAs is needed, and that it should be made public how much each individual authority receives. A member of the European Federation of Pharmaceutical Industries and Associations (EFPIA) commented that there is lack of transparency regarding the use of annual fees. An academic respondent felt that it is not transparent and clear enough why academic institutions have to pay the same for scientific advice as large pharmaceutical companies.

There are a few specific areas where more transparency is needed for NCAs. One NCA respondent noted that the breakdown of fees is not transparent enough, that is, how much an individual activity would 'cost' and to what extent each activity would be reimbursed. Examples include remuneration for scientific advice and line extensions. Related to that, in cases of waived or reduced fees, an NCA interviewee reported that the amount of the remuneration an NCA would receive is not clear, particularly at the stage of agreeing to undertake an activity. Some NCA representatives also indicated that in general fee exemptions and reductions are not transparent enough. Another NCA representative indicated that there is not enough clarity regarding the rationale for the fee share between EMA and NCAs (i.e. why it is 50-50 in some cases but 60-40 or 70-30 in others; see EMA 2017d, 24–5).

The current cooperation agreement between EMA and NCAs stipulates that payments to NCAs 'shall be made when the [NCA] has fulfilled its obligation in accordance with this Agreement, including compliance with the Key Performance Indicators described in Annex III' (EMA 2016c, Article 4(1)). NCA consultees, however, pointed to a lack of transparency regarding the timing of remuneration, which complicates NCAs' internal accounting and billing. The specific example of inspections was given, where late payments affect reporting periods. While NCA representatives did not provide any specific examples of the lack of transparency with regard to timing, Article 12(2) of the agreement indicates that the payment period to NCAs may be suspended in case obligations have not been fulfilled. NCA consultees indicated that being paid at least a part of their remuneration upfront would be more appropriate, considering that the EMA receives fees from the industry before the requested services are conducted.

The EMA's approach to remunerate NCAs after they have fulfilled their obligations is similar to ECHA's approach: Article 14(3) of Commission Regulation (EC) No 340/2008 stipulates that remuneration for ECHA NCAs will be provided only after submission of the relevant report of the task undertaken. However, ECHA's Management Board may also permit pre-financing or interim payments (Regulation (EC) No 340/2008, Article 14(3)). EASA's regulation on fees and charges does not include any information on payment timelines.

NCA representatives, wider stakeholders and respondents to the open public consultation identified several aspects of the fee and remuneration system that lack proportionality. While all consulted groups suggested that, overall, fees charged to industry and services provided are proportionate, there are some specific areas that lack proportionality.

Wider stakeholders consulted for this study reported that in general, particular types of medicines for which no fees are foreseen (e.g. orphan designated medicines, veterinary medicines for MUMS, products for paediatric use) should be extended to other areas (e.g. on additional fees for each presentation, non-food-producing animals). Consultees noting that fee reductions should be extended to fees for medicines for non-food-producing animals indicated that this would create more fairness across the veterinary medicine industry; this comment was raised by both representatives of SMEs and large

pharmaceutical companies. While 38.4 per cent of wider stakeholder survey respondents (n=26; excluding respondents who chose the answer options 'don't know' or 'not applicable') agreed or strongly agreed that such specific fee arrangements are appropriate and 34.6 per cent were neutral, 26.9 per cent disagreed or strongly disagreed. No other justifications were provided for these suggestions.

Wider stakeholders across stakeholder type (i.e. large pharmaceutical companies, SMEs, representatives of research organisations as well as representative groups) highlighted other activities which they felt were not proportionately charged. Examples included fees for variations (type IA, simple and grouped type II), annual fees for MUMS, fees for initial scientific advice requests, general maintenance fees, post-authorisation measures (PAMs) comprising submissions of a single report, fees for transfer of a marketing authorisation holder (MAH), fees for changing the local representative, fees for changing detailed descriptions of the pharmacovigilance system (DDPS), and fees for products for emergency purposes. Two respondents (a representative of a large pharmaceutical company and an industry organisation representative) also indicated that they do not find it appropriate that each MAH has to pay the full inspection fee when only one inspection is carried out.

Although half of respondents to the open 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 (38.9 per cent neither agreed nor disagreed, 11.1 per cent disagreed, and no respondent strongly disagreed), they also highlighted areas where more proportionality is needed. Similar to wider stakeholder respondents, two respondents to the open public consultation (a representative of a company with direct relevance to the EMA, and a representative of EFPIA) felt that fees for variations (grouped variations, type IA, type IB and type II variations) are not proportionate.

Specifically, a representative of a company with direct relevance to the EMA highlighted that each change associated with variations is charged separately, even if changes are only minor. A representative of EFPIA felt that fees for grouped variations are too high as they only require one review process. Moreover, the same respondent noted that type II variation fees are not proportionate to the size and content of the report (same fee irrespective of the length of the report, whether or not the benefit-risk is changed or whether or not an assessment is needed). Two respondents (a company and an EFPIA representative) also highlighted the disproportionality of fees for additional strengths, and one respondent each felt that the following fees are not proportionately charged: fees for PSURs, fees for homeopathic medicinal products, fees for updates to a dossier and annual fees (in particular for products that do not require any regular regulatory activity). The representative of EFPIA also felt that in general fees do not always reflect the level of service for a particular activity, as they do not consider the complexity of an individual product.

2.5. Fee system ability to meet needs in exceptional or particular circumstances

In this section we report on the answers to the study question regarding the extent to which the fee system enables needs to be met in exceptional circumstances or under particular priorities/imperatives. The question is addressed by looking at: (A) whether reductions and exemptions enable authorisations for special categories of medicinal products that are prioritised by the EU; (B) whether the fee system provides flexibility for exceptional circumstances; and (C) evidence of satisfaction with the provisions made in exceptional circumstances or under particular priorities/imperatives.

The study found that key elements of the current fee system are its ability to respond to exceptional circumstances and related to that a certain degree of flexibility to allow doing

so. However, it was also shown that other areas lack flexibility, including the fee system's ability to respond to increasing complexity of activities. Overall, industry representatives indicated satisfaction with the provisions made in exceptional circumstances, although they highlighted areas where more flexibility is needed. Academic stakeholders, however, reported that more incentives for academic and non-profit institutions are needed.

More specifically, key findings relating to the fee system's ability to meet needs in exceptional or particular circumstances are as follows:

F16. 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.

F17. The system of having a 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 impeded fee reductions under exceptional circumstances (see also finding F13).

F18. The current fee system does not enable enough flexibility when it comes to the time NCAs need for activities (time needed for accomplishing an activity of the same kind often varies).

F19. The current fee system is not flexible enough to meet time and budget needs regarding increasing complexity of activities. The study identified activities related to the following areas which already include and will likely include even more complexity in the future for both the EMA and NCAs: companion diagnostic reviews, activities related to big data, real-world data analysis, highly innovative products without sufficient clinical data, health technology assessments and novel therapies.

F20. Overall, stakeholders from industry, academia and representative organisations are satisfied with provisions made in exceptional circumstances or under particular priorities/imperatives, but they highlighted areas where more incentives and focus on particular user groups are needed, such as incentives for academic and non-profit institutions as well as patient organisations.

A. The reductions and exemptions enable authorisations for special categories of medicinal products that are prioritised by the EU.

The current fee system provides enough flexibility to the EMA to finance their EMA-related activities to meet particular needs, such as activities related to advanced therapies. As discussed in section 2.1, the current fee and remuneration system allows the EMA as well as NCAs to fund activities offering fee reductions and exemptions to industry stakeholders (see also Regulation (EC) No 141/2000, Regulation (EC) No 1902/2006 and Regulation (EC) No 1394/2007). EMA representatives reported that this flexibility, and in particular the availability of EU and EEA contributions, is crucial to fully operating regardless of fee income fluctuations.

B. The fee system provides flexibility for exceptional circumstances in several areas, while other areas are insufficiently flexible.

The system of a Fee Regulation and implementing rules is important to enable a certain degree of flexibility with regards to, for example, fee reductions and exemptions. EMA representatives noted that the combination of the Fee Regulation (Council Regulation (EC) No 297/95, and most recent amendment Commission Regulation (EU) 2017/612) and implementing rules (EMA 2017d) allow adjustments of

the fee level to regulatory changes, and thus enables them to provide fee reductions and exemptions that would not be foreseen otherwise. Article 9 of Council Regulation (EC) No 297/95 stipulates that reductions and exemptions of fees may be granted 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'.

In contrast to EMA, ECHA and EASA do not have systems of fee regulations and implementing rules, but include the amount of fees and charges payable in their regulations (e.g. Commission Implementing Regulation (EU) 2018/895, Commission Regulation (EU) No 319/2014).

The study team compared the EMA fee system with the U.S. FDA's fee system regarding flexibility for exceptional circumstances such as public health or animal health emergencies. The FDA's Prescription Drug User Fee Act (PDUFA) – applicable to human medicines – indicates that section 736(d) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) provides for fee exemptions to be granted in cases where 'a waiver or reduction is necessary to protect the public health' (FDA 2016b). The study did not find any other evidence of exemptions or reductions for exceptional circumstances in the other user fee acts of the FDA.

However, changes to the pharmacovigilance legislation impeded fee reductions under exceptional circumstances. EMA interviewees indicated that although amendments to the pharmacovigilance legislation made the fee system more cost-based and simpler, the changes also included restrictions regarding granting exemptions or reductions, as fee reductions are not allowed after 30 calendar days from the date of the invoice (Regulation (EU) No 658/2014, L 189/117).

The current fee system does not enable enough flexibility when it comes to the time NCAs need for activities (time needed for accomplishing an activity of the same kind very often varies) and the time period over which some activities are undertaken. Several NCA representatives consulted indicated that both the workload and the time needed for accomplishing an activity can vary widely even for the same activities. Remuneration to NCAs is not adjusted in such situations; instead, NCAs have to fund such activities through fee remuneration from other less complex procedures that are remunerated at the same rate, through annual fees and through the use of their national budget. The validation exercise also showed evidence that the same NCAs charge different times for the same activities. For example, there are large variations in the time reported by the same NCAs for marketing authorisation activities. Such differences are likely to reflect the level of complexity of the different procedures. The validation exercise did not provide evidence of any NCAs consistently reporting a longer time to complete an activity than other NCAs for the same activities.

The current fee system is not flexible enough to meet time and budget needs regarding increasing complexity of activities. Related to the lack of flexibility with regards to different workloads for the same tasks, NCA representatives also indicated that the fee system needs to be adapted to reflect the increasing complexity of activities resulting from new and complicated innovations and advances in science. It is expected that such changes will affect both time and budget needs. Examples of activities where increasing complexity is already observed and expected in the near future include companion diagnostic reviews, activities related to big data, real-world data analysis, highly innovative products without existing or insufficient clinical data, health technology assessments, novel therapies, and personalised medicine. NCA representatives raised the concern that the current fee system is not flexible enough to address such changes.

There are areas where industry and academic representatives require more flexibility. In the open public consultation, several stakeholders highlighted such areas.

Two respondents, for instance, noted that there is only little flexibility when it comes to providing fee reductions or waivers to academic and non-profit institutions. An industry representative commented that the current payment period of 30 days for companies is too short and that more flexibility is needed regarding payment timelines (e.g. general extension of the payment timelines or exception rules). A member of an industry organisation noted that there is lack of flexibility regarding sharing of costs between MAHs; the respondent specifically referred to homeopathic products, where only one MAH (for PSURs or PASS) is charged, and that fees cannot be shared between MAHs.

C. Overall, there is satisfaction with the provisions made in exceptional circumstances or under particular priorities/imperatives.

Overall, stakeholders from industry, academia and representative organisations are satisfied with provisions made in exceptional circumstances or under particular priorities/imperatives, such as exemptions and reductions for certain types of medicines. However, they highlighted areas where more incentives and focus on particular user groups are needed. The wider stakeholder survey asked respondents for their level of agreement with the statement 'The specific fee arrangements made for particular types of medicines (orphan medicines, veterinary medicines for MUMS, medicines for paediatric use, etc.) are appropriate'. Overall, 38.4 per cent of respondents (n=26; excluding respondents who chose the answer options 'don't know' or 'not applicable') agreed or strongly agreed that such fee arrangements are appropriate, while 34.6 per cent were neutral and 26.9 per cent disagreed or strongly disagreed. SME representatives and stakeholders who did not identify as SME, large pharmaceutical company or research organisation representatives, however, were less satisfied with the fee arrangements compared to other stakeholder groups: 20 per cent of SME and 25 per cent of other respondents agreed, 50 per cent of SME and 25 per cent of other respondents were neutral and 30 per cent of SME and 50 per cent of other respondents disagreed or strongly disagreed (n=10, excluding respondents who chose the answer options 'don't know' or 'not applicable'). Representatives of research organisations, by contrast, showed a higher degree of satisfaction: 80 per cent strongly agreed or agreed, while the remaining 20 per cent disagreed (n=5, excluding respondents who chose the answer options 'don't know' or 'not applicable').

Only three respondents to the survey further explained their level of agreement with the statement. One respondent emphasised the importance to maintain fee reductions for orphan designated medicines. The remaining comments were provided by respondents disagreeing with the statement (a representative of a large pharmaceutical company and an SME representative), who commented that financial incentives for products with MUMS only apply to food producing species, but not to other animals.

In comments on other questions, consultees identified additional areas where they believe exemptions or reductions are needed. For instance, a respondent reported that incentives for emergency purposes are insufficient and that there should be exemptions or reductions for these cases. As stated in Article 9 of Council Regulation (EC) No 297/95, fee reductions for public or animal health emergency purposes should be decided on a case-by-case basis by the Executive Director. Another survey respondent, a representative of a veterinary medicine representative group, noted that there should be fee reductions for inspections for two or more products, which have the same pharmaceutical form. A consultee mentioned that fee incentives could be introduced for type IA variation groupings and work-sharing procedures if the change applies to several centrally authorised products of the same MAH.

In the open public consultation, the extent of agreement with the statement 'The EMA fee system rules provides adequate incentives and support' was higher than the extent of agreement with the statement on the provision of adequate incentives in the wider

stakeholder survey. Overall, 57.5 per cent of respondents (n=40; excluding respondents who chose the answer option 'do not know') agreed or strongly agreed that there are adequate incentives and support, while 20 per cent disagreed or strongly disagreed (eight respondents) and 22.5 per cent (nine respondents) neither agreed nor disagreed.

In open-text comments, several respondents highlighted areas where they believe more incentives or support are needed. Twelve respondents indicated that the reductions provided by EMA to the fees related to parallel distribution notices should be re-introduced, as they feel that this has a positive effect on the parallel distribution market, which is under continuous commercial pressure.[52]

Three academic/research respondents explained that there is a lack of incentives for academic institutions and research organisations. The respondents felt that academic/research institutions and organisations should receive incentives similar to those provided to SMEs. A patient organisation representative also commented that there is a need for supporting the involvement of patients in EMA activities (as for example per Article 102 of Directive 2010/84/EU on pharmacovigilance), including providing compensation to patients. A member of an industry organisation also indicated that there is a lack of focus on the specific needs of MAHs of homeopathic medicinal products.

2.6. SME support through effective cost reductions to use the centralised system

This section discusses answers to the study question regarding the extent to which SMEs are supported through effective reductions in their costs to use the centralised system. The question is addressed by looking at: whether (A) SMEs are able to participate in the centralised system without undue burdens.

Overall, the study found that current support provided to micro enterprises and SMEs (fee incentives and administrative support) allows smaller businesses to use the current centralised system.

More specifically, findings relating to the fee system's ability to support SMEs are as follows:

F21. Indicators such as numbers of registered SMEs and authorisations to SMEs suggest that SME incentives and guidance enable them to participate in the centralised system.

F22. Compared to the European Chemicals Agency (ECHA),[53] the EMA offers higher fee reductions. The EMA fee system also offers fee exemptions, which are not provided for SMEs in the ECHA fee system. However, ECHA breaks its reductions down by the size of the enterprise (micro, small and medium-sized enterprises), providing significantly higher reductions to micro-sized businesses.

F23. 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 individual definitions for micro, small or medium-sized enterprises.

[52] The 12 respondents who provided this input submitted the same verbatim (or almost verbatim) comment.

[53] ECHA uses a similar approach to providing fee incentives to SMEs, while other EU agencies analysed for this study (EASA and OHIM) do not provide such incentives.

A. SMEs are in general able to participate in the centralised system without undue burdens.

The study showed mixed views on incentives for SMEs. Wider stakeholders responding to the survey provided mixed answers to the statement 'The specific fee arrangements made for SMEs are appropriate'. Overall, no respondent strongly agreed, 20.5 per cent agreed, 17.9 per cent felt neutral about the statement, 25.7 per cent strongly disagreed or disagreed (10.3 disagreed, 15.4 per cent strongly disagreed) and 17.9 per cent each chose the answer option 'don't know' and 'not applicable'.

Stakeholders who identified their organisation as an SME in the survey were less satisfied than the group of respondents as a whole: a majority of 53.8 per cent of self-identified SME respondents disagreed or strongly disagreed with the statement that fee arrangements for SMEs are appropriate (23.1 per cent disagreed, 30.8 per cent strongly disagreed), while only 7.7 per cent agreed, 30.8 per cent felt neutral about it, and 7.7 per cent indicated that the statement is not applicable to them.

Five wider stakeholder respondents (three SME and two industry organisation representatives) and one representative of industry representative organisation in the open public consultation provided follow-up comments on their level of agreement with the statement indicating that the EU definition of an SME is not sufficient and requires an update. However, this is an EU-wide definition and cannot be addressed through the fee system; it is therefore outside the scope of this study.

The criteria for fee reductions and exemptions for SMEs are defined in Commission Regulation (EC) No 2049/2005. The document uses the European Commission's definition of micro-sized enterprises and SMEs provided in Commission Recommendation 2003/361/EC. The Recommendation emphasises that the staff headcount criterion is considered the main criterion for SMEs; by contrast, criteria such as turnover are not seen as relevant, as there are major differences among sectors. The turnover criterion should thus only be used in combination 'with that of the balance sheet total, a criterion which reflects the overall wealth of a business, with the possibility of either of these two criteria being exceeded' (Commission Recommendation 2003/361/EC, L 124/36). Recommendation 2003/361/EC provides that enterprises of fewer than 250 employees, having an annual turnover of maximum €50 million and/or an annual balance sheet of maximum €43 million fall within the SME category. Table 7 shows the criteria for determining whether a company within the SME category is defined as a small or micro-sized enterprise.

Table 7: Recommendation 2003/361/EC definition of micro, small and medium-sized enterprises

Category	Staff headcount	Annual turnover	or	Annual balance sheet total
Medium-sized	< 250	EUR 50 million	*or*	EUR 43 million
Small-sized	< 50	EUR 10 million	*or*	EUR 10 million
Micro-sized	< 10	EUR 2 million	*or*	EUR 2 million

Source: Commission Recommendation 2003/361/EC (L 124/39)

Commission Regulation (EC) No 2049/2005 was adopted with the aim of promoting innovation and the development of new medicinal products by SMEs, and thus defines SME reductions and exemptions of costs for centralised procedure authorisations of medicinal products for both human and veterinary use. In addition to fee incentives, the Regulation also established an SME Office to provide advice to applicants on administrative and procedural activities, to ensure that all requests from the same applicant related to a particular product are monitored, and to organise workshops and training sessions for applicants to ensure they comply with the requirements in Regulation (EC) No 726/2004. The Regulation also stipulates the publication of a detailed

User Guide for SMEs (see SME Office 2016). In 2016, the User Guide was substantially revised with the aim to better explain the legislative framework as well as EMA requirements to SMEs (EMA 2017a, 43).

Commission Regulation (EC) No 2049/2005 defines fee deferrals, exemptions and reductions as well as multiple fee reductions. As outlined in Article 5, fees for applications for marketing authorisation and inspections for assessing market authorisation are deferred until a final decision on the authorisation is issued or if the application is withdrawn. The fees are then payable within 45 days of the final decision or application withdrawal. Article 6 on conditional fee exemptions notes that SMEs that have submitted medicinal products for which scientific advice has been given will not have to pay a fee if their application for market authorisation has been rejected.

As defined in Articles 7 to 9, there are a number of services for which SMEs are eligible for fee reductions or exemptions. While Commission Regulation (EC) No 2049/2005 does not break down reductions or exemptions by the size of an enterprise, the amended pharmacovigilance legislation in 2012 provides incentives based on the category of a company (micro-sized enterprise or SME). In addition, there have been further introductions of fee incentives after the adoption of Commission Regulation (EC) No 2049/2005, such as total or partial exemptions for post-authorisation activities in 2014 (EMA 2014c). Table 8 provides an overview of incentives for micro-sized enterprises and SMEs as of October 2017.

Table 8: Incentives for micro-sized enterprises and SMEs

Type of procedure/service	Incentive
Scientific advice	• 90% reduction to the total applicable fee for non-orphan medicinal products • 100% reduction to the total applicable fee for designated orphan medicinal products • 100% reduction to the total applicable fee for products eligible to the PRIME scheme[54]
Inspections (pre-authorisation)	• Deferral of total applicable fee • 90% reduction to the total applicable fee • 100% reduction to the total applicable fee for designated orphan medicinal products[55]
Inspections (post-authorisation)	• 90% reduction to the total applicable fee
Applications for a marketing authorisation	• Deferral of total applicable fee • Conditional fee exemption (unsuccessful application)
Scientific services (e.g. certification, Article 58 procedures)	• 90% reduction to the total applicable fee for non-orphan medicinal products • 100% reduction to the total applicable fee for designated orphan medicinal products
Establishment, extension or modification of maximum residue limits (MRL) for a veterinary medicinal product	• 90% reduction to the total applicable fee
Administrative services (excluding parallel distribution)	• 100% reduction to the total applicable fee
Post-authorisation activities[56]	• Micro-sized enterprises: 100% reduction to the total applicable fee • SMEs: 40% reduction to the total applicable fee • 100% reduction to the total applicable fee for designated orphan products during the first year after marketing authorisation[57]
Pharmacovigilance services	• Micro-sized enterprises: 100% reduction to the total applicable fee • SMEs: 40% reduction to the applicable fee or share of fee[58]

Sources: EMA (2016e, 8), EMA (2017c, 41–43), EMA (n.d.-e)

[54] In 2016, the EMA launched the PRIME (PRIority MEDicines) scheme to support developers of medicinal products 'that may offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options' (EMA n.d.-d).

[55] The full waiver of the total applicable fee for designated orphan medicinal products is not listed in the explanatory note on general fees payable (EMA 2017c), but on the EMA's website (EMA n.d.-e).

[56] 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' (EMA 2017c, 42).

[57] Fee reduction only listed on the EMA website (EMA n.d.-e).

[58] The EMA website notes that SMEs only receive a fee reduction of 40 per cent for pharmacovigilance services (EMA n.d.-e).

Indicators such as numbers of registered SMEs and authorisations to SMEs suggest that SME incentives and guidance enable them to participate in the centralised system. As shown in the EMA's annual reports, the number of SMEs registered continuously increased in the last six years. While in 2011 a cumulative total of 679 SMEs were registered, the cumulative number increased by 167 per cent to 1,810 registered SMEs in 2016 (EMA 2012a, 16; 2013a, 34; 2014a, 36; 2015a, 31; 2016a, 46; 2017a, 43). Similarly, the number of requests for renewal of SME status steadily increased from 349 in 2011 to 1182 in 2016 (increase of 239 per cent). By contrast, requests for administrative assistance have varied over time; they decreased from 158 in 2011 to 135 in 2012 and 131 in 2013, then increased to 163 in 2014, followed by a decrease to 141 in 2015 and an increase to 174 in 2016 (EMA 2014a, 36; 2015a, 31; 2016a, 46; 2017a, 43).

The number of initial marketing authorisation applications for human medicines submitted by SMEs also showed significant fluctuations in the past five years: while in 2012 EMA registered 20 SME applications, they received only 8 in 2013 and 7 in 2014. The number increased by more than 100 per cent to 15 applications in 2015 and by another 80 per cent to 27 in 2016 (EMA 2017a, 44).

Overall, SMEs are very active in submitting marketing authorisation applications for veterinary medicines compared to non-SME businesses. In total, the EMA received 21 applications for marketing authorisation for veterinary medicines in 2016; out of those, nine applications (43 per cent) were submitted by SMEs. In the case of scientific advice, 50 per cent came from SMEs (EMA 2017a, 60).

The study team compared incentives for micro-sized businesses and SMEs as well as their definitions with the U.S. FDA as well as the ECHA. We did not compare the EMA with the EASA and the EUIPO in the context of SME support, as both agencies do not offer any reductions or exemptions to SMEs. Table 9 provides an overview of the three agencies' definitions of micro-sized businesses and SMEs as well as their incentives.

