Study for the evaluation of the EMA fee system

Methodology Note

SANTE/2016/B5/021

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Unit B.5 — Medicines: policy, authorisation and monitoring

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List of acronyms

Acronym	Description
AD	Scientific staff
AST	Non-scientific/administrative staff
ATMP	Advanced Therapy Medicinal Products
CAP	Centrally authorised product
CAT	Committee for Advanced Therapies
CHMP	Committee for Medicinal Products for Human Use
CVMP	Committee for Medicinal Products for Veterinary Use
DG SANTE	Directorate General for Health and Food Safety
EEA	European Economic Area
EMA	European Medicines Agency
EMA MB	EMA Management Board
EMEA	European Medicines Evaluation Agency (now the EMA)
EU	European Union
GCP	Good clinical practice
GMP	Good manufacturing practice
GVP	Good pharmacovigilance practices
HMA	Heads of Medicines Agencies
HMPC	Committee on Herbal Medicinal Products
HTA	Health technology assessment
IT	Information technology
MA	Marketing authorisation
MBDG	EMA Management Board Data Gathering
MRL	Maximum residue limit
MUMS	Minor-use-minor-species
NAP	Nationally authorised product
NCA	National Competent Authority
PAES	Post-authorisation efficacy study
PASS	Post-authorisation safety study
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
VAMF	Vaccine Antigen Master File

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 NCA survey, data provided by EMA and model. Administrative staff are 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 an SME) making the application, among other things and is assumed to be fixed for the typical year.
Committee and Working Groups activities	Time spent in and preparing for EMA committee and Working Group meetings.
Cost-based	In a cost-based fee 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.

[1] The NCA survey is included as Appendix 7 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 revenue	EMA revenue consists of the fee revenue from industry and EU and EEA budget contributions minus NCA remuneration.
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 are 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 are 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.

1. INTRODUCTION

This methodology note to support the 'Study for the Evaluation of the Fee System' for the Directorate General for Health and Food Safety (DG SANTE) is provided as a formal deliverable alongside the final report. The note explains the methodology used for the quantitative modelling undertaken as part of the evaluation of the current fee system. The model was designed to:

- Assess the extent to which the fee and remuneration levels under the current financial model correspond to the costs of the European Medicines Agency (EMA) and the National Competent Authorities' (NCAs') contribution to EMA activities.
- Test the impact of theoretical cost-based fee systems on the EMA financial model, including the EU/EEA budget contributions, NCA remuneration and industry fees.

A single model was developed that enabled both of these analytical activities to be conducted. The model first determined the cost to EMA and NCAs of undertaking EMA-related activities. Fees and remuneration levels under the current fee system were then calculated. These were compared to EMA and NCA costs (i.e. the extent to which the current fee system is cost-based). Then, by changing the model parameters, different theoretical cost-based scenarios were tested. The model facilitated the analysis of the current and theoretical fee systems.

2. MODEL OVERVIEW

This section presents an overview of the model and the stages of the modelling process. These are discussed in more detail in subsequent sections.

2.1. Financial model

The model consists of two parts:

a) A **cost** model of the costs for NCAs to undertake EMA-related activities and for EMA to undertake its own activities.

- NCA costs for undertaking **EMA-related** activities cover procedural activities, work undertaken in relation to Working Groups and committees and additional EMA-related activities that NCAs report they undertake. ***NCA costs from other (non-EMA-related) activities were not included***.
- EMA costs comprise only the activities they undertake as an organisation. EMA also makes payments to NCAs for undertaking certain procedural activities in accordance with the legislation. **To avoid confusion, payments by EMA to NCAs were not included as EMA costs in the model but instead were entered in the revenue model as a reduction in the EMA share of fee income from industry.**
- Overhead costs and direct non-staff costs were added to the salary costs to determine the total costs of activities undertaken by both EMA and NCAs.
- A **costing methodology** was developed to calculate costs for all activities undertaken by EMA and NCAs using information on salary costs, overhead costs and direct non-staff costs, time spent on individual activities and the numbers of activities undertaken.

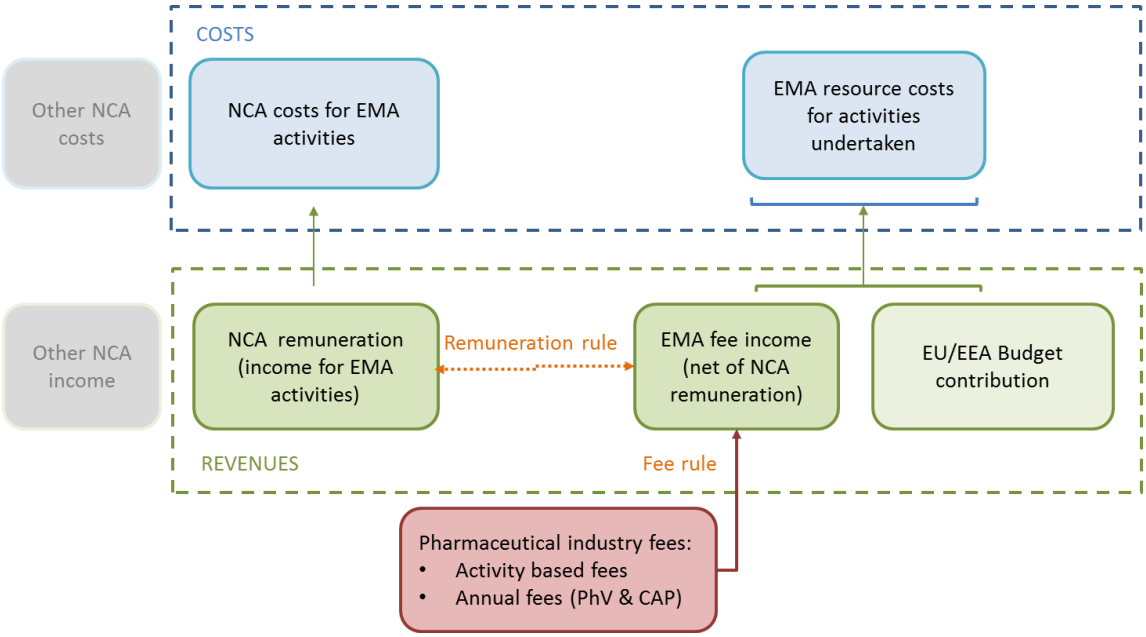
b) A **revenue** model of the income that NCAs receive from EMA for the EMA-related activities they undertake and the share of total revenue that EMA retains (i.e. EMA fee income), as well as the EU/EEA budget contributions.

- NCA income in this model consists of the payments they receive from EMA (NCA income from other sources was not included).

- 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.

The model is illustrated in Figure 1. Costs and income not included in the model have been greyed out. NCAs receive their remuneration for EMA activities from EMA rather than directly from industry: the payment is treated as a transfer of income and is therefore included in the revenue model only.

Figure 1: Schematic presentation of the cost and revenue model



Two rules were implemented in the model:

a) A **fee rule** that establishes the fees paid by industry for the services they receive. EMA fee income per procedure depends on the fee rules and the incentives that are applied to the fees.
b) An **NCA remuneration rule** that establishes NCA income for EMA-related activities. NCA income depends on the remuneration rule. EMA net income after making payments to NCAs also depends on the remuneration rule as this rule determines the payments EMA makes to NCAs.

The rules are shown in Figure 1.There is no *a priori* reason for the two rules to be connected. However, in the existing fee system, NCA remuneration is partly linked to the fees charged to industry, as NCA remuneration is a fixed percentage of the fee EMA charges industry (with the exception of pharmacovigilance activities). Hence the remuneration rule *de facto* currently depends on the fee rule. In a cost-based approach, the remuneration rule depends on the costs of carrying out the procedures and this determines the fee rule.

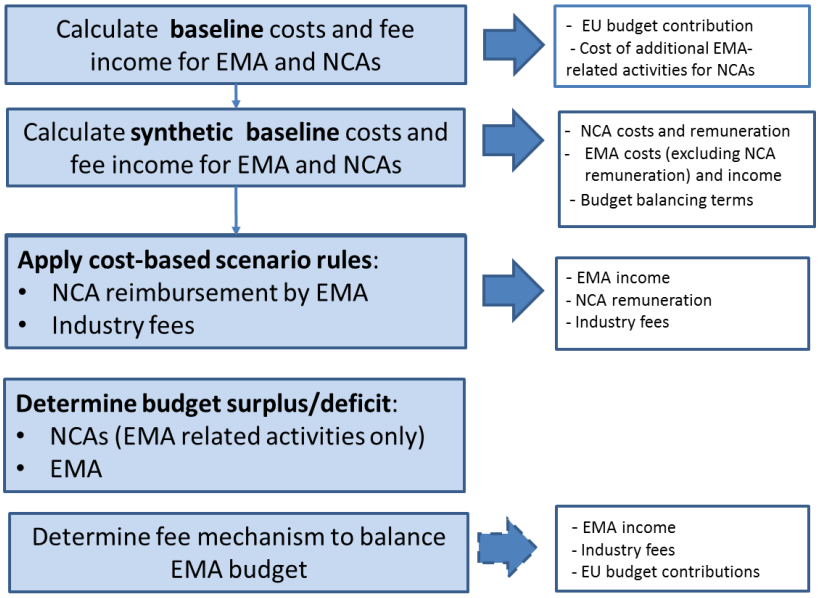
The model has been developed to use actual data provided by EMA and NCAs with the aim of understanding how well the existing fee system reflects the costs of the activities undertaken and what the impact of different cost-based theoretical fee systems would be on EMA, NCAs and industry. The detailed implementation of the cost model and revenue models for different fee systems is presented in section 3 and a further discussion of the data provided by EMA and NCAs can be found in Section 5. In order to use the model to compare costs and fees under the existing fee system and under different theoretical fee

system scenarios in a consistent manner, the study team had to make assumptions. The study team developed a synthetic baseline to represent a 'typical' year, for which, in particular, the incentive rates and numbers of procedures are fixed. The rationale and method for the synthetic baseline are presented in section 4.

2.2. Steps in the modelling process

The modelling process followed a series of steps to calculate the different components of the costs and revenues shown in Figure-1 from the data; for the existing fee system and for the theoretical cost-based scenarios. The stages of the modelling process and the corresponding outputs are shown in Figure-2.

Figure-2: Stages of modelling process



The boxes on the left hand side of the figure show the calculations made at each stage of the modelling process. The boxes on the right hand side show the model output at each stage. The different stages are explained below.

The first step was to calculate the actual baseline costs and shares of fee income for EMA and NCAs. The baseline year is the year for which data were reported by EMA and NCAs. The model uses data from three sources:

- The NCA survey conducted by the study team;
- The Management Board Data Gathering (MBDG) exercise carried out by the EMA Management Board; and
- Information on EMA costs and revenues provided by EMA.

These sources provide information on the number of activities that were undertaken by EMA and the NCAs and the time taken to carry them out, in addition to cost and revenue data. The activities include fee- and non-fee-generating activities. A validation of the time data from the MBDG data was undertaken before it was used in the model (section 5).

In the baseline, data reported by EMA and NCAs for the baseline year and the validated time data were used in the model to calculate costs and fees. Costs were calculated using an activity based approach. Fees and NCA remuneration were calculated using the fee and remuneration rules that pertain under the current fee system. The modelling

approach is described in more detail in section 3; the implementing rules for the existing fee system are described in section 3.3.

The baseline model serves two purposes. It firstly provides a top-down verification of the modelling approach in which the costs calculated for EMA could be compared with the actual costs EMA reported, and the total calculated fee remuneration for NCAs could be compared with the NCA remuneration reported by EMA. These comparisons indicate whether the model calculations are of the right order of magnitude. Secondly, the baseline model determines the EMA-related costs of additional activities reported by NCAs that are captured in the modelling approach. The additional NCA activities are discussed in more detail in section 3. The actual 2016 EU and EEA budget contributions are used as fixed inputs in the model in the baseline. A balancing term is also calculated which represents other sources of EMA income in the reporting year. The verification of the EMA data is discussed in section 5.2.

The model was designed to represent a 'typical' year for both EMA and NCAs in terms of services provided and activities undertaken. Therefore, the next step was to determine the fees and costs for a **synthetic baseline**. The synthetic baseline relies on assumptions about a common set of activities for both EMA and NCAs in one synthetic year. In particular, in the synthetic baseline the number of procedural activities involving NCA activities that EMA undertakes for the pharmaceutical industry in a typical year is constrained to be the same as the number of activities undertaken by NCAs at EMA's request and by EMA itself. The fee revenue is also based on this number of activities. For procedural activities undertaken by EMA not involving NCAs, the invoiced number of procedures is used to calculate fees and costs in both the baseline and synthetic baseline. All other activities are also assumed to be the same as in the baseline. This includes time spent in committees and Working Groups by NCAs and on additional activities by EMA and NCAs. The costs for these activities are therefore unchanged from the baseline.

The synthetic baseline was used to determine NCA costs as well as EMA costs excluding NCA remuneration for a typical year. NCA costs are different in the synthetic baseline compared with the baseline because they are based on a different number of procedures. EMA costs are the same in both the baseline and the synthetic baseline.

The synthetic baseline costs are used for all the fee and remuneration rules. The current fee and remuneration rules were then applied to the synthetic baseline year to determine revenues (EMA share of fee income and NCA remuneration). The revenues for procedure based activities are different in the synthetic baseline year compared with the actual baseline because for some activities, EMA remunerates NCAs for a different number of procedures (as stated in the preceding paragraph). Hence, the actual EU budget contributions and other sources of income do not act to balance the EMA's revenues with its costs in the synthetic baseline. It turns out that additional income is needed to balance the EMA's revenues with its costs in the synthetic baseline. This is added to 'other sources of income'.

The final stage of the model was to implement a number of cost-based scenarios with different fee rules, using data from the synthetic baseline year. The starting point for the scenarios was the implementation of cost-based remuneration for NCAs as a whole. The average cost for undertaking a procedure for a given activity, for both EMA and NCAs, was determined from the synthetic baseline cost calculations. For NCAs, this was effectively a weighted average across NCAs, weighted by the number and cost of remunerated and unremunerated roles undertaken by different NCAs in the typical year. For all scenarios, NCAs were then remunerated for procedural activities at average cost. In the scenarios, changes in EU budget contributions and industry fees were considered as mechanisms to pay for different levels of NCA remuneration. The implementation of the scenarios in the revenue model is presented in section 3.3.

2.3. Model outputs

The model calculates and generates the NCA costs and EMA costs for EMA-related activities undertaken. These costs are independent of the fee and NCA remuneration rules and are the same for both the current financial model and the scenarios tested.

The model generated the following outputs, which depend on the fee and NCA remuneration rule applied:

- NCA remuneration, to identify how much of the costs incurred are remunerated;
- EMA income, to identify whether the EMA's budget is balanced by the existing European Union (EU) and European Economic Area (EEA) budget contributions; and
- Pharmaceutical industry fees: that is, fees both before and after incentives are applied.