Table 9: Overview of fee reductions for SMEs provided by the EMA, the ECHA and the U.S. FDA

	EMA	ECHA	U.S. FDA
Definition of micro-sized enterprises	• Staff headcount: < 10 employees • Annual turnover or annual balance sheet total of maximum €2 million	• Staff headcount: < 10 employees • Annual turnover or annual balance sheet total of maximum €2 million	• Definition for 'small businesses' only • Staff number, including employees of affiliates: < 500
Definition of small-sized enterprises	• Staff headcount: < 50 employees • Annual turnover or annual balance sheet total of maximum €10 million	• Staff headcount: < 50 employees • Annual turnover or annual balance sheet total of maximum €10 million	
Definition of medium-sized enterprises	• Staff headcount: < 250 employees • Annual turnover of maximum €50 million or annual balance sheet total of maximum €43 million	• Staff headcount: < 250 employees • Annual turnover of maximum €50 million or annual balance sheet total of maximum €43 million	
Incentives for micro-sized enterprises	• 90–100% fee reduction (same for micro, small and medium-sized enterprises) • 100% fee reduction for post-authorisation activities and pharmacovigilance services (micro-sized enterprises only) • No other incentives for micro-sized enterprises only	• Approximately 95% fee and charges reduction for all services	• 25–50% reduction to fees defined by the Medical Device User Fee Act (MDUFA), except for the Annual Establishment Registration Fee • 100% reduction to fees for some first applications for small businesses with gross receipts or sales of 30 million USD (MDUFA) • 100% reduction to fees for first biosimilar product application as defined by the Biosimilar User Fee Act (BsUFA) • 100% reduction to fees for first human drug application as defined by the Prescription Drug User Fee Act (PDUFA)
Incentives for small-sized enterprises	• 90–100% fee reduction (same for micro, small and medium-sized enterprises) • 40% fee reduction for post-authorisation activities (small and medium-sized enterprises only) • 60% fee reduction for pharmacovigilance services (small and medium-sized enterprises only)	• Approximately 65% fee and charges reduction for all services	

	EMA	ECHA	U.S. FDA
Incentives for medium-sized enterprises	• 90–100% fee reduction (same for micro, small and medium-sized enterprises) • 40% fee reduction for post-authorisation activities (small and medium-sized enterprises only) • 60% fee reduction for pharmacovigilance services (small and medium-sized enterprises only)	• Approximately 35% fee and charges reduction for all services	• No incentives for fees defined by the Generic Drug User Fee Act (GDUFA) and for fees defined by the Animal Generic Drug User Fee Act (AGDUFA) • 100% reduction to fees for first animal drug application as defined by the Animal Drug User Fee Act (ADUFA)

Sources: Commission Implementing Regulation (EU) 2015/864 (L 139/3–11), EMA (2016d, 8), EMA (2017c, 41–43), EMA (n.d.-e), FDA (2016a, 2016b, 2017a, 2017b), US Department of Health and Human Services et al. (2009, 8; 2017, 9–10)

As defined in Commission Regulation (EC) No 340/2008, the ECHA provides reduced fees and charges for micro, small or medium-sized enterprises. Unlike the EMA, the ECHA breaks its fees and charge reductions down by the size of the business, and they offer SME reductions for all of their services. In addition, micro-sized businesses and SMEs can receive further reductions in the case of some joint submissions (Commission Implementing Regulation (EU) 2015/864, L 139/3–11).

Commission Implementing Regulation (EU) 2015/864, the most recent amendment of Regulation (EC) No 340/2008, shows that medium-sized enterprises are eligible for a reduction of approximately 35 per cent of the total fees or charges, small enterprises for a reduction of approximately 65 per cent and micro-sized enterprises for a reduction of approximately 95 per cent (Commission Implementing Regulation (EU) 2015/864, L 139/3–11). Each of the current reductions is five per cent higher than those initially defined in Regulation (EC) No 340/2008. The ECHA justified the increase of the reductions as a result of financial gain made from incorrect SME company size declarations (ECHA 2015b).

Overall, the EMA offers SME incentives for many of their services and procedures and the ECHA for all their services, while the FDA provides significantly fewer reductions and exemptions. The provision of incentives can be seen as a strength of the ECHA and EMA fee systems when compared to the FDA. As shown in Table 9, the FDA does not distinguish between 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 (FDA 2016b). The maximum staff size is thus twice as high as that of the EMA and the ECHA. The FDA waives fees 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 per cent reduction to fees defined by the MDUFA, except for the Annual Establishment Registration Fee. There are no incentives for fees defined by the Generic Drug User Fee Act (GDUFA) or for fees defined by the Animal Generic Drug User Fee Act (AGDUFA)..

A particular strength of the EMA fee and remuneration system compared to the ECHA and the FDA is that it offers comparably high fee reductions and exemptions for several fees regardless of the size of the SME. Such reductions and exemptions include: 90 per cent reductions to the total applicable fee for scientific advice for non-orphan medicinal products, inspections, scientific services, and establishments, extensions or modifications of maximum residue limits for a veterinary medicinal product; and fee exemptions and reductions for a wide range of activities related to products eligible to the PRIME scheme as well as for designated orphan medicinal products[59] (EMA 2017c, 41–3; see also Table 8). The ECHA, by contrast, does not offer full fee exemptions at all, and fee reductions for small- and medium-sized enterprises are on average lower than EMA fee reductions for companies of the same size. However, as outlined above, ECHA fee reductions apply to all services, while the EMA only offers fee exemptions and reductions for selected services. As discussed in section 2.4, some respondents to the wider stakeholder survey indicated that fee incentives currently offered by the EMA are not sufficient; two SME respondents also noted that there should be more fee incentives for SMEs, for example fee reductions for marketing authorisations for non-orphan medicinal products.

[59] Fee reductions for designated orphan medicinal products are also available to companies regardless of their size, but both the number of different fee incentives for designated orphan medicinal products and their degree are higher for SMEs.

3. ASSESSMENT OF RELEVANCE

The relevance criterion refers to an assessment of the relationship between the EU intervention being evaluated and the needs and problems related to activities that fall within the remit of EMA. The assessment includes identification of any possible mismatch between the objectives of the intervention and existing needs or problems.

For this study, the problems and needs that the EMA fee and NCA remuneration system was designed to address were assessed and compared with existing needs and any problems identified to determine whether the fee system is still fit for purpose and if any changes are needed.

This chapter reports on the findings with regard to the study questions referring to relevance (Table 10).

Table 10: Study questions referring to relevance

Study question	Section in the report
Q7. 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?	Section 3.1
Q8. Is the fee system relevant in terms of current needs?	Section 3.2

3.1. Ability of the current fee system to address original problems and needs

In this section we report on the answers to the study question asking to what extent the fee system addresses the problems and needs originally identified to fund the relevant legislative tasks of the EMA, including NCA remuneration. This question is addressed by looking at: (A) the extent to which needs identified when the fee system was developed are addressed by the fee system.

Overall, the analysis showed that the current fee and remuneration system responds to needs originally identified at the time the fee system was established. In particular, the underlying legislation and the fee system itself address the requirement of a funding model based both on fee income paid by industry applicants and general EU and EEA contributions. The fee system provides for remuneration to NCAs for undertaking EMA-related activities, although the fee charged and remuneration provided are not cost-based across all activities. The study also found that the current fee system overall provides lower fees for activities for veterinary medicinal products; however, there are indications that such lower fees are not aligned with present needs. Alignment was found between the original requirement to offer incentives to respond to public or animal health threats and the current fee system.

More specifically, key findings relating to the ability of the current fee system to address original problems and needs are as follows:

F24. Overall, the fee and remuneration system addresses the problems and needs identified at the time of the establishment of the EMA as well as requirements set out in the main legislation for the fee and remuneration system. It considers the requirement to partially fund the EMA through fees collected from industry and EU/EEA contributions.

F25. The fee system provides for remuneration to NCAs for undertaking EMA-related activities. However, the study indicates that the current remuneration system is not cost-based across all activities and while it enables NCAs to cover their costs for procedural activities and for working groups and committees, it does not

cover all of the activities that NCAs consider to be EMA-related that they undertake.

F26. The current fee and remuneration system offers lower fees for veterinary medicinal products than for human medicinal products. However, there are indications that the lower fees are not aligned with present needs.

F27. The originally identified requirement to provide fee incentives to address public health or animal health threats is still relevant and in general met by the current fee system. Additional fee incentives introduced in later years indicate that the fee system responds to the requirement to allow fee reductions and exemptions under exceptional circumstances.

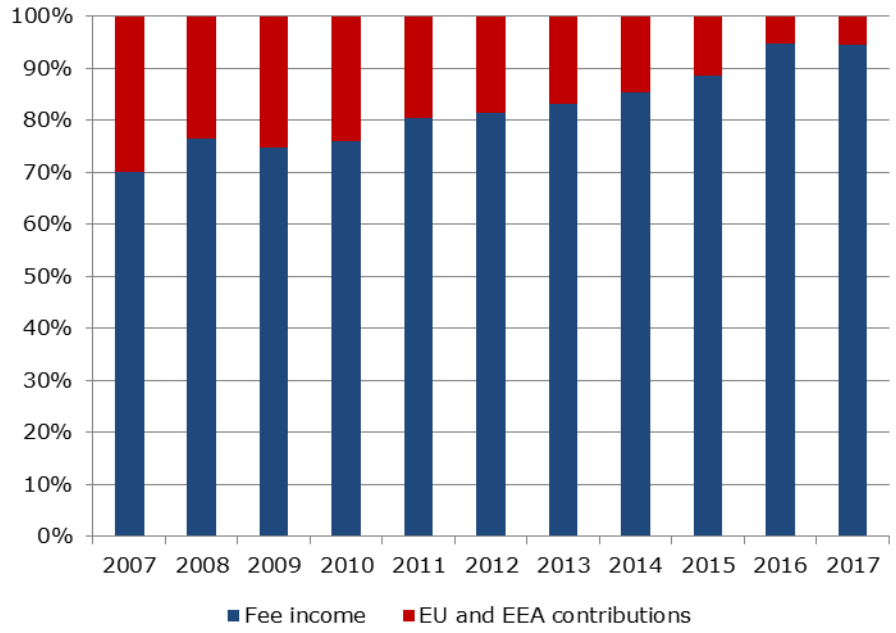
A. Overall, the fee system addresses needs identified when the fee system was developed.

Overall, the fee and remuneration system addresses the problems and needs identified at the time of the establishment of the EMA as well as requirements set out in the main legislation for the fee and remuneration system. It considers the requirement (Article 57 (1) of Council Regulation (EC) No 297/95) to primarily fund the EMA through fees collected from industry. The first legal document on the establishment of a centralised European authority and its network with national competent authorities is Council Regulation (EEC) No 2309/93, which indicates the necessity to enable centralised authorisation procedures for medicinal products for use in humans and food-producing animals in the European Community, and related to that the decision to found a European agency for the Evaluation of Medicinal Products ('the Agency').

The Agency should work in close collaboration with authorities in the Member States. Its main task should be to provide scientific advice, while Member States' main tasks should be to undertake authorisations and supervisions of medicinal products. Article 6 of the regulation stipulates that in order to place a medicinal product for human use on the European market, applicants should submit an application to the Agency, 'accompanied by the fee payable to the Agency for the examination of the application' (Council Regulation (EEC) No 2309/93, 134). Similarly, as determined in Article 28, applications for a marketing authorisation of a medicinal product are subject to a fee. Article 58 states that the Council shall create a structure as well as the amount of fees. The structure and amount of fees are also addressed in Article 70(1) of the 'founding regulation' of the EMA, Regulation (EC) No 726/2004, and were established through Council Regulation (EC) No 297/95 on general fees payable to the EMA, the implementing rules (EMA 2017d) and Regulation (EU) No 658/2014 on fees payable for pharmacovigilance activities.

Interviewed EMA and NCA representatives emphasised the importance of the fees to undertake EMA-related activities. The annual budget reports of the EMA from 2007 to 2017 also show the relevance of the fee income to the overall budget of the Agency. As shown in Figure 20, over the past ten years, the proportion of the fees of the revenues in the budget has steadily increased (except for 2009 and 2015) from 66.6 per cent in 2007 to 88.5 per cent in 2017 (EMEA 2006, 2007b, 2008, 2009a, 2011, 2012; EMA 2012b, 2013b, 2014b, 2015b, 2016b).

Figure 20: EMA budget division from 2007 to 2017



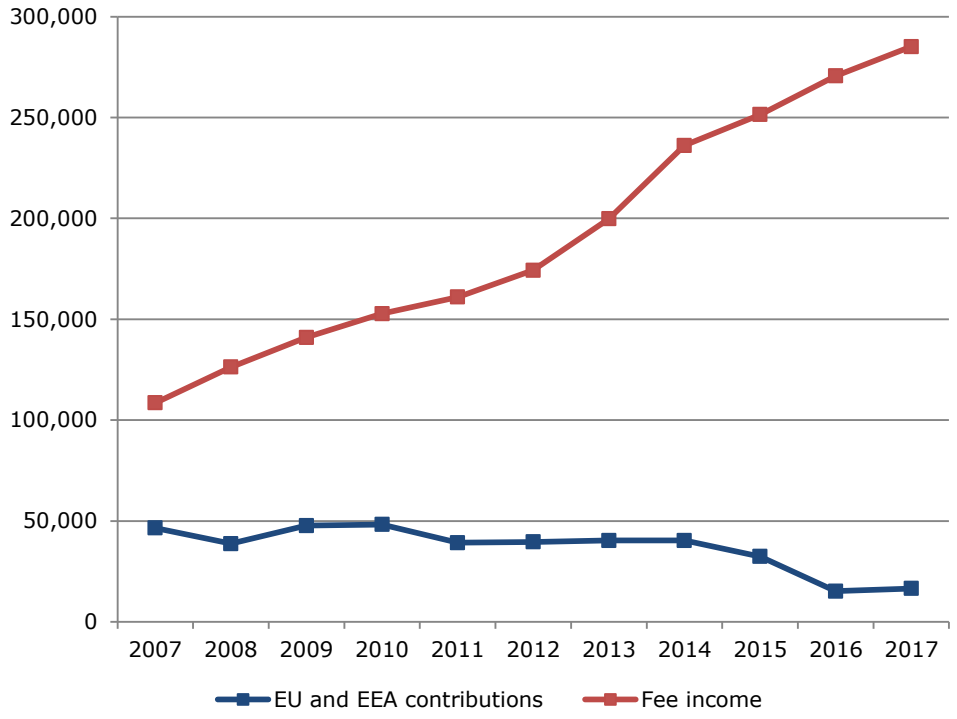
Sources: EMEA 2006, 2007b, 2008, 2009a, 2011, 2012; EMA 2012b, 2013b, 2014b, 2015b, 2016b

The fee system funds EMA-related activities through fees paid by industry and EU/EEA budget contributions. Article 57 of Council Regulation (EEC) No 2309/93 dealing with financial provisions as well as the revenue and expenditure of the Agency, provides that the 'revenues of the Agency shall consist of a contribution from the Community, and the fees paid by undertakings for obtaining and maintaining a Community marketing authorization and for other services provided by the Agency' (Council Regulation (EEC) No 2309/93, 158). The passage on the revenue structure is also cited in Council Regulation (EC) No 297/95, showing that it is still valid. Article 57 states that the revenue should be spent on staff, administration, infrastructure and other operational activities as well as on expenses for contracts with third parties, whereas 'Revenue and expenditure shall be in balance' (Council Regulation (EEC) No 2309/93, 158).

EMA interviewees confirmed the importance of a system based on fees paid by industry and EU/EEA contributions. The latter are found to be particularly important and still relevant, as they allow flexibility when it comes to funding activities and to counterbalance fee income fluctuations (see also section 2.1B). However, as shown in Figure 21, the total amount of EU and EEA contributions only slightly increased from 2011 (€39,204,000) to 2014 (€40,314,000), and decreased in the following years (2015: €32,435,315; 2016: €15,233,000; 2017: €16,523,000).[60] Similarly, EU and EEA contributions' proportion of the revenue (EU and EEA contributions and fee income combined) steadily decreased from 2007 to 2017 (except for 2009 and a slight increase in 2017) from 30 per cent in 2007 to 5.5 per cent in 2017 (EMEA 2006, 2007b, 2008, 2009a, 2011, 2012; EMA 2012b, 2013b, 2014b, 2015b, 2016b).

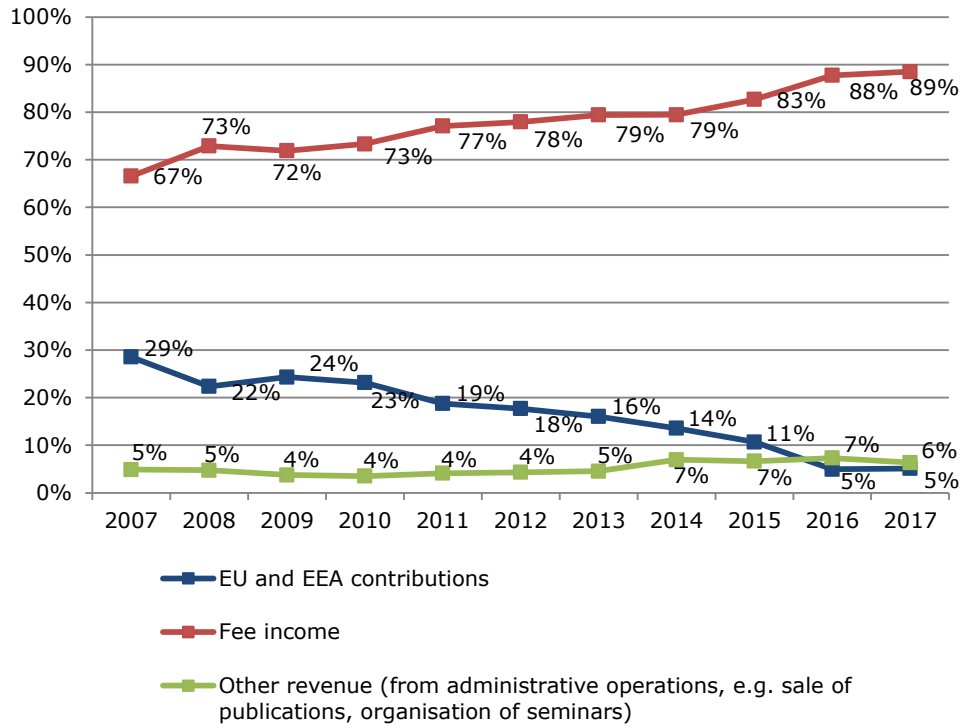
[60] EMA received additional income, predominantly made up of a one–off rent rebate due to exchange rate fluctuations, in 2016 so that smaller EU and EEA budget contributions were required to balance the EMA budget. The projected EU/EEA contributions for 2016 were €25,151,000 (published in December 2015, see EMA 2015b).

Figure 21: Total amount of EU and EEA contributions as well as fee income from 2007 to 2017 (in €1,000)



Sources: EMEA 2006, 2007b, 2008, 2009a, 2011, 2012; EMA 2012b, 2013b, 2014b, 2015b, 2016b

Figure 22: Percentage of EU and EEA contributions, fee income and other revenue of the overall EMA budget from 2007 to 2017



Sources: EMEA 2006, 2007b, 2008, 2009a, 2011, 2012; EMA 2012b, 2013b, 2014b, 2015b, 2016b

The fee system remunerates NCAs for undertaking EMA-related activities. However, NCAs are not remunerated for all of the EMA-related activities that they report undertaking. EMA-related activities undertaken by NCAs that are not remunerated include both legally required activities that are not remunerated and additional activities, which were reported through the NCA survey.

Article 53(1) of Council Regulation (EEC) No 2309/93 states that the relevant committee[61] shall appoint a rapporteur from one of the Member States' agencies and if applicable a co-rapporteur from a second agency. Article 53(3) notes that the Agency and the expert/rapporteur (or the rapporteur's national agency) should set up a written contract on the provision of services, which 'shall be remunerated in accordance with a fixed scale of fees to be included in the financial arrangements established by the Management Board' (Council Regulation (EEC) No 2309/93, 156). Article 11(1) of Council Regulation (EC) No 297/95 on general fees payable to the EMA addresses the decision to create rules for partial payment of the annual fees to NCAs undertaking EMA-related activities. The implementing rules (EMA 2017d) applicable to Council Regulation (EC) No 297/95 as well as the Annexes to Regulation (EU) No 658/2014 on fees payable for pharmacovigilance activities describe the amounts paid to NCAs for the respective activities covered by these two pieces of legislation.

EMA, NCA and wider stakeholder representatives agree overall regarding the need to remunerate NCAs for performing EMA-related activities. NCA representatives noted that remuneration is not always sufficient to cover the costs for remunerated procedural activities, and in most instances it is insufficient to fund unremunerated activities. This was confirmed through the modelling exercise for some procedural activities but in other cases the remuneration is more than sufficient to cover costs (e.g. variations) (see also findings in section 2.1 and 2.3).

They also indicated imbalance between the amount of fees and the services they provide; this finding suggests that the requirement set out in Council Regulation (EC) No 297/95, stating that 'the calculation of the amount of fees charged by the Agency must be based on the principle of the service actually provided', is currently not met in all instances. Wider stakeholders (across stakeholder groups) also referred to fees for some EMA services which do not match the provided services (e.g. fees for variations (type IA, single and grouped type II), annual fees for MUMS, fees for initial scientific advice requests, general maintenance fees, post-authorisation measures (PAMs) comprising submissions of a single report, fees for transfer of a MAH, fees for changing the local representative, fees for changing Detailed Descriptions of the Pharmacovigilance System (DDPS), and fees for products for emergency purposes). This perception was confirmed by our estimates resulting from the modelling exercise (see also findings in section 2.1 and section 2.4 for specific activities).

The current fee and remuneration system offers lower fees for veterinary medicinal products than for human medicinal products. However, there are indications that these lower fees are not aligned with present needs. Council Regulation (EC) No 297/95 states that differences in the markets for veterinary medicinal products and human medicinal products justify general fee reductions for the veterinary sector. The current fee structure provides lower fee levels for veterinary medicinal products, as compared to fee levels for human products; for example, the fee for a full application for products for human use is €282,100, while that for products for

[61] Committee for Proprietary Medicinal Products, today: Committee for Medicinal Products for Human Use (CHMP); or Committee for Veterinary Medicinal Products, today: Committee for Medicinal Products for Veterinary Use (CVMP).

veterinary use is €141,300 (EMA 2017d, 26, 30). Some NCA and EMA representatives noted that significantly lower fees for veterinary medicinal products do not reflect the workload and complexity of services provided. By contrast, some wider stakeholder respondents (large pharmaceutical company, SME and industry organisation representatives) emphasised that the fee system should remain proportionate to the size of the veterinary sector market.

The quantitative analysis shows that the EMA share of fee income for veterinary procedural activities is not sufficient to match the EMA staff costs of these activities and there is some funding of veterinary activities by other fee income for procedural activities (section 2.1, Table 3 and Figure 11). For NCAs, remuneration for veterinary procedural activities covers costs, within the accuracy of the modelling, and definitely does so when annual fees are taken into account (section 2.1, Figure 12). However, there is little funding available for additional, unremunerated activities. For NCAs undertaking activities for both human and veterinary medicines, human medicine income can be used to fund veterinary activities. This is not the case for NCAs that only carry out activities related to veterinary medicines. For four of these NCAs, remuneration did not cover total costs. Moreover, in 2014, a proposal for a new regulation on veterinary medicinal products was published (Proposal Regulation COM(2014) 558). This new regulation should address issues related to veterinary medicines which are not met by the current legislation, such as to deliver a single market in veterinary medicines and meet current regulatory requirements. As it is likely that the new regulation will introduce new or changed procedures – including potentially additional unremunerated activities – covering all costs may become even more challenging for NCAs undertaking activities for veterinary medicines.

The originally identified requirement to provide fee incentives to address public health or animal health threats is still relevant and in general met by the current fee system. Additional fee incentives introduced in later years indicate that the fee system responds to the requirement to allow fee reductions and exemptions under exceptional circumstances. Article 9 of Council Regulation (EC) No 297/95 states that the Executive Director may grant – after consulting with the relevant scientific committee – fee reductions 'in exceptional circumstances and for imperative reasons of public or animal health' (Council Regulation (EC) No 297/95, Article 7(1)). Such reductions should be decided on a case-by-case basis. Wider stakeholders and EMA representatives indicated that fee reductions in emergency cases are still relevant. However, an industry respondent noted that fixed incentives instead of case-by-case assessments would be preferred. Article 9 of Council Regulation (EC) No 297/95 in its currently applicable wording states that 'A total or partial exemption from payment of the fees laid down in this Regulation may be granted, in particular for medicinal products for treating rare diseases or diseases affecting minor animal species or for extension of existing MRLs to additional animal species or for medicinal products available for compassionate use'.

Since 2005, the EU has introduced additional incentives for micro-sized businesses and SMEs (Commission Regulation (EC) No 2049/2005), medicinal products for paediatric use (Regulation (EC) No 1902/2006), advanced therapy medicinal products (Regulation (EC) No 1394/2007) and reductions for academic sector applicants in the case of scientific advice requests for PRIME products (EMA 2016d).

3.2. Relevance of the fee system in relation to current needs

This section describes answers to the study question relating to the relevance of the fee system in terms of current needs by looking at: (A) whether needs identified by EMA, NCAs and stakeholders as relevant currently are addressed by the fee system.

While the fee and remuneration system is still relevant in relation to originally identified needs, the study identified problems that are currently not taken into account. In particular, there are indications that the fee and remuneration system does not consider increasing complexity of the regulatory system as well as of activities, which might have an impact on EMA's and NCAs' ability to meet their costs in the future.

More specifically, key findings related to the relevance of the fee system with respect to current needs are as follows:

F28. There is no need for a dispute settlement procedure between the EMA and industry.

F29. The current fee and remuneration system does not address current and future needs regarding changing requirements and increasing complexity of activities, and particularly the increasing complexity of procedures related to innovative medicines.

F30. The current fee and remuneration system does not consider potential future changes related to proposed changes to the EMA legislation, such as a new regulation on veterinary medicinal products (Proposal Regulation COM(2014) 558) and potential changes to the orphan and paediatric medicines legislation (Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006; see European Commission (2017)).

A. The current fee system does not require a dispute settlement procedure. However, there are other needs identified by EMA, NCAs and stakeholders as relevant.

There is no need for a dispute settlement procedure between the EMA and industry. The consultation activities of this study also sought to find out whether there is a need for a procedure to mediate between the EMA, NCAs and industry, similar to ECHA's dispute settlement procedure (ECHA n.d.). While EMA interviewees agreed that payers sometimes have queries, issues raised are usually quickly clarified. According to EMA interviewees, most of the concerns are related to the complexity of the fee system. EMA interviewees were not aware of any disputes between the EMA and NCAs, and none of the interviewees indicated a need for a dispute settlement procedure. Similarly, responses to the open public consultation showed that there is no need for such a procedure. Only one respondent, a member of an industry organisation, indicated a need for a dispute settlement procedure. They explained that they think that the EMA is not always objective when deciding the amount of fees charged. The respondent did not provide any suggestions for an appropriate form of a dispute settlement procedure.

The current fee and remuneration system does not consider current and future needs regarding changing requirements and increasing complexity of activities. In particular, increasing complexity of procedures related to innovative medicines are not reflected. EMA interviewees noted that they have observed increasing complexity of coordination activities in the past years. While the current financial model enables the EMA to fund activities exceeding the expected unitary costs, interviewees raised 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. As outlined in section 3.2B, such increasing complexity is for instance observed in fields where already a high number of products have been approved. Assessments of applications for a product in these fields have become increasingly complex, as EMA and NCA experts need to consider already approved products in their review in order to ensure consistency in approvals. 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.

NCAs also indicated that the workload and time needed for the same type of activity can vary significantly. An interviewee provided the example of renewal procedures for marketing authorisations under exceptional circumstances (Article 14(8) of Regulation (EC) No 726/2004), which they argued are more work-intensive than regular renewals. As noted by NCA representatives, the current fee system neither provides sufficient flexibility in such cases (e.g. through increasing the remuneration) nor reflects general increases in complexity (see also section 2.5).

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. Interviewees referred to very innovative products without clinical data or that have insufficient data, which would require more time to assess than regular products (and therefore cost more for the NCA), as assessors cannot build on existing data or previous reviews, and NCA staff need to gain the right skills to be able to assess these products. Another example relates to changes in how products are approved: as NCA representatives noted, personalised medicine or complex molecules will not only change the way medicines are developed, but will also change approval processes. For example, an interviewee explained that they 'used to have a single indication for a product and now […] they may have 30 or more'. Other areas where increasing complexity is expected include control activities for medicinal products (including falsified medicinal products, see Directive 2011/62/EU), big data, analysis of real-world data and patient experience data (including how to address differences in data standardisation), health technology assessments[62] and companion diagnostic reviews. In the veterinary medicine sector, increasing complexity is also expected in activities related to monoclonal antibodies and stem cells.

The current fee and remuneration system does not consider potential future changes related to proposed changes to the EMA legislation.[63] Changes include a new regulation on veterinary medicinal products (Proposal Regulation COM(2014) 558) and a new regulation for orphan and paediatric medicines (Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006; see European Commission (2017)). The new regulation on veterinary medicinal products may introduce new procedures, of which some might not be remunerated, which could have an impact on veterinary medicine NCAs' ability to meet their costs. The legislation for orphan and paediatric medicines will be evaluated and, potentially, amended to meet current needs and address challenges related to these types of medicines and their regulation. The evaluation will include an assessment of current incentives, and may result in an update of them. Any changes to the legislation may thus result in changes to the available budget for the EMA and NCAs as well as in additional challenges to meet EMA-related costs.

[62] See Proposal Regulation COM(2018) 51 for a proposal on health technology assessment and amending Directive 2011/24/EU.

[63] Changes related to the veterinary legislation were not within scope of the current study. The current study presents veterinary data based on the existing fee system.

4. ASSESSMENT OF COHERENCE

Coherence refers to how well or not different aspects of a system work together (e.g. to achieve common objectives). This can take place at several levels, including: i) internally, ii) with other EU interventions, and iii) with non-EU related aspects.

In this study, the assessment of fee system coherence focuses: i) internally (e.g. fee structure, remuneration levels), ii) nationally, with Member State fee systems, and iii) at EU level, with other EU policies and programmes.

This chapter reports on the findings with regard to the study questions referring to coherence (Table 11).

Table 11: Study questions referring to coherence

Study question	Section in the report
Q9. To what extent is the fee system coherent internally?	Section 4.1
Q10. To what extent is the fee system coherent with Member State fee systems?	Section 4.2
Q11. To what extent is the fee system coherent at EU level with other EU policies?	Section 4.3

4.1. Internal coherence of the fee system

This section provides answers to the study question relating to the internal coherence of the fee system by looking at: (A) the internal coherence of the fee system in terms of the fees charged; (B) internal coherence of the fee system in terms of the remuneration provided; and (C) internal coherence of the fee system in terms of the Agency's strategy and objectives.

Broadly, the fees charged for procedural activities align with the costs for undertaking the activities.

However, as noted elsewhere, the fee system is not cost-based at the level of specific activities and this contradicts Council Regulation (EC) No 297/95 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'. Additionally, it does not take into account changes since 2005 resulting from additional legislation. More specifically, key findings are as follows:

F31. Overall, Council Regulation (EC) No 297/95 and the implementing rules (EMA 2017d) are internally coherent. However, the study identified minor aspects of incoherence between the documents.

F32. Regulation (EU) No 658/2014 and Council Regulation (EC) No 297/95 on the general fees payable are internally coherent.

F33. The EU legislation on fees is complex and would benefit from streamlining.

F34. The study did not find any incoherence regarding the fee system, remuneration provided and the legislation determining the remuneration to NCAs.

F35. Overall, the fee system is coherent with the EMA's strategy and objectives. However, there are some areas where more coherence is needed: flexibility in the case of pharmacovigilance activities, financing of innovation-related activities, and efficiency and cost-effectiveness.

A. There are elements of internal incoherence of the fee system in terms of the fees charged.

Broadly, the fees charged for procedural activities align with the costs for undertaking the activities. Average cost-based fees as calculated in section 2.1 could help to redress the imbalance between individual fees and between the fees retained by EMA and those remunerated to NCAs to bring the fee system more in line with Council Regulation (EC) No 297/95, which indicates that 'the calculation of the amount of the fees charged by the Agency must be based on the principle of the service actually provided' (Council Regulation (EC) No 297/95, 2). Additional revenue would be required, however, to enable EMA and NCAs to meet their costs under this fee system as discussed in section 2.1.

For NCAs in total, the costs of procedural activities do not exceed the remuneration for these activities (section 2.1, Figure 12). At the activity level, costs are not aligned with remuneration for NCAs, with fees for some activities financing the costs of others (section 2.1, Figure 5 and Figure 6). In particular, for human medicines, costs exceed remuneration for initial marketing authorisations, while fees exceed remuneration for type II variations. The misalignment is less pronounced for veterinary activities. When modelling average cost pricing however, although total NCA costs are calculated to be recovered for each activity, this is not the case for all individual NCAs (section 2.1, Figure 13).

The EMA fee system approach to the level of the fees distinguishes EMA from ECHA's and EASA's approaches, which can change the level of their fees based on the costs they need to cover. As stated in regulations on fees and charges payable to ECHA – most recently in Commission Implementing Regulation (EU) 2018/895 – 'the structure and amount of the fees provided for in that Regulation shall take account of the work required to be carried out by the European Chemicals Agency ('the Agency') 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 the Agency's revenue is sufficient to cover the cost of the services delivered' (Implementing Regulation (EU) 2018/895, L160/1). Similarly, Commission Regulation (EU) No 319/2014 stipulates that EASA's 'tariffs need to be adjusted in order to ensure a balance between the costs incurred by the Agency for related certification tasks and services provided, and the revenues to cover said costs' (Commission Regulation (EU) No 319/2014, L 93/58).

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' (ECHA 2018). The revision brought increased fees for each additional use covered by an application, but fees for additional applicants were removed to encourage joint applications.

Overall, Council Regulation (EC) No 297/95 and the implementing rules (EMA 2017d) are internally coherent. However, the study identified minor aspects of incoherence between the documents. The review of the general Fee Regulation and its related implementing rules showed that there are some inconsistencies in the wording used in the documents. Council Regulation (EC) No 297/95 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' (Council Regulation (EC) No 297/95, 2). The implementing rules to the Fee Regulation (EMA 2017d), however, uses 'applicable full fee' to describe initial application fees. Council Regulation (EC) No 297/95 also sets out that 'a ceiling should be established' for the fees for each additional strength and/or pharmaceutical form; the study team could not find any specification of such limits in the implementing rules.

Council Regulation (EC) No 297/95 describes cases for which reduced fees for applications should be made. For example, reductions may be granted 'for applications concerning a medicinal product for use in non-food producing animals' (Council Regulation (EC) No 297/95, 2). In the past years, EMA's policy on incentives for veterinary medicines has undergone several adaptations, most recently in June 2013, when the EMA restricted fee incentives to products for food-producing animals only (EMA 2013c; see also related revised policy: EMA 2014f). These changes are not aligned with the existing Fee Regulation.

Regulation (EU) No 658/2014 and Council Regulation (EC) No 297/95 on the general fees payable are internally coherent. Unlike Council Regulation (EC) No 297/95, Regulation (EU) No 658/2014 is not complemented by implementing rules. Instead, Regulation (EU) No 658/2014 includes the rules for fees, the fees to be charged to industry as well as the share of fees for rapporteurs and co-rapporteurs. According to an EMA interviewee, the decision to not complement the regulation with implementing rules was justified by the aim to reduce administrative burdens and to make the regulation as simple as possible. Regulation (EU) No 658/2014 also includes detailed information on exemptions from payment and the amount of fees for micro-sized enterprises and SMEs. By contrast, exemptions for micro-sized enterprises and SMEs are not addressed in Council Regulation (EC) No 297/95 at all, but are listed in the implementing rules and in Commission Regulation (EC) No 2049/2005.

EMA and NCA representatives interviewed for this study indicated that, overall, the pharmacovigilance legislation is very clear and fulfils the aim to simplify the fee system. However, as discussed in section 2.5, EMA representatives prefer a combination of fee regulations and implementing rules, as such a fee system enables more flexibility regarding fee reductions and exemptions under exceptional circumstances. As Regulation (EU) No 658/2014 is not combined with implementing rules but sets out fees and rules for exemptions in the regulation itself, any adaptions responding to exceptional circumstances would require a change to the overall legislation.

The EU legislation on fees is complex and would benefit from streamlining. Council Regulation (EC) No 297/95 has not been amended since 2005. Since then, new legislation has been introduced including Regulation (EC) No 1902/2006 on medicinal products for paediatric use, Regulation (EC) No 1394/2007 on advanced therapy medicinal products and Commission Regulation No 2049/2005 on incentives for micro-sized enterprises and SMEs. 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' (EMA n.d.-d). The scheme offers fee reductions for scientific advice requests for micro enterprises and SMEs as well as applicants from the academic sector (EMA 2016d). Some EMA representatives indicated that they would prefer an overall revision of all legislative documents and consolidating them into one coherent piece of legislation.

B. There is no evidence of internal incoherence of the fee system in terms of the remuneration provided

The study did not find any incoherence 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 Council Regulation (EC) No 297/95, the implementing rules (EMA 2017d) and Regulation (EC) No 726/2004 did not show any incoherence.

The remuneration of NCAs was first addressed in Article 11 of Council Regulation (EC) No 297/95, which stipulates that the EMA Management Board shall, based on 'a proposal from the Executive Director and following a favourable opinion from the Commission […] fix the rules for repaying a part of the resources deriving from the annual fees to the competent national authorities in Community market supervision'. According to the implementing rules, 30 per cent of the annual fees are distributed to rapporteurs and co-rapporteurs (i.e. 15 per cent for each), 30 per cent to the EMA to cover staff costs for pharmacovigilance and inspection activities, 30 per cent to special activities, which shall be 'determined by the Management Board, in consultation with the Agency's scientific committees' (EMA 2017d, 25), and (up to) 10 per cent are attributed to the sampling and testing of centralised products.

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 per cent of the fees. The scale of fees as outlined in the implementing rules corresponds with Article 62(3) of Regulation (EC) No 726/2004, which states that 'The provision of services by rapporteurs or experts shall be governed by a written contract between the Agency and the person concerned, or where appropriate between the Agency and his employer. The person concerned, or his employer, shall be remunerated in accordance with a scale of fees to be included in the financial arrangements established by the Management Board'. However, although EMA interviewees noted that NCAs receive the full share of the fee for activities related to the general Fee Regulation regardless of exemptions or reductions, as outlined in section 2.1, most NCA interviewees noted that they do not receive remuneration for some activities, such as orphan designated or paediatric medicines or in cases of incentives for SMEs.

4.2. External coherence of the fee system with Member State fee systems

This section presents answers to the study question relating to the external coherence of the fee system with Member State fee systems by looking at: whether (A) the fee system is consistent with and does not overlap with national fees.

The analysis of the alignment of the EMA fee system with Member State fee systems showed that the EMA fee system is coherent with Member State fee systems.

More specifically, key findings relating to the external coherence of the fee system with Member State fee systems are as follows:

F36. There is no evidence regarding an overlap or gaps between fees for EMA-requested activities and fees charged for national activities.

F37. The study showed that national-level fee systems and the EMA fee and remuneration system differ in their financing structures and in the amount of fees charged. Considering the complexity of the EMA fee system resulting from its size and scope, EMA's comparatively higher fees are considered to be fair.

A. The EMA fee system is consistent with and does not overlap with national fee systems

The study question on the external coherence of the EMA fee system with Member State fee systems was mainly answered using views of EMA, NCA and wider stakeholder representatives gained through interviews and surveys. It does not include any review of legislation or policy documents on the Member States' fee systems, nor does it provide information on national priorities not mentioned by the consultees.

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-requested activities do not overlap with fees charged for national activities. A review of the Fee Regulation (Council Regulation (EC) No 297/95) and implementing rules (EMA 2017d) by the study team does not indicate any potential overlaps between EMA and national fees. In the case of the pharmacovigilance legislation, Regulation (EU) No 658/2014 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 (Regulation (EU) No 658/2014, L 189/113).[64] NCA interviewees confirmed that there is no double-charging for the activities regulated by Council Regulation (EC) No 297/95 nor pharmacovigilance activities.

The study showed that national-level fee systems and the EMA fee and remuneration system differ in their financing structures and in the amount of fees charged. Several NCA interviewees indicated that their national fee systems and the EMA fee system are different in how they are financed. At least some national fee systems uses real costs of activities to determine the fees, while the EMA uses a fee that is not based on costs and does not consider individual differences of NCAs (e.g. living costs). Another example provided was the basis of the annual fee in national fee systems, which is annually adapted to turnover in at least one Member State. By contrast, the EMA's annual fees do not consider turnover of the Agency. Other interviewees also reported that their fee systems do not include annual fees at all. NCA representatives indicated that differences between national fee systems and the EMA fee system with respect to the structure, financing and underlying legislation do not hinder the effective conduct of EMA-related activities.

Both NCA representatives and wider stakeholders reported differences between the EMA fee system and national fee systems regarding the amount of fees charged to industry, indicating that EMA fees are in general higher. **However, considering the complexity of the centralised system as a result of its size and scope (i.e. approval of a product in 31 countries), EMA's higher fees are considered to be fair.** As noted by several respondents to the NCA survey, the current fees charged by the EMA are appropriate, as authorisations provide access to the overall EU population of more than 510 million people. NCA representatives also indicated that they find some fees (e.g. for scientific advice, annual fees) too low considering the size of the market. Several wider stakeholders (i.e. a large pharmaceutical company, an SME and industry organisation representatives) commented that EMA fees are significantly higher than those charged by national authorities; however, many large pharmaceutical company respondents noted that higher fees are reasonable considering the complexity of the regulatory system and the size and scope of the market.

4.3. External coherence of the fee system at EU level

This section summarises answers to the study question relating to the external coherence of the fee system at EU level with other EU policies by looking at: (A) the coherence of the fee system with requirements set out in other EU policies.

Overall, the study found that there is external coherence of the fee system with priorities set out in other EU policies analysed for this study.

[64] Based on a previous recommendation in Proposal Regulation COM(2013) 472, which suggested that fees charged for 'the activities performed at national level […] should, however, not overlap with the fees laid down in [Proposal Regulation COM(2013) 472]' (Proposal Regulation COM(2013) 472, 2)

More specifically, key findings relating to the external coherence of the fee system at EU level are as follows:

F38. Overall, the EMA fee system is coherent with the third EU health programme (2014-2020). It shows strong synergies with the programme's four main objectives.

F39. The current EMA fee system is coherent with the priorities set out in the Strategic Plan of DG Health & Food Safety for 2016 to 2020.

F40. The current EMA fee system is coherent with EU policy on the support of micro, small and medium-sized businesses.

A. Overall, the fee system is coherent with requirements set out in other EU policies

EMA, NCA and wider stakeholder representatives did not report any inconsistencies between the EMA fee system and other EU policies. The following analysis on the coherence of the EMA fee system with requirements set out in other EU policies is based on a review of the following EU policies:

- Third EU health programme (2014-2020), in particular requirements set out in Regulation (EU) No 282/2014.
- DG Health & Food Safety's Strategic Plan 2016-2020 (DG Health & Food Safety 2016).
- EU policy on the support of micro, small and medium-sized enterprises:
  - Commission Communication COM(2008) 394.
  - Commission Recommendation 2003/361/EC.

Overall, the EMA fee system is coherent with the third EU health programme (2014-2020). The European Union's third health programme for the years 2014 to 2020 is considered the main initiative of the European Commission to implement the EU's health priorities. Article 12 of Regulation (EU) No 282/2014 specifies that the programme shall be aligned with and complementary to other EU policies, actions and instruments as well as those of EU agencies. The programme has four specific objectives:

- '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' (Regulation (EU) No 282/2014, L 86/6–7).

The study found general coherence between the EMA fee system and the four main objectives. In particular, the first objective on the promotion of health, disease prevention and advancement of supportive environments for healthy lifestyles is addressed by the EMA's overall mission, 'to foster scientific excellence […] for the benefit of public and animal health in the European Union (EU)' (EMA, n.d.-f). Similarly, the main legislative documents of the EMA fee system – Council Regulation (EC) No 297/95, its implementing rules (EMA 2017d) and Regulation (EU) No 658/2014 – 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. In addition, pharmacovigilance activities of the EMA and its related reductions for specific medicinal products, therapies and micro-sized businesses and SMEs are aligned with the first objective (Regulation (EU) No 658/2014).

Council Regulation (EC) No 297/95 and its implementing rules (EMA 2017d) are consistent with the second objective of the third EU health programme, as they support fee exemptions and reductions in emergency cases such as threats to public and animal health. As outlined in the implementing rules, total fee exemptions are granted for core dossier medicinal products to be used in human pandemic situations (EMA 2017d, 38).

The aim to support public health capacity-building of the programme's third objective is aligned with 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). In addition, centralised procedures for the marketing authorisation of medicinal products underpin the priority to enhance public health capacity-building as well as to support efficiency and sustainability of health systems. The EMA's PRIME scheme – including its related fee reductions for micro-sized enterprises, SMEs and academic sector applicants – is an additional initiative to support innovative health systems.

In 2010, the first legislation on the renewal and extension of pharmacovigilance activities was adopted (Directive 2010/84/EU and Regulation (EU) 1235/2010). This was complemented by Commission Implementing Regulation (EU) No 520/2012 on the performance of pharmacovigilance activities, Regulation (EU) No 1027/2012 amending Regulation (EC) No 726/2004 as regards pharmacovigilance, and Directive 2012/26/EU amending Directive 2001/83/EC as regards pharmacovigilance in 2012. In 2014, EMA's new pharmacovigilance legislation was completed by Regulation (EU) No 658/2014 on fees for pharmacovigilance activities. The new pharmacovigilance legislation is aligned with the fourth main objective of the third EU health programme, to enable access to better and safer healthcare. In particular, the legislation's simplified fee structure and its related fee incentives (see also section 2.4) are indicators that the EMA fee system is aligned with this objective.

The current EMA fee system is coherent with the priorities set out in the Strategic Plan of DG Health & Food Safety for 2016 to 2020. DG Health & Food Safety has identified strategies to address challenges related to public health in its most recent strategic plan. The strategies should support the overall mission of DG Health & Food Safety, to:

- 'Improve and protect human health, and support the modernisation of Europe's health systems;
- Ensure that all food, feed and medicinal products marketed in the EU are safe and that EU
- standards are promoted globally;
- Protect animal health and welfare and plant health; and
- Contribute to a well-functioning and fair internal market in food, feed, agricultural and medical products.' (DG Health & Food Safety 2016, 4).

Aligned with that mission, three general objectives and related specific objectives were defined in the strategic plan. The study team compared the following specific objectives against the EMA fee system:[65]

- 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 (DG Health & Food Safety 2016, 13–24).

Specific objective 1.1 includes the aim to tackle cross-border health threats related both to human and animal health, showing coherence with objective 2 of the third EU health programme, 'to protect Union citizens from serious cross-border health threats' (Regulation (EU) No 282/2014, L 86/6). As demonstrated above in the discussion of the EMA fee system's alignment with the third EU health programme, the current fee system includes adequate measures including fee incentives to address threats to public health, including cross-border health problems.

Specific objective 1.4 addresses the aim to promote innovation in healthcare, as also outlined in the European Commission's Digital Single Market Strategy (Commission Communication COM(2015) 192). 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 the 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.

One of the key priorities related to specific objective 1.7 is to contribute to harmonisation in the pharmaceutical sector. As outlined above in relation to the third objective of the third EU health programme, this objective is aligned with the EMA fee system and particularly the overall mission of the EMA (Regulation (EC) No 726/2004, L 136/1).

Specific objective 2.1 relates to the aim to use HTA to ensure more effective and safer assessments of medicinal products. While 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 bodies since 2008 and intends to increase such engagement (EMA n.d.-c; HMA & EMA 2015, 9).

Specific objective 2.2 outlines the aim to ensure high standards regarding safety and quality of medicinal products on the European market as well as to provide European citizens access to new and innovative products and services. The objective directly addresses the EMA, indicating that it would introduce the PRIME scheme in 2016 to reach this goal. The implementation of the PRIME scheme in 2016 and related fee incentives show that the current fee system is coherent with specific objective 2.2 of DG Health & Food Safety's strategic plan.

[65] The analysis only included objectives that showed direct relevance to the EMA's fee and remuneration system.

The current EMA fee system is coherent with EU policy on the support of micro, small and medium-sized businesses. EU policy on research and innovation is characterised by its strong focus on the support of smaller businesses. The main policy documents addressing micro-sized enterprises and SMEs are the European Commission's Communication on a 'Small Business Act' for Europe (Commission Communication COM(2008) 394) and Commission Recommendation 2003/361/EC on SME size definitions. As outlined in Commission Communication COM(2008) 394, the European Commission considers SMEs to be important players to ensure employment as well as to sustain and support wellbeing of EU citizens. The document sets out principles to ensure SME support, which should be implemented in both Member State and EU policies, such as: the creation of an SME-friendly environment, financial incentives, administrative support to SMEs, enabling SMEs' participation in public procurement, and implementing measures to build up SME skills and support innovation.

Commission Regulation No 2049/2005 defines the rules regarding fee reductions and exemptions for EMA services, and outlines administrative support measures offered to micro enterprises and SMEs. The regulation sets out the main aim to enhance innovation and support the development of medicinal products by SMEs, which is strongly aligned with the principles defined in Commission Communication COM(2008) 394. Besides fee incentives for a wide range of EMA services, the regulation also includes measures to provide SMEs with administrative services, such as the establishment of an SME office, workshops and training sessions as well as the publication of a User Guide for SMEs (see EMA 2017a and SME Office 2016).

As discussed in section 2.6 on SME support, the fee incentives can be found in the EMA's main legislation as well as other documents related to SME support (e.g. implementing rules for Council Regulation (EC) No 297/95 (EMA 2017d); Regulation (EU) No 658/2014; PRIME-related documents such as EMA 2016d; EMA 2017a; SME Office 2016), and thus show coherence with EU policy on the support of micro enterprises and SMEs.

5. ASSESSMENT OF SUSTAINABILITY

The sustainability criterion refers to the likelihood that an intervention will succeed over time. This study focused on the extent to which the fee system is based on costs, taking into account the need to finance some activities (i.e. reductions and exemptions), cross-cutting activities and the needs of the EMA and NCAs to meet evidence-based trends. The assessment includes analysis of the fee system's flexibility to adjust to changing trends.

This chapter reports on the findings with regard to the study question referring to sustainability (see Table 12).

Table 12: Study question referring to sustainability

Study question	Section in the report
Q12. To what extent does the current financial model ensure the financial stability of the EMA including its ability to remunerate NCAs?	Section 5.1

5.1. Financial stability of the EMA

This section outlines answers to the study question relating to the sustainability of the current fee system by looking at: (A) the correspondence of fees charged with EMA costs and remuneration provided with NCA costs; and (B) the extent to which the total fees earned enable the EMA to meet its costs, taking into consideration the availability of EU and EEA contributions within the seven-year ceiling.