All of the cost, revenue and fee components can be calculated at different levels of aggregation:

- Overall, as yearly totals over all activities for EMA, NCAs and industry. These were further disaggregated by NCA so that it was possible to look at yearly totals for human and veterinary medicine products separately and at different types of NCAs; i.e. those responsible for veterinary products, for human products and for both veterinary and human products. The yearly totals were used to identify to what extent costs are covered by, or exceed, fee income for EMA and remuneration for NCAs; including taking into account the cost of activities that are currently not fee generating for EMA or are unremunerated for NCAs. Scenarios based on average-cost fees show whether individual NCAs cover their costs and what would be the impact on the EU, EMA and industry of addressing any funding gaps.
- At the activity level, as yearly totals for procedural activities. Since costs and fee income are based on the same number of procedures in the synthetic baseline, the yearly totals by activity show how closely or otherwise current fees relate to the EMA plus NCA costs of the activities they are paying for.[5]
- As unitary values, calculated per procedure for procedural activities and annual fees covering other services. Unitary full fees and actual fees (after incentives are applied) provide information on what the fees would be, independent of the number of procedures or average incentive rates. The unitary fees for procedural activities and for annual fees under the existing fee system were determined from the total fee income before incentives reported by EMA divided by the invoiced number of procedures. These do not exactly match the fees in the legislation because the reported values already take account of different factors that affect the calculation of the underlying fee, such as inflation and pharmaceutical strength and form. For procedural activities, a unitary cost for EMA and NCAs can be determined for each activity. These were determined as a weighted average from the total costs for EMA and NCAs in total divided by the total number of procedures undertaken for a given activity in the synthetic baseline.[6] Together these form the full, average cost-based unitary fees that are used in the scenarios. The unitary full fees for the existing fee system and the average-cost

[5] The model calculations are made by organisation (EMA, individual NCAs), activity and role and summed to provide the relevant aggregate output.

[6] Different numbers of procedures for a given activity may be undertaken by NCAs with different costs so that the average cost is weighted. For EMA, the average cost depends on the hourly costs and average time taken for a procedure of a given activity.

based unitary fees are presented in the fee grid, which is a separate document accompanying the final report. The costs over the one year period depend on the number of procedures completed for each activity type and the time taken to undertake these as well as the costs per hour of scientific and administrative staff time (see section 3). These were considered to be fixed inputs for the typical year. Changes to the number of activities completed and the time taken can be implemented in the model as policy scenario tests, in light of new data or as new assumptions.

For the fee and remuneration rules implemented in both the current fee system and the cost-based scenarios, comparing NCA remuneration and costs indicates the degree to which the remuneration covers the costs of the EMA-related activities the NCAs undertake. The current EMA financial model requires that the EMA share of fee income, once NCAs have been remunerated, is sufficient to maintain a balanced budget for the EMA with the existing EU contribution. Equally, the EU budget contributions could be manipulated to change the required fee income; and the effect on the EU budget contributions from a change in the required fee income of EMA, and hence on industry fees can be assessed with the model.

In summary, the model applies rules to a set of inputs for a typical year to calculate industry fees and NCA remuneration amounts as well as EMA fee income that can be compared to NCA and EMA costs (both yearly and per activity). The inputs to the model were determined using data from three sources at the baseline stages of the modelling process, and a number of assumptions were required; in particular a synthetic baseline was established. Once calculated, the inputs were 'fixed' and independent of the fee and remuneration rules applied. The EU budget contribution is not a fixed input in the model as it can be changed to ensure that the EMA's net income balances its costs.

3. COMPONENTS OF THE FINANCIAL MODEL

The following sections present the cost and revenue components of the model in detail, including data sources, assumptions made and data validation, as well as the calculation process for the fixed inputs to the model.

3.1. The EMA resource cost model

This section describes the costing methodology applied to EMA. EMA costs can be broadly categorised as the costs of activities they undertake as an organisation (including direct non-staff costs), the costs of remunerating NCAs for EMA-related activities they undertake, and overhead costs.

The EMA activity costs consist of three types:

i) Costs for the scientific and administrative work they undertake as part of fee- and non-fee-generating services they provide to industry, which also involve NCAs.
ii) Costs for the scientific and administrative work they undertake as part of fee-generating services they provide to industry which do not involve NCAs, plus costs incurred for the administration of annual fees.
iii) Costs for additional non-fee-generating activities.

For each of the above cost types, EMA provided granular data for activities for the calendar year 2016.[7] This table was designed by the study team to capture cost (and

[7] The EMA data is available in a spreadsheet as a separate electronic supplement.

revenue) data related to the three types of activities EMA undertakes (as listed above) and the remuneration they pay to NCAs. The same level of disaggregation of activities was used in this spreadsheet and in the NCA survey conducted by the study team.

The first activity type, which involves NCAs, comprises a set of 40 procedural activities for human medicines and 32 activities for veterinary medicines. These are predominantly fee-generating activities, with a few exceptions.[8] Both EMA and Heads of Medicines Agencies (HMA) were consulted in the identification of these activities.

The second activity type covers seven procedural activities for human medicines that EMA undertakes without NCA involvement and three for veterinary medicines. EMA also incurs costs for the administration of centrally authorised product (CAP) annual fees, for both human and veterinary medicines, and annual pharmacovigilance (PhV) fees for human medicines.

Finally, EMA undertakes additional activities that are neither procedural nor fee-generating. EMA provided cost data for 11 such activities, covering human and veterinary medicines, as listed in Table-1. EMA staff costs related to Working Groups and guidelines are included under "guidelines for good practice". More details on the type of additional activities undertaken within these broad categories can be found in the EMA Work Programme 2016 (EMA, 2016).

Table-1: 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

EMA costs were provided as scientific and administrative staff salary costs, meeting costs, other direct (non-staff) costs and overhead costs. Staff costs that were not directly related to activities were included in overhead costs.

In the data provided by EMA, staff costs related to the plenary meetings of committees were included under the relevant activity – for example, COMP was included under "orphan designation" and PDCO was included in the Paediatrics activities – whereas the staff costs for the CHMP and CVMP were re-allocated to the relevant activities using "staff" as the allocation key. This approach was applied to the reported costs because almost all EMA time spent in committees is related to procedural activities. In the model,

[8] The exceptions are: paediatric activities and orphan designation.

committee time costs are also allocated to procedural activities (see section 5.2 for additional details.)

An activity-based costing methodology was used to determine costs for the EMA's procedural activities involving NCAs (i.e. costs for the scientific and administrative work EMA undertakes as part of fee- and non-fee-generating services they provide to industry that also involve NCAs). This approach allocates overhead costs as well as non-staff direct costs and staff costs to individual activities, thus enabling fees to be compared with full costs for individual activities in the modelling.

The study team followed a two-step procedure to calculate the costs of the activities undertaken by EMA at a disaggregate level:

- Step 1: Determine the full cost per hour of an activity. Salary costs per hour for two staff types (scientific and administrative) were calculated from total EMA salary costs divided by total annual number of hours worked (number of FTEs x annual hours per FTE). Overhead and direct costs were then allocated to each of these staff types according to staff numbers because direct costs are more likely to be aligned with staff numbers than to, say, staff costs. The costs per hour were then uplifted by multiplying by a factor of 1.2 to allow for FTEs spending some time on non-assessment activities. This is in line with the approach taken in the pilot costing exercise (EMEA 2009). Meeting costs were allocated separately.
- Step 2: Multiply full cost per hour by hours spent on an activity. The total time spent on an activity by each staff type was determined from the time taken to carry out a procedure for the given activity and the number of procedures undertaken. Total costs were calculated by multiplying the time taken by the costs per hour for each staff type and activity.

This approach was followed for the EMA fee- and non-fee generating activities involving NCAs. For other EMA activities, staff salary costs were provided by EMA at a detailed level so that only overhead and non-staff direct costs had to be allocated according to the specified allocation rule.

The following data sources and assumptions were used:

- EMA staff were categorised as one of two staff types - scientific or administrative staff – these definitions were consistent with those used by EMA in the MBDG Exercise. This categorisation was made by EMA.
- The number of FTEs of each staff type was provided to the study team by EMA.
- The annual number of hours worked per FTE is based on 41 working weeks per year (after allowing for holidays, sick leave etc.) of 40 hours per week for both staff types. This is based on data provided by EMA.
- The hourly cost of each staff type was assumed to be independent of the type of activity they undertake (e.g. the salary cost of scientific staff time is the same for all activities). Costs of staff not involved in scientific activities were included as overhead costs.
- The allocation of overheads in relation to staff time was specified in the model. EMA also provided its own allocation of overheads and direct costs to activities. This was used for procedural activities involving EMA only and additional activities.
- Committee time costs were allocated across procedural activities. This was done by multiplying the costs/hour for scientific and administrative staff by a scaling factor. The scaling factors were determined from the ratio of total reported procedural costs involving NCAs to the total calculated costs of procedural activities involving NCAs. This approach allocates committee time costs proportionately across all relevant activities.

- Any administration cost for NCA remuneration was allocated across activities by EMA.
- Data for Scientific Advice and Protocol Assistance were combined as EMA provided data for these activities at a more detailed level than in the NCA survey. Data were weighted according to the number of procedures.
- Data for Initial Marketing Authorisations were provided at a more aggregated level than in the NCA survey and costs could only be calculated at this level in the baseline. In the synthetic baseline, procedures were imputed at a more disaggregate level based on the proportion of procedures reported by NCAs.
- In the data reported by EMA, inspection activities were combined for human and veterinary medicines. In the model these were not separated in the baseline for data validation purposes (see section 5.2). In the synthetic baseline, procedures for these activities were allocated between human and veterinary medicines in proportion to the allocation of total reported NCA procedures. It is assumed that the cost of these activities (i.e. time taken per procedure) is the same for human and veterinary medicines.
- PIP-modifications (labelled as PIP-activities) were included as an activity in the EMA reported costs. PIP-modifications were not part of the agreed list of activities included in (Q17 of) the NCA Survey (see final report, Appendix 7 for the NCA Survey – Survey Instrument). PIP-modifications were therefore not included in the cost-based analysis. The MBDG dataset was used as the main source of data on time taken for procedural activities by the two EMA staff types (scientific and administrative).
- There is not a complete correspondence between the activities included in the NCA survey or provided by EMA (and used the modelling exercise) and the MBDG dataset. The MBDG dataset does not provide time data for a small number of activities included in the NCA survey, namely: scientific services[9], Certification of Advanced Therapies and PSUSAs undertaken for human medicines. Only limited data was available for PASSs and PSURs; these were means for EMA and all NCAs only, not disaggregated by staff type. These times were very similar to times reported in the KPI (2016) study for EMA on the Pharmacovigilance Fee Regulation that provides aggregate data on post-authorisation safety studies (PASS), periodic safety update reports (PSURs), and also on periodic safety update report single assessments (PSUSAs). It was then assumed that these values apply to scientific staff as no staff type distinction was available. There were also no time data for Type II variations - level III for both human and veterinary medicines. EMA-reported cost data was used to back-calculate time taken for scientific services. No costs for Certification of Advanced Therapies were calculated in the model as no time data for them were available. No procedures were reported by EMA for compassionate use opinions and consequently no costs were calculated for these. For good clinical practice (GCP) inspections inside and outside Europe, a single inspection time was used for both geographies. The MBDG dataset also does not distinguish levels for line extensions. In the model the same time was used for all levels. For veterinary medicines, it was additionally necessary to use a single value for all scientific advice and protocol assistance follow-up activities and to apply the time taken for initial marketing authorisations for known active substances to initial marketing authorisations for fixed combination. No procedures were reported by EMA or NCAs for initial marketing authorisations covering informed consent, well established use and hybrids, and consequently no costs were calculated for these in the model.

[9] The scientific services are: PMF, VAMF, ancillary medicinal substances consultation, Advanced Therapy Medicinal Products (ATMP) certification, traditional herbals, compassionate use opinions, and Art. 58.

The costs to EMA of remunerating NCAs for the EMA-related activities the NCAs undertake depend on the remuneration rule applied. This remuneration rule may be linked to the fees charged to industry, as is mostly the case under the existing fee system. Since all fee revenue from industry is collected by EMA, the remuneration costs can be considered as a transfer of fee income from EMA to NCAs, subject to an administration cost. Under the existing fee system EMA also reimburses travel and subsistence costs for NCA committee and Working Group members attending meetings.[10] The travel and subsistence costs paid to NCA delegates for meeting attendance (NCA reimbursement) have been allocated across activities and cost types by EMA; this remains fixed in the model.

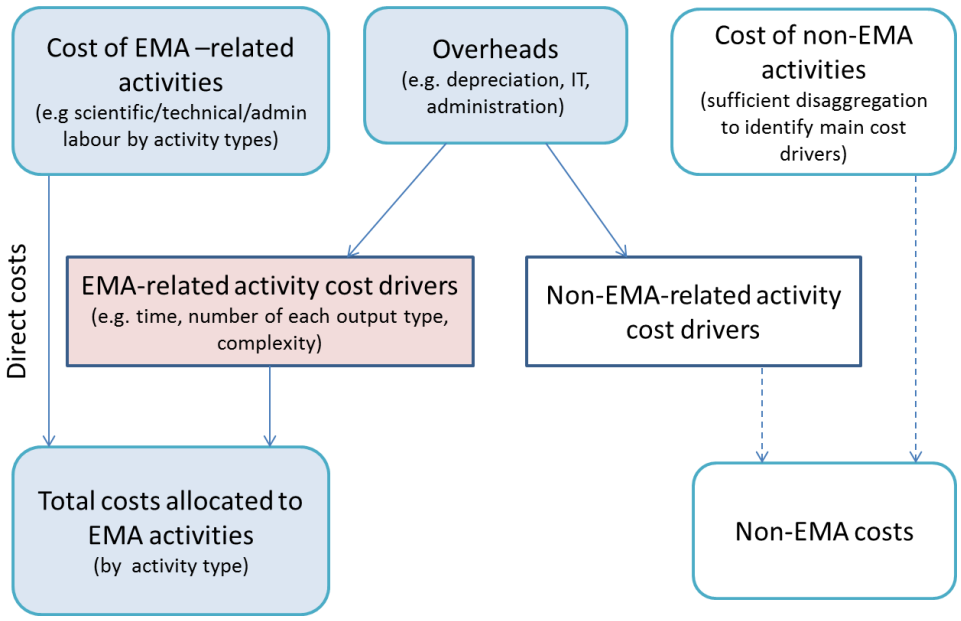
3.2. The NCA cost model

This section describes how the study team used the available data sources to determine the costs to NCAs of undertaking EMA-related activities. Data for the NCA cost model was predominantly taken from the NCA survey conducted by the study team. This survey provides data for a one-year period. Thirty NCAs completed the survey, of which 11 undertook activities relating to human medicines only, 6 relating to veterinary medicines only and 13 to both. Of the respondent NCAs, one had a separate inspectorate. Responses for the inspectorate were included in the survey responses of the relevant NCA and incorporated in the model calculations for that NCA. For 28 NCAs, information was provided for the calendar year 2016; for two NCAs, the financial year spanned twelve months from April 2015 to March 2016.

NCA costs can be considered to consist of three types: costs for EMA-related activities, costs for other (non-EMA-related) activities they undertake, and overhead costs. The current study is concerned only with costs from EMA-related activities by NCAs and the proportion of NCA overheads that can be attributed to these. Costs associated with all other non-EMA-related activities undertaken by NCAs were explicitly excluded from the model. This is illustrated in Figure-3.

[10] NCAs are reimbursed for delegates and their alternates only.

Figure-3: Cost allocation for NCAs



The cost calculations for NCAs followed a similar approach to that used for EMA.

The hourly costs of EMA-related activities and the cost of EMA-related activities by activity type were calculated for each NCA. The following steps were applied to each NCA separately:[11]

1. determine hourly costs of EMA-related activities
2. determine the cost of EMA-related activities by activity type.

[11] The model is based on cost data from 29 respondent NCAs. The one other respondent NCA did not report any EMA related activities. It is not possible to determine an average over all 48 NCAs from the available data. However, the respondent NCAs cover 23 countries and 95 per cent of workload undertaken by NCAs for EMA.

Step 1: determine hourly costs of EMA-related activities

Overheads and non-staff costs were allocated to the annual salary costs to determine the annual costs of undertaking EMA activities for two different staff types: administrative and scientific. The cost per hour of EMA activities for each staff type was calculated by dividing the annual costs by the annual hours worked. The cost per hour was (as for EMA) multiplied by a factor of 1.2 to allow for FTEs working on EMA-related activities spending some time on non-assessment activities. This is in line with the approach taken in the pilot costing exercise (EMEA 2009).