The study found that the current fee system has important elements that contribute to its sustainability. In particular, the flexibility to fund unremunerated activities, as well as incentives for specific medicinal products and SMEs are considered to be essential. However, the study also identified elements of the fee system that create challenges for its long-term sustainability.

Specifically, key findings relating to sustainability are as follows:

F41. The current fee system enables EMA and NCAs overall to meet their costs for procedural activities, although some flexible funding across procedures is needed where incentives and exemptions are applied.

F42. The current fee system enables both the EMA and NCAs to undertake cross-cutting activities. This characteristic of the fee system is considered an important element of the fee system which should be maintained in order to ensure its sustainability (see also findings F7, section 2.2, and F16, section 2.5).

F43. However, the current financial model does not enable NCAs to cover all costs for undertaking cross-cutting activities. The remuneration and payments provided to NCAs are not sufficient to compensate for all costs of EMA-related activities (see also finding F9, section 2.3).

F44. The current fee system does not address the increasing complexity of existing and new procedures (e.g. specialised/personalised medicine).

F45. Exemptions and reductions for SMEs and exemptions for specific products and procedures (e.g. orphan medicinal products, medicinal products for paediatric use, advanced therapy medicinal products) are considered to be important elements of the current fee system and contribute to the fee system's

sustainability. Such incentives enable relevant stakeholders who otherwise might not be able to use the centralised system to do so (see also finding F21, section 2.6).

F46. Increased transparency in areas highlighted in finding F14 (see section 2.4) would contribute to more sustainability of the fee system.

F47. Proposed changes to the EMA legislation, such as a new regulation on veterinary medicinal products (Proposal Regulation COM(2014) 558) and potential changes to the orphan and paediatric medicines legislation (Regulation (EC) No 141/2000 and Regulation (EC) No 1901/2006; see European Commission (2017)), could affect the fee system in the future.

A. Overall, fees charged correspond with costs for procedural activities

The current fee system enables both the EMA and NCAs overall to meet their costs for procedural activities and also to undertake cross-cutting activities, which is considered to be important to ensure the fee system's sustainability (see section 2.1). The study has shown that the current financial model and its underlying legislation enable the EMA and the NCAs to undertake cross-cutting activities, and hence to fund activities that are not directly covered by a fee. As outlined in section 2.2, 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 and EEA contributions additionally 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. EU and EEA contributions also ensure that all participating groups – industry stakeholders, EMA and NCAs – can expect that their objectives and work are not affected by fee income fluctuations, as noted in the 2010 evaluation of the EMA (Ernst & Young 2010, 112). While a fee-for-service system could contribute to a fairer fee system, EMA representatives raised concerns that a cost-based fee system limited to procedures only could make the fee system less flexible and as a consequence also less sustainable.

The quantitative analysis shows that under the current financial model other tasks undertaken by EMA are funded by both fee income for procedural activities and EU/EEA budget contributions (section 2.1, Figure 11). **According to EMA interviewees, the current financial system of fee income and general budget is sustainable and sufficient in order to continue their work in its present form.**

NCA representatives consulted for this study agree with EMA interviewees that some flexibility of funding is a vital element of the fee system. **However, all interviewed NCA representatives as well as most of the NCA survey respondents indicated that they are not able to fund in this way all of their EMA-related activities with payments received from the EMA** (see also section 2.3).

The quantitative analysis shows that for NCAs, there is some flexible funding of costs by remuneration at the activity level (section 2.1, Figure 5 and Figure 6). This is seen to a greater extent for human medicine-related activities, with fees for type II variations effectively funding the costs of initial marketing authorisations. The modelling exercise showed that NCAs may use the remuneration they receive from EMA for human procedural activities and related annual fees to partially fund costs associated with working groups, committees and other additional, unremunerated activities they undertake. However, in the model, costs for EMA-related activities exceed remuneration by approximately €50 million/year. At the level of the individual NCAs, 6 out of 29 NCAs fully funded their additional costs with overall EMA remuneration (section 2.1, Figure 13).

Interviewed NCAs compensate for the additional EMA-related costs with their national budget.[66] Consequently, none of the interviewed NCA representatives considers the current fee system to be sustainable. As discussed in section 2.3, NCAs acknowledge the importance of the EMA network and are highly committed to the work they do as part of it, including unremunerated activities declared by NCAs in the NCA survey but for which costs for specific activities could not be determined. However, they identified current approaches that should be changed as well as activities that should be remunerated in the future in order to ensure the fee system's sustainability. One of the activities that is currently not remunerated is peer reviews: according to NCA representatives, remuneration for peer reviews is particularly important, as they are very time consuming and a highly relevant part of the regulatory system. In the modelling exercise, for each relevant procedural activity, peer review was included in one category of other roles with PRAC rapporteurs and co-rapporteurs. Averaged over all NCAs, these other roles were found to take up to between 20 and 50 per cent of rapporteur time, depending on the activity.

Other currently unremunerated activities, which NCAs indicated should be covered by fees include: activities of committee and working party members (e.g. preparatory work), development of guidelines, orphan designation assessments, and herbal monographs). Several of these unremunerated activities have already been identified by the HMA in the 2010 report on the European Regulatory Medicines Network, which noted activities that should be remunerated in the future: PIPs, assessments of orphan designation applications, rapporteurships of herbal monographs, safety referrals as well as committee work and EMA meetings including travel and preparatory work (HMA 2010, 7–8).[67]

NCA representatives emphasised that there are activities that are currently unremunerated and that this should be reconsidered. In the current fee system, only NCAs acting as rapporteurs and co-rapporteurs are remunerated for undertaking EMA-requested activities (except PRAC rapporteurs and co-rapporteurs, who are not remunerated for their work during initial marketing authorisation activities). As determined in the implementing rules of Council Regulation (EC) No 297/95, payments made by the EMA shall be divided equally between the two NCAs, 'who are responsible for the allocation of resources within their evaluation team(s)' (EMA 2017d, 26). The implementing rules do not stipulate how much should be paid to other involved NCAs. As pointed out by several NCA interviewees however, the current fee distributions among all involved NCAs do not reflect the actual workload of each of them. NCA interviewees thus suggested a predefinition of the share of fees between rapporteurs, co-rapporteurs and other involved actors corresponding to the time invested by each. In addition, according to the implementing rules, only Committee for Medicinal Products for Human Use (CHMP) rapporteurs and co-rapporteurs receive a share of the annual fees for scientific evaluation services. Several NCA representatives noted that they would find it fair if other NCAs also received a share of the annual fees since they are 'also intended to contribute to other activities carried out by Member States under their European Union obligations' (EMA 2017d, 25).

More than half of the wider stakeholders surveyed for this study prefer a fee system that is cost-based. Overall, 55.3 per cent indicated that they agree or strongly agree with the idea of a fee system based on costs, while only 13.2 per cent disagreed or strongly disagreed; the remaining consultees felt neutral about the idea (26.3 per cent) and 5.3

[66] Only one interviewed NCA indicated that they do not use their national budget to compensate for EMA-related costs because their national legislation does not allow doing so.

[67] Fees for safety referrals as well as related remuneration to NCAs have been addressed in Article 6 of Regulation (EU) No 658/2014 on fees payable for pharmacovigilance activities.

per cent indicated that they 'don't know'. However, agreement was significantly higher among large pharmaceutical company representatives and from respondents of industry organisations, patient and other representative groups: 72.7 per cent of large pharmaceutical company representatives agreed or strongly agreed with a cost-based fee system (the remaining 27.3 per cent were neutral), and 75 per cent of 'other' respondents showed agreement or strong agreement (12.5 per cent neutral, 12.5 per cent 'don't know'). By contrast, only 30.8 per cent of SME representatives agreed and 30.8 per cent disagreed or strongly disagreed (30.8 per cent neutral, 7.7 per cent 'don't know'). Half of the research organisation respondents agreed or strongly agreed with a cost-based fee system, 33.3 per cent were neutral and 16.7 per cent disagreed.

Some respondents who were either not in favour of or felt neutral about a cost-based fee system provided further explanations. A representative of a large pharmaceutical company indicated that such a fee system 'would be detrimental to innovation', and other respondents noted that a cost-based fee system would endanger the sustainability of the fee system as well as independence from the interests of the industry (highlighted by an industry association representative, an SME respondent and a research organisation respondent). A respondent from a large pharmaceutical company commented that higher fees, respectively a fully fee-based system, could be a barrier for regulatory approval and lead to cost pressures, and as a further consequence could hamper patients' access to affordable medicine. In addition, only larger companies (as well as SMEs, if incentives continue to exist) might have the financial means to submit new applications; smaller companies that do not meet SME criteria could be excluded through higher fees.

Exemptions and reductions for SMEs and exemptions for specific products and procedures are considered to be important elements of the current fee system and contribute to the fee system's sustainability. All consulted stakeholders – EMA, NCA and wider stakeholder representatives – highlighted the importance of exemptions and reductions for specific products and medicines as well as incentives for micro, small and medium-sized companies. Such incentives, as several consultees emphasised, ensure that public health needs can be addressed; in the case of SMEs, incentives enable stakeholders who otherwise might not be able to use the fee system to do so.

The study found that increased transparency in some areas could contribute to more sustainability of the fee system. As discussed in section 2.4, NCA representatives and wider stakeholder consultees identified areas that need more transparency. According to them, increasing transparency in these 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, a large pharmaceutical company representative indicated that more clarity on the basis for fees is required. In addition, the consultee noted that fee invoices should show the breakdown of fees. NCA representatives emphasised that more transparency would be needed regarding the extent to which they would be remunerated for individual activities; the criteria for exemptions and reductions to industry; the amount of remuneration to NCAs in the case of waived or reduced fees; the rationale for the fee share between the EMA and NCAs (i.e. why it is 50-50 for some activities, but 70-30 for others; see EMA 2017d, 24–5); and the timing of remuneration to NCAs.

Proposed changes to the EMA legislation could pose additional future challenges for the EMA fee and remuneration system.[68] In 2014, a proposal for a regulation on veterinary medicinal products (Proposal Regulation COM(2014) 558) was published, which should be better able to address current needs related to veterinary

[68] Changes related to the new veterinary legislation are outside of the scope of the study because there is no available data on the changes; therefore, the changes were not taken into consideration.

medicines. The new regulation should not have any financial impact on the EU/EEA contributions, but any new rules should be covered by fees charged to industry (Recital 73 of Proposal Regulation COM(2014) 558). The dependency on fee income, however, could become a challenge to the EMA and its available budget. Similarly, it was proposed that the legislation on orphan designated medicines and paediatric medicines should be evaluated and amended to meet current needs and to address observed challenges, such as concerns that therapeutic advances often failed to materialise despite fee incentives. An evaluation of the orphan and paediatric legislation will also include an assessment of current incentives, and any possible revisions of the legislation may have an impact on the current EMA fee and remuneration system (European Commission 2017).

6. CROSS-CUTTING CONCLUSIONS

This study set out 12 questions linked to the five evaluation criteria prescribed by the Better Regulation guidelines. The study findings and conclusions for each of these questions have been addressed in the previous Chapters 2 to 5. This chapter summarises the main challenges and limitations of the study, and draws together cross-cutting messages.

6.1. The study findings are limited due to several main issues

The study relied on the best available data and information to arrive at the findings and conclusions presented in this report. The reported results 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 the current fee implementing rules. However, there are several issues that limit the conclusions that can be drawn:

- Additional activities are a large component of overall EMA and NCA costs modelled in the synthetic baseline. However, no data is available to analyse in any detail the additional activities reported by NCAs in the survey; data available from EMA on its additional activities was also highly limited. Further research is required to assess the specific costs in this category, which is beyond the scope of the present study.
- The centralised system was acknowledged by NCAs as having considerable benefits; however, this study could not quantify or in other respects assess in detail the implied benefits of the centralised system vis-à-vis national markets, such as access to products in their countries without undertaking national procedures.
- For veterinary medicines, data samples were small, with a large degree of variation across the reported values for some activities. This is to be expected, given the small volume of activities undertaken relative to human medicines during the period of the MBDG exercise. The small 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.

6.2. The current fee system is generally efficient and effective but it is not cost-based at a granular level

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

NCA remuneration covers the aggregate costs of their procedural activities as well as, in aggregate, their involvement in working groups and committees. Alignment of remuneration with costs for individual NCAs varies, however, and in some cases there is a high degree of variation for NCAs in the extent to which remuneration aligns with costs. There are also differences in the extent to which remuneration covers costs for organisations that undertake human medicine activities only, human and veterinary medicine activities, and veterinary medicine activities only. NCAs that undertake veterinary activities only are less likely to cover their costs. Moreover, the total value of remuneration NCAs receive from EMA does not cover all of the additional EMA-related

activities that NCAs report undertaking. A closer analysis of the additional EMA-related activities reported by NCAs would be required in order to better assess whether and to what extent these activities might require additional remuneration.

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, some activities are not charged for at all.

Some fees may have 'incentives' applied, or be exempted, for certain types of medicines and certain types of company. Incentives and exemptions result in activities for which costs cannot be covered (fully or at all) by fees and so fees charged for other activities and annual fees support these costs, 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 purpose of the modelling exercise was to provide cost-based benchmarks for comparison with the current fee system. The exercise shows that using average cost pricing and remuneration could help to balance unitary fees against costs. But the overall effect would be that EMA income would need to increase to balance its costs, due to the effect of incentives and exemptions which are absorbed by EMA and not passed on to NCAs. The mechanism used to achieve this would have an impact either on EU and EEA budget contributions or industry fees (or potentially both, if the shortfall is met by a combination of increased fees and EU and EEA budget contribution). Average cost pricing would by definition cover costs for procedural activities for NCAs overall (with the assumption that their remuneration continues to be based on full fees without incentives applied), but it would not cover costs for all individual NCAs.

If NCAs were also remunerated to take into account costs for their time spent in committees and working groups, and for additional EMA-related activities that are currently unreimbursed, the additional revenue required by EMA would increase. In the scenarios, the overall budget of the EMA would only be larger than its existing budget under the current system if NCAs were remunerated for all activities they reported undertaking. This would include additional activities that have not been analysed in detail in the study.

6.3. The existing fee and remuneration system provides for a certain degree of flexibility, which is beneficial to its current operation; in other respects, the fee system is less flexible, which creates challenges for its current operation

The current fee system provides flexibility that enables EMA and NCAs to fund some of their activities. In particular, the flexibility to fund unremunerated activities, as well as incentives for specific medicinal products and SMEs are considered to be essential. Flexibility is important in relation to incentives and exemptions, which respondents to the consultation for this study largely view as important in order to support the development of veterinary medicines; facilitate the development of orphan designated medicines, products for paediatric use and advanced therapies; and support SMEs to participate in the centralised system.

Additionally, the current fee system of having a Fee Regulation and implementing rules provides further flexibility in regards to the introduction and implementation of reductions and exemptions, for example, to respond to needs under exceptional circumstances. EMA representatives noted that Regulation (EU) No 658/2014 on fees

payable for pharmacovigilance activities does not have implementing rules, resulting in less flexibility with regard to fee exemptions and reductions.

6.4. The fee system responds to needs originally identified at the time the fee system was established

The current fee system responds to needs originally identified at the time the fee system was established. In particular, the underlying legislation and the fee system itself address the requirement of a funding model based both on fee income paid by industry applicants and general EU and EEA contributions. 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 study also found that the current fee system overall meets the need to provide lower fees for activities for veterinary medicinal products; however, there are indications that such lower fees are not aligned with present needs. Alignment was also found between the original requirement to offer incentives to respond to public or animal health threats and the current fee system.

6.5. The fee system is complex and increasing complexity across many dimensions is viewed as a challenge for a well-functioning fee system

The EMA fee and NCA remuneration system has become more complex over time, which has created challenges for its effective operation and this complexity is expected to increase in the future.

Both EMA and NCA representatives observed that a perpetual challenge in the fee system is the increasing complexity of their activities. In both cases, this is a result of changes in the field of medicine; for example, highly innovative products may lack sufficient clinical data and novel therapies present assessment challenges as well. Other changes in the regulatory system, such as companion diagnostic reviews, activities related to big data, and real-world data analysis, add to the complexity of EMA and NCA work. In some cases this means that there can be wide variation in the costs associated with undertaking any given procedure.

For the EMA, increasing complexity is also related to its coordination activities and to managing a fee system that has a large number of activities, all of which have different associated fees, and related incentives and exemptions. Legislative amendments and the introduction of new legislation have meant that the fee system has changed considerably since its implementation in 2005. EMA representatives generally reported a highly complex fee system to coordinate and manage, and one that is growing ever-more complex.

NCAs, conversely, reported that given the complexities in the fee system, the current fee and remuneration system itself is generally simple to understand and implement. Legislative changes in recent years have generally contributed to the fee system's simplicity. Any additional simplifications (e.g. with respect to the legislation) would be welcomed by all stakeholders.

EMA, NCAs and industry are generally satisfied that the fee system is clear and transparent, although NCAs and industry would like to see more information from EMA regarding the basis for each fee.

6.6. The flexibility in the fee system contributes to its sustainability

The flexibility in the fee system to fund unremunerated activities, as well as incentives for specific medicinal products and SMEs are considered to be important for the fee system's long-term sustainability.

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8. APPENDICES

Appendix 1. Evaluation matrix

Effectiveness & efficiency

Evaluation Criterion	Effectiveness & efficiency
Definition	Effectiveness: Assessment of progress made towards achieving the objectives of the intervention, looking for evidence of why, whether or how these changes are linked to the EU intervention. Identification of factors driving or hindering progress and how they are linked (or not) to the EU intervention. Efficiency: Assessment of the relationship between the resources used by an intervention and the changes generated by the intervention and of both the costs and benefits of the EU intervention as they accrue to different stakeholders.
Approach proposed	In this study, effectiveness was closely tied to efficiency and so these evaluation criteria were considered together. Effectiveness in general was based on the extent to which the objectives of the fee system have been achieved in relation to the general needs of the fee system. This included an assessment of the extent to which the fee system: allows the EMA to perform its tasks, allows the EMA to remunerate NCAs adequately, is fair and transparent, is flexible to take into account exceptional circumstances, and supports SMEs. Linked to this, efficiency (cost-effectiveness) was assessed by examining the relationship between costs and fees for the activities covered by the EMA.
Risks and challenges	A challenge for addressing this evaluation criterion identified at the inception stage of the study was the availability of data from the EMA and NCAs in relation to the costs and time data for various activities – in terms of the quality, quantity and timeliness in receiving the data. In order to mitigate against these challenges, we requested the opportunity to review the time data already collected at an early stage in the study so that we could identify where we will need to collect additional data through the consultation. Interviews served as a means of both validating data gathered through desk research and the surveys, and to address any gaps identified. We used more than one data source wherever possible and as many data sources as possible to triangulate the findings and ensure the most robust response possible. We indicates where possible the data sources that provided the most robust evidence and used these as the basis for our answers to the study questions, supplemented and supported by other data sources.

Evaluation question	Judgement criteria	Indicators	Data sources	Methods
Q1. To what extent do the fees charged correspond with EMA and NCA costs?	JC.1.1 Fees charged are aligned with the services performed JC.1.2 Total fees earned enable the EMA to meet its costs, taking into consideration the availability of EU and EEA contributions; the remuneration paid to NCAs allow them to meet the costs of EMA-requested activities	I.1.1 Specific fees charged align with costs identified by the EMA and by the NCAs with regard to their remuneration I.1.1a Specific fees charged align with legislative requirements (e.g. exemptions and reductions) where the fees do not align with the costs identified by the EMA	DS.1.1 Time data collected by the EMA MB Data Gathering exercise DS.1.2 Cost data collected by the study team DS.1.3 Fee grid of EMA fees and remuneration to NCAs DS.1.4 EU legislation that sets specific requirements for fee exemptions and reductions DS.1.5 Comparison of fees system approach in other EU agencies and third countries	M.1.1 Time data analysis M.1.2 Cost data analysis M.1.3 Interviews with EMA and with NCAs M.1.4 Desk research of EU legislation and supporting documents: EU2020 budget; EMA budget; NCA budgets M.1.5 Analysis of approach taken in other EU agencies and countries, notably, ECHA and the U.S. FDA, as well as Canada, Japan and Australia, where appropriate
Q2. To what extent does the current financial model allow the EMA to effectively perform the activities in its remit?	JC.2.1 The financial model enables the EMA to perform procedural tasks within its remit JC.2.2 The financial model enables the EMA to perform other (i.e. cross-cutting, horizontal and related) tasks within its remit	I.2.1 The financial model enables EMA to perform procedural and other tasks effectively I.2.2 The EMA is not hindered by their charging and remuneration arrangements	DS.2.1 Views of EMA DS.2.2 Views of NCAs DS.2.3 Views of stakeholders DS.2.4 Documents that comment on the ability of EMA to perform their tasks effectively DS.2.5 EU Court of Auditors reports regarding EMA fee system	M.2.1 Interviews with EMA and NCAs and survey of stakeholder representatives M.2.2 Document review of EMA annual reports, 2010 EMA evaluation, NCAs and HMA

Evaluation question	Judgement criteria	Indicators	Data sources	Methods
Q3. To what extent does the current financial model allow the EMA to remunerate NCAs adequately for the activities they perform?	JC.3.1 Remuneration provided to NCAs aligns with the actual costs to NCAs for the activities they perform JC.3.2 Evidence of any issues regarding the current model's ability to adequately remunerate NCAs	I.3.1 Remuneration to NCAs aligns with the time spent and overhead costs identified by NCAs to perform activities within their remit I.3.2 The current model allows adequate remuneration to NCAs	DS.3.1 Information on remuneration currently provided to NCAs (fee grid) DS.3.2 Time data on actual time spent by NCAs, collected by the EMA MB data gathering DS.3.3 Overheads and other costs for NCAs to undertake the work, collected by the study team DS.3.4 EU Court of Auditors reports regarding EMA fee system DS.3.5 Views of EMA and NCAs	M.3.1 Desk research of EU Court of Auditors reports and other data sources M.3.2 Time data analysis M.3.3 Cost data analysis M.3.4 Interviews with EMA representatives M.3.5 Interviews with NCAs M.3.6 Survey of NCAs
Q4. To what extent is a balance struck between a fee and remuneration system based on actual costs and simplicity of the fee system?	JC.4.1 Evidence of satisfaction (or dissatisfaction) with the balance between costs and simplicity	I.4.1 EMA, NCAs and payers are satisfied that the fee system is balanced between costs and simplicity I.4.2 The fee system is clear, transparent and proportionate, and aligned with the underlying legislation	DS.4.1 Views of EMA, NCAs and stakeholders DS.4.2 Documents that comment on the balance between simplicity and cost basis	M.4.1 Interviews with EMA and NCAs M.4.2 Survey of NCAs and stakeholder representatives M.4.3 Public consultation M.4.5 Document review of position papers and other supporting information that indicates satisfaction

Evaluation question	Judgement criteria	Indicators	Data sources	Methods
Q5. To what extent does the fee system enable needs to be met in exceptional circumstances or under particular priorities/imperatives?	JC.5.1 The reductions and exemptions enable authorisations for special categories of medicinal products that are prioritised by the EU JC 5.2 Fee system provides flexibility for exceptional circumstances JC 5.3 Evidence of satisfaction with the provisions made in exceptional circumstances or under particular priorities/imperatives	I.5.1 Number of authorisations under exceptional circumstances or to meet particular needs (e.g. public health or animal health emergencies, orphan medicines, paediatric medicines, advanced therapy medicines) I.5.2 Other evidence that the fee system enables needs to be met in exceptional circumstances or to meet particular needs I.5.3 Stakeholders are satisfied with the provisions	DS 5.1 Applicable fee rules DS.5.2 Authorisations data held by the EMA DS.5.3 Views of stakeholders DS.5.4 Views of EMA and NCAs DS.5.5 Comparison of authorisation data in other countries	M.5.1 Analysis of applicable fee regulations and implementing rules M.5.2 EMA authorisation data analysis M.5.3 Interviews with EMA, NCAs and survey of stakeholders (targeted consultation) M.5.4 Public consultation M.5.5 Comparative Information on authorisations for special circumstances in third countries
Q6. To what extent are SMEs supported through effective reductions in their costs to use the centralised system?	JC.6.1 SMEs are able to participate in the centralised system without undue burdens	I.6.1 Number of authorisations to SMEs I.6.2 SMEs are able to access the centralised system given the costs	DS.6.1 Authorisations data held by the EMA DS.6.2 Views of SMEs DS.6.3 Comparison of SME provisions and any information on views of SMEs to obtain authorisation in other countries DS.6.4 SME regulation	M.6.1 Analysis of EMA authorisations data and SME office activities M.6.2 Interviews with SME representatives M.6.3 Public consultation M.6.4 Information on SME provisions in other EU agencies and third countries

Relevance

Evaluation Criterion	Relevance
Definition	Assessment of the relationship between the EU intervention and the needs/problems related to activities that fall within EMA's remit. Identification of any possible mismatch between the objectives of the intervention and the (current) needs or problems.
Approach proposed	The problems and needs that the fee system was designed to address were assessed and compared with existing needs and any problems identified to determine whether the fee system is still fit for purpose and if any changes are needed.
Risks and challenges	The main challenge for this criterion identified at the inception stage was related to collecting and synthesising the views of a wide range of stakeholders in relation to the main needs relating to the EMA fee system, taking into account the different priorities set by various groups of stakeholders. In order to address this challenge, the study team gathered the information collected into an evidence grid which enabled comparison of responses to the questions asked in interviews, surveys and gathered through document review. This internal document enabled the team to analyse the responses of numerous groups of stakeholder in a synthetic way and compare current needs and problems with those existing when the fee system was first developed.

Evaluation question	Judgement criteria	Indicators	Data sources	Methods
Q7: 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?	JC.7.1 Needs identified when the fee system was developed are addressed by the fee system.	I.7.1 Alignment between the fee system and the problems and needs originally identified I.7.2 Divergence between the fee system and the problems and needs originally identified	DS.7.1 EMA and NCA views DS.7.2 Stakeholder views DS.7.4 Supporting documents	M.7.1 EMA and NCA interviews M.7.2 NCA and stakeholder survey M.7.3 Public consultation M.7.4 Desk research of supporting documents
Q8: Is the fee system relevant in terms of current needs?	JC.8.1 Needs identified by EMA, NCAs and stakeholders as relevant currently are addressed by the fee system.	I.8.1 Alignment between the fee system and current problems and needs I.8.2 Divergence between the fee system and current problems and needs	DS.8.1 EMA and NCA views DS.8.2 Stakeholder views DS.8.3 Supporting documents	M.8.1 EMA and NCA interviews M.8.2 NCA and stakeholder survey M.8.3 Public consultation M.8.4 Desk research of supporting documents

Coherence

Evaluation Criterion	Coherence
Definition	Assessment of how well or not different aspects of the fee system work together (e.g. to achieve common objectives). This can take place at several levels, including: (i) internally, (ii) with other EU interventions, and (iii) with non-EU interventions
Approach proposed	The study assessed the coherence of the fee system: (i) internally (e.g. fee structure, remuneration levels), (ii) nationally, with Member State fee systems, (iii) at EU level, with other EU policies and programmes.
Risks and challenges	The main challenge identified at inception stage was to identify the synergies and potential overlaps between national fee systems and the EMA fee system. This point was raised through interviews with the EMA and with stakeholders and cross checked in interviews with the NCAs in order to validate findings.

Evaluation question	Judgement criteria	Indicators	Data sources	Methods
Q9: To what extent is the fee system coherent internally?	JC.9.1 The EMA fee system is internally coherent in terms of the fees charged JC.9.2 The EMA fee system is internally coherent in terms of the remuneration provided JC.9.3 The EMA fee system is coherent in terms of the agency's strategy and objectives	I.9.1 The internal components of the fee system work well together, including: 1.1 with the legal basis and other related rules, 2.1 between the fees charged to industry and the remuneration provided to NCAs, and 3.1 the funding required for the EMA to conduct the activities in its remit taking into consideration EU and EEA contributions	DS.9.1 Views of EMA, NCAs and industry representatives DS.9.2 Time and cost data provided by EMA and collected by the study team DS.9.3 EU legislation on medicines DS.9.4 Supporting documents, as appropriate	M.9.1 EMA and NCA interviews; survey of stakeholders M.9.2 Analysis of time and cost data M.9.3 Desk research of EMA-related EU legislation and supporting documents
Q10: To what extent is the fee system coherent with Member State fee systems?	JC.10.1 The EMA fee system is consistent with and does not overlap with national fees	I.10.1 Synergies observed between national fee systems and the EMA system I.10.2 Risks of overlaps observed between national fee systems and the EMA fee system	DS.10.1 Views of EMA and NCA representatives DS.10.2 Views of other stakeholders, as appropriate	M.10.1 EMA and NCA interviews M.10.2 NCA and stakeholders' survey
Q11: To what extent is the fee system coherent at EU level, with other EU policies?	JC.11.1 The fee system is coherent with requirements set out in other EU policies	I.11.1 Synergies observed between EU policies and the EMA fee system I.11.2 Overlaps observed between EU policies and the EMA fee system	DS.11.1 Views of EMA and COM representatives DS.11.2 EU policy documents	M.11.1 EMA and COM interviews M.11.2 Document review of EU policies, including legislation and supporting materials

Sustainability

Evaluation Criterion	Sustainability
Definition	Assessment of the likelihood that the intervention will succeed over time.
Approach proposed	The study focused on the extent to which the fee system is based on costs, taking into account the need to finance some activities (i.e. reductions and exemptions), cross-cutting activities and the needs of the EMA and NCAs to meet evidence-based trends. The study team assessed the flexibility of fee system to adjust to changing trends.
Risks and challenges	The main challenge identified at inception stage was to identify the long term costs associated with EMA and NCA activities. In order to mitigate against this, consultees were asked to reflect on how costs may change in the future.

Evaluation question	Judgement criteria	Indicators	Data sources	Methods
Q12: To what extent does the current financial model ensure the financial stability of the EMA including its ability to remunerate NCAs?	JC.12.1 Fees charged correspond with EMA and NCA costs JC.12.2 Total fees earned enable the EMA to meet its costs, taking into consideration the availability of EU and EEA contributions	I.12.1 Specific fees charged align with all costs identified by the EMA and NCAs I.12.2 Specific fees charged align with legislative requirements (e.g. exemptions and reductions) where fees do not align with the costs identified by the EMA I.12.3 Fees charged enable cross-cutting activities I.12.4 EU and EEA contributions are sufficient and will continue to be available to the EMA where fees collected do not meet actual costs, taking into consideration the reductions and exemptions required under EU law	DS.12.1 Time data collected by the DGSG DS.12.2 Cost data collected by the study team DS.12.3 EU legislation that sets specific requirements for fee exemptions and reductions DS.12.4 Information on cross-cutting activities funded by fees or that could be funded by fees DS.12.5 Information on EMA and NCA needs with regard to ongoing and medium to long-term investments	M.12.1 Analysis of time data provided by DGSG M.12.2 Analysis of cost data collected by the study team M.12.3 Interviews with EMA and NCAs M.12.4 NCA and stakeholders' survey M.12.5 Public consultation M.12.6 Desk research of EU legislation and supporting documents

Appendix 2. Documents and data sources

The following documents were identified through our research and/or provided by the EMA.

Legislation

Regulations

- Regulation (EU) 2016/461 of 30 March 2016 amending Council Regulation (EC) No 297/95 as regards the adjustment of the fees of the European Medicines Agency to the inflation rate (OJ L 80/25, 31.3.2016)
- Regulation (EU) No 658/2014 on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use (OJ No. L 189, 27.6.2014)
- Regulation (EU) No 520/2012 Performance of pharmacovigilance activities provided for in Regulation (EC) No 726/2004 of the European Parliament and of the Council and Directive 2001/83/EC of the European Parliament and of the Council
- Regulation (EU) No 1235/2010 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
- Regulation (EC) 1234/2008 of 28 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)
- 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) No726/2004 (ATMP Regulation) (OJ L 324, 10.12.2007)
- Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use (OJ L 378, 27.12.2006)
- Regulation (EC) No 1902/2006 of the European Parliament and of the Council of 20 December 2006 amending Regulation 1901/2006 on medicinal products for paediatric use (OJ L 378, 27.12.2006)
- 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. L329, 16.12.2005)
- Regulation (EC) No 726/2004 of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ No. L 136, 30.4.2004)
- Regulation (EC) No 45/2001 of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data (OJ. L8, 12.01.2001)
- Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products (Orphan Regulation) (OJ L 18, 22.1.2000)

- 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)
- Regulation (EU) 2017/612 of 30 March 2017 amending Council Regulation (EC) No 297/95 as regards the adjustment of the fees of the European Medicines Agency to the inflation rate with effect from 1 April 2017 (OJ L 86, 31.3.2017)

Directives

- Directive 2001/82/EC of 6 November 2001 on the Community code relating to veterinary medicinal products (OJ L311, 28.11.2001)
- 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)
- Directive 2010/84/EU Amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use (OJ L 348, 31.12.2010)

Proposals

- Proposal for a Regulation of the European Parliament and of the Council on veterinary medicinal products COM (2014) 557, final.
- Proposal for a Regulation of the European Parliament and of the Council on veterinary medicinal products COM (2014) 558, final.
- Proposal for a Regulation on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use, COM (2013) 472 final.

Other

- Commission Recommendation of 6 May 2003 concerning the definition of micro, small and medium-sized enterprises (2003/361/EC)
- Corrigendum to Council Regulation (EC) No 594/2008 of 16 June 2008 on certain procedures for applying the Stabilisation and Association Agreement between the European Communities and their Member States, of the one part, and Bosnia and Herzegovina, of the other part, and for applying the Interim Agreement on trade and trade-related matters between the European Community, of the one part, and Bosnia and Herzegovina, of the other part
- Revised policy for classification and incentives for veterinary medicinal products indicated for minor use minor species (MUMS)/limited market (EMA/308411/2014 Adopted, 1.12.2014).

Administrative documents

- 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, 27.5.2017)
- Roadmap on the evaluation of EMA Fees of December 2015: http://ec.europa.eu/smart-regulation/roadmaps/index_en.htm
- Renewal of the Cooperation Agreement between the NCAs and the EMA (EMA/MB/99041/2015 Noted, 19.3.2015): http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/03/WC500184861.pdf
- Cooperation Agreement between the NCAs and the EMA
- EMA/NCA Memorandum of Understanding

- Executive Director's decision on fee reductions for designated orphan medicinal products (EMA/317270/2014, 9.9.2014)
- Guidance on the classification of veterinary medicinal products indicated for minor use minor species (MUMS) / limited market (EMA/CVMP/388694/2014, 18.12.2014)
- Commission Staff Working Document Impact Assessment accompanying document to the Proposal for a Regulation of the Council and the European Parliament on the fees payable to the European Medicines Agency (EMA) for the conduct of pharmacovigilance activities in respect of medicinal products for human use SWD (2013) 234, final.
- Commission Staff Working Document Impact Assessment accompanying document to the Proposal for a Regulation of the Council and the European Parliament on the fees payable to the European Medicines Agency (EMA) for the conduct of pharmacovigilance activities in respect of medicinal products for human use SWD (2013) 235, final.
- Information from European Union Institutions, Bodies, Offices and Agencies. Guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products and on the documentation to be submitted pursuant to those procedures (2013/C 223/01)
- Processing of requests for fee reduction falling under paragraph 1 of Article 9 of Council Regulation (EC) No 297/95 (SOP/EMA/0028. Effective date 09-MAR-17)
- Rules for the implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures. Revised implementing rules to the Fee Regulation as of 1 April 2017 (EMA/MB/97423/2017, 16.3.2017)

EMA documentation

- European Medicines Agency. Budgetary reporting. Available from:
- http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/document_listing/document_listing_000158.jsp&mid=WC0b01ac0580029337 (Accessed 19 August 2016)
- Annual accounts. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/document_listing/document_listing_000158.jsp&mid=WC0b01ac0580029337 (Accessed 19 August 2016)
- European Medicines Agency. Funding. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000130.jsp&mid=WC0b01ac0580029336 (Accessed 19 August 2016)
- European Medicines Agency. Annual reports. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/document_listing/document_listing_000208.jsp&mid=WC0b01ac058002933a#section3 (Accessed 19 August 2016)
- European Medicines Agency. Work programmes. Available from: http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/document_listing/document_listing_000208.jsp&mid=WC0b01ac058002933a#section3 (Accessed 19 August 2016)

- European Court of Auditors reports, e.g. Report of December 2012 on the annual accounts of the European Medicines Agency for the financial year 2011, together with the Agency's replies (OJ. C388/116, 15.12.2012)
- Pharmacovigilance http://www.ema.europa.eu/docs/en_GB/document_library/Leaflet/2011/03/WC500104236.pdf
- Explanatory note on pharmacovigilance fees payable to the European Medicines Agency http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/03/WC500183456.pdf
- Explanatory note on general fees payable to the European Medicines Agency http://www.ema.europa.eu/docs/en_GB/document_library/Other/2016/06/WC500208145.pdf
- Guideline on good pharmacovigilance practices (GVP): Module VII - periodic safety update report http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2013/04/WC500142468.pdf
- European Medicines Agency post-authorisation procedural advice for users of the centralised procedure http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500003981.pdf
- List of Organisations which provided comments during the public consultation on the EU reference dates list http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/10/WC500133158.pdf

EMA Management Board Data Gathering (MBDG) documentation, as provided by the EMA

- Draft report to EMA MB in Dec 2016 and raw data
- Agenda and summary notes for the Steering Group meetings (1-34) on MBDG), Proposal, agendas and minutes Management Board
- HMA Proposal to bring forward the EMA MB data gathering initiative at 83rd Management Board
- Management Board minutes on MBDG
- Report by the Steering Group on MBDG at the 85th-94th Management Board
- Time data collected by the Data Gathering Steering Group, EMA Management Board, 2014-2016.
- Pilot project data, EMA Management Board, 2008-2009.Pilot Scientific Advice Protocol Assistance Reports (Human and Veterinary)
- Explanatory notes
- Fee Generating Analysis & Datasets
- PDCO & OD Analysis & Dataset

EMA fee system study related documents and data, as provided by the European Medicines Agency

- European Commission introduction of plans for the Evaluation of EMA fee system
- European Commission Roadmap outlining planned evaluation of EMA fee system
- 2015 EMA Revenue & Expenditure
- Human medicines fee grid
- Documents outlining non-fee and fee generating EMA activities
- SME Office user guide on fee incentives

- Costing Group - Outcome of the pilot exercise. Management Board meeting 10 December 2009. Agenda point 12a for discussion (EMEA/MB/780575/2009).

Documents relevant to the EMA fee system study

- Ernst and Young (2010). Evaluation of the European Medicines Agency. Available from: http://ec.europa.eu/health/files/pharmacos/news/emea_final_report_vfrev2.pdf (Accessed 19 August 2016)

Documents relevant to EMA activities

- European Medicines Agency. Fees payable to the European Medicines Agency. Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000327.jsp
- Heads of Medicines Agencies - Role of the European Regulatory Medicines Network and its relation to a revision of the fees regulation, HMA, December 15, 2010:http://www.hma.eu/fileadmin/dateien/HMA_joint/04_HMA_Induction/07_HMA_Position__on_Rev_fees_2010_12.pdf
- Example of a report on the annual accounts of the EMA for the financial year 2011 from the European Court of Auditors regarding the need for the remuneration for services provided by Member State authorities to be based on costs: http://eur-lex.europa.eu/legalcontent/EN/TXT/?uri=uriserv:OJ.C_.2012.388.01.0116.01.ENG

Appendix 3. Summary of the available time data

Table 13: Activities included in the MBDG report

Activities	Time period for data collection
HUMAN ACTIVITIES	
Scientific Advice/Protocol Assistance (initial request and follow-up request (Level I, II and III))	February – June 2015
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
Line extensions (phase I, II and III)	January – September 2016
Type II variations (new clinical indication, clinical, clinical safety and quality)	January – September 2016
Type IB variations	July 2016
Type IA variations	July 2016
Renewals	January – September 2016
Transfer of marketing authorisation	January – October 2016
Pharmacovigilance Referrals	January – October 2016
PSUR	January – October 2016
PASS	January – October 2016
PIP (phase I and II)	March – September 2016
PIP modification	March – September 2016
PIP waiver	March – September 2016
PIP compliance check	March – September 2016
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
VETERINARY ACTIVITIES	
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

Activities	Time period for data collection
Referral procedures (Art. 34 and Art. 35 (phase I, II and III) and Art. 45 (total procedure))	March – August 2016
Inspections/Parallel Distribution & Certificates	
Parallel distribution	February – October 2016
Certificates	February – October 2016
GMP Inspections	February – October 2016
GCP Inspections*	February – October 2016
Pharmacovigilance Inspections*	February – October 2016
Scientific committee activities (CHMP, PRAC, CVMP, PDCO, CAT, HMPC, COMP)	September – October 2016
Working party activities (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
Activities	Time period for data collection

* Human only

Table 14: Overall summary of the total mean hours declared by EMA Secretariats and NCAs for the principal fee generating procedures by means and percentages

	EMA AD[a]	EMA AST[b]	EMA Total	NCA AD[a]	NCA AST[b]	NCA Total	EMA %	NCA %
Initial Marketing Authorisations – Human								
BioSimilar	275.51	98.89	***363.43***	2830.27	67.69	***2897.97***	11	89
Fixed Combination	388.59	79.67	***468.25***	1485.13	53.70	***1538.83***	23	77
Generics	189.40	88.34	***272.49***	475.23	31.96	***507.19***	35	65
Hybrid	316.51	51.54	***368.05***	1344.70	60.05	***1404.75***	21	79
Known active substance	413.36	86.88	***500.24***	2448.88	104.99	***2553.88***	16	84
New active substance	420.43	109.83	***523.19***	2841.20	69.98	***2911.18***	15	85
Well-established use	665.46	81.13	***746.59***	2562.78	76.37	***2639.15***	22	78
Informed Consent	29.75	27.32	***57.07***	55.83	6.42	***62.25***	48	52
Scientific advice - Human								
Scientific advice	42	32	***73.58***	97	5	***101.17***	42	58
Type II variations, Line extensions and renewals - Human								
Clinical Indication	75.70	11.36	***86.46***	391.00	6.66	***397.66***	18	82
Clinical Safety	9.78	4.51	***13.98***	42.50	3.25	***45.75***	23	77
Clinical	8.83	4.45	***12.92***	44.66	2.44	***47.10***	22	78
Quality	6.60	2.85	***9.39***	33.09	1.80	***34.89***	21	79
Line Extensions	172.76	65.95	***232.28***	706.37	32.14	***738.50***	24	76
Renewals	19.77	12.45	***32.22***	47.44	10.17	***57.61***	34	66
Pharmacovigilance procedures - Human								
PSUR only	-	-	***33.05***	-	-	***75.12***	31	69
PASS	-	-	***64.31***	-	-	***79.75***	45	55
Referrals (Art.31, Art.20, Art.107i)	-	-	***589.82***	-	-	***454.42***	56	44
Inspections – Human & Veterinary								
GCP*	56.21	14.62	***70.83***	616.50	66.83	***845.34***	8	92
GMP	15.59	0.81	***16.40***	81.63	3.50	***126.88***	10	90
GVP*	31.10	28.35	***59.45***	102.00	26.00	***162.00***	27	73
Maximum Residue Limits and Initial Marketing Authorisations - Veterinary								
Maximum residue limits	139.91	30.16	***158.25***	250.74	10.12	**260.87**	38	62
New active substance	292.23	105.50	***396.07***	1196.29	29.84	***1226.13***	25	75
Known active substance	265.77	75.44	***341.21***	970.13	19.68	***989.81***	26	74
Generic application	205.97	85.26	***276.83***	427.00	19.34	***446.34***	38	62

	EMA AD[a]	EMA AST[b]	EMA Total	NCA AD[a]	NCA AST[b]	NCA Total	EMA %	NCA %
Scientific advice – Veterinary								
Scientific advice	19.22	22.35	***41.57***	51.30	0.77	***52.08***	44	56
Post authorisation procedures - Veterinary								
Extensions (with re-examination)	352.83	119.47	***470.40***	379.08	14.54	***393.63***	54	46
Extensions (without re-examination)	115.56	52.56	***168.12***	284.83	13.79	***298.63***	36	64
Type II quality/clinical	54.22	65.25	***119.47***	205.17	10.67	***215.83***	36	64
Type II clinical	42.41	72.41	***114.82***	87.89	2.42	***89.96***	56	44
Type II quality	11.96	36.94	***45.04***	23.38	1.09	***24.48***	65	35
Type IB	0.67	18.25	***19.32***	9.79	0.83	***10.62***	65	35
Type IA**	0.21	12.73	***12.94***	-	-	-	100	-
MAH Transfers**	0.56	12.35	***12.91***	-	-	-	100	-

* Human only ** EMA only [a] AD = scientific staff [b] AST = non-scientific/administrative staff

Table 15: Overall summary of the total mean hours declared by EMA Secretariats and NCAs for the non-fee generating procedures by percentage

	EMA AD[a]	EMA AST [b]	EMA Total	NCA AD[a]	NCA AST[b]	NCA Total	EMA %	NCA %
Compliance check, PIP Modification, exemption and new PIP and Orphan designation – Human								
PIP Compliance Check	9.36	4.23	***13.63***	11.50	0.64	***12.14***	53	47
PIP Modification	15.06	5.96	***20.16***	19.05	1.24	***20.29***	50	50
PIP Waiver	15.26	7.23	***18.34***	24.33	1.10	***25.43***	42	58
New PIP	43.66	16.69	***60.74***	58.22	2.82	***61.04***	50	50
Orphan designation	21.93	9.00	***30.93***	12.16	0.37	***12.52***	70	30
Post authorisation procedures – Veterinary								
Referral Art 35	264.05	56.67	***320.72***	830.42	21.16	***851.57***	27	73
Referral Art 34	344.04	56.33	***400.38***	651.25	16.98	***668.23***	37	63
Referral Art 45	25.5	12.25	***37.75***	572.00	22.00	***594.00***	6	94
PSUR	4.68	9.74	***14.42***	9.45	0.61	***10.15***	59	41
Surveillance/ signal detection	0.33	3.32	***3.65***	4.01	0.12	***4.13***	47	53
MUMS**	10.75	7.05	***17.80***	-	-	-	100	-

The red figures indicate types of procedure where in one or more phases data had to be extrapolated from the most similar type of procedure due to lack of data

** EMA only [a] AD = scientific staff [b] AST = non-scientific/administrative staff

Table 16: Categorisation of additional activities reported by NCAs

Activity/working group/committee	Number of NCAs
Member EMA Management Board /Scientific Coordination board	4
Surveys/questionnaires!	2
Transparency	1
Communication/stakeholder engagement	1
Guidelines drafting	6
Establishment and maintenance of terminology standards	1
Databases	11
Training (participation and delivery)	9
Preparation/briefing/comments on non (co)rap procedures	4
Drafting responses	2
Translation checks	4
Quality defects (incl non-GMP compliance + Incident Management Plan meetings)	3
Rapid Alert/Incident Management	2
Adverse events	1
ADR reporting covering both national and EMA approved pharmaceuticals	
EFSA, AMEG, RONAFA and CADVVA, VICH	3
PRIME	5
ESVAC (European Surveillance of Veterinary Antimicrobial	2

Activity/working group/committee	Number of NCAs
consumption)	
ECVAM (3Rs)	2
Lumpy Skin Disease and FishMed	2
Surveillance and Signal detection/management (includes PRAC signal)	10
Classification ATMP	6
Herbal related	6
Post-Authorisation Efficacy Studies (PAES)	6
Post authorisation measurements (PAM)	6
Eligibility +Accelerated assess/procedure	4
Annual re-assessment/ re-examination procedures	3
Similarity report	3
Significant benefit	3
Referrals (NonPhV)	3
PhV activities	1
Innovation	1
Ph Vig veterinary Inspections	2
Inspections – GDP/GLP/national	2
safety type II	3
Plasma Master File (PMF) (various)	2
PSURs mixed CAPS/NAPS	2
Derogation of orphan status/ Review of orphan designation for orphan medical product for MA (criteria time of marketing)	2
PIP modifications	3
Other evaluation reports for the EU:RMP in the context of MAA or line extension; renewals, RUP	1
Non- (co)rap procedure roles or committee time	9
Pharmacopeia work	1
OMCL lab work (Official Medicines Control Laboratories)	1
No information provided	6

Appendix 4. Stakeholder mapping

The aim of the stakeholder mapping is to:

- Identify relevant stakeholder groups, namely National Competent Authorities (NCAs) and European-level industry, research, healthcare, patient, consumer, and other relevant associations and representative groups.
- Assess their involvement in, and the influence they exert on, the fee system.
- Determine the potential impact of changes to the fee system on, and the differences in views across, stakeholder groups.

The study team has consulted with DG SANTE, DG GROW, DG RTD, EMA and HMA representatives to refine the list of stakeholders. In addition, the study team assessed the level of involvement across three areas to determine stakeholders':

- Level of interest in the study of the fee system.
- Level of influence in the fee system.
- Dependency on the outcome of the fee system study and other stakeholders' actions.

The next section lists the NCAs for EU Member States and for EEA countries who were contacted for the study (two inspectorates, one in the Netherlands and one in Poland, were not directly contacted). This is followed by lists of the European-level industry associations, research bodies, healthcare associations, patient and consumer groups, and other groups.

National Competent Authorities

NCAs have been assessed to have a high level of interest in the activities of the EMA vis-à-vis the fee system (Table 17). The underlying rationale is that NCAs, as members of the EMA committees, and as executors of scientific assessments and other EMA-requested activities, have a high level of interest regarding both the EMA's activities and the outcome of the current study of the fee system. Given that the current study is dependent on the information collected from NCAs regarding their costs and other information about the fee system, the level of influence the NCAs have on the study has been assessed as high. Each of the NCAs listed in Table 17 received a survey to complete; some NCAs were invited to elucidate their views in further detail. Table 17 provides a list of all EU Member State NCAs consulted for this study, indicating whether they have responsibility for human medicines, veterinary medicines or both. Two Member States, Poland and the Netherlands, have separate inspectorates. In the Netherlands, the MEB included data from the Healthcare Inspectorate with their survey responses. Poland was not included in the modelling exercise as the Polish Office for Registration of Medicinal Products, Medical Devices and Biocidal Products did not respond to the survey.