The following data sources and assumptions were used:

- NCAs provided data for two staff types - scientific and administrative staff – in order to ensure consistency with the time data provided by the EMA MBDG Exercise, which refers to these two employee types only.
- The number of FTEs of each staff type involved in EMA activities was provided by NCAs in the survey.
- The number of annual hours per FTE was entered in the model for each NCA. The same hours were used for both staff types. NCAs were requested to provide data on weekly working hours per FTE and number of weeks worked per year per FTE. 21 NCAs responded and of these, 9 reported more than 48 working weeks per year. This indicated that they had not excluded annual leave from their reported numbers. One NCA reported working hours but no working weeks. The average number of working weeks across the remaining NCAs is approximately 43.5. This is in line with EMEA 2009 which used 44 working weeks. For all NCAs that reported working hours per week per FTE and working weeks per FTE greater than 48, the stated number of working hours per week was used as provided but the stated number of working weeks per year was replaced by 43.5. The annual hours were then calculated by multiplying working hours per week by weeks worked per year. For NCAs that did not provide any data, 1640 annual hours per FTE was assumed. This is lower than the overall NCA average because most of the NCAs for which data was not provided were larger, Western European NCAs whereas the overall NCA average contained a higher proportion of smaller, Eastern European agencies that reported longer working hours per year. These values were adjusted for sick leave and other parental leave by reducing the number of weeks worked annually by 2 weeks.[12]
- The hourly cost of each staff type was assumed to be independent of the type of activity they undertake (e.g. the salary cost of scientific staff time is the same for EMA and non-EMA related activities and for rapporteur, co-rapporteur or other, unremunerated roles). Costs of staff not involved in scientific activities were included as overhead costs.
- NCAs provided information in the survey as to the overhead cost allocation rule they applied in their own cost calculations. To ensure consistency in our model, however, overheads were allocated in relation to staff time for all NCAs (and EMA) in the model.[13] Explicitly this means that all reported overhead costs (scientific staff, administrative staff and non-staff) were summed. These were first allocated between EMA-related and other NCA activities in proportion to the

[12] This is in line with findings from Eurofound (https://www.eurofound.europa.eu/observatories/eurwork/comparative-information/absence-from-work) and the approach used by EMA in the calculation of their annual hours worked.

[13] 15 NCAs reported a cost based overhead allocation rule, 11 a staff time or staff numbers based rule; i.e. consistent with the overhead allocation rule. Two NCAs specified a different rule but it was not clear how this would be implemented. One NCA did not specify a rule. In these cases, the staff numbers rule was used as the default. If overheads were already allocated by staff type, then both rules would allocate the same proportion between EMA and non-EMA activities.

number of FTEs working on these two types of activities. For EMA related activities, the overheads were then further allocated between scientific and administrative staff in proportion to the number of these staff types working on these activities.

Step 2: determine the cost of EMA-related activities by activity type

The cost of EMA-related activities was calculated based on a categorisation according to three different types of activities:

1. Procedural activities (NCA involvement)
2. Committees and Working Groups
3. Additional activities.

1. Procedural activities (NCA involvement)

This first activity type comprises a set of 40 activities related to human medicines and 32 activities related to veterinary medicines. These are predominantly fee-generating activities, with a few exceptions.[14] Both EMA and HMA were consulted in the identification of these activities, which formed the basis for Questions 17 and 18 respectively in the NCA survey. For these activities, NCAs provided information on the number of times they undertook a given activity and their role.

Three types of procedural roles were distinguished in Q17 and Q18 of the NCA survey:

- Rapporteur or equivalent lead role
- Co-rapporteur or equivalent support
- Any other role that is required for completion of a procedure. Other roles include PRAC rapporteur and co-rapporteur and peer-reviewer but also membership of multi-national assessment teams.

The term 'procedural role' is used by the study team to refer to each instance that an NCA undertakes a particular activity. For any given procedure,[15] a number of NCAs may carry out different procedural roles. For example, for 5 procedures of the activity 'Type II variation – level I', NCA X could undertake three rapporteur roles, NCA Y two rapporteur roles and NCA Z five co-rapporteur roles.

For a given activity and role, the total cost was calculated based on the time taken multiplied by the number of procedures undertaken. These costs were summed across the different roles (rapporteur, co-rapporteur and other) and activities to provide the total yearly procedural activity cost of a given NCA. The total yearly activity costs are presented separately for human and veterinary medicines.[16] A weighted yearly average cost per procedure for each procedural activity was calculated from the total yearly cost divided by the number of procedures.

The following data sources and assumptions were used:

[14] Namely the majority of paediatric activities and orphan designations.
[15] See Glossary for the definition of procedure used in this study.
[16] Keeping costs for human and veterinary medicines separate is in line with the study's terms of reference and enabled the implications of cost-based fees for different stakeholders to be better understood.

- The MBDG exercise was the main data source for the time to undertake a procedure for each activity in a given role. The exercise covered the three types of procedural roles (rapporteur, co-rapporteur or equivalent and other).
- The MBDG dataset was used to determine an NCA average time[17] for each procedural role for a given activity that was used as the default for each NCA in the model. The 'other' roles were combined into a single category for each activity and an average time taken was applied to all procedural roles reported as 'other' for an activity type in the NCA survey.
- There is not a complete correspondence between the activities included in the NCA survey or provided by EMA (and used the modelling exercise) and the MBDG dataset. The MBDG dataset does not provide time data for a small number of activities, namely: scientific services[18], Certification of Advanced Therapies and PSUSAs undertaken for human medicines. Only limited data was available for PASSs and PSURs; these were means for EMA and all NCAs only, not disaggregated by staff type. These times were very similar to times reported in the KPI (2016) study for EMA on the Pharmacovigilance Fee Regulation that provides aggregate data on post-authorisation safety studies (PASS), periodic safety update reports (PSURs), and also on periodic safety update report single assessments (PSUSAs). It was then assumed that these values apply to scientific staff as no staff type distinction was available. EMA reported cost data was used to back calculate time taken for scientific services and these were assumed to also apply to NCAs. No costs for Certification of Advanced Therapies or for GCP inspections outside Europe were calculated in the model.
- For good clinical practice (GCP) inspections inside and outside Europe, a single inspection time was used with different travel times. The MBDG dataset also does not distinguish levels for line extensions. Consequently, in the model the same time was used for all levels. For veterinary medicines, it was additionally necessary to use a single value for all scientific advice and protocol assistance follow-up activities and to apply the time taken for initial marketing authorisations for known active substances to initial marketing authorisations for fixed combinations. No procedures were reported by EMA or NCAs for initial marketing authorisations covering informed consent, well established use and hybrids, and consequently no costs were calculated for these in the model.
- Data on the number of procedural roles for each of the three types (rapporteur/lead, co-rapporteur/support and other) are taken from the NCA survey. For 'other' roles in particular, where it is not possible to verify the data from another source (see section 5.3), it is possible that NCAs may have under or over-reported the number of roles they undertook. This would result in an under or over-estimation, respectively, of the procedural costs with a corresponding opposite effect on the estimated costs of additional activities.
- Data on the number of POs for annual CAP fees for each NCA was provided by EMA. NCAs were not asked about roles related to annual fees in the NCA survey.

2. Committees and Working Groups

The second type of activity relates to time spent in and preparing for EMA committee and Working Group meetings. NCAs were asked to provide information on these activities in Question 19 of the NCA survey. Of the 30 survey respondents, 12 provided total cost information and 4 provided travel costs only. For committees, the MBDG

[17] In this case the average is based on the NCAs that provided data to the MBDG exercise for the period that it covered.

[18] The scientific services are: PMF, VAMF, ancillary medicinal substances consultation, Advanced Therapy Medicinal Products (ATMP) certification, traditional herbals, compassionate use opinions, and Art. 58.

exercise provides monthly average data on time spent on meeting preparation by a committee member and their scientific and administrative support, as well as time spent at the meeting and travelling. The MBDG dataset also presents the average monthly workload for Working Group members and their support staff.

Data from the MBDG exercise was used in the first instance to ensure a consistent approach to the calculation across NCAs. Hence cost data for work related to committees and Working Groups was only included in the model for NCAs that provided time data for these activities in the MBDG exercise and an average NCA value was not applied. For each NCA for which data were available in the MBDG exercise, the average monthly time spent in or preparing for meetings by committee members and their support staff was multiplied by the number of time the committees met. For Working Groups, a combined value over all groups was used and Working Groups are each assumed to meet 11 times per year.[19] All committees meet 11 times per year, except the PDCO, which meets 12 times/year, and the HMPC, which meets 6 times/year. However, for those NCAs that provided data on this in responding to the NCA survey, the time they reported being spent in committees was compared with the MBDG data and any discrepancies noted – see the discussion in section 5.3. The costs of time spent in committees were calculated for each NCA by multiplying the annual time taken by the cost per hour for each staff type.

The following data sources and assumptions were used:

- Data from the MBDG exercise was used to determine the average time spent across all committees and Working Groups by each NCA for which data were available.
- Member State delegates (or their alternates) travel costs are reimbursed by EMA. It is assumed that only additional travel costs that are not reimbursed by EMA are included in the NCA costs as the reimbursed costs are transfers.

3. Additional activities

The third type of activity includes those that NCAs consider to be EMA-related but which were not already covered under the first two activity types. NCAs were asked to provide information on additional activities in Question 20 of the NCA survey. Ten NCAs provided data on time spent on additional activities, while a further six NCAs indicated the number of additional activities they undertook.

NCAs provided a variety of responses for these activities, both in terms of the types of activities undertaken and the information provided about them. Some NCAs provided monetary costs, others provided time spent on activities or numbers of activities undertaken. Therefore the study team's approach was to determine the total cost of additional activities, which was calculated as the sum of costs of fee- and non-fee-generating activities with NCA involvement (activity type no. 1) plus the cost of time spent on committees and Working Groups (activity type no. 2), all subtracted from the total costs of EMA-related activities for each NCA as declared by the NCAs in the survey.

The study team's approach to analysing the data was to map the additional activities reported by the individual NCAs onto a common set of categories, shown in Table-2.

[19] A single value was used for all Working Groups. This may result in an overestimation of costs for some.

Table-2 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

The following data sources and assumptions were used:

- Total costs for NCA activities, with non-staff costs and overheads allocated according to the overhead rule based on staff time, were calculated from data provided in the NCA survey.
- Additional costs are independent of the fee and remuneration rules and are treated as a fixed cost in the model.

3.3. The revenue model

In this section the revenue model and the different fee and remuneration rules that are applied under the existing fee system and in the scenarios are presented.

There are three stages to the revenue model as follows.

First, EMA receives fees from the pharmaceutical industry for the services it provides. The total fees paid by industry depend on the fee rule and the incentive rate and the number of procedures for a given activity. The fee rule determines the full fee, which is the maximum fee that could be paid. Incentives (discounts or waivers) are applied to the full fees depending on the nature of the product and the industry organisation (e.g. whether an SME) making the application, as well as for other reasons. A procedure is the smallest chargeable unit used in the model and, for a given activity, the model calculates the unit full fee, which is the full fee per procedure (before any incentive, i.e. discount or waiver), as well as the total fees paid by industry. Three types of fees may be covered by the fee rule. These are procedural-activity based fees for CAPs, annual fees for CAPs and annual PcV fees for nationally authorised products.

Second, NCA income takes the form of a payment from EMA to recompense it for the EMA-related activities it has undertaken. The amount of this payment is determined by the **remuneration rule**. NCA delegates are additionally also reimbursed by EMA for travel and subsistence costs for attending meetings. The EMA's net fee income was calculated as the total fee revenue minus the NCA remuneration. For both NCAs and EMA, fee income from annual fees and procedural-activity based fees are provided separately for both human and veterinary medicines.

Finally, in the financial model for EMA, the budget is balanced so that EMA costs do not exceed the revenue it receives. In addition to revenue from its share of industry fee income, EMA receives EU and EEA budget contributions. In the baseline the total reported EU and EEA budget contributions were used and an additional balancing term, denoted 'other income', was calculated as the difference between the EMA costs and revenues from fees and EU budget contributions. The balancing term takes account of other non-fee sources of income that EMA received in the reporting year (this is discussed in more detail in section 5.2). In the synthetic baseline this balancing term was adjusted so as to balance the EMA budget (see section 4). 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 following data and assumptions were used:

- The number of procedures of each activity type and the allocation of these across NCAs and EMA is fixed in the model. This was determined from NCA survey and EMA-provided data in the synthetic baseline. The NCA survey data determined the allocation of roles across NCAs at the disaggregate level.[20] The EMA data determined the total number of procedures for a given activity.
- The average incentive rate applied to each activity type for the baseline year was provided by EMA and this was assumed to remain the same for all fee and remuneration scenarios.

[20] NCA-specific PO data was not provided at the same level of disaggregation and contains no information on other roles that were not remunerated or rapporteur/lead and co-rapporteur/support roles for paediatric and orphan activities that were also not remunerated.

- Travel and subsistence cost reimbursement for Member State delegates remains fixed for all scenarios. It does not enter the model as it is a transfer from EMA to NCA delegates either directly or via NCAs.
- Data provided by DG SANTE was used to separate the contributions into general and orphan contributions. As the amount of orphan contributions has remained relatively constant since 2013, these contributions are considered to be fixed inputs in the revenue model.

Fee and remuneration rules under the existing fee system

Under the current fee system, each procedural activity (or service) for which a fee can be charged has a full fee associated with it. This is the maximum fee that an organisation could be asked to pay for a given activity (i.e. if there were no discount or waiver) and has a specific legal basis. The different full fees were the main basis for the level of disaggregation of procedural activities in the NCA survey and hence in the model. In addition, there are a number of procedural activities for which no fees are charged currently.

In the model, the unitary full fees were derived from the total theoretical full fee revenue from industry before incentives are applied divided by the number of invoiced procedures. These may differ from published values because:

- A yearly inflationary adjustment is applied to the fees charged every April.
- The fee charged for some procedures (full application for marketing authorisation and line extensions) contains a fixed and a variable fee. The variable part is linked to the requests from the applicants for additional "strength, pharmaceutical forms and presentations, so the higher the number of additional requests the higher fee charged.

Under the current fee system, the incentives that can be applied to full fees mean that there are around 150 different possible fee combinations. The actual incentives that apply in any given year depend on the combination of product type (e.g. whether an orphan medicinal product), the applicant for each procedure (e.g. whether an SME) and the procedure type itself. EMA provided the monetary value of the incentives that were applied in 2016 based on the invoiced procedures for a given activity in that year. From this, the study team calculated the average incentive rate for a given activity, in percentage terms, as:

(monetary value of the incentives/ full fee revenue) x 100

The combination of product and applicant types observed in 2016 was assumed to be representative of a typical year. This average discount rate for each activity was used as an input in the model.[21]

The rule for the remuneration of NCAs under the existing fee system is as follows:

1) For a rapporteur or co-rapporteur role for a non-pharmacovigilance, fee generating procedural-activity,[22] the NCA receives 50 per cent of the full fee before incentives are applied. Where more than one NCA undertakes a

[21] The alternative to this would be to run the model for all possible combinations of products and applicant types, of which there are over 150. Using an average incentive rate for each activity means that a manageable output can be generated on which to base fee and remuneration rules.

[22] PRAC rapporteur and co-rapporteur roles, as well as peer-reviewers, are not remunerated under the current fee system, where they appear in conjunction with other rapporteur or co-rapporteur roles (e.g. CHMP).

remunerated role for the same procedure, the remuneration is distributed equally between them. For pharmacovigilance activities, NCAs are remunerated a fixed amount, which is reduced in proportion to the incentive applied to the full fee.[23]

2) Rapporteurs and co-rapporteurs of eligible procedures receive 30 per cent (15 per cent each) of the CAP annual fees for human and veterinary medicines. NCAs do not receive a share of pharmacovigilance annual fees.