Table 17: EU Member State NCAs

Level of interest	Level of influence	Dependency on outcome
High	High	Medium/High

State	National Competent Authority	Human medicine	Veterinary medicine
Austria	Austrian Medicines and Medical Devices Agency (AGES MEA)	✓	✓
	Federal Office for Safety in Health Care (BASG)	✓	✓
Belgium	Federal Agency for Medicines and Health Products (FAMHP)	✓	✓
Bulgaria	Bulgarian Drug Agency (BDA)	✓	
	Bulgarian Food Safety Agency (BFSA)		✓
Croatia	Agency for Medicinal Products and Medical Devices (HALMED)	✓	
	Ministry of Agriculture - Veterinary and food safety directorate (*abbreviation not available*)		✓
Cyprus	Ministry of Health - Pharmaceutical Services (MOH)	✓	
	Veterinary Services, Ministry of Agriculture, Natural Resources and Environment (MOA)		✓
Czech Republic	State Institute for Drug Control (SÚKL, CZ)	✓	
	Institute for State Control of Veterinary Biologicals and Medicines (ÚSKVBL)		✓
Denmark	Danish Medicines Agency (DKMA)	✓	✓
Estonia	State Agency of Medicines (Ravimiamet)	✓	✓
Finland	Finnish Medicines Agency (Fimea)	✓	✓
France	National Agency for the Safety of Medicine and Health Products (ANSM)	✓	
	French Agency for Veterinary Medicinal Products (ANMV)		✓
Germany	Federal Institute for Drugs and Medical Devices (BfArM)	✓	
	Paul Ehrlich Institute (PEI)	✓	
	Federal Office of Consumer Protection and Food Safety (BVL)		✓
Greece	National Organization for Medicines (EOF)	✓	✓
Hungary	National Institute of Pharmacy and Nutrition (OGÉYI)	✓	
	Directorate of Veterinary Medicinal Products (MgSzH)		✓
Ireland	Health Products Regulatory Authority (HPRA)		✓
Italy	Italian Medicines Agency (AIFA)	✓	

State	National Competent Authority	Human medicine	Veterinary medicine
	Ministry of Health – Directorate General for Animal Health and Veterinary Medicines (*abbreviation not available*)		✓
Latvia	State Agency of Medicines of the Republic of Latvia (ZVA)	✓	
	Food and Veterinary Service (PVD)		✓
Lithuania	State Medicines Control Agency of Lithuania (VVKT)	✓	
	National Food and Veterinary Risk Assessment Institute (NMVRVI)		✓
Luxembourg	Ministry of Health (MS)	✓	✓
Malta	Medicines Authority (*abbreviation not available*)	✓	
	Veterinary Medicines Section within the Veterinary and Phytosanitary Regulation Division (VMANS)		✓
Netherlands	Medicines Evaluation Board (MEB)	✓	✓
Poland	Office for Registration of Medicinal Products, Medical Devices and Biocidal Products (URPL)	✓	✓
Portugal	National Authority of Medicines and Health Products (Infarmed)	✓	
	National Authority for Animal Health (DGAV)		✓
Romania	National Medicines Agency (ANM)	✓	
	Institute for Control of Biological Products and Veterinary Medicines (ICBMV)		✓
Slovakia	State Institute for Drug Control (SÚKL, SK)	✓	
	Institute for State Control of Veterinary Biologicals and Medicaments (USKVBL)		✓
Slovenia	Agency of the RS for Medicinal Products and Medical Devices of the Republic of Slovenia (JAZMP)	✓	✓
Spain	Spanish Agency for Medicines and Health Products (AEMPS)	✓	✓
Sweden	Medical Products Agency (MPA)	✓	✓
UK	Medicines and Healthcare products Regulatory Agency (MHRA)	✓	
	Veterinary Medicines Directorate (VMD)		✓

EEA countries (i.e. Iceland, Lichtenstein, and Norway) have limited influence and impact on the study of the fee system and also comparatively less dependency on the outcome, given their observer status in EMA committees and their relatively small share of EMA commissioned work (Table 18). Table 18 provides a list of all EEA NCAs consulted for this study, indicating whether they have responsibility for human medicines, veterinary medicines or both.

Table 18: EEA NCAs

Level of interest		Level of influence	Dependency on outcome
Medium		Low	Low
Country	Organisation	Human medicine	Veterinary medicine
Iceland	Icelandic Medicines Agency (IMCA)	✓	✓
Liechtenstein	Office of Health/ Medicinal Products Control Agency (*abbreviation not available)*	✓	✓
Norway	Norwegian Medicines Agency (*abbreviation not available*)	✓	✓

Other stakeholders

The following section identifies industry, research, healthcare professional, consumer, patient and other stakeholder groups with a likely interest in the EMA fee system study. Table 19 provides definitions for each category that was used by the study team to assess their appropriateness for targeted consultation.

Table 20 provides a list of industry associations and representatives operating in the human, veterinary, SME and pharmacovigilance sectors and an assessment of their interest in the study, level of influence and dependency of the study outcome. Table 21 lists European-level patient and consumer, Table 22 European-level research associations and Table 23 European-level healthcare professionals' associations.

Table 19: Stakeholders' level of interest in, influence and dependence on EMA fee system study

Category	Level of interest in the study	Level of influence	Dependency on outcome
High	EMA-listed stakeholder organisation or EMA suggestion, belongs to a niche medicines area (e.g. orphan medicines), and/or an SME.	High level of interaction with the EMA, large number of and/or active/influential members	A change in the fee system could have a high impact on a stakeholder group, i.e. their ability to fund market authorisation activities, decrease in exemptions, etc.
Medium	Some degree of interaction with the EMA. EMA suggestion but less relevant to the aims of the study.	Small to medium number of members but representing an important area for the study (e.g. paediatric medicine, orphan medicine, SMEs, pharmacovigilance, research and development)	Limited impact on their ability to access authorisation procedures
Low	Little or no interaction with the EMA. EMA suggestion but less relevant to the aims of the study.	Small number of members or relatively inactive/non-influential members	No impact on their ability to access authorisation procedures, or no likely change to fees as they are enshrined in legislation (e.g. paediatric medicines)

Table 20: European-level industry stakeholder associations

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
Human medicines				
European Federation of Pharmaceutical Industries and Associations (EFPIA)	• Represents approximately 1,900 companies across Europe in research and development and marketing of medicines. • Hosts two specialised groups: • Vaccines Europe • European Biopharmaceutical Enterprises (EBE) for biotechnology • Listed member of the ENCePP committee in the 2015 EMA annual report[69]	High	Medium	Medium

[69] EMA. 2014. *Budget for 2015: EMA/MB/73904/2014*. London: EMA.

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
Vaccines Europe	• Specialised group in EFPIA • Represents research-based vaccine companies • In addition, represents SMEs	High	Medium	Medium
Medicines for Europe	• Focus on: • Generic medicines • Biosimilar medicines • Value added medicines • Full members and affiliate members include national associations and pharmaceutical companies • Has collaborated with the EMA through meetings and organising workshops, namely on Bioequivalence Guideline for Modified Release Products[70]	High	Medium	Medium
Alliance for Regenerative Medicine (ARM)	• Listed EMA stakeholder • International voice on regenerative medicine • Focus on support for R&D of regenerative medicine	High	Medium	Medium
European Association of Euro-Pharmaceutical Companies (EAEPC)	• Represents industry, with a focus on increasing member competitiveness and helping with implementation of legislation • Roughly 80 wholesaler members	High	Medium	Medium
Active Pharmaceutical Ingredients Committee (APIC)	• Represents industry producing active pharmaceutical ingredients in Europe	High	Medium	Medium
Plasma Protein Therapeutics Association (PPTA)	• International • Represents manufacturers of plasma protein therapies • Focus on biologics, biotechnologies and rare diseases	High	Medium	Medium
Association of the European Self-Medication Industry	• Represents industry for non-prescription drugs	High	Medium	Medium

[70] EMA. 2014. *Budget for 2015: EMA/MB/73904/2014*. London: EMA.

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
European Paediatric Formulation Initiative (EuPFI)	• Focus on research for children's medicines • Members from pharmaceutical industry, academy and hospital	High	Medium	Low
European Biopharmaceuticals Enterprises (EBE)	• Focus on healthcare technologies and innovation	Medium	Medium	Medium
European Alliance for Personalised Medicines (EAPM)	• Focus on personalised medicine and regulatory environment	Medium	Medium	Medium
European Coalition on Homeopathic and Anthroposophic Medicinal Products (ECHAMP)	• Focus on homeopathic and anthroposophic medicinal products • Roughly 50 members from across the EU working in the development and production of these products	Medium	Medium	Medium
Association of Clinical Research Organization (ACRO)	• Represents clinical research organisations	Medium	Low	Low
European CRO Federation (EUCROF)	• Focus on clinical research	Medium	Low	Low
European Healthcare Distribution Association (GIRP)	• Represents and supports approximately 750 pharmaceutical wholesalers in Europe	Medium	Low	Low
Parenteral Drug Association (PDA)	• Association which aims to assist in the development of regulation and manufacturing science in the pharmaceutical and bio-pharmaceutical industries	Medium	Low	Low
European Federation of Statisticians in the Pharmaceutical Industry (EFSPI)	• Represents statisticians in research and development, and production of medicines • Promoting standards of statistics	Low	Low	Low
Confédération Européenne des Syndicats	• Represents trade unions	Low	Low	Low
IndustriAll	• Represents workers in mining, manufacturing and energy	Low	Low	Low

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
Veterinary medicine				
European Group for Generic Veterinary Products (EGGVP)	• Focus on generic medicinal products • Represents 21 member organisations with market authorisations	High	High	Medium
European Animal Health Industry (IFAH-Europe)	• Represents manufacturers in: ○ Veterinary medicines ○ Vaccines ○ Animal health products	High	Medium	Medium
Animal Cell Technology Industrial Platform (ACTIP)	• Focus on animal cell technology biopharmaceuticals, vaccines and therapies • Approximately 44 member companies	High	Low	Medium
SMEs				
European Network of Centres for Pharmaco-epidemiology and Pharmacovigilance (ENCePP)	• Hosted by the EMA • Pharmacoepidemiology and pharmacovigilance	High	High	Medium
The European Association for Bioindustries (EuropaBio)	• Focus on the area of biotechnology • Represents associations and corporate members which feed into a network of approximately 1,800 SMEs across the European Union. • Focus on three areas of biotechnology: healthcare biotechnologies agri-food, and industrial. • Priority areas include orphan medicines, advanced-therapy medicinal products and personalised medicine	High	Medium	Medium
Europharm SMC	• Represents roughly 200 SMEs across Europe	High	Medium	Medium
European Confederation of Pharmaceutical Entrepreneurs (EUCOPE)	• Pharmaceutical and biotechnology • Represents mid-sized companies (approximately 900)	High	Medium	Medium

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
European Federation for Exploratory Medicines Development (EUFEMED)	• Established in 2015, supporting development of medicines	Medium	Medium	Medium
European Quality Assurance Confederation (EQAC)	• Focus on quality assurance • National organisation members • Member experience in good clinical, laboratory and manufacturing practices	Medium	Medium	Low

Table 21: European-level patient and consumer associations

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
European Patients' Forum (EFP)	• Patient and patient organisations • Focus on community wellbeing	Medium	Low	Low
BEUC	• Represents interests of consumers in Europe	Medium	Low	Low
HOPE	• Represents national hospital associations and owners (both public and private)	Low	Low	Low
International Association of Mutual Benefit Societies (AIM)	• Non-profit healthcare payers, mutual and insurance funds	Low	Low	Low
European Social Insurance Platform (ESIP)	• Focus on social protection • Represents 40 social security organisations across 15 Member States and Switzerland	Low	Low	Low
European Renal Association/European Dialysis and Transplantation Association/European Renal Best Practice	• Focus on improving outcomes for patients with kidney disease	Low	Low	Low

Table 22: European-level research associations

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
EuFEPS	• Represents scientists in Europe across industry, government, academia, and other institutions involved in drug research, development, regulation and policymaking • 22 member societies, roughly 15,000 individual members	Medium	Medium	Medium
Federation of European Academies of Medicine (FEAM)	• Create cooperation between national academies of medicine and science in Europe • Represents approximately 5,000 scientists across the network	Medium	Medium	Medium
Science Europe	• Represents research funding organisations and research performing organisations • Objective to work with key partners to strengthen the European Research Area	Medium	Medium	Medium
European Academy of Allergy and Clinical Immunology (EAACI)	• Represents approximately 50 allergy societies at a national level • Focus on basic and clinical research • Roughly 9,500 academics, researchers and clinicians • Globally active	Medium	Medium	Medium
ELIXIR	• Infrastructure to integrate research data, particularly biological data, produced by researchers.	Medium	Medium	Low
Infrastructure for Systems Biology (ISBE)	• Focus on creating a research infrastructure for health, bio-economy and quality of life. • Working to create technical specifications for the infrastructure	Medium	Low	Medium
ECRIN-ERIC	• Supports the conduct of clinical trials (multinational) in Europe. • Represents 7 member countries and 2 observer countries	Medium	Medium	Medium
EATRIS-ERIC (European Infrastructure for Translational	• Focus on preclinical and early clinical development of drugs, vaccines and diagnostics.	Medium	Low	Medium

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
Medicine)				
ERA-EDTA	• Physicians' association • Approximately, 7,000 members	Medium	Low	Low
BBMRI-ERIC	• European research infrastructure of biobanks and biomolecular resources. • Approximately 19 Member State members and an international organisation	Medium	Low	Low
European Society of Endocrinology (ESE)	• Society for public benefit • Focus on research, education and clinical practice in endocrinology	Medium	Low	Low
INFRAFRONTIER	• Seeks to inform on role of genome in human health (through mouse models, data and scientific platforms)	Medium	Low	Low
Network of Coordinating Centres for Clinical Trials (KKS Netzwerk)	• Platform for communication on clinical trials in Europe • Helps patients and population understand clinical trials	Medium	Low	Low

Table 23: European-level healthcare professionals' associations

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
Pharmaceutical Group of the European Union (PGEU)	• Healthcare professionals' organisation • Represents community pharmacy	Medium	Medium	Medium
European Association for Clinical Pharmacology and Therapeutics (EACPT)	• Represents all European national organisations for clinical pharmacology • Objective to add expertise to decisionmaking around regulation of medicines	Medium	Medium	Medium
European Respiratory Society	• Members include physicians, scientists, healthcare professionals and others involved with respiratory medicine • Members from over 140 countries • Promotes research and standards	Medium	Low	Low

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
Comité Permanent des Médecins Européens/ Standing Committee of European Doctors (CPME)	• Representative of national medical associations in Europe	Medium	Low	Low
European Union Geriatric Medicine Society	• Focus on research into ageing, and on regulation of medicine	Medium	Medium	Low
European Society of Oncology Pharmacy	• Aim is to get optimal treatment for patients • Promotes of clinical and oncology pharmacy (education, research and development, quality management, etc.)	Medium	Medium	Low
European Academy of Paediatrics (EAP)	• Focus on children and young people's health	Medium	Medium	Low
European College of Neuropsychopharmacology (ECNP)	• Promotes experimental and clinical research in Europe • Promotes translation of knowledge into medicines and clinical applications	Medium	Low	Low
European League Against Rheumatism (EULAR)	• Promotes education and research in arthritis/rheumatism • Represents people living with arthritis/rheumatism, professionals and scientific societies	Low	Low	Low
European Society for Medical Oncology (ESMO)	• Professional organisation for medical oncology • Approximately 15,000 members across 130 countries	Low	Low	Low
European Society of Cardiology	• Global network of cardiology societies, and professionals in the domain, organised by volunteers •	Low	Low	Low
European Society of Endocrinology	• Promotes education and clinical practice in endocrinology	Low	Low	Low
European Society of Radiology (ESR)	• Almost 70,000 members worldwide • Promoting radiology profession	Low	Low	Low

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
European Specialists Nurses Organisations	• Represents organisations across Europe	Low	Low	Low
European Union of General Practitioners	• Promote training, practice and patient care • Works with other groups in the medical profession	Low	Low	Low
European working group on Gaucher Disease	• Promotes clinical and basic research into Gaucher Disease	Medium	Low	Low
Health Care Without Harm Europe	• Group of hospitals, healthcare professionals, research professionals, local authorities, etc. • Represents on a range of issues, including pharmaceuticals	Low	Low	Low
International League Against Epilepsy	• Promote research and education in epilepsy[71]	Medium	Low	Low
United European Gastroenterology (UEG)	• Promotes research and education on digestive disease	Medium	Low	Low
European Academy of Neurology (EAN)	• Network of those working in neurology and neuroscience (institutions, researchers, clinicians, etc.) • Share information in the network (Europe and more widely) • Roughly 23,000 members	Low	Low	Low
European Federation of Internal Medicines (EFIM)	• Promotes internal medicine (education, ethics and professionally) • Little information on member organisations	Low	Low	Low
European Association for the Study of Diabetes (EASD)	• Support research for diabetes	Low	Low	Low
European Association of Hospital Pharmacists (EAHP)	• Represents hospital pharmacists (approximately 19,000) in Europe • Promotes improvement of care and patient outcomes in hospitals	Low	Low	Low

[71] For more information: http://www.ilae.org/Visitors/About_ILAE/Index.cfm

Organisation	Relevance	Level of interest	Level of influence	Dependency on outcome
European Association of Urology (EAU)	• Promotes urological care • Approximately 15,000 medical professionals	Low	Low	Low
European Forum for Primary Care (EFPC)	• Focus on primary care, and evidence generation	Low	Low	Low
European Hematology Association (EHA)	• Promotes research, education and patient care	Low	Low	Low
European Society for Blood and Marrow Transplantation (EBMT)	• Promotes research and education on blood and marrow transplantation and cell therapy to treat and improve the lives of patients with blood cancers and other life-threatening diseases	Medium	Low	Low
International Society for Cellular Therapy Society (ISCT)	• Promotes research and education on cellular therapies	Medium	Low	Low

Appendix 5. Survey of NCAs – Survey instrument

Evaluation of the European Medicines Agency Fee System

Introduction

The European Commission Directorate General for Health and Food Safety has commissioned RAND Europe to conduct a study supporting the evaluation of the European Medicines Agency (EMA) fee system, including the remuneration paid by EMA to National Competent Authorities (NCAs). [*The terms of reference for the study are available* here]

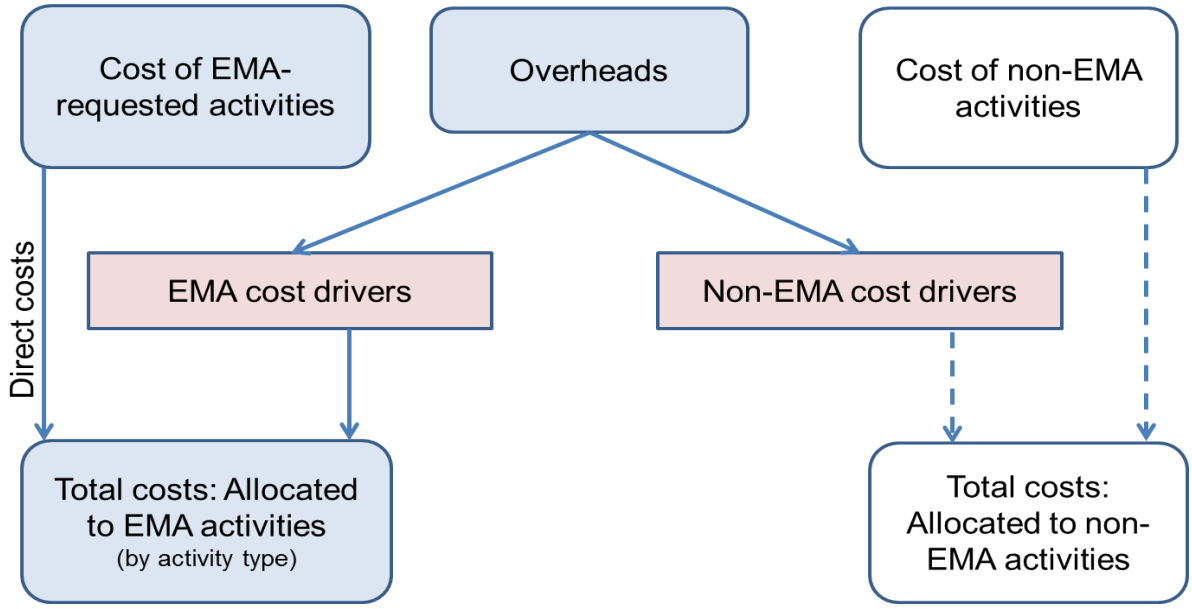
The study runs from December 2016 to February 2018 and focuses on the fee and remuneration system with reference to its effectiveness, efficiency, relevance, coherence and sustainability. This evaluation is expected to provide a sound basis to consider the review of the entire fee system of EMA based on needs identified and described in the evaluation process.

The present survey is part of the study which aims to collect views from multiple perspectives, including NCAs, EMA, industry representatives and other interested parties, who are in a position to comment on the fee system and its implementation. The objective of this NCA consultation is to obtain information that, together with information from other sources, particularly the EMA Management Board (MB) data gathering exercise, will enable the study team to assess the extent to which the current fee and remuneration system is cost-based, fair, proportionate and not unduly complex.

Scope of this survey

This online survey will be sent to all of the EU and EEA competent authorities that undertake EMA-requested activities related to either human or veterinary medicines. This includes all activities requested by EMA regardless of whether or not they are currently remunerated. The survey is divided into two parts.

Part I of the survey covers NCAs' costs currently incurred as a result of undertaking EMA activities, and the number of each of these activities that NCAs undertake. The objective is to understand the current **cost** implications for NCAs of the existing system. It is recognised that NCAs operate in different national contexts and have different legal structures and, as such, a pragmatic approach is applied. The basic model is illustrated below:



This model requires that full economic costs are allocated between EMA-requested activities and the totality of other, non-EMA-requested, activities (a definition of full economic costs is provided in Part I of the survey). This allocation will be estimated by the study taking into account the NCA survey responses to this survey and time data from the EMA MB data gathering exercise. We are asking for detailed information on EMA-requested activities undertaken by each individual NCA (whether remunerated by EMA currently or not) and their costs. **We are not asking for detailed information on non-EMA activities**. The survey requests information on:

- the portion of NCA total (full economic) costs that are related to EMA activities and the portion that is related to non-EMA activities, and the total amount of overhead costs that support both of these categories of activity;
- the method applied by NCAs for allocating its overhead costs between EMA-requested and non-EMA activities, and the rationale for that allocation method;
- the portion of NCA total (full economic) costs for EMA activities that are based on work undertaken by scientific vs. administrative staff members;
- NCAs' level of engagement with the EMA in terms of staff hours allocated to EMA-requested activities and the number of each of those activities they are involved in, including EMA-requested activities and respective costs that are not currently covered by the EMA remuneration system.

The responses from NCAs will inform RAND Europe's analysis of the relationship between costs and the existing fee and remuneration system. To aid comparability, cost and activity data are requested for the most recent calendar or financial year for which they are available. While cost structures may change over time, for example, due to changes in staffing levels, the focus of the exercise is to determine how fee remuneration compares to actual costs incurred now, and not how they might be expected to change in future. It is important to note that the purpose is not to analyse the efficiency of NCAs in carrying out EMA-requested activities. NCA funding that is not related to EMA-requested activities is similarly out of scope.

Part II of the survey provides an opportunity for NCAs to provide additional comment on the current fee system.

We would like to stress the importance of providing the most accurate data at your disposal regarding the costs incurred by your organisation for the provision of services to

the EMA, bearing in mind the responsibility of EMA to coordinate 'the existing scientific resources put at its disposal by Member States for the evaluation, supervision and pharmacovigilance of medicinal products'. Your contribution will be treated confidentially and stored securely at RAND Europe (for more details on the confidentiality clauses associated with the data provided, please see here).

Thank you very much in advance for your participation. If you have any queries regarding your responses to specific survey questions or on the survey in general, please do not hesitate to contact the RAND Europe project manager, Elta Smith, at EMA-fees-eval@RAND.org

Background

1. Please provide the name of your organisation:

2. Please indicate the country your organisation is located in: [single choice]

- Austria
- Belgium
- Bulgaria
- Croatia
- Cyprus
- Czech Republic
- Denmark
- Estonia
- Finland
- France
- Germany
- Greece
- Hungary
- Iceland
- Ireland
- Italy
- Latvia
- Liechtenstein
- Lithuania
- Luxembourg
- Malta
- Netherlands
- Norway
- Poland
- Portugal
- Romania
- Slovakia
- Slovenia
- Spain
- Sweden
- United Kingdom

3. Please indicate the role of your NCA in relation to other public bodies in your country in [single choice]

- My agency is a department in a Ministry
- My agency is subordinated to another institution (e.g. Ministry)
- My agency is an independent public body
- Other, please specify

4. Please indicate the areas of responsibility of your NCA: [multiple choice]

- Human medicines
- Veterinary medicines
- Other, please specify

Part I: Cost data associated with EMA-related activities

The following questions focus on the costs incurred by your organisation to conduct the work contributing to EMA activities. If your organisation provided time data to the EMA Management Board Data Gathering (MBDG) Initiative, please note that we will be provided with the time data collected for that initiative and you do not need to provide that information here. We are collecting cost data on the full range of EMA-requested activities, not limited to the ones included in the time data gathering exercise.

Costs in the present survey are **full economic costs**. A definition of full economic costs is provided below for reference when answering the questions in this section.