The net fee income that EMA receives from fee-generating activities is the remainder of the full fee income less NCA remuneration and the incentives applied. Hence, for procedural activities, other than pharmacovigilance activities, they receive:

Full fee x (100% – 50% paid to NCAs – incentive rate (%))

For pharmacovigilance activities, EMA fee income is calculated as:

(Full fee – NCA remuneration) x (100% – incentive rate (%))

EMA receives 70 per cent of the annual fees for CAPs and 100 per cent of the annual pharmacovigilance fees. In both cases the EMA fee income is net of incentives.

Based on the above rules, the fee income for EMA and remuneration for NCAs was calculated as follows:

- The total theoretical full fee income was calculated as the product of the full fee per activity and the number of invoiced procedures for a given activity.
- Data on the number of CAP and PhV annual fee procedures, the incentive rates and the number of POs for CAP annual fees sent to individual NCAs was provided by EMA. These data were used to determine the eligibility of NCAs for CAP annual fees and the share of fee income they received.
- The EMA net fee income is the total fee income net of the NCA share and incentives.
- NCA remuneration was calculated for a given activity according to the rules outlined above. The remuneration was allocated across NCAs according to the number of rapporteur/co-rapporteur roles undertaken and the number of POs per procedure. (The formula is modified slightly for pharmacovigilance activities.)

  Remuneration of NCA X = NCA share of fee x unit full fee x (no. rap + no. co-rap NCA X)
  /(no. rap + no. co-rap per procedure)

Fee and remuneration rules for cost-based scenarios

The scenarios implemented in the model are shown in Table-3 below. Remuneration rules are shown in the columns and fee mechanisms are shown in the rows. Nine combinations of fee and remuneration rules were developed.

For all scenarios, the remuneration rule applied to NCAs for procedural activities was that they should be remunerated at average cost. This is enacted in the model as follows:

[23] The combined NCA remuneration for rapporteurs and co-rapporteurs for PASS is €7280 for the draft report and a further €10920 for the final report. For PSURs and PSUSAs, it is €13100. The remuneration is scaled proportionally to the incentive rate applied to the full fee (EU Regulation 658/2014).

- The average cost was determined as the total yearly cost of all procedural roles undertaken for an activity by all NCAs divided by the total number of procedures undertaken for that activity (see NCA cost model).
- For fee generating procedural-activities, 'other' roles that are currently unremunerated under the current fee system are included in these costs.
- NCAs are not remunerated for paediatric and orphan activities for which they are not remunerated under the current fee system.
- The average-cost remuneration is allocated across NCAs in proportion to the number and type of roles they undertake.

The scenarios are based on the synthetic baseline so that the number of procedures for which NCAs carried out roles for an activity is the same as the number of procedures for which applications from industry are received and, where appropriate, invoiced.

Under the cost-based scenarios, NCAs do not receive remuneration from annual fees.

For scenarios A1, B1 and C1, NCAs are remunerated for procedural-activity costs only. Two further sets of scenarios are developed in which NCAs are remunerated for:

- Procedural-activities and time spent in committees and Working Groups (A2, B2, C2)
- All activities undertaken including additional activities (A3, B3, C3)

Under these remuneration rules, each individual NCA is remunerated for: a) the time spent in committees and Working Groups calculated in the model for that NCA; and b) the cost of additional activities determined in the model for that NCA. An average is not used for these activities.

Table-3: Scenarios to assess the impact of different fee and remuneration mechanisms

NCA Remuneration / Fees[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 remunerated (procedural activities, Working Groups and committees, and additional activities)
Remainder in EU and EEA budget (existing annual fee)[b]	A1	A2	A3
Remainder in CAP annual fee (existing EU and EEA budget)	B1	B2	B3
Remainder spread proportionally across fees (existing EU and EEA budget contribution, existing annual fee)	C1	C2	C3

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

Cost-based full fees are also applied to procedural activities in the scenarios. These are calculated as the sum of the average cost to EMA and to NCAs of undertaking a procedure of a given activity.[24] A cost based fee is not used for annual fees. Applying cost-based full fees and cost-based NCA remuneration may result in a shortfall in EMA income as incentives or exemptions reduce the actual fee income from industry.

[24] For NCAs, this is the same average cost used in the remuneration rule described above.

Three fee mechanisms are used to ensure the EMA budget balances with cost-based fees and the different levels of NCA remuneration. These are the EU and EEA budget contributions, the CAP annual fee and a common mark-up on the cost-based fees for procedural activities.

4. SYNTHETIC BASELINE CALCULATIONS

In the actual baseline, two different sources of data were used to determine the number of procedures and roles undertaken for procedural activities, from which costs and revenue were calculated for NCAs and EMA. These were the NCA survey and the data provided directly by EMA on invoiced procedures. NCA costs and fee income were calculated using data on procedural roles provided in the NCA survey. EMA costs and fee income was based on the number of procedures invoice to industry.

In order to assess how far the fees under the existing fee system are cost-based and to compare the impact of different fee and remuneration rules, a common number of procedures for each activity type is needed for the cost and fee calculations for both EMA and. Otherwise it is not possible to determine how much of any difference between costs and the revenues raised by the fees is due to the fees not being cost-reflective and how much is due to costs being calculated for one set of activities while fee revenues are calculated for a different set of activities.

4.1. Approach to synthetic baseline calculations

To ensure consistent calculations could be made, the following approach was adopted.

First, the number of invoiced procedures provided by EMA for each procedural activity type and for annual fees was used to calculate the total full fee income in the revenue model. The number of POs per procedure for each activity was calculated from the EMA data on the number of invoiced procedures and total POs issued. Under the existing fee system, this determines when the NCA share of fee income is split between rapporteur and co-rapporteur roles.

Second, the number of invoiced procedures for each procedural activity and for CAP annual fees provided by EMA was used to determine the costs in the NCA cost model:

- The total number of POs per activity was calculated from the number of invoiced procedures for a given activity multiplied by the number of POs per procedure.
- The number of POs by NCA provided by EMA was adjusted to match the total number of POs per activity. The study team assumed in effect that the 29 respondent NCAs undertake all of the activities in the synthetic baseline year – and in practice 95 per cent of all POs were indeed issued to these NCAs in 2016.[25]
- The number of procedures for a given activity as rapporteur/co-rapporteur provided by NCAs was adjusted to match the number of POs corresponding to the invoiced procedures for a given activity. To do this, a scaling factor was applied to the NCA values. 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.
  Scaled procedural roles=reported procedural roles x (total number of purchase orders reported by EMA)/(total reported sum of rapporteur and co-rapporteur roles)

[25] This assumption implies that the activities not undertaken by respondent NCAs are assumed to be undertaken at the same average cost as the average cost of the respondent NCAs.

- The number of roles undertaken by a given NCA relative to other NCAs was determined by the NCA survey data.
- POs only cover rap/lead and co-rap roles that are remunerated. The only data on 'other' procedural roles that are unremunerated was provided directly by the NCAs. The study team assumed that these should be scaled in the same way as the remunerated roles. A further constraint was added so that the total unremunerated roles do not exceed three times the total number of remunerated roles for a given activity. This constraint was added to ensure that the number of unremunerated roles reported by NCAs in total was consistent with the number of remunerated roles, while at the same time allowing that NCAs considered a number of such roles to be procedural. Where the constraint was exceeded, the excess costs were included as part of the costs of additional activities for the relevant NCAs.
- For activities for which no fees are charged to industry or where fees are completely waived, the number of invoiced procedures reported by EMA is used to determine NCA costs.

EMA costs were calculated based on the number of procedures in the EMA resource cost model. In this case invoiced procedures for PhV annual fees were also included.

4.2. Implications for cost calculation

For EMA costs (excluding NCA remuneration), the activity based approach was used to calculate the costs of procedural activities, as discussed in section 3.1. In both the baseline and the synthetic baseline these calculations were based on the number of invoiced procedures for procedural activities.[26]. Costs of additional activities undertaken by EMA were assumed to be the same in the synthetic baseline as the actual costs for these activities reported by EMA.

The costs to NCAs of procedural activities were calculated using the scaled numbers of procedures determined in section 4.1 above. The methodology described in section 3.2. was followed. The costs are therefore based on slightly different numbers of activities than reported by NCAs in the baseline. The costs of time spent in and preparing for Working Groups and committees were calculated based on data from the MBDG data gathering exercise. They were assumed to be independent of the number of procedures. The NCA costs of additional EMA-related activities were calculated in the baseline as the total costs of EMA-related activities as declared by NCAs in the survey minus the activity-based costs (costs for activity no. 1) and the time based costs for committee work (costs for activity no. 2). These additional costs were then carried forward as a fixed term into the synthetic baseline and were not recalculated.

The NCA and EMA costs (excluding NCA remuneration) calculated in the synthetic baseline are independent of the fee and remuneration rules.

4.3. Implications for revenue calculation

The rules of the existing fee system were applied in the synthetic baseline. The rules used to determine the fees are described in section 3.3.

[26] In the baseline, inspections were reported as a combined activity by EMA. In the synthetic baseline, inspection costs for EMA were allocated across human and veterinary medicines in proportion to the human and veterinary inspections reported by NCAs. For procedural activities where no fees were charged, the number of completed procedures was used.

The main implication is that NCA remuneration is based on the number of invoiced procedures and not the number of procedures NCAs reported in the survey. Total fee revenue is unchanged from the baseline because this is determined from the number of invoiced procedures as well as incentive rates and unit full fees, which are fixed. The EMA share of total fee income is affected because this is calculated as total fee income minus NCA remuneration.

The existing EU and EEA budget contributions remain fixed in the synthetic baseline. However, an adjustment to the balancing, 'other income' term is also required to balance the EMA budget. This results from the change in the EMA fee revenue due to the change in NCA remuneration. The adjustment to the balancing term effectively represents the effect of the remuneration of procedures being completed in the 'typical year' and not being carried over more than one year as would normally be the case. The balancing term also still accounts for other sources of income and the different methodologies used by EMA in their reported costs and their accounts.

5. DATA VALIDATION

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 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.

5.1. MBDG exercise

EMA produced a detailed report on the MBDG initiative and its outcomes.[27] Only a brief overview is provided here.

5.1.1. Data overview

The data were collected under the guidance and oversight of the MBDG Steering Group over the period December 2015-March 2017, and show the number of input hours per activity, by EMA and NCA staff respectively, for each of a range of EMA activities.

Table-4 presents the activities for which data were collected and the time period of the data collection.[28]

Data was provided to the study team in a spreadsheet format. The validation of data was carried out on this data only and not on the survey data that was processed by EMA to generate the spreadsheet content or the processing methodology employed to do this. Additional documentation comprised the MBDG report on the outcome of the exercise with Annexes: Annex III contained the methodology and templates for the data reporting.

The MBDG time data is for two main types of activities:

[27] EMA MBDG. Report on the outcome of the exercise. April 2017.

[28] These were the time periods provided to the study team. For some activities, the collection period was extended to March 2017.

1) Fee- and non-fee-generating activities that are procedure based. The term 'procedure' is used by the study team, for the purposes of the report, to mean instances of the activities listed in Questions 17 and 18 of the NCA survey and the procedural activities without NCA involvement listed by EMA. That does not mean that procedures are identical. For each procedure, roles are undertaken by EMA and, if appropriate, NCAs, for which time spent was recorded.
2) Horizontal activities. This is time spent in committees, working parties and groups that is not specific to a procedure (fee- or non-fee-generating). Time spent on these activities includes time spent at meetings and preparing for meetings and was allocated across different roles.

Initial Marketing Authorisations and Line Extensions are undertaken in three phases. The time taken to complete each phase was recorded separately in the MBDG data. Due to the length of the collection period and the time taken to complete all three phases of a procedure, the number of procedures for which data were available on all three phases was small. The majority of MBDG data refers to procedures for which data are available for only one or two of the three phases.

For all activities, time data for two staff types are provided for both EMA and NCAs. These are scientific staff (labelled AD by EMA) and non-scientific/administrative staff (labelled AST). There is no further subdivision of staff roles for EMA. For NCAs, a number of roles are provided for each staff type, depending on the particular activity. These encompass rapporteur, co-rapporteur from the relevant committee for the procedural activity, co-ordinator and inspector roles and other roles including peer-reviewer, PRAC rapporteur and co-rapporteur.

Table-4: 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
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 Committees activities (CHMP, PRAC, CVMP, PDCO, CAT, HMPC, COMP)	September – October 2016
Working Parties 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

* Human only

5.1.2. Validation

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 for both EMA and NCAs. The allocation of time spent on activities by scientific and administrative staff, and for NCAs on all rapporteur, co-rapporteur and equivalent and 'other'[29] 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 2009). 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. The validation steps are summarised in Table-5.

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

Table-5: Summary of validation steps

Validation step	Organisation	Outcome
Summary table of procedures	EMA/NCA	Summary info for reference: mean time spent, sample size. Identifies number of outliers per procedure
Table-of outliers	EMA/NCA	Identifies outliers by procedure, role, staff type and organization for given activity. Provides indication of complexity.
AD vs AST plots, all data	NCA	Identifies range, outliers, mean trend
AD vs AST plots NCA + EMA averages	EMA/NCA	Identifies range, outliers, mean trend and trend across NCAs
Rapporteur vs co-rapporteur plots, all data	NCA	Identifies range, outliers, equality of rapporteur/co-rapporteur time, mean trend
Rapporteur vs co-rapporteur plots, NCA average	NCA	Identifies range, outliers, equality of rapporteur/co-rapporteur time mean trend and trend across NCAs
Comparison with previous cost data collection	NCA	Limited sense check magnitude of values

As well as determining outliers, the data validation process identified patterns in NCA reported values for different roles and staff types. These are interesting to note, particularly for the cost modelling exercise where costs can be based on different time values for individual NCAs and roles that are currently remunerated and non-remunerated are considered separately. However, these patterns are not a reason to exclude data as they may reflect the real behaviour of a particular organisation. An NCA may, for example, consistently use more administrative time and less scientific time than the average across all activities.

The main findings of the data validation exercise are that:

- Overall, outliers do not appear to be associated with particular procedures or activities, are not associated with particular organisations, and are not associated with particular roles or staff types.
- For most activities, there is wide variation in the time taken by individual NCAs to undertake procedures for the same activity. However, procedures may also differ in complexity. The variation in time taken is supported by the evidence from the previous cost exercise (2008-2009).[30]
- For most activities, where procedures take more scientific time to complete, they also take more administrative time. Type II and Type IB variations are the main exception.
- The time taken by rapporteurs and co-rapporteurs is approximately equal for Phase 1 of Initial Marketing Authorisations but not for subsequent phases or Line Extensions.
- Comparison of average times taken to complete procedures for activities with outliers excluded (adjusted averages) does not significantly change the patterns observed when outliers are included.

The conclusion of the data validation exercise was that, given the relatively short time period for data collection and the range of complexity in the procedures for which time was reported, **there were insufficient grounds to exclude the outliers**. All the available data from the MBDG exercise was therefore used to calculate average NCA values for time taken to undertake a procedure for a given activity for the two staff types

[30] The three sources used are EMEA/MB/780575/2009 Costing Group – Outcome of the pilot exercise, NCA hours and costs from 2009 exercise, and Costing Method for 2009 exercise.

and three roles (rapporteur, co-rapporteur and other). These averages were then used in the model. Two different sensitivity tests were carried out: the average values were recalculated without outliers, and averages for individual NCAs were used where data were available instead of the overall NCA average. The findings of the validation exercise for procedural activities are discussed in more detail for each of the validation steps in Appendix 1. Initial Marketing Authorisations are used to illustrate the results. All the figures generated as part of the analysis are contained in further appendices to this note.

5.2. Data provided by EMA

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. This was found not to be the case for a number of reasons.

- The reported costs were not based on the number of invoiced procedures or completed procedures provided to the study team, although they most closely matched invoiced procedures, except for activities where no invoices were raised. In this case they were based on completed procedures. In the model, invoiced procedures were used for fee generating activities and completed procedures for non-fee generating activities. It is not clear whether the different number of procedures underlying the reported costs would result in an over or underestimation of the calculated costs.
- Time data were not available for Certification of Advanced Therapies and costs were therefore not calculated. Costs were calculated for all other procedural activities for which procedures were reported.
- Costs for time spent in committees were allocated to the procedural activities in the EMA reported costs. The rationale for this approach is that most of the EMA staff time spent in committees is related to procedural activities as EMA will be involved in almost all of the activities discussed in the plenary sessions. In the model, this approach is replicated as far as possible. In the MBDG exercise, time spent on procedural activities was available for disaggregate activities and for scientific and administrative staff separately. This data is used in the activity based costing for EMA. Data for monthly time spent in committees was available for EMA staff in the MBDG exercise only as a combined total for scientific and administrative staff. This data is not used in the model. Instead a scaling factor is used to match the calculated activity costs to the reported costs. Separate scaling factors are used for scientific and administrative staff. This approach is roughly equivalent to allocating committee time to activities, proportionately across all activities. There will not be an exact match at the activity level. As the scaling approach effectively reallocates the residual costs (difference between the modelled and reported costs) to procedures, the committee time data reported in the MBDG survey was used to check the scaling. Multiplying the committee time by 11 (i.e. the number of meetings per year for most committee types), to obtain an annual value and by scientific staff costs provided an order of magnitude comparison for the residual time costs obtained from the model. This value is used as a maximum for the scaling so that potential omitted costs (noted above) are accounted for and the calculated EMA procedural costs are not over-estimated.
- There were some differences between costs presented in the EMA accounts for 2016 and the reported costs for 2016 provided by EMA for the modelling exercise. These amounted to approximately €4 million and were explained by the use of cash-accounting to determine the reported costs whereas the accounts are based on accruals.

5.3. NCA survey data

A number of specific checks were undertaken:

- NCAs were contacted if there were obvious discrepancies in the data they reported. In total, 13 email queries were sent to NCAs. Data from one NCA was excluded from the final modelling as the NCA did not report any EMA-related activities.
- Data on costs from Question 10 and on FTEs from Question 13 in the NCA survey were used to allocate overhead and other non-staff costs to scientific and administrative staff costs for EMA related activities. As the data requested in these questions was interpreted differently across the NCAs, the overhead rule calculations were adjusted to ensure the same rule was applied to all given the data provided.
- NCAs reported the numbers of rapporteur and co-rapporteur roles and other, unremunerated roles for procedural activities at the level of disaggregation agreed with EMA and HMA (Questions 17 and 18 of the NCA survey). The combined number of rapporteur and co-rapporteur roles reported by NCAs could be compared with purchase order information from EMA. A PO is provided for each rapporteur or co-rapporteur role (or equivalent, remunerated role) for each procedure of a given activity. However, this was only possible at a more aggregate level and it was not possible to verify the allocation of roles between rapporteurs and co-rapporteurs or to verify the number of rapporteur and co-rapporteur roles undertaken for paediatric and orphan activities that are not remunerated under the current fee system. Where an NCA indicated that it did not know how many procedures were undertaken for a given activity, PO data were used. The PO data were used to adjust the entries for individual NCAs at the aggregate level for Type II variations and inspections where these were found to be significantly different from the reported POs.
- The number of 'other' procedural roles that are unremunerated that were reported by NCAs in the survey could not be validated in this way as EMA does not issue POs for these.
- In the modelling exercise, NCA reported data was used so that the costs and activities they report can be assumed to be mutually consistent. The study team has subjected the NCA reported data to as much validation as possible. There are a number of ways in which the study team has tried to control for the fact that NCAs may not have the data available in the format requested in Questions 17 and 18 of the NCA survey or may have misinterpreted what was being asked.
  - NCAs enter too many 'other' roles for a given procedural-activity. The ratio of other roles to rapporteur + co-rapporteur roles was calculated from the total numbers reported across all NCAs for each activity. This ratio has a median value of 1 and an interquartile range of 0.33 to 1.62 (i.e. for 75 per cent of reported activities, the number of other roles is less than 1.62 times the number of rapporteur +co-rapporteur roles. This does not seem unreasonable because for some activities the rapporteur and co-rapporteur would be supported by a PRAC rapporteur and co-rapporteur and a peer reviewer. For only 5 activities out of 72 is the number of other roles greater than 3x rapporteur +co-rapporteur. These are for Type II variations and two full MA types. When checked against individual NCA inputs, these larger values are mainly driven by a few particular NCAs that reported large numbers of other roles. It seems likely that these few NCAs misinterpreted the information to be included in column 3 and these roles should not be considered 'other' roles for a procedure and should rather be counted as time spent in committees or as additional activities that are excluded from the 'other' procedural-activity costs. Over-reporting was addressed by setting a constraint in the model for other roles for a given activity not to exceed 3 x rapporteur +co-rapporteur. This cap was chosen because it is possible, although it may not be likely, that a procedure could have 1 rapporteur, a PRAC rapporteur and co-rapporteur, and a peer reviewer. Hence the limit is set to strike a balance between what NCAs have reported as what they realistically do and what could be reasonable.

This approach means that roles that should not be considered 'other' roles for a procedure and should rather be counted as time spent in committees or as additional activities are excluded from the 'other' procedural-activity costs. These costs are not lost from the model because additional costs are calculated as the difference between calculated costs and total reported costs.

- NCAs enter too few 'other' procedural roles. This is more difficult to identify because there is no other source to verify the 'other' reported roles against. The ratio of 'other' to rapporteur + co-rapporteur roles indicates that for 25 per cent of reported procedural activities there is less than one other role per procedure. Again this does not appear unreasonable as not all procedures necessarily require other roles. Where the number of other roles has been under-reported by an NCA these costs were not lost and appear in the costs of additional activities. This means that the additional activity costs may be inflated as they contain an element of procedural costs.

- Five NCAs reported data on roles at a more aggregate level than was requested in the survey for scientific advice, line extensions, Type II variations and paediatrics. A proportion of the NCA entry was allocated to the disaggregate categories (e.g. Type II levels I-III) for these five NCAs using the overall proportions of procedures invoiced by EMA for these activities (i.e. the approach is not NCA-specific). The same scaling approach is used for rapporteurs, co-rapporteurs and other entries. For veterinary activities, the same approach is used for scientific advice, line extensions and Type II variations as for human activities above. The overall number of procedural roles reported is not changed under this approach.
- Two NCAs reported aggregate data from MAs. For human marketing authorisations, purchase order data was available EMA for three categories of MA: full MA (new, known, fixed combination), biosimilar, and abridged/generics. The MAs within each category have the same fee but may take different amounts of time. Using the PO data therefore means that the correct number of procedural roles will be allocated to the correct fee level but may not be allocated to the correct time taken. The approach is to allocate the roles to the MA with the highest time taken within the fee group. This means the cost estimate represents an upper bound. This is considered the most appropriate approach given the lack of more detailed information.
- NCAs were able to report time spent on committee and Working Group activities or the cost of that time in the NCA survey (Q19). Time data for committees and Working Groups was also provided in the MBDG exercise. The MBDG data was used in the model because: a) it allowed a consistent approach to be applied to the calculation of this time for all NCAs that reported; and b) time spent on Working Groups could be distinguished from committee time. The data from the NCA survey was used as an order of magnitude check for the model, with the caveat that NCAs may have calculated the time spent differently. Of the NCAs that provided data in this category, 8 provided a description only, 7 provided travel costs and a further 9 provided costs, although it was not always clear that these were associated with time in committees and working groups and not travel. For 3 NCAs, there was a good fit with the reported data, the model underestimated for 2 NCAs and overestimated for the remaining 4.As with the procedural roles, any difference in the costs of Working Groups and committees that NCAs report and those calculated using the MBDG data are accounted for in the additional costs of EMA-related activities, which are determined as the residual between total NCA reported costs of EMA-related activities and the calculated model costs for procedural-activities and Working Groups and committees.

- NCAs reported additional EMA-related activities in the survey (Q20) in a variety of formats; these included costs, time taken, number of activities, or a list.[31]
- Total NCA income calculated using the revenue model with the existing fee and remuneration rules was compared with the total NCA remuneration reported by EMA. This is an order of magnitude comparison as the number of procedures used in the model calculations was taken from the NCA survey, with the exception of those NCAs for which PO data were used for some procedural activities as described above, while the NCA remuneration reported by EMA was based on the number of POs issued. The EMA data is also based on remuneration for 46 NCAs and not the 29 included in the model. The comparison indicated that the model implementation of the current fee rules resulted in NCA remuneration of the right order of magnitude.

31 Additional details of the activities can be provided on request in a separate Excel file.

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Regulation (EU) No 658/2014 of the European Parliament and of the Council of 15 May 2014 on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use (OJ L 189, 27.6.2014). As of 1 November 2017: https://ec.europa.eu/health//sites/health/files/files/eudralex/vol-1/reg_2014_658/reg_2014_658_en.pdf

7. APPENDICES

Appendix 1. Summary of validation of data from MBDG exercise

Tabulation of outliers by activity

For the purposes of this exercise, a data point is considered to be an outlier if it is more than two standard deviations from the mean, where the mean is calculated from all procedures undertaken for a given activity. For each activity a first summary table of procedures was produced. This contains information on the sample size, mean time taken for EMA and NCAs (averaged) by staff type and number of outliers. A second summary table provides details on the outliers, including information on related types of procedure, roles, and NCAs. The samples sizes for different activities reflect the volume of activities undertaken during the MBDG exercise and are much smaller for veterinary medicines than for human medicines.

For Initial Marketing Authorisation, most of the outliers (30 out of 34) were recorded in the New Active Substance procedures, but this is also the activity with the largest sample. Outliers are quite widespread across NCAs and do not appear to be associated with any particular organisation. Similarly, outliers are also evenly spread across roles. In very few cases, outliers were recorded for the same procedure for more than one role, which is most likely to signal that the procedure was particularly complex.

Similar considerations apply to the other activities. Line extensions are the activity with the highest number of outliers recorded (as a percentage of the sample), while Type IB variations and orphan designations are the activities with the smallest number of outliers (as a percentage of the sample). When both the Committee for Medicinal Products for Human Use (CHMP) and Pharmacovigilance Risk Assessment Committee (PRAC) are involved (as in the case of Type II variations) the large majority of outliers are recorded in the CHMP. Lastly, outliers were very rarely recorded for both the scientific staff for a role and the administrative staff providing support for the same role (e.g. for the scientific and administrative time reported for the rapporteur role for a procedure); thus it appears that the complexity of a procedure is unlikely to affect simultaneously the time spent by administrative and scientific staff.

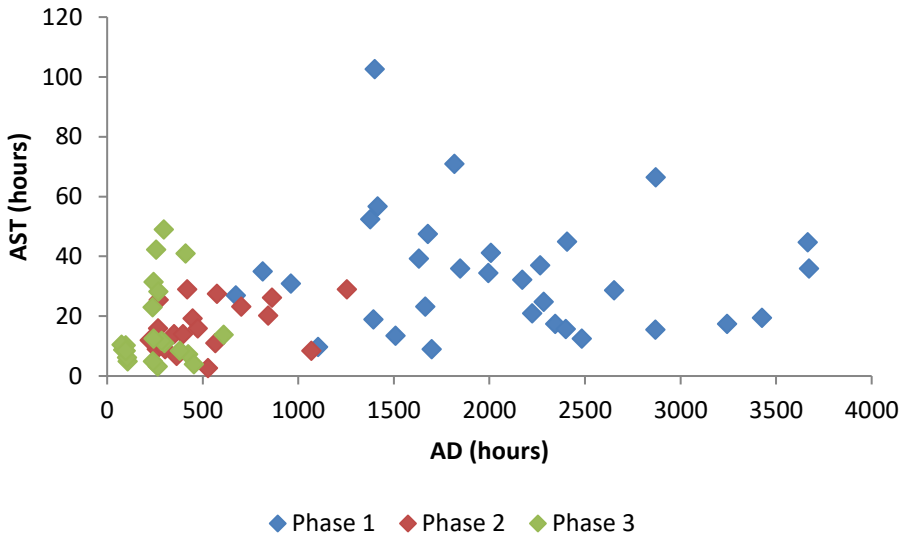
Comparison of the allocation of time spent on activities by scientific and administrative staff

Where there is sufficient data, scatter plots were produced to compare the allocation of time spent on activities by scientific and administrative staff. First, the time spent by scientific and administrative staff was calculated using all NCA data for the given activity. Second and where possible, the time spent was calculated using averages for each NCA and the EMA. These plots show the range of reported time taken to undertake procedures by NCA staff, the sample size and whether there is a consistent relationship between scientific and administrative time. The plots with data aggregated by NCA are generated with and without outliers.

The plots for the Initial Marketing Authorisations (human medicines) (Appendix 2) show that in each of the three phases there is a wide variation in the time declared by NCA: while some procedures took a few hundred hours, other procedures took thousands of hours. On average, phase 1 took longer than phase 2, which in turn took longer than phase 3. Administrative time and scientific time appear to be positively correlated in all three phases of the Initial Marketing Authorisations: as administrative time increases, scientific time increases as well. For biosimilars, generics, and new active substances, there were enough data to provide specific plots. The trends are similar to those observed for all procedures, notably the range of data is broad, and administrative time increases with scientific time. Although the data show wide variation across the NCAs,

the mean trend line shows that there is a consistent relationship between scientific and administrative time spent across NCAs. This relationship holds when the plots are generated both with and without outliers. The relationship is less consistent when looking at the Initial Marketing Authorisation for veterinary procedures: although the mean trend line still has a positive slope, it is evidently flatter than for human procedures. The hours spent for all phases of Initial Marketing Authorisations for new active substances for human medicinal products are presented in Figure-4.

Figure-4: Total time spent (hours) by NCAs – all new active substance procedures for human medicinal products



For scientific advice procedures, the mean trend lines indicate a positive relationship between the time spent by NCA scientific and administrative staff. This relationship holds for the different levels of scientific advice, and for initial and follow-up procedures. When the data were aggregated by NCA the positive relationship also appeared, especially when the outlier values were removed. Similar considerations hold for line extensions, good manufacturing practice (GMP) and good clinical practice (GCP) inspections, although the data samples are small.

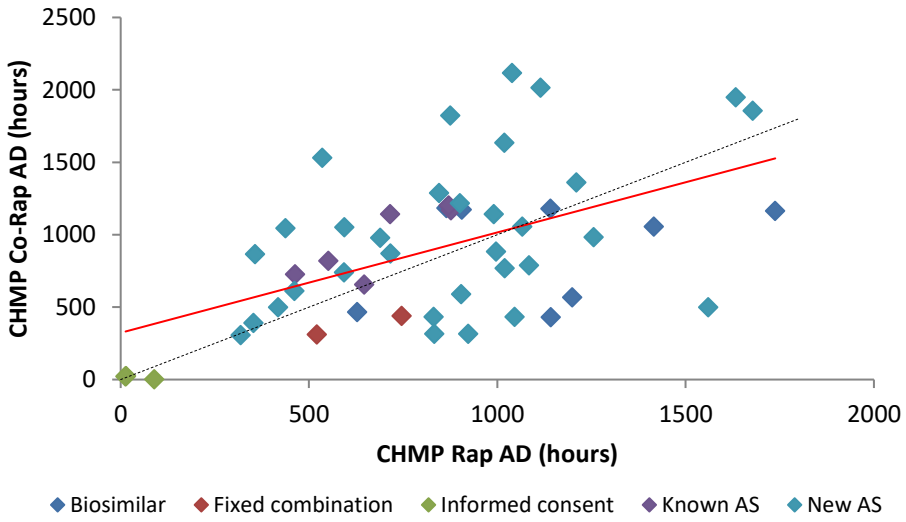
Type II variations for applications in the categories 'clinical', 'clinical safety', and 'quality', and Type IB variations, show wide variation in the time declared by NCAs and there is no clear relationship between the time spent by scientific and administrative staff. For renewals applications, the time declared by the NCAs does not suggest any consistent relationship between the time spent by scientific and administrative staff: when data from all of the procedures are plotted, the slope of the mean trend line is slightly negative; when the procedures are aggregated by NCA and the averages for each NCA is calculated the slope of the mean trend line is slightly positive.