Full economic costs include both directly attributable and overhead costs. Some costs will be directly attributable to specific activities whether EMA-requested activities or other activities. Other costs are overheads that are not directly attributable to specific activities. It is for the responding organisation to decide which costs to include under the heading of overheads and which to include under the heading of costs directly attributable to specific activities. Respondents are requested to provide a list of the types of costs included as overheads and the types of costs included as directly attributable costs, respectively.

- Full economic costs include all costs incurred by the organisation:
- All staff costs incurred by the employer, gross of any taxes, including superannuation, training and other staff-related costs
- Costs of all staff hired on contracts as well as employees
- All non-staff operating costs: consumables (stationery, telecommunications, etc.); facilities costs (heating, lighting, cleaning, security, etc.); business travel expenses; etc.
- All annual costs of buildings and equipment (IT, etc.). This should include the annual depreciation costs of all capital assets that are used and owned by the organisation and associated capital charges including interest payments. Where assets are leased rather than owned, full economic costs include the annual lease payments. Where assets are used free of charge – for example they have been donated to the organisation – an attempt should be made to estimate the annual opportunity costs of those assets (e.g. what lease payments would be due had the assets been leased commercially rather than donated).

Please provide the information for the **most recent calendar or financial year** for which you have the valid data as requested.

5. State the currency in which all financial figures are given:

6. State the complete, one-year period for which the information you provide applies (use the most recent 12 month period for which you have data):

Please provide your answer in the format DD/MM/YYYY

From

To

7. State the total costs for your NCA in this time period (EMA and non-EMA related, see definition above):

8. Do you have any supporting documentation for this figure? [single choice]

- Yes
- No

[If Yes] Please can you provide the name(s) of the supporting document(s) – if you prefer, please send us a list separately to EMA-fees-eval@RAND.org:

9. Of the total costs (EMA and non-EMA related) provided in question 7, please separate the costs into the following categories:

Total staff costs, including all contracted staff as well as employed staff (see above for definition)	
Total non-staff costs, that is, all other costs that make up full economic costs (see above for definition)	

10. Please separate your organisation's costs into the following three ***mutually exclusive*** categories. If you do not have exact data, please provide estimates.

Note: Please apply the same criteria as used in the time data from the EMA MB data gathering exercise.

- *Scientific/technical staff members for NCAs are defined as the scientifically qualified staff acting as rapporteur, co-rapporteur, co-ordinator, quality, safety or efficacy assessor, inspector, peer reviewer, quality assurance, and/or external expert.*
- *Administrative staff members for NCAs are defined as all staff other than scientific/technical staff*

	Scientific staff costs (including sub-contracted personnel)	**Administrative staff costs (including sub-contracted personnel)**	**Non-staff costs**	**TOTAL**
Costs of undertaking all EMA-requested activities – excluding overhead costs				
Costs of all other activities in your NCA – excluding overhead costs				
Overhead costs - i.e. costs that cannot be directly attributed to specific activities				
TOTAL				

11. Please indicate for the question above whether the data are estimated or actual: [single choice]

- Estimated
- Actual
- Part actual/part estimate

[If Part actual/part estimate] Please explain what part is based on actual costs, and what part is estimated:

12. Do you have any supporting documentation for this figure? [single choice]

- Yes
- No

[If Yes] Please can you provide the name(s) of the supporting document(s) – if you prefer, please send us a list separately to EMA-fees-eval@RAND.org:

13. How many full-time equivalent (FTE) staff members did your organisation employ (or subcontract) on average during the 12 month reporting period?

Note: Please apply the same criteria as used in the time data from the EMA MB data gathering exercise.

Number of FTE scientific staff

Number of FTE administrative staff

14. Please list the cost categories and their amounts you have included as overhead costs (*e.g. capital depreciation, rent, general administration, IT, etc.)*:

15. Do you have any supporting documentation for this figure? [single choice]

- Yes
- No

[If Yes] Please can you provide the name(s) of the supporting document(s) – if you prefer, please send us a list separately to EMA-fees-eval@RAND.org:

16. In the cost modelling exercise that will be undertaken for this study (see Terms of reference here), overheads will be allocated between EMA-requested activities and non-EMA activities. Which of the following approaches to allocating overheads do you feel is the most suitable for your NCA? [single choice]

- The allocation of overheads is proportionate to staff costs
- The allocation of overheads is proportionate to staff numbers
- Other, please specify

Engagement in EMA-requested activities

We will now ask a series of questions regarding the types of EMA-requested activities that your organisation undertakes.

During the year for which you are reporting data, your staff may have:

- completed EMA activities commenced in the previous year
- commenced EMA activities and completed them during the same year
- commenced EMA activities that will be continued into the next year

For the purposes of this survey, we will only ask you about activities that your staff have **completed** in the reporting year [items (1) and (2) from the list above]. For initial marketing authorisations and line extensions in particular, this means that only procedures for which phase 3 (including clock stops) was completed in the reporting year should be included.

We will ask you to indicate the number of activities that were completed in the reporting year.

17. Please provide the number of EMA procedures for human medicines listed in the following table that your staff members completed during the reporting year:

This includes activities commenced in a previous year and completed in the reporting year and those commenced and completed in the reporting year

	Number of EMA-requested activities completed within the reporting year (Rapporteurs)	**Number of EMA-requested activities completed within the reporting year (Co-rapporteurs)**	**Number of EMA-requested activities completed within the reporting year (Other, incl. multi-national teams)**
Scientific advice & protocol assistance - Initial scientific advice - I			
Scientific advice & protocol assistance - Initial scientific advice - II			
Scientific advice & protocol assistance - Initial scientific advice - III			
Scientific advice & protocol assistance			

	Number of EMA-requested activities completed within the reporting year (Rapporteurs)	**Number of EMA-requested activities completed within the reporting year (Co-rapporteurs)**	**Number of EMA-requested activities completed within the reporting year (Other, incl. multi-national teams)**
- Follow-up scientific advice - I			
Scientific advice & protocol assistance - Follow-up scientific advice - II			
Scientific advice & protocol assistance - Follow-up scientific advice - III			
Full application for marketing authorisation - New active substances			
Full application for marketing authorisation - Known active substances			
Full application for marketing authorisation – Fixed combination			
Full application for marketing authorisation - Biosimilars			
Full application for marketing authorisation - Informed consent			
Full application for marketing authorisation – Generics			
Full application for marketing authorisation - Well established use			
Full application for marketing authorisation – Hybrids			
Paediatrics – PIPs			
Paediatrics - Waivers			
Paediatrics - Compliance checks			
Orphan designation			
Scientific services – Plasma Master File (PMF), VAMF, Ancillary medicinal substances consultation, ATMP certification, Traditional herbals			
Scientific services - Compassionate use opinions			
Scientific services - Art.58			
Line extensions - Level I			
Line extensions - Level II			
Line extensions - Level III			

	Number of EMA-requested activities completed within the reporting year (Rapporteurs)	Number of EMA-requested activities completed within the reporting year (Co-rapporteurs)	Number of EMA-requested activities completed within the reporting year (Other, incl. multi-national teams)
Renewals			
Certification for Advanced Therapies			
Referrals of disputes from decentralised and mutual recognition procedures (Art.29(4), Art.30, Art.31, Art.20)			
Type II variations - Level I			
Type II variations - Level II			
Type II variations - Level III			
Type 1B variations			
Pharmacovigilance referrals (Art.31, Art.20, Art.107i)			
Post-Authorisation Safety Studies (PASS)			
Periodic Safety Update Reports for CAPs (PSUR)			
Periodic Safety Update Reports for NAPs (PSUSA)			
Inspections - GMP in Europe			
Inspections - GMP outside Europe			
Inspections - GCP in Europe			
Inspections - GCP outside Europe			
Inspections - GVP			

18. Please provide the number of EMA-requested activities for veterinary medicines listed in the following table that your staff members completed during the reporting year:

This includes activities commenced in a previous year and completed in the reporting year and those commenced and completed in the reporting year.

	Number of EMA-requested activities completed within the reporting year (Rapporteurs)	Number of EMA-requested activities completed within the reporting year (Co-rapporteurs)	Number of EMA-requested activities completed within the reporting year (Other, incl. multi-national teams)

	Number of EMA-requested activities completed within the reporting year (Rapporteurs)	Number of EMA-requested activities completed within the reporting year (Co-rapporteurs)	Number of EMA-requested activities completed within the reporting year (Other, incl. multi-national teams)
Scientific advice & protocol assistance - Initial scientific advice I			
Scientific advice & protocol assistance - Initial scientific advice II			
Scientific advice & protocol assistance - Initial scientific advice III			
Scientific advice & protocol assistance - Follow-up scientific advice I			
Scientific advice & protocol assistance - Follow-up scientific advice II			
Scientific advice & protocol assistance - Follow-up scientific advice III			
Full application for marketing authorisation - New active substances			
Full application for marketing authorisation - Generics			
Full application for marketing authorisation - Known active substances			
Full application for marketing authorisation – Fixed combination			
Full application for marketing authorisation - Informed consent			
Full application for marketing authorisation - Well established use			
Full application for marketing authorisation - Hybrids			
Full application for marketing authorisation - Immunologicals			
Full application for marketing authorisation - MUMS			
Maximum residue limit applications			
Line extensions - Level I			
Line extensions - Level II			
Line extensions - Level III			
Renewals			

	Number of EMA-requested activities completed within the reporting year (Rapporteurs)	**Number of EMA-requested activities completed within the reporting year (Co-rapporteurs)**	**Number of EMA-requested activities completed within the reporting year (Other, incl. multi-national teams)**
Referrals of disputes from decentralised and mutual recognition procedures and Pharmacovigilance referrals (Art.33, Art.34, Art.35, Art.78, Art.13.2, Art.30.3)			
Type II variations - Level I			
Type II variations - Level II			
Type II variations - Level III			
Type II variations - Level IV (Immunological)			
Type 1B variations			
Post-Authorisation Safety Studies (PASS)			
Periodic Safety Update Reports (PSUR)			
Inspections - GMP in Europe			
Inspections - GMP outside Europe			
Inspections - GCP in Europe			
Inspections - GCP outside Europe			

19. What additional costs were incurred, if any, by your staff members, in the reporting year, for their participation in EMA Scientific Committees, Ad-hoc Expert Groups, Working Parties and other expert groups?

Please include travel and subsistence if these have been included in the costs you reported in Part I of the survey.

20. What additional EMA activities, if any, were staff members from your organisation involved and for which you incurred costs in the reporting year? How much time was involved per activity?

These can include non-remunerated activities.

Part II Views on the current EMA fee and remuneration system

The following questions are designed to obtain your views more broadly about the EMA fee and remuneration system.

21. What are the main strengths of the EMA fee and remuneration system?

22. What are the main weaknesses of the EMA fee and remuneration system?

23. How can the weaknesses you have identified be improved?

24. Do you have any additional comments on the current EMA fee and remuneration system:

25. If you have any additional information to share with the study team in relation to this evaluation please provide contact details in the box below:

Name

Contact email address

You may also provide information directly at the following email address: EMA-fees-eval@RAND.org

Appendix 6. Survey of wider stakeholders – Survey instrument

Evaluation of the European Medicines Agency Fee System – Survey of targeted stakeholders

Introduction

The European Commission Directorate General for Health and Food Safety has commissioned RAND Europe to conduct a study in support of an evaluation of the European Medicines Agency (EMA) system of fees charged mainly to market authorisation holders and applicants, including remuneration paid to national competent authorities (NCAs) that work on EMA activities. [The terms of reference for the study are available here]

The study runs from December 2016 to February 2018 and looks at the fee and remuneration system with reference to its effectiveness, efficiency, relevance, coherence and sustainability. The results of this study are expected to provide the Commission with a basis for an evaluation from which to consider launching a separate project for a possible review of the EMA fee and remuneration system.

The present survey aims to collect views from multiple perspectives, including industry, relevant associations and other interested parties, who are in a position to comment on the fee system and its implementation.

It is important to note that this is a targeted consultation survey. An open public consultation will take place in the second half of 2017.

The objective of the present targeted survey is to obtain information that, together with information from other sources such as the open public consultation, will enable the study team to assess how far the current fee and remuneration system is cost-based, fair, proportionate and not unduly complex.

All information collected in the survey will be kept strictly confidential and any quotes included in the final report will be anonymised.

Thank you very much in advance for your participation. If you have any queries regarding your responses to specific survey questions or on the survey in general, please do not hesitate to contact the RAND Europe project manager, Elta Smith, at EMA-fees-eval@RAND.org

Background

1. Please provide the name of your organisation

2. Which of the following statements best describes the work of your organisation/members: [multiple choice]

- My organisation/members primarily work at the national level
- My organisation/members primarily work at the EU-level
- My organisation/members primarily work at the global level

[If at the national level] In which country?

3. Please select the category that best describes your organisation: [single choice]

Small and medium-sized enterprises (SMEs) are defined in the EU recommendation 2003/361 as having a staff headcount of less than 250 and either a turnover of less than €50m or a balance sheet total of less than €43m.

- Pharmaceutical Industry (Large)
- Pharmaceutical Industry (SME)
- Industry organisation
- Research organisation
- Healthcare professional association
- Patient association
- Wholesalers association
- Public Health NGO
- Other, please specify

4. Please indicate the areas of responsibility of your organisation: [multiple choice]

- Human health
- Veterinary health
- Other, please specify

Engagement with the EMA

5. Which of the following EMA services are relevant to you or your members? [multiple choice]

- Scientific advice and protocol assistance
- Full application for marketing authorisation – New active substances
- Full application for marketing authorisation – Known active substances
- Full application for marketing authorisation – Biosimilars
- Full application for marketing authorisation – Informed consent
- Full application for marketing authorisation – Generics
- Full application for marketing authorisation – Well established use
- Full application for marketing authorisation – Hybrids
- Full application for marketing authorisation – Immunologicals
- Full application for marketing authorisation – Minor-use-minor-species (MUMS)
- Paediatrics (PIPs, Waivers or Compliance checks)
- Orphan designation
- Veterinary MUMS designation
- Scientific services (e.g. Art 58, compassionate use opinions, etc.)

- Maximum residue limit (MRL) applications
- Line extensions
- Renewals
- Certification for Advanced Therapies
- Variations
- Inspections (GMP, GCP or GVP)
- Pharmacovigilance activities
- Non-product specific engagement (e.g. working parties for professionals, patients, consumers and academia, etc.)
- None of the above
- Other, please specify

Reflections on the EMA fee system

To what extent do you agree or disagree with the following statements:

6. Overall, the level of fees charged by the EMA is appropriate given the services they provide [single choice]

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree
- Don’t Know

7. If you have any reflections on the statement above please elaborate in the box below:

8. The fees for additional strengths or presentations are proportionate [single choice]

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree
- Don’t Know
- Not applicable

9. If you have any reflections on the statement above please elaborate in the box below:

10. The specific fee arrangements made for SMEs are appropriate [single choice]

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree
- Don’t Know
- Not applicable

11. If you have any reflections on the statement above please elaborate in the box below:

12. The specific fee arrangements made for particular types of medicines (orphan medicines, veterinary medicines for MUMS, medicines for paediatric use, etc.) are appropriate [single choice]

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree
- Don’t Know
- Not applicable

13. If you have any reflections on the statement above please elaborate in the box below:

14. Overall, the fee system is straightforward and easy to understand [single choice]

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree
- Don’t Know

15. If you have any reflections on the statement above please elaborate in the box below:

16. Overall, the fees charged for different EMA services are transparent [single choice]

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree
- Don’t Know

17. If you have any reflections on the statement above please elaborate in the box below:

18. Fees should be based on the costs incurred by EMA and experts in delivering the services [single choice]

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree
- Don’t Know

19. If you have any reflections on the statement above please elaborate in the box below:

Comparisons with other fee systems

20. To what extent do you agree with the following statement:

The EMA fee system is consistent with fees charged for similar services by national regulatory authorities in the EU [single choice]

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree
- Don't Know

21. Please elaborate in the box below on any differences or inconsistencies in the fees charged (if applicable):

22. Do you have experience with other fee systems outside of the EU? [single choice]

- Yes
- No

[If yes] How does the EMA's fee system compare with those in other regions (e.g. the US Food & Drug Administration (FDA), etc.) in terms of simplicity, transparency and proportionality of the system?

Final comments

23. Do you have any suggestions for the way in which the current fee system could be improved?

24. If you are willing for the evaluation team to contact you should we require further information, please provide your information in the box below:

Name

Contact email address

You may also provide information directly at the following email address: EMA-fees-eval@RAND.org

Appendix 7. Open public consultation – Survey instrument

Study supporting the Evaluation of the European Medicines Agency Fee System: Open Public Consultation

I. Introduction

The European Medicines Agency (EMA) is the European Union's (EU) central regulatory body operating centralised pre-authorisation and post-authorisation procedures for medicinal products for human and veterinary use across the EU and the European Economic Area (EEA). The Agency is funded by EU and EEA contributions as well as fees paid by industry for obtaining and maintaining marketing authorisations and providing other services. The EMA works in close collaboration with national competent authorities (NCAs) in EU and EEA Member States. NCAs are represented in the EMA committees and in this setting they carry out assessments of medicinal products for human and veterinary use in the context of EU marketing authorisations. Other activities related to centrally-authorised medicinal products are also undertaken, including pharmacovigilance activities at EU level. NCAs receive remuneration by the EMA for activities for centralised procedures at EU level.

The EMA fee system is set up by Council Regulation (EC) No 297/95 and Regulation (EU) No 658/2014) and implementing arrangements. It provides fee incentives for specific types of products (including medicines for rare diseases, medicines for children, advanced therapies, and veterinary medicines for minor use/minor species) and specific applicants and MAHs such as micro, small and medium-sized enterprises (SMEs).

This public consultation is part of a study supporting the evaluation of the EMA fee system. The consultation aims to elicit information, views and concerns of all groups having an interest in the EMA fee system and its implementation, including the remuneration to NCAs. In particular, it seeks to gather input from groups having experience with the fee and remuneration system on its effectiveness and efficiency, relevance, coherence and sustainability.

Your input will help the study team to assess the extent to which the current fee and remuneration system is cost-based, fair, proportionate and not unduly complex. It will complement information from other sources, particularly time and cost data provided by the EMA and NCAs, insights gained from EMA and NCA representatives as well as views provided by wider stakeholders, covering European level industry, research, healthcare, patient, consumer and other relevant associations and representative groups.

You can contribute to this public consultation by filling in the online questionnaire below. The questionnaire is available in English, French and German, and responses can be submitted in any EU language.

The final question of the questionnaire allows you to upload one supplementary document (max. 2 pages).

Please **only** include any personal data or any other information that can lead to your direct identification in your replies **where specifically requested in the questionnaire**. Please **do not** enter such data in any of your other replies, in particular in the free text boxes of the questionnaire. See further the privacy statement attached to this consultation for information on how your personal data and contribution will be dealt with.

*[NOTE: * represents questions that are mandatory for the respondent]*

II. About you

1. Publication of your contribution* [single choice]

Note that, whatever option chosen, your answers may be subject to a request for public access to documents under Regulation (EC) No 1049/2001.

- **My contribution can be published with my personal information** (I consent the publication of all information in my contribution in whole or in part including my name or my organisation's name, and I declare that nothing within my response is unlawful or would infringe the rights of any third party in a manner that would prevent publication).
- **My contribution can be published only without my identification and contact details (i.e. name, surname and e-mail address)** (I consent to the publication of any information in my contribution in whole or in part (which may include quotes or opinions I express) provided that it is done without publishing my name, surname and e-mail address. I declare that nothing within my response is unlawful or would infringe the rights of any third party in a manner that would prevent the publication).

2. Please provide your:

First name*

Last name*

E-mail address (Your e-mail address is needed in case we have questions about your reply and need to ask for clarifications. If you do not have an email address or do not wish to be contacted by us for further clarifications, please write "Not available")*

3. You are welcome to answer the questionnaire in any of the 24 official languages of the EU. Please indicate in which language you are replying*

- Bulgarian
- Croatian
- Czech
- Danish
- Dutch
- English
- Estonian
- Finnish
- French
- Gaelic

- German
- Greek
- Hungarian
- Italian
- Latvian
- Lithuanian
- Maltese
- Polish
- Portuguese
- Romanian
- Slovak
- Slovenian
- Spanish
- Swedish

4. You are replying as a(n)* [single choice]

- Individual citizen in your personal capacity
- Member of a central government/ministry or public authority at national or regional level in a Member State or the EEA
- Member of a central government or public authority at EU level
- Member of an inter-governmental organisation
- Member of a non-governmental organisation (NGO)
  - Type of NGO: [single choice]
    - Public health NGO
    - Other NGO
- Member of a civil society organisation
- Member of a representative organisation:
  - Type of organisation: [single choice]
    - Healthcare organisation
    - Patient association
    - Consumer association
    - Other representative group/organisation
      - Please specify:
        200 character(s) maximum
- Member of a Member State/EEA medicine regulation agency
- Member of a non-EU medicine regulation agency
- Member of a think-tank/consultancy
- Member of a research organisation/academic institution
- Representative of a company with direct relevance to the EMA (e.g. pharmaceutical company)
  - How many employees does your company have?* [single choice]
    - More than 250 employees (large enterprise)
    - 50 to 250 employees (medium-sized enterprise)
    - 10 to 49 employees (small enterprise)
    - Max. 9 employees (micro enterprise)
    - I am self-employed

- Please describe the areas of responsibility of your organisation:* [multiple choice]
  - Human health
  - Veterinary health
  - Innovative medicinal products
  - Generic medicinal products and biosimilars
  - Other
    - Please specify:
      200 character(s) maximum
- Name of your organisation:*
  200 character(s) maximum
- Postal address of your organisation:*
  200 character(s) maximum

- Representative of a company with no direct relevance to the EMA
  - How many employees does your company have?* [single choice]
    - More than 250 employees (large enterprise)
    - 50 to 250 employees (medium-sized enterprise)
    - 10 to 49 employees (small enterprise)
    - Max. 9 employees (micro enterprise)
    - I am self-employed
  - Name of your organisation:*
    200 character(s) maximum
  - Postal address of your organisation:*
    200 character(s) maximum
- Legal professional
- Other
  - Please specify:
    200 character(s) maximum

5. Is your organisation included in the Transparency Register?* [single choice]
   [If you do not respond as a representative of an organisation, please click 'Not applicable']

   If your organisation is not registered, we invite you to register here, although it is not compulsory to be registered to reply to this consultation. Please also read: Why a transparency register?

   - Yes
     - Please indicate your register ID number:

- No
- Not applicable

6. Country of your residence* [single choice]

- Austria
- Belgium
- Bulgaria
- Croatia
- Cyprus
- Czech Republic
- Denmark
- Estonia
- Finland
- France
- Germany
- Greece
- Hungary
- Iceland
- Ireland
- Italy
- Latvia
- Liechtenstein
- Lithuania
- Luxembourg
- Malta
- Netherlands
- Norway
- Poland
- Portugal
- Romania
- Slovakia
- Slovenia
- Spain
- Sweden
- United Kingdom
- Other
  - Please specify:
    200 character(s) maximum

7. Country of your organisation's headquarters* [single choice]
   [If you do not respond as a representative of an organisation, please click 'Not applicable']

- Austria
- Belgium
- Bulgaria

- Croatia
- Cyprus
- Czech Republic
- Denmark
- Estonia
- Finland
- France
- Germany
- Greece
- Hungary
- Iceland
- Ireland
- Italy
- Latvia
- Liechtenstein
- Lithuania
- Luxembourg
- Malta
- Netherlands
- Norway
- Poland
- Portugal
- Romania
- Slovakia
- Slovenia
- Spain
- Sweden
- United Kingdom
- Other
  - Please specify:
    200 character(s) maximum

III. Awareness

8. To what extent are you familiar with the EMA?* [single choice]

- 1 – I am very familiar with the EMA
- 2 – I am familiar with the EMA
- 3 – I am not very familiar with the EMA
- 4 – I am not at all familiar with the EMA

9. To what extent are you familiar with the EMA fee system for medicinal products?* [single choice]

- 1 – I am very familiar with the EMA fee system
- 2 – I am familiar with the EMA fee system
- 3 – I am not very familiar with the EMA fee system

- 4 – I am not at all familiar with the EMA fee system

10. Have you ever had direct contact or engagement with the EMA?* [single choice]

- Yes
- If yes, please specify:* [multiple choice]
  - As an employee/former employee of the EMA
  - As a representative of an EU medicines regulatory agency
  - As a representative of a pharmaceutical company
  - As an academic/researcher
  - Other
    - Please specify:
      200 character(s) maximum
- No
- Do not know

IV. Experience

11. To what extent do you agree with the following statements related to the EMA fee system for medicinal products?

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly Disagree	Do not know
The EMA fee system rules are clear and easy to understand*						
The operation of the EMA fee system is transparent*						
The EMA fee system rules are easy to apply in practice*						
The EMA fee system reflects the overall costs of the services charged for*						
The EMA fee system provides adequate incentives and support (e.g. SMEs, orphan, paediatric, advanced therapy medicinal products, veterinary medicines for minor use/minor species, academia)*						

Note: Any additional comments to your reply can be provided under Question 16.

12. For the next set of questions, please consider how the EMA fee system compares to the fee system for medicinal products in the following countries.