With regards to paediatrics procedures and orphan designation procedures, although the slope of the mean trend line suggests a positive relationship between the time spent by NCA scientific and administrative staff for most of the paediatrics procedures, there is wide variation across the data (see Appendices 7 and 8). Notably, for many procedures the reported time spent by administrative staff was zero.

Comparison of the time spent on rapporteur and co-rapporteur roles across organisations and activities.

Where there is sufficient data, scatter plots were produced to compare the time spent on rapporteur and co-rapporteur roles across organisations and activities. For Initial Marketing Authorisations, the plots compare the rapporteur and the co-rapporteur role using all of the available data in each of the three phases. For phase 1, the (red) mean trend line shows that there is a consistent relationship between rapporteur and co-rapporteur in phase 1, and the 45 degree (broken) line shows that rapporteur and co-rapporteur time is approximately equal. For phase 2 and 3, the relationship between the two roles is not consistent; this result is driven by a few Initial Marketing Authorisations for new active substances which involved many hours of rapporteur time and few hours of co-rapporteur time. The scatter plots also compare the allocation of time spent on Initial Marketing Authorisations by rapporteur and co-rapporteur roles for scientific staff with averages for each NCA. Again, the relationship between rapporteur and co-rapporteur is consistent only in phase 1. This is illustrated in Figure-5.

Figure-5: Time spent (hours) as CHMP Rapporteur and Co-rapporteur - All Initial Marketing Authorisation procedures phase 1



For line extensions, the data show a wide variation in the distribution of time between rapporteur and co-rapporteur (Appendix 3). In particular, the time spent by the rapporteur varies widely, while for the majority of the procedures the time spent by the co-rapporteur is similar. For renewals procedures (Appendix 6), the positive slope of the mean trend line appears to suggest a positive relationship between the two roles.

A further check on the time data for NCAs is provided by comparison with the pilot cost exercise undertaken in 2008-2009.[32] The study team's understanding of this exercise is that:

[32] The three sources used are EMEA/MB/780575/2009 Costing Group – Outcome of the pilot exercise, NCA hours and costs from 2009 exercise and Costing Method for 2009 exercise.

- Time data were reported by NCAs for rapporteurs only for eight aggregate activities, of which only six correspond to activities used in the current study.
- In the 2008-2009 cost exercise, total time reported was divided by the number of procedures reported to obtain an average time spent per procedure. This is a different approach to the MBDG exercise in which time was recorded for each reported procedure.
- Although 18 NCAs took part in the 2008-2009 exercise, it is not possible to compare data for individual NCAs in 2008-2009 and in the MBDG exercise because the NCAs are anonymised.
- It was not clear whether time data reported in the 2008-2009 exercise was for scientific staff only. It is assumed that this is the case because administrative staff costs are included as overhead costs. From the notes under the figure on p12 of *Costing Group – Outcome of the pilot exercise*, it appears that only rapporteur time has been recorded. Hence scientific rapporteur data from the MBDG exercise was used in the comparison.

The comparison is therefore limited to average times taken by rapporteurs for six aggregate activities common to both studies, noting that the averages for the 2008-2009 exercises contain data for both human and veterinary medicines combined. These are presented in Table-6.

Table-6: Comparison of hours per procedure reported in 2008 cost exercise and MBDG exercise

Activity	2008-2009 cost exercise (mean)	MBDG (AD average) – rapporteur human medicines[1]
Full application	435	880
Line Extension	278	113
Type II Variation	64	39
Renewal	116	25
Scientific Advice	42	49
Consultation procedure	100	Not known[2]

1 Data were reported at a more disaggregate activity level in the MBDG exercise. Simple (unweighted) averages across the disaggregate activities have been used to determine the averages presented here.

2 Activities were categorized differently in the 2008-2009 exercise compared with the MBDG exercise and it was not clear how Consultation procedures related to the activities covered in the MBDG exercise.

There are differences in the reported time spent on a procedure for the different aggregate activities in 2008-2009 and the MBDG exercise. 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.

Appendix 2. Data validation – Human medicines activities – Initial marketing authorisations

Table-7: Summary table for initial marketing authorisations, average time spent (hours) by the EMA and NCAs – MBDG 2016 Report

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers[33]
Biosimilar P1	Jan'16 -Sep'16	8	112.84	47.84	8	2158.45	42.38	
Biosimilar P2	Jan'16 -Sep'16	6	61.25	7.14	5	433.88	16.35	
Biosimilar P3	Jan'16 -Sep'16	8	101.42	43.91	5	211.10	8.60	
Total Biosimilars	Jan'16 -Sep'16	22	275.51	98.89	18	2803.43	67.33	
New AS P1	Jan'16 -Sep'16	37	164.55	57.54	32	2061.24	33.85	13
New AS P2	Jan'16 -Sep'16	31	87.84	27.14	23	519.28	19.87	7
New AS P3	Jan'16 -Sep'16	28	168.04	25.16	21	260.67	16.25	10
Total New AS	Jan'16 -Sep'16	96	420.43	109.83	76	2841.20	69.98	
Generic P1	Jan'16 -Sep'16	16	73.71	34.60	13	285.12	16.04	1
Generic P2	Jan'16 -Sep'16	15	53.21	22.22	9	112.11	9.61	1
Generic P3	Jan'16 -Sep'16	12	62.48	31.53	8	78.00	6.31	1
Total generics	Jan'16 -Sep'16	43	189.40	88.34	30	475.23	31.96	
Known AS P1	Jan'16 -Sep'16	6	168.15	54.79	6	1788.35	54.75	1
Known AS P2	Jan'16 -Sep'16	1	100.25	5.50	0[34]	519.28	19.87	
Known AS P3	Jan'16 -Sep'16	6	144.96	26.58	2	141.25	30.38	
Total Known AS	Jan'16 -Sep'16	13	413.36	86.88	8	2448.88	104.99	
Fixed combin.P1	Jan'16 -Sep'16	3	135.25	40.67	2	1101.88	25.08	
Fixed combin.P2	Jan'16 -Sep'16	2	73.88	7.13	1	210.50	7.75	
Fixed combin.P3	Jan'16 -Sep'16	2	179.46	31.88	2	172.75	20.88	
Total Fixed Combination	Jan'16 -Sep'16	7	388.59	79.67	5	1485.13	53.70	
HybridP1	Jan'16 -Sep'16	3	103.83	28.14	1	1028.50	40.75	
HybridP2	Jan'16 -Sep'16	6	90.14	13.71	5	246.95	14.30	
HybridP3	Jan'16 -Sep'16	4	122.54	9.69	1	69.25	5.00	
Total Hybrid	Jan'16 -Sep'16	13	316.51	51.54	7	1344.70	60.05	
Well-established use P1	Jan'16 -Sep'16	2	155.93	45.38	0[35]	1788.35	54.75	
Well-established use P2	Jan'16 -Sep'16	1	116.66	8.00	0[36]	519.28	19.87	
Well-established use P3	Jan'16 -Sep'16	2	392.88	27.75	1	255.50	1.50	
Total Well-established use	Jan'16 -Sep'16	5	665.46	81.13	1	2563.13	76.12	
Informed consent P1	Jan'16 -Sep'16	4	29.75	27.32	3	55.83	6.42	

[33] Outliers are defined as being more than two standard deviations from the mean.

[34] Due to missing data from the NCA side, the MBDG report used data extrapolated from phase II New Active Substance.

[35] Due to missing NCA data, the MBDG report used data extrapolated from phase I Known Active Substance.

[36] Due to missing data from the NCA side, the MBDG report used data extrapolated from phase II New Active Substance.

Table-8: Table of outliers

Type	Procedure number	CHMP Rap AD	CHMP Rap AST	CHMP Co-Rap AD	CHMP Co-Rap AST	CHMP Peer Review AD	CHMP Peer Review AST	PRAC Rap AD	PRAC Rap AST	PRAC Co-Rap AD	PRAC Co-Rap AST
Generic	EMEA/H/C/000000/0001	692.00	20.00								
Known AS	EMEA/H/C/000000/0001										
New AS	EMEA/H/C/000000/0002									304.75	0.50
New AS	EMEA/H/C/000000/0003					177.50	17.00				
New AS	EMEA/H/C/000000/0004					222.75	6.00				
New AS	EMEA/H/C/000000/0005							212.00	1.00		
New AS	EMEA/H/C/000000/0006	832.50	49.00	316.00	9.50	85.25	25.20				
New AS	EMEA/H/C/000000/0007			1634.00	48.50					66.50	9.00
New AS	EMEA/H/C/000000/0008	1633.00	7.00								
New AS	EMEA/H/C/000000/0009	1678.00	35.00								
New AS	EMEA/H/C/000000/0010							112.00	24.00		
New AS	EMEA/H/C/000000/0011			1050.00	50.00						
New AS	EMEA/H/C/000000/0012							219.00	0.00		
New AS	EMEA/H/C/000000/0013	1056.50	55.00								
New AS	EMEA/H/C/000000/0014			2115.00	13.00						
New AS	EMEA/H/C/000000/0015							180.00	32.00		
Generic	EMEA/H/C/000000/0016	210	18								
New AS	EMEA/H/C/000000/0017	428.25	82.50								
New AS	EMEA/H/C/000000/0018	845.00	0.50								
New AS	EMEA/H/C/000000/0019					138.00	3.50				
New AS	EMEA/H/C/000000/0020			295.00	12.00						
New AS	EMEA/H/C/000000/0021									67.00	0.50
New AS	EMEA/H/C/000000/0022			498.00	7.00			188.50	6.00		
New AS	EMEA/H/C/000000/0023							82.00	24.00		

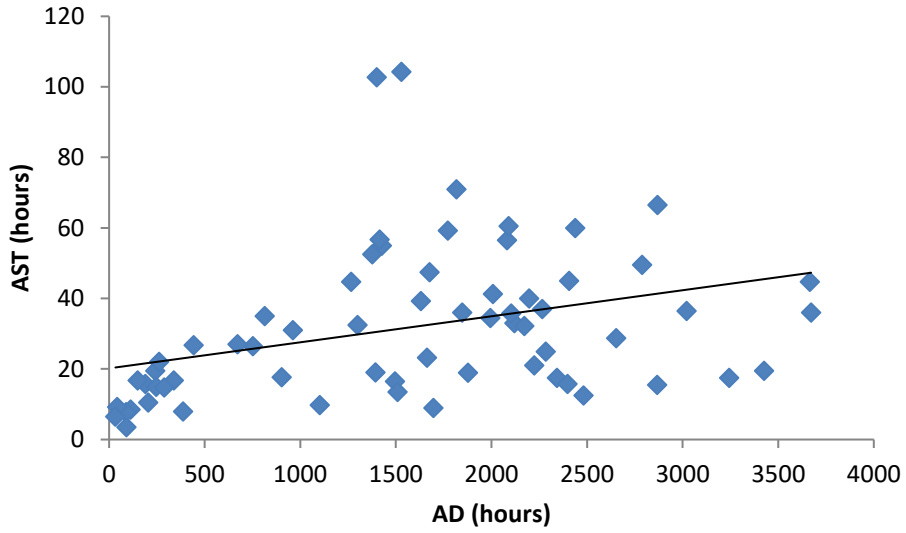
Type	Procedure number	CHMP Rap AD	CHMP Rap AST	CHMP Co-Rap AD	CHMP Co-Rap AST	CHMP Peer Review AD	CHMP Peer Review AST	PRAC Rap AD	PRAC Rap AST	PRAC Co-Rap AD	PRAC Co-Rap AST
Generic	EMEA/H/C/000000/0024	200.00	9.00								
New AS	EMEA/H/C/000000/0025	525	6.15								
New AS	EMEA/H/C/000000/0026							116.00	2.50		
New AS	EMEA/H/C/000000/0027					159.00	1.75				
New AS	EMEA/H/C/000000/0028					128.00	22.00	3.00	15.00		
New AS	EMEA/H/C/000000/0029	332.25	33.00								
New AS	EMEA/H/C/000000/0030									48.00	2.00
New AS	EMEA/H/C/000000/0031	198.50	28.50								
New AS	EMEA/H/C/000000/0032			194.25	6.00			136.00	3.50		
New AS	EMEA/H/C/000000/0033									44.50	0.50
New AS	EMEA/H/C/000000/0034			125.50	19.25						

Notes: AS = active substance.

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

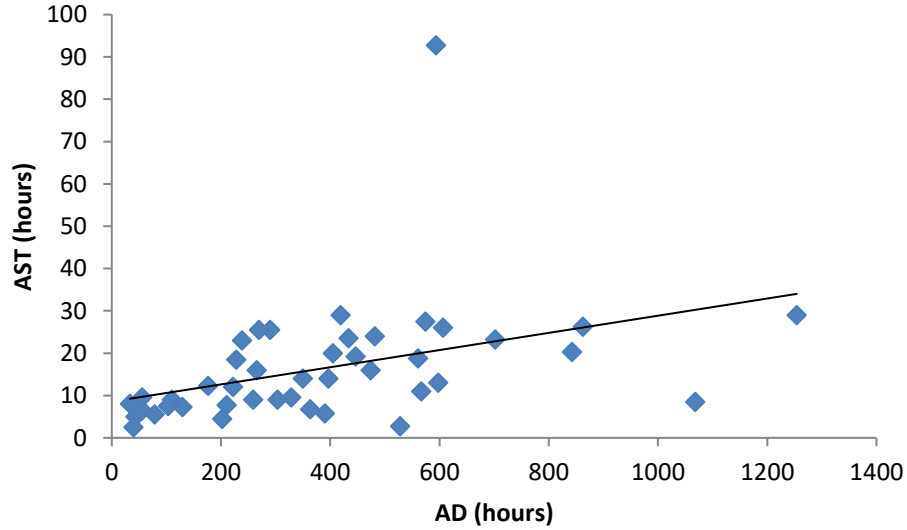
Initial marketing authorisations: scientific staff (AD) and administrative staff (AST)

Figure-6: Total time spent (hours) by NCAs - all procedures in phase 1



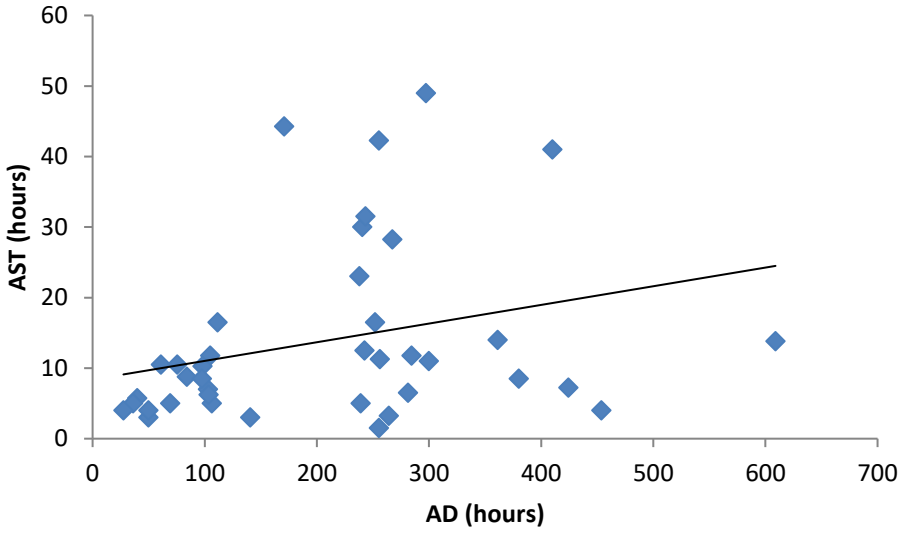
Note: Each point in the figure represents an individual procedure