12.1. Thinking first about the EMA fee system for medicinal products compared to the fee system of the Food and Drug Administration in the United States:

- Considering the clarity of the rules of each fee system:*
  - The EMA fee system rules are clearer and easier to understand than those of the U.S. fee system.
  - The EMA fee system rules and the U.S. system rules are comparably clear and easy to understand.
  - The U.S. fee system rules are clearer and easier to understand than those of the EMA fee system.
  - Do not know
- Considering the transparency of each fee system:*
  - The EMA fee system is more transparent than the U.S. fee system.
  - The EMA fee system and the U.S. fee system are comparably transparent.
  - The U.S. fee system is more transparent that the EMA fee system.
  - Do not know
- Considering the ease of applying the rules in practice for each fee system:*
  - The EMA fee system rules are easier to apply in practice than those in the U.S. fee system.
  - The EMA fee system and the U.S. fee system have rules that are comparably easy to apply in practice.
  - The U.S. fee system rules are easier to apply in practice than those in the EMA fee system.
  - Do not know
- Considering the extent to which each fee system is cost-based:*
  - The EMA fee system is more cost-based than the U.S. fee system.
  - The EMA fee system and the U.S. fee system are comparably cost-based.
  - The U.S. fee system is more cost-based than the EMA fee system.
  - Do not know
- Considering the appropriateness of the incentives provided by each fee system (e.g. SMEs, orphan, paediatric, advanced therapy medicinal products, veterinary medicines for minor use/minor species, academia):*
  - The EMA fee system provides more appropriate incentives than the U.S. fee system.
  - The EMA fee system and the U.S. fee system provide comparably appropriate incentives.
  - The U.S. fee system provides more appropriate incentives than the EMA fee system.
  - Do not know

Note: Any additional comments to your reply can be provided under Question 16.

12.2. Thinking next about the EMA fee system for medicinal products compared to the fee system of the Pharmaceuticals and Medical Devices Agency in Japan:

- Considering the clarity of the rules of each fee system:*

  - The EMA fee system rules are clearer and easier to understand than those of the fee system in Japan.
  - The EMA fee system rules and the fee system rules in Japan are comparably clear and easy to understand.
  - The fee system rules in Japan are clearer and easier to understand than those of the EMA fee system.
  - Do not know
- Considering the transparency of each fee system:*
  - The EMA fee system is more transparent than the fee system in Japan.
  - The EMA fee system and the fee system in Japan are comparably transparent.
  - The fee system in Japan is more transparent that the EMA fee system.
  - Do not know
- Considering the ease of applying the rules in practice for each fee system:*
  - The EMA fee system rules are easier to apply in practice than those in the fee system in Japan.
  - The EMA fee system and the fee system in Japan have rules that are comparably easy to apply in practice.
  - The fee system rules in Japan are easier to apply in practice than those in the EMA fee system.
  - Do not know
- Considering the extent to which each fee system is cost-based:*
  - The EMA fee system is more cost-based than the fee system in Japan.
  - The EMA fee system and the fee system in Japan are comparably cost-based.
  - The fee system in Japan is more cost-based than the EMA fee system.
  - Do not know
- Considering the appropriateness of the incentives provided by each fee system (e.g. SMEs, orphan, paediatric, advanced therapy medicinal products, veterinary medicines for minor use/minor species, academia):*
  - The EMA fee system provides more appropriate incentives than the fee system in Japan.
  - The EMA fee system and the fee system in Japan provide comparably appropriate incentives.
  - The fee system in Japan provides more appropriate incentives than the EMA fee system.
  - Do not know

Note: Any additional comments to your reply can be provided under Question 16.

12.3. Thinking next about the EMA fee system for medicinal products compared to the system of Health Canada in Canada:

- Considering the clarity of the rules of each fee system:*
  - The EMA fee system rules are clearer and easier to understand than those of the fee system in Canada.
  - The EMA fee system rules and the fee system rules in Canada are comparably clear and easy to understand.

  - The fee system rules in Canada are clearer and easier to understand than those of the EMA fee system.
  - Do not know
- Considering the transparency of each fee system:*
  - The EMA fee system is more transparent than the fee system in Canada.
  - The EMA fee system and the fee system in Canada are comparably transparent.
  - The fee system in Canada is more transparent that the EMA fee system.
  - Do not know
- Considering the ease of applying the rules in practice for each fee system:*
  - The EMA fee system rules are easier to apply in practice than those in the fee system in Canada.
  - The EMA fee system and the fee system in Canada have rules that are comparably easy to apply in practice.
  - The fee system rules in Canada are easier to apply in practice than those in the EMA fee system.
  - Do not know
- Considering the extent to which each fee system is cost-based:*
  - The EMA fee system is more cost-based than the fee system in Canada.
  - The EMA fee system and the fee system in Canada are comparably cost-based.
  - The fee system in Canada is more cost-based than the EMA fee system.
  - Do not know
- Considering the appropriateness of the incentives provided by each fee system (e.g. SMEs, orphan, paediatric, advanced therapy medicinal products, veterinary medicines for minor use/minor species, academia):*
  - The EMA fee system provides more appropriate incentives than the fee system in Canada.
  - The EMA fee system and the fee system in Canada provide comparably appropriate incentives.
  - The fee system in Canada provides more appropriate incentives than the EMA fee system.
  - Do not know

Note: Any additional comments to your reply can be provided under Question 16.

12.4 Thinking next about the EMA fee system for medicinal products compared to the system of the Therapeutic Goods Administration in Australia:

- Considering the clarity of the rules of each fee system:*
  - The EMA fee system rules are clearer and easier to understand than those of the fee system in Australia.
  - The EMA fee system rules and the fee rules in Australia are comparably clear and easy to understand.
  - The fee system rules in Australia are clearer and easier to understand than those of the EMA fee system.
  - Do not know
- Considering the transparency of each fee system:*
  - The EMA fee system is more transparent than the fee system in Australia.

  - The EMA fee system and the fee system in Australia are comparably transparent.
  - The fee system in Australia is more transparent that the EMA fee system.
  - Do not know
- Considering the ease of applying the rules in practice for each fee system:*
  - The EMA fee system rules are easier to apply in practice than those in the fee system in Australia.
  - The EMA fee system and the fee system in Australia have rules that are comparably easy to apply in practice.
  - The fee system in Australia rules are easier to apply in practice than those in the EMA fee system.
  - Do not know
- Considering the extent to which each fee system is cost-based:*
  - The EMA fee system is more cost-based than the fee system in Australia.
  - The EMA fee system and the fee system in Australia are comparably cost-based.
  - The fee system in Australia is more cost-based than the EMA fee system.
  - Do not know
- Considering the appropriateness of the incentives provided by each fee system (e.g. SMEs, orphan, paediatric, advanced therapy medicinal products, veterinary medicines for minor use/minor species, academia):*
  - The EMA fee system provides more appropriate incentives than the fee system in Australia.
  - The EMA fee system and the fee system in Australia provide comparably appropriate incentives.
  - The fee system in Australia provides more appropriate incentives than the EMA fee system.
  - Do not know

Note: Any additional comments to your reply can be provided under Question 16.

13. In your experience, have you ever encountered difficulties related to the EMA fee system for medicinal products?* [single choice]

- Yes
- No
- Do not know
- Not applicable
- If yes, please indicate the areas where you experienced difficulties (multiple choice possible):
- Lack of transparency of the fee system (rules and/or implementation).
  - Please explain the difficulties you have experienced with respect to the transparency of the fee system:
    1000 character(s) maximum
- Complexity of the fee system.
  - Please explain the difficulties you have experienced with respect to the complexity of the fee system:

1000 character(s) maximum

- Misalignment between fees charged and services provided.
  - Please explain the difficulties you have experienced with respect to the misalignment between fees charged and services provided:
    1000 character(s) maximum
- Lack of flexibility of the fee system
  - Please explain the difficulties you have experienced with respect to the lack of flexibility of the fee system:
    1000 character(s) maximum
- Insufficient focus on the needs of particular users (e.g. SMEs, orphan medicinal products, paediatric medicinal products, ATMPs, academia)
  - Please identify the particular category of 'user' for which there is insufficient focus on their needs and the difficulties you have experienced:
    1000 character(s) maximum
- Other
  - Please explain the other difficulties you have experienced with respect to the fee system:
    1000 character(s) maximum

14. Based on your experience, have you ever had a need for a dispute settlement procedure between the EMA and industry?* [single choice]

- Yes
  - Please explain the reason why a dispute settlement procedure would have been needed:
    1000 character(s) maximum
  - Please provide suggestions for the most appropriate form for the dispute settlement procedure:
    1000 character(s) maximum
- No
- Do not know
- Not applicable

15. For a typical year for your organisation, please indicate what is the proportion of your total annual expenditure on EMA fees of, respectively, pre-authorisation fees (i.e. scientific advice and initial marketing authorisation) and post-authorisation fees (e.g.

variation, extension, renewal, pharmacovigilance procedure, annual fee).* [single choice]

- The percentage of pre-authorisation fees and post-authorisation fees are as follows:

  Percentage of pre-authorisation fees

  Please fill in the field below with numbers only – please avoid using % symbol for example

  Only values of at most 100 are allowed

  Percentage of post-authorisation fees

  Please fill in the field below with numbers only – please avoid using % symbol for example

  Only values of at most 100 are allowed

  Please note that the total of pre and post authorisation fees should make 100%.

- Do not know
- Not applicable

V. Document upload and final comments

16. If you wish to provide additional comments or information within the scope of this questionnaire, including possible recommendations, please do so here.

2000 character(s) maximum

17. If you wish to provide additional supporting information within the scope of this questionnaire you may also upload a document, such as a position paper, related to your responses (max. 2 pages):

The maximum file size is 1 MB.

Please note that the uploaded document will be published alongside your response to the questionnaire which is the essential input to this open public consultation. The document is an optional complement and serves as additional information to better understand your position.

Appendix 8. Overview of received survey responses

Table 24: Overview of NCAs respondents to the survey of NCAs (n=29)

Name of agency	State	Areas of responsibility
Austrian Medicines and Medical Devices Agency (AGES MEA)	Austria	Human and veterinary health
Federal Agency for Medicines and Health Products (FAMHP)	Belgium	Human and veterinary health
Agency for Medicinal Products and Medical Devices (HALMED)	Croatia	Human health
State Institute for Drug Control (SÚKL, CZ)	Czech Republic	Human health
Danish Medicines Agency (DKMA)	Denmark	Human and veterinary health
State Agency of Medicines (Ravimiamet)	Estonia	Human and veterinary health
Finnish Medicines Agency (Fimea)	Finland	Human and veterinary health
French Agency for Veterinary Medicinal Products (ANMV)	France	Veterinary health
Federal Institute for Drugs and Medical Devices (BfArM)	Germany	Human health
Paul Ehrlich Institut (PEI)	Germany	Human and veterinary health
Federal Office of Consumer Protection and Food Safety (BVL)	Germany	Veterinary health
National Organization for Medicines (EOF)	Greece	Human and veterinary health
National Institute of Pharmacy and Nutrition (OGÉYI)	Hungary	Human health
Health Products Regulatory Authority (HPRA)	Ireland	Human and veterinary health
Italian Medicines Agency (AIFA)	Italy	Human health
Ministry of Health – Directorate General for Animal Health and Veterinary Medicines (*abbreviation not available*)	Italy	Veterinary health
Food and Veterinary Service (PVD)	Latvia	Veterinary health
State Agency of Medicines of the Republic of Latvia (ZVA)	Latvia	Human health
State Medicines Control Agency of Lithuania (VVKT)	Lithuania	Human health
National Food and Veterinary Risk Assessment Institute (NMVRVI)	Lithuania	Veterinary health
Malta Medicines Authority (*abbreviation not available*)	Malta	Human health
Medicines Evaluation Board (MEB)	Netherlands	Human and veterinary health
Norwegian Medicines Agency (*abbreviation not available*)	Norway	Human and veterinary health
State Institute for Drug Control (SÚKL, SK)	Slovakia	Human health
Agency for Medicinal Products and Medical Devices of the Republic of Slovenia (JAZMP)	Slovenia	Human and veterinary health
Spanish Agency for Medicines and Medical Devices (AEMPS)	Spain	Human and veterinary health
Medical Product Agency (MPA)	Sweden	Human and veterinary

Name of agency	State	Areas of responsibility
		health
Veterinary Medicines Directorate (VMD)	United Kingdom	Veterinary health
Medicines and Healthcare products Regulatory Agency (MHRA)	United Kingdom	Human health

Figure 23: Areas of responsibility of responding NCAs to the survey of NCAs (n=29)

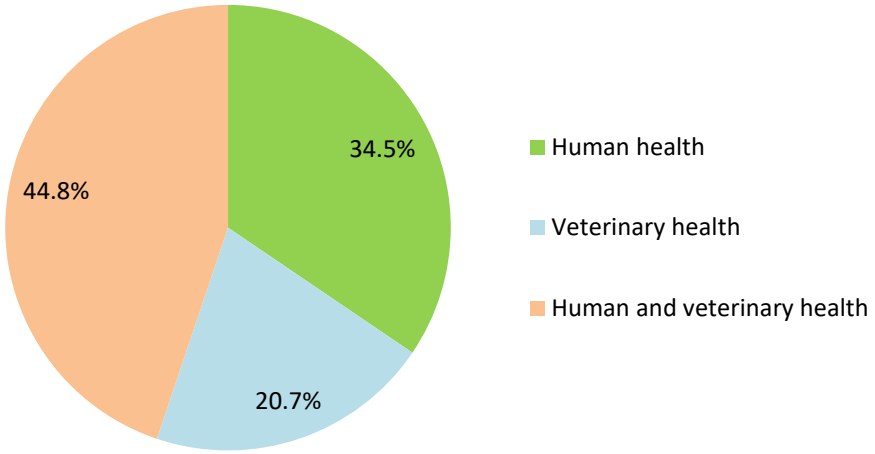


Table 25: Breakdown of respondent types to the survey of wider stakeholders (n=40)

Type of respondent	Count	Share
Pharmaceutical Industry (SME)	14	35.0%
Pharmaceutical Industry (Large)	11	27.5%
Research organisation	7	17.5%
Industry organisation	3	7.5%
Patient association	1	2.5%
Wholesalers association	1	2.5%
Other	2	5.0%
(blank)	1	2.5%
Total	**40**	**100.0%**

Table 26: Geographic level of activity of respondents to the survey of wider stakeholders (n=40)

Geographic level of activity	Count	Share
Organisation/members primarily work at the global level	15	37.5%
Organisation/members primarily work at the EU level	12	30.0%
Organisation/members primarily work at the national level	13	32.5%
France	*4*	*10.0%*
Italy	*3*	*7.5%*
Portugal	*1*	*2.5%*
Czech Republic/Slovakia	*1*	*2.5%*
Germany	*1*	*2.5%*
Greece	*1*	*2.5%*
Spain	*1*	*2.5%*
UK	*1*	*2.5%*
Turkey	*1*	*2.5%*
Total	**40**	**100.0%**

Note: Respondents indicating that their organisation/members primarily work at the national level were asked to provide the main country they work in.

Figure 24: Areas of responsibility of wider stakeholder survey respondents' organisations (n=40)

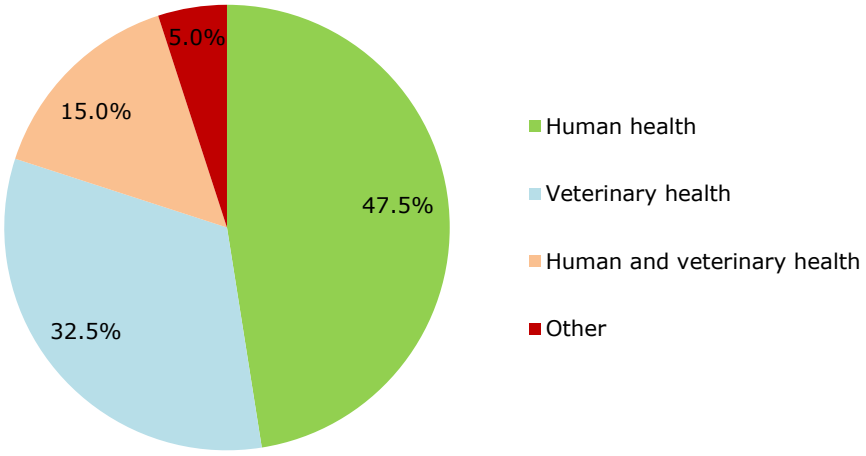


Table 27: Breakdown of open public consultation respondent types (n=51)

Type of respondent	Count	Share of n=51
Representative of a company with direct relevance to the EMA (e.g. pharmaceutical company)	22	43.1%
More than 250 employees (large enterprise)	*10*	*19.6%*
50 to 250 employees (medium-sized enterprise)	*3*	*5.9%*
10 to 49 employees (small enterprise)	*4*	*7.8%*
Max. 9 employees (micro enterprise)	*5*	*9.8%*
Member of a research organisation/academic institution	9	17.6%
Individual citizen in their personal capacity	6	11.8%
Member of a representative organisation	5	9.8%
Patient association	*2*	*3.9%*
Other representative group/organisation[72]	*3*	*5.9%*
Member of a non-governmental organisation (NGO)	3	5.9%
Public health NGO	*2*	*3.9%*
Other NGO	*1*	*2.0%*
Member of a Member State/EEA medicine regulation agency	2	3.9%
Member of a central government or public authority at EU level	1	2.0%
Member of a civil society organisation	1	2.0%
Member of a think-tank/consultancy	1	2.0%
Representative of a company with no direct relevance to the EMA	1	2.0%
More than 250 employees (large enterprise)	*1*	*2.0%*
Member of a central government/ministry or public authority at national or regional level in a Member State or the EEA	0	0.0%
Member of an inter-governmental organisation	0	0.0%
Member of a non-EU medicine regulation agency	0	0.0%
Legal professional	0	0.0%
Other	0	0.0%
Total	**51**	**100.0%**

[72] One respondent specified their organisation as 'parallel wholesale', one respondent as 'industry of homeopathic and anthroposophic [sic!] medicinal products', and one respondent as the European Federation of Pharmaceutical Industries and Associates (EFPIA).

Table 28: Open public consultation respondents' countries of residence (n=51)

Country of residence	Count	Share of n=51
Italy	9	17.6%
Germany	7	13.7%
Greece	5	9.8%
United Kingdom	5	9.8%
Austria	4	7.8%
Netherlands	4	7.8%
Belgium	3	5.9%
Spain	3	5.9%
Denmark	2	3.9%
France	2	3.9%
Bulgaria	1	2.0%
Cyprus	1	2.0%
Hungary	1	2.0%
Ireland	1	2.0%
Sweden	1	2.0%
Other	2	3.9%
Switzerland	*1*	*2.0%*
Canada	*1*	*2.0%*
Total	**51**	**100.0%**

Table 29: Location of open public consultation respondents' organisations'/companies' headquarters (n=45)

Location of the organisation's/company's headquarters	Count	Share of n=45
Italy	9	20.0%
Germany	7	15.6%
Netherlands	6	13.4%
Greece	3	6.8%
United Kingdom	3	6.8%
Belgium	2	4.4%
Denmark	2	4.4%
France	2	4.4%
Spain	2	4.4%
Austria	1	2.2%
Bulgaria	1	2.2%
Ireland	1	2.2%
Sweden	1	2.2%
Other	5	11.0%
Canada	*1*	*2.2%*
Republic of Korea	*1*	*2.2%*
Switzerland	*1*	*2.2%*
[blank]	*2*	*4.4%*
Total	**45**	**100.0%**

Appendix 9. List of agreed activities

The activities presented below were agreed with EMA and HMA for the purposes of undertaking the modelling exercise and were divided into two groups. These activities are listed in the fee grid provided separately with this report.

The first set of activities consists of procedural activities that involve EMA and NCAs. There are 35 procedural activity types for human medicines and 26 procedural activity types for veterinary medicines that involve both EMA and NCAs. Five further inspection activities were combined for human and veterinary medicines. The activities are mainly fee-generating but also include non-fee-generating activities for which NCAs do not receive remuneration under the current fee system (e.g. paediatrics and orphan designations).

The activities are differentiated either in the legal basis for the associated fee or because of the time taken to undertake a procedure. The activities can be grouped into more aggregate categories that reflect the type of work undertaken. The aggregate activities, which are used to illustrate the main results in section 2.1, are shown in Table 30. The remuneration rule for NCAs under the current financial model is also included.

The second set of activities involves seven fee-generating, procedural activities undertaken by EMA only (without NCA involvement). These are also combined in the analysis.

In addition to fees generated from procedural activities, there are two types of annual fees: annual fees for CAPs for human and veterinary use and annual pharmacovigilance fees for NAPs for human use. EMA incurs costs for the administration of both of these fees. NCAs receive a share of annual CAP fee income but EMA retains all of the fee income from the annual pharmacovigilance fees.

Table 30: Summary of procedural activities included in the financial modelling

Type		Aggregate activity	NCA remuneration under current financial model*
Activities involving EMA and NCAs	Human	Scientific Advice/Protocol Assistance (initial request and follow-up request (Level I, II and III))*	50% of full fees
		Initial marketing authorisations (new active substance, known active substance, fixed-dose combination, generic, hybrid, biosimilar, informed consent, well-established use)	
		Line extensions (Level I, II and III)	
		Scientific services (PMF, VAMF, ancillary medicinal substances consultation, ATMP certification, traditional herbals; compassionate use opinions; Art.58)	
		Renewals	
		Referrals of disputes from decentralised and mutual recognition procedures (Art.29(4), Art.30, Art.31, Art.20)	
		Type II variations (Level I, II and III)	
		Type IB variations	Not remunerated
		Pharmacovigilance referrals (Art.31, Art.20, Art.107i)	€119,333, scaled according to incentives applied
		Post-Authorisation Safety Studies (PASS)	Fixed amount, scaled according to incentives applied (€18,200 in total for PASS, €13,100 for PSUR/PSUSA)
		Periodic Safety Update Reports for CAPs (PSUR)	
		Periodic Safety Update Reports for NAPs & CAP/NAP (PSUSA)	
		PIP (phase I and II), , PIP waiver, PIP compliance check (PIP modifications were not included in the list agreed for the NCA survey)	Not remunerated
		Orphan Designation	
	Human/veterinary	Inspections (GMP, GCP, GVP)	50% of full fee
	Veterinary	Scientific Advice (initial request and follow-up request (Level I, II and III))	50% of full fee
		Initial marketing authorisations (new active substance, known active substance, generic (phase I, II and III)	
		Line extensions (Level I, II and III))	
		Maximum residue limits (phase I,	

Type		Aggregate activity	NCA remuneration under current financial model*
		II and III)	
		Renewals	
		Referral procedures (Art. 34 and Art. 35 (phase I, II and III) and Art. 45 (total procedure))	
		Type II variations (Level I, II and III)	
		Type IB variations	Not remunerated
		MUMS	
EMA only	Human and Veterinary	Type IA variations, MAH transfers, issuing certificates, parallel distribution	Not applicable

* For most Scientific Advice/Protocol Assistance procedures, NCAs receive 50% of the full fee. However, NCAs do not receive remuneration for Scientific Advice for paediatric products, unless such product is also labelled as ATMP or an orphan product.

** Only applies to rapporteur and co-rapporteur roles; each receive an equal share of the remuneration. Procedural activities performed as peer reviewer or commenting member state are not remunerated.

Appendix 10. Lists of additional activities reported by EMA and by NCAs

Table 31 Additional EMA related activities reported by EMA

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
Transparency on non-fee generating areas e.g. Access to documents and publication of clinical trials	7,121,070
Literature monitoring (PhV)	758,840
Signal detection (PhV)	4,936,648
International Activities	4,056,230
Coordination Group (Cmd) Human & Vet	2,555,085

Table 32 Categorisation of additional activities reported by NCAs

Activity/Working Group/Committee	Number of NCAs
Member EMA Management Board /Scientific Coordination board	4
Surveys/questionnaires!	2
Transparency	1
Communication/stakeholder engagement	1
Guidelines drafting	6
Establishment and maintenance of terminology standards	1
Databases	11
Training (participation and delivery)	9
Preparation/briefing/comments on non (co)rap procedures	4
Drafting responses	2
Translation checks	4
Quality defects (incl non-GMP compliance + Incident Management Plan meetings)	3
Rapid Alert/Incident Management	2
Adverse events	1
ADR reporting covering both national and EMA approved pharmaceuticals	1
EFSA, AMEG, RONAFA and CADVVA, VICH	3
PRIME	5
ESVAC (European Surveillance of Veterinary Antimicrobial consumption)	2
ECVAM (3Rs)	2
Lumpy Skin Disease and FishMed	2
Surveillance and Signal detection/management (includes PRAC signal)	10
Classification ATMP	6
Herbal related	6
Post-Authorisation Efficacy Studies (PAES)	6
Post authorisation measurements (PAM)	6
Eligibility +Accelerated assess/procedure	4
Annual re-assessment/ re-examination procedures	3
Similarity report	3
Significant benefit	3
Referrals (NonPhV)	3
PhV activities	1
Innovation	1
Ph Vig veterinary Inspections	2
Inspections – GDP/GLP/national	2
safety type II	3
Plasma Master File (PMF) (various)	2
PSURs mixed CAPS/NAPS	2
Derogation of orphan status/ Review of orphan designation for orphan medical product for MA (criteria time of marketing)	2
PIP modifications	3
Other evaluation reports for the EU:RMP in the context of MAA or line extension; renewals, RUP	1
Non- (co)rap procedure roles or committee time	9
Pharmacopeia work	1
OMCL lab work (Official Medicines Control Laboratories)	1
No information provided	6

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