Figure-7: Total time spent (hours) by NCAs - all procedures in phase 2



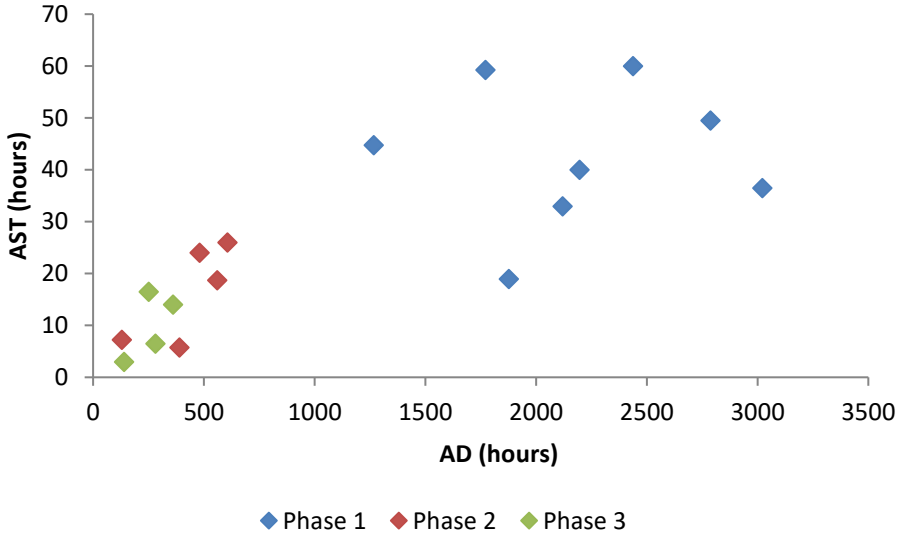
Note: Each point in the figure represents an individual procedure

Figure-8: Total time spent (hours) by NCAs - all procedures in phase 3



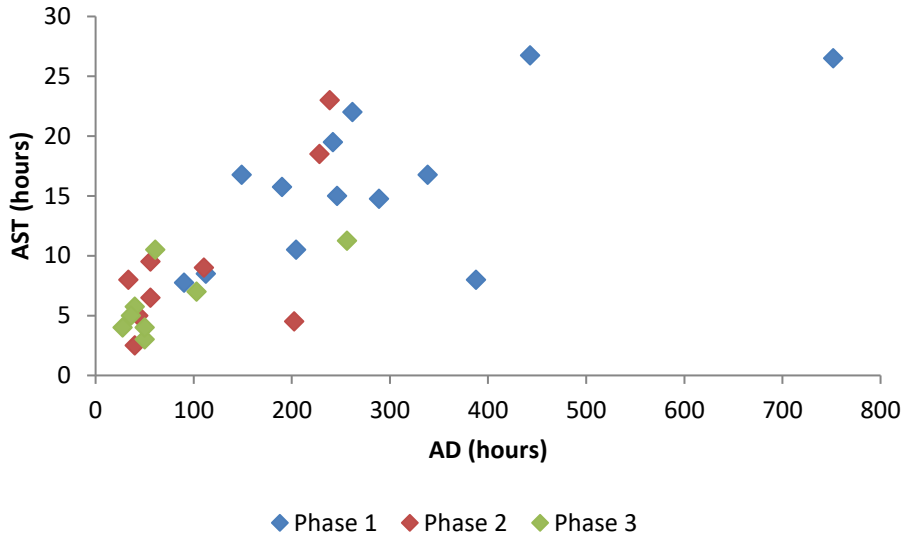
Note: Each point in the figure represents an individual procedure

Figure-9: Total time spent (hours) by NCAs – all biosimilar procedures



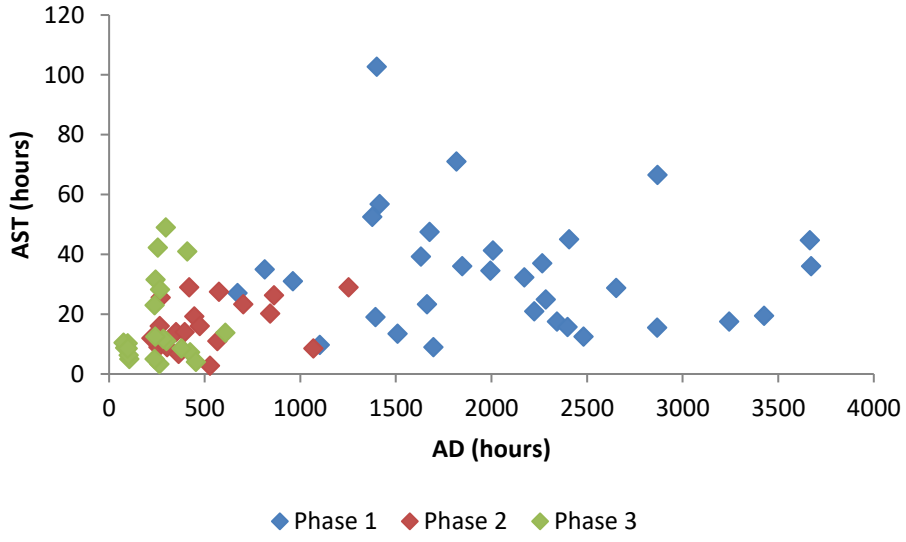
Note: Each point in the figure represents an individual procedure

Figure-10: Total time spent (hours) by NCAs – all generic procedures



Note: Each point in the figure represents an individual procedure

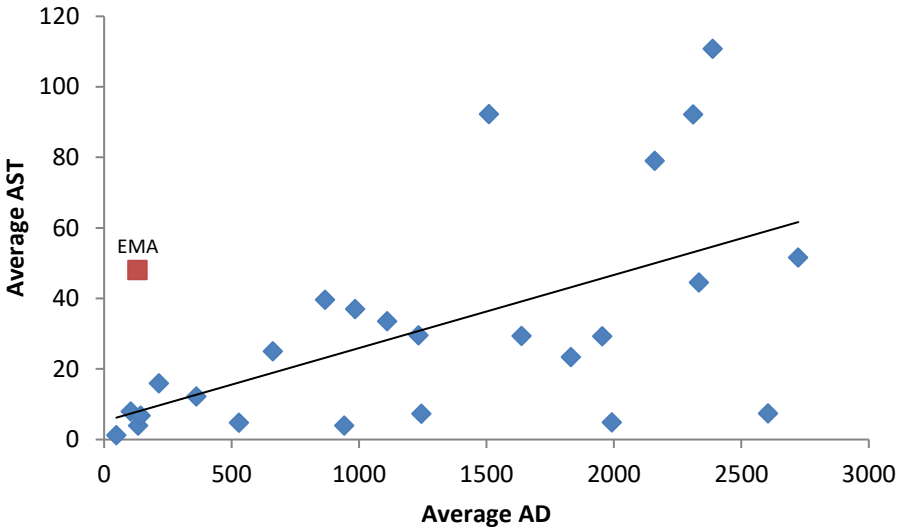
Figure-11: Total time spent (hours) by NCAs – all new active substance procedures



Note: Each point in the figure represents an individual procedure

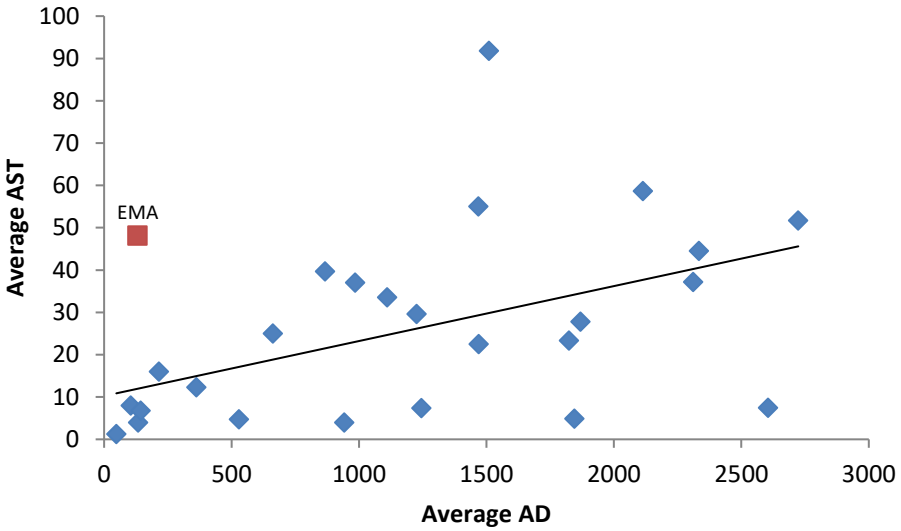
Initial marketing authorisations: NCAs scientific staff (AD) and administrative staff (AST)

Figure-12: Average[37] time spent (hours) for each NCA and EMA - All procedures phase 1



Note: Each point in the figure represents an individual NCA

Figure-13: Adjusted[38] average time spent (hours) for each NCA and EMA - All procedures phase 1

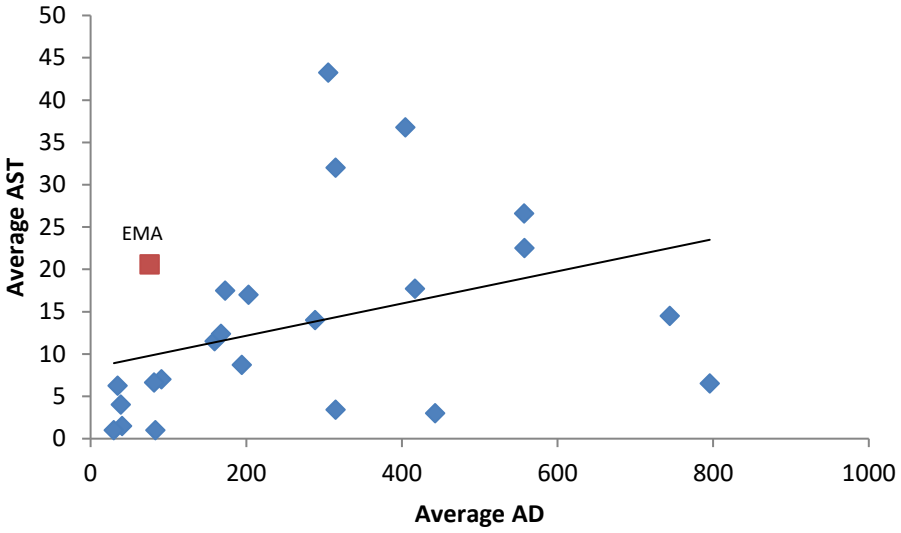


Note: Each point in the figure represents an individual NCA

[37] Average NCA1 = Average of CHMP Rap + Average of CHMP Co-Rap + Average of CHMP Peer Reviewer + Average of PRAC Rap + Average of PRAC Co-Rap

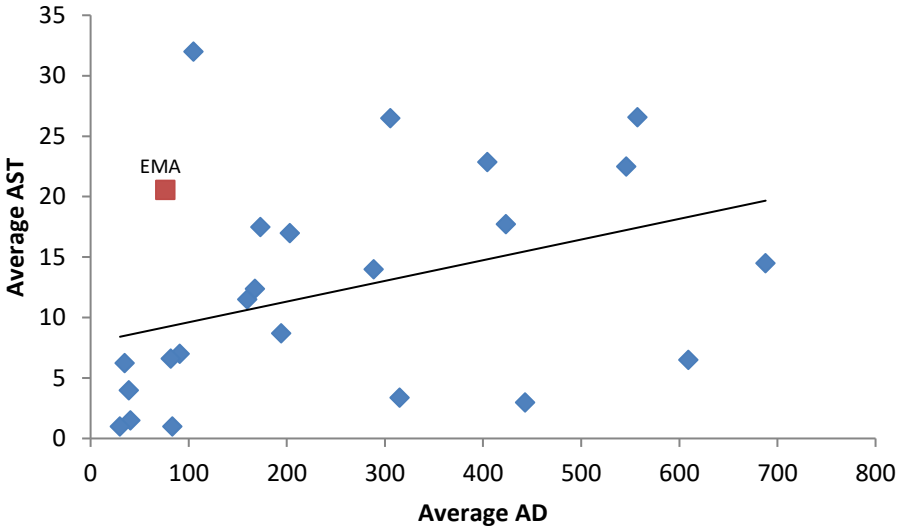
[38] Outliers excluded; outliers are defined as being more than 2 standard deviations from the mean.

Figure-14: Average time spent (hours) for each NCA and EMA - All procedures phase 2



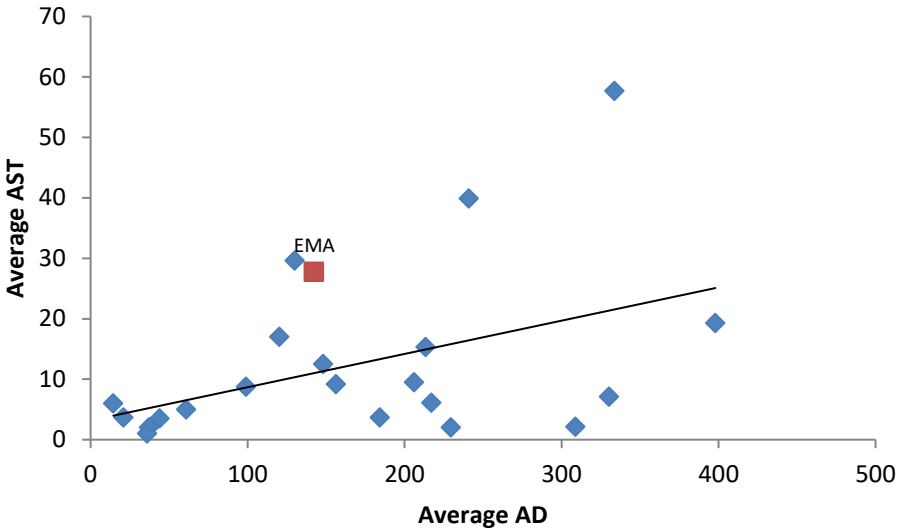
Note: Each point in the figure represents an individual NCA

Figure-15: Adjusted average time spent (hours) for each NCA and EMA - All procedures phase 2



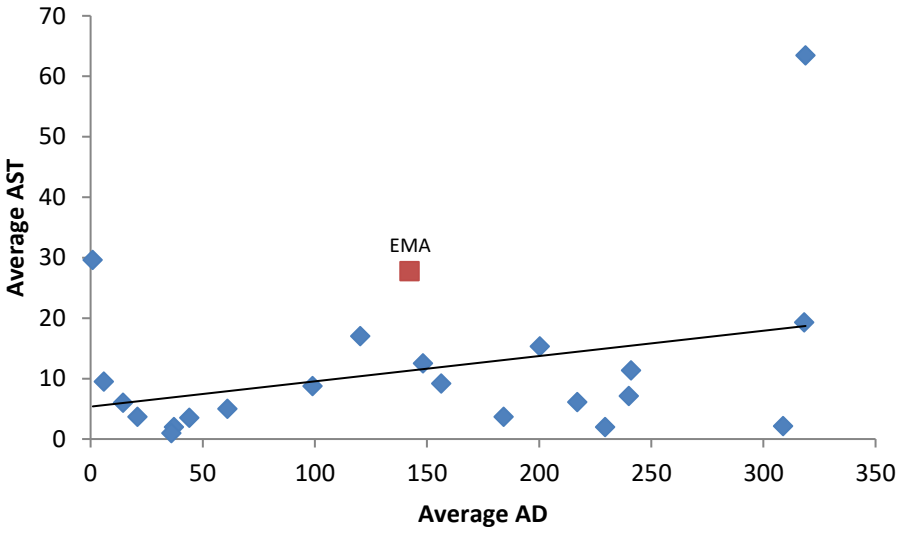
Note: Each point in the figure represents an individual NCA

Figure-16: Average time spent (hours) for each NCA and EMA - All procedures phase 3



Note: Each point in the figure represents an individual NCA

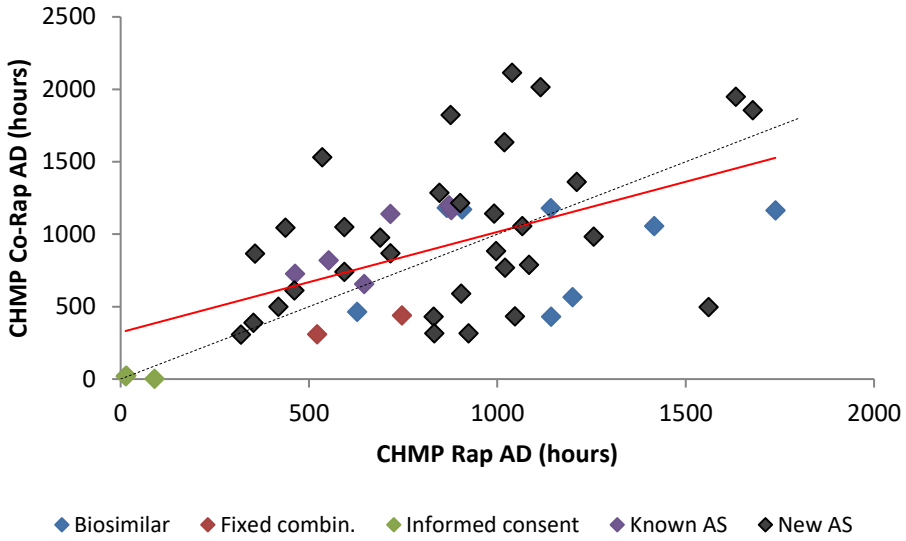
Figure-17: Adjusted average time spent (hours) for each NCA and EMA - All procedures phase 3



Note: Each point in the figure represents an individual NCA

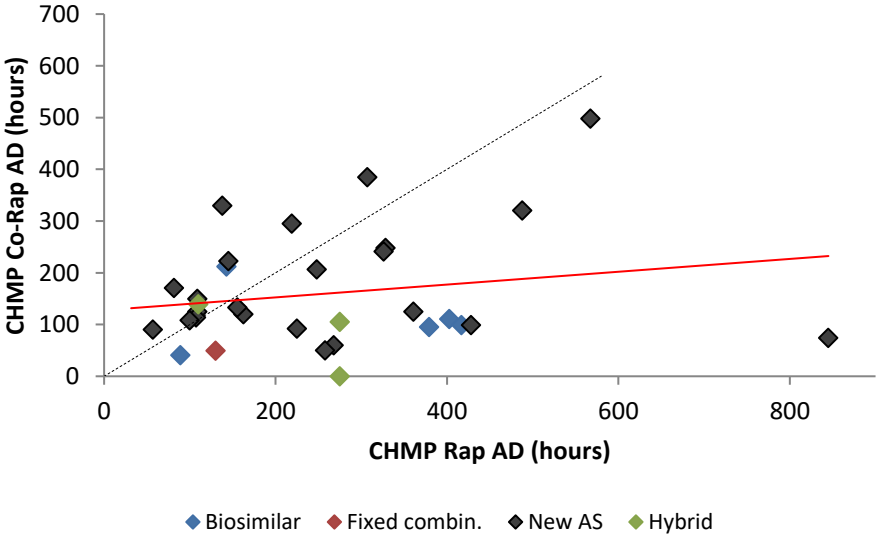
Initial marketing authorisations: Rap and Co-Rap

Figure-18: Time spent (hours) by CHMP Rap and Co-Rap - All procedures phase 1



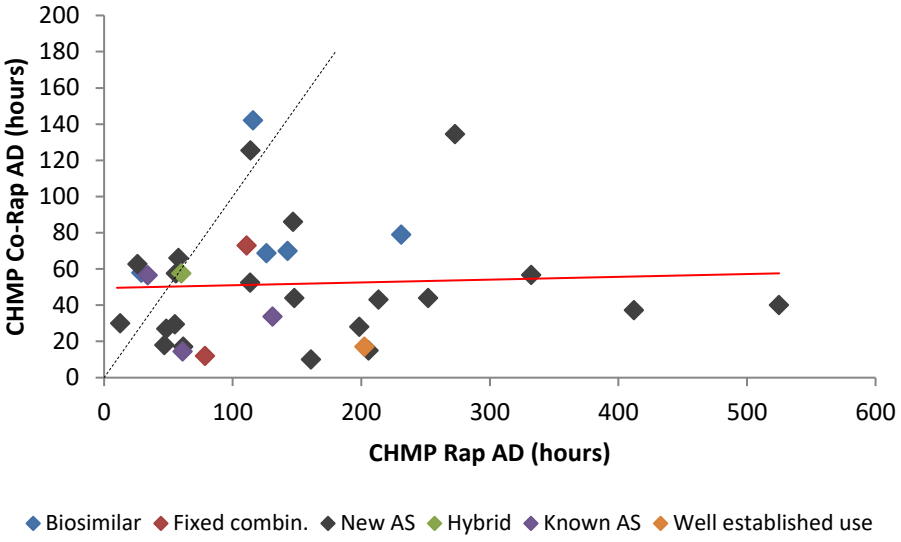
Note: Each point in the figure represents an individual procedure. The red line is the linear trendline. The dotted line is a 45 degree line.

Figure-19: Time spent (hours) by CHMP Rap and Co-Rap - All procedures phase 2



Note: Each point in the figure represents an individual procedure. The red line is the linear trendline. The dotted line is a 45 degree line.

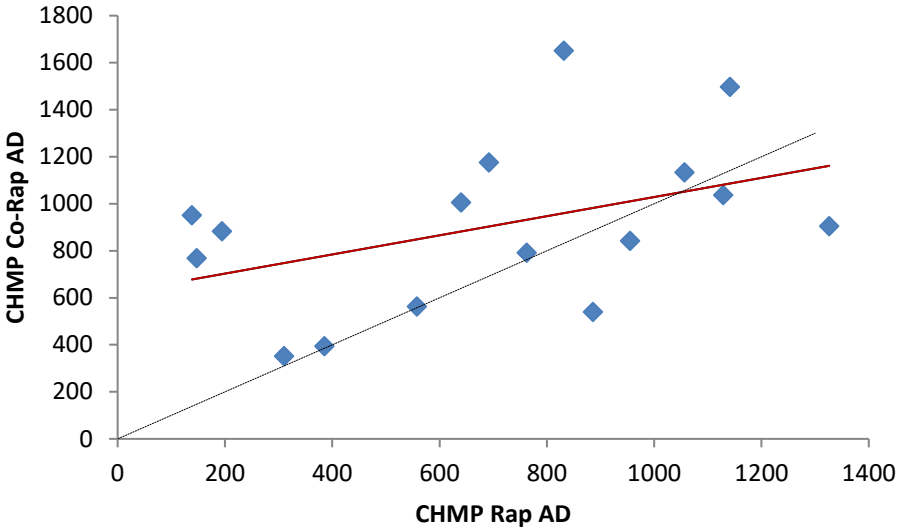
Figure-20: Time spent (hours) by CHMP Rap and Co-rap - All procedures phase 3



Note: Each point in the figure represents an individual procedure. The red line is the linear trendline. The dotted line is a 45 degree line.

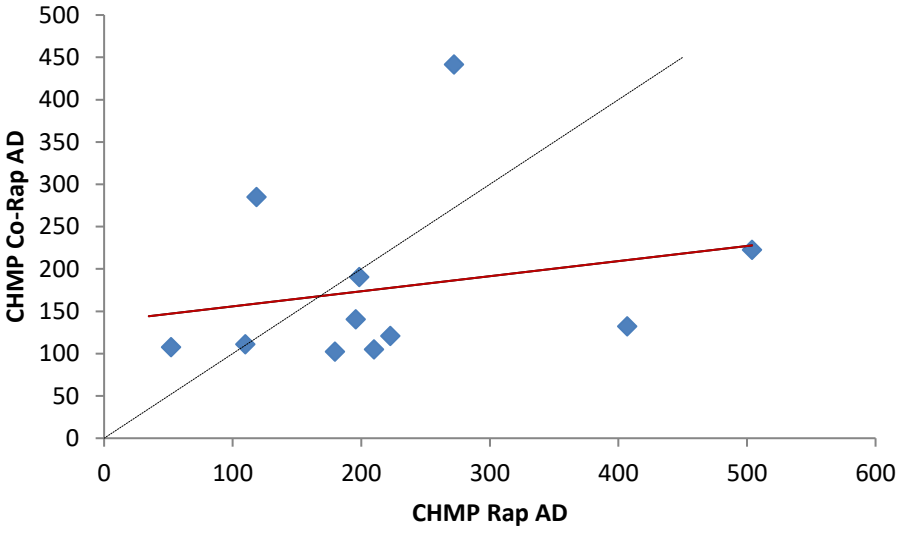
Initial marketing authorisations: Rap and Co-Rap per NCAs

Figure-21: Average time spent (hours) for each NCA as CHMP Rap and Co-Rap - All procedures phase 1



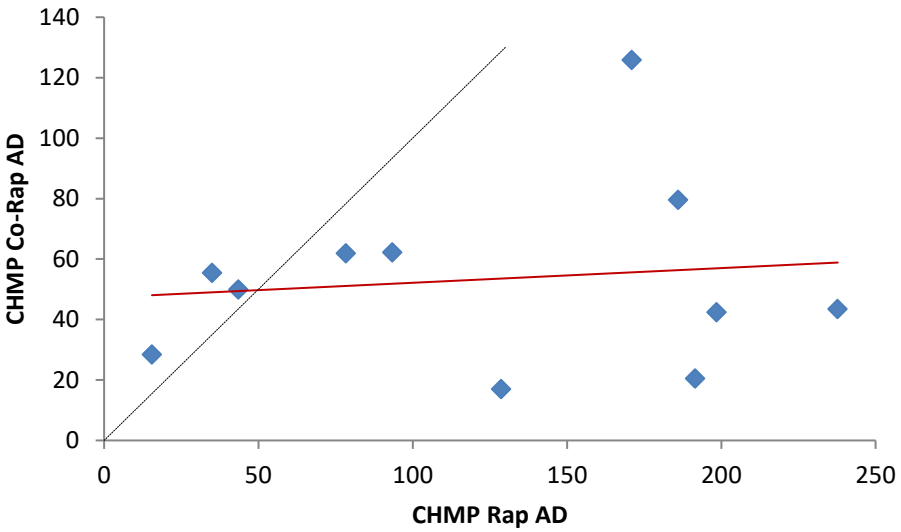
Note: Each point in the figure represents an individual NCA. The red line is the linear trendline. The dotted line is a 45 degree line.

Figure-22: Average time spent (hours) for each NCA as CHMP Rap and Co-Rap - All procedures phase 2



Note: Each point in the figure represents an individual NCA. The red line is the linear trendline. The dotted line is a 45 degree line.

Figure-23: Average time spent (hours) for each NCA as CHMP Rap and Co-Rap - All procedures phase 3



Note: Each point in the figure represents an individual NCA. The red line is the linear trendline. The dotted line is a 45 degree line.

Appendix 3. Data validation – Human medicines activities – Line extensions

Table-9: Summary table for line extension - MBDG 2016 Report

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
Line extension Phase 1	Jan'16 - Sep'16	17	54.21	31.02	11	425.95	12.36	5
Line extension Phase 2	Jan'16 - Sep'16	10	74.00	22.36	5	190.60	11.96	2
Line extension Phase 3	Jan'16 - Sep'16	6	44.54	12.56	4	89.81	7.81	1

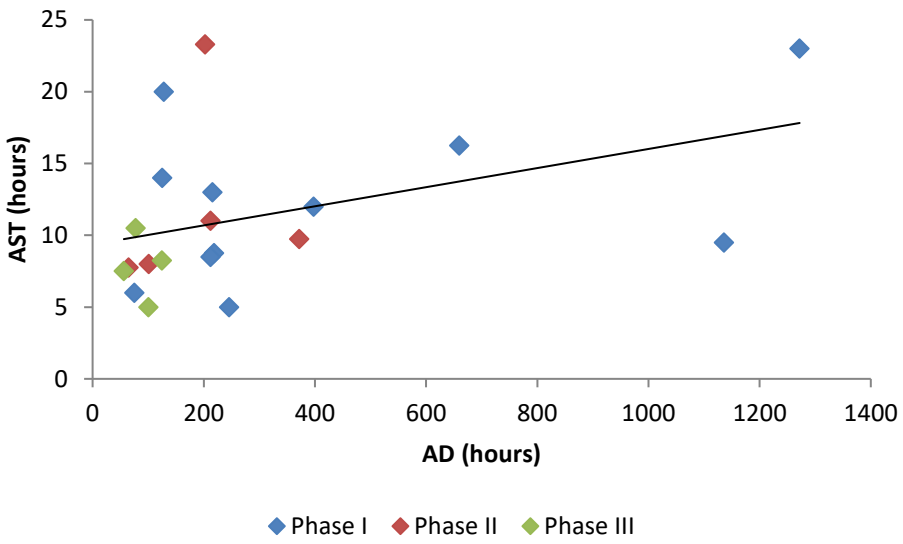
Table-10: Table-of outliers

	CHMP Rap		CHMP Co-Rap		PRAC Rap		PRAC Co-Rap	
Proc number	AD	AST	AD	AST	AD	AST	AD	AST
EMEA/H/C/000000/X/0001			851.75	15.00			33.00	0.00
EMEA/H/C/000000/X/0002			765.50	9.50	91.25	0.00		
EMEA/H/C/000000/X/0003	153.25	16.80						
EMEA/H/C/000000/X/0004	364.00	2.00						
EMEA/H/C/000000/X/0005					41.00	3.50		

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

Line extensions: scientific staff (AD) and administrative staff (AST)

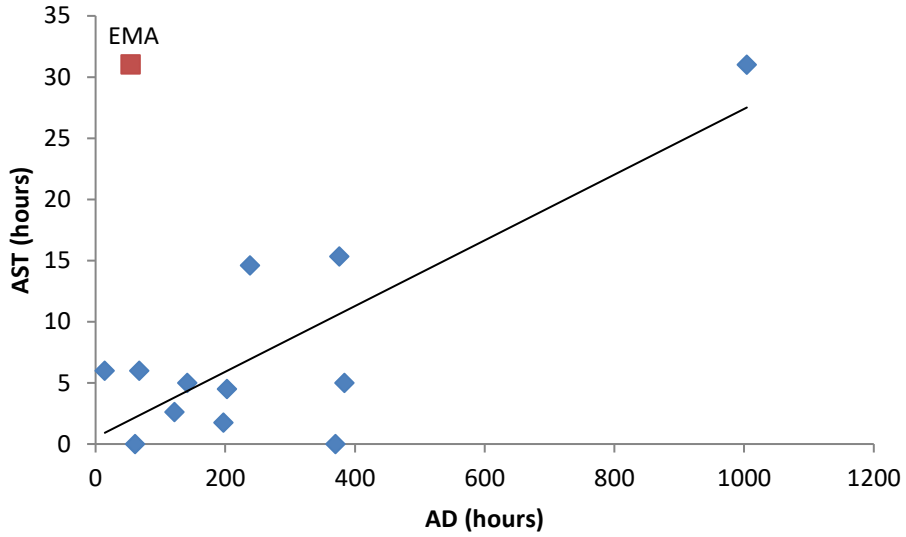
Figure-24: Total time spent (hours) by NCAs - all procedures



Note: Each point in the figure represents an individual procedure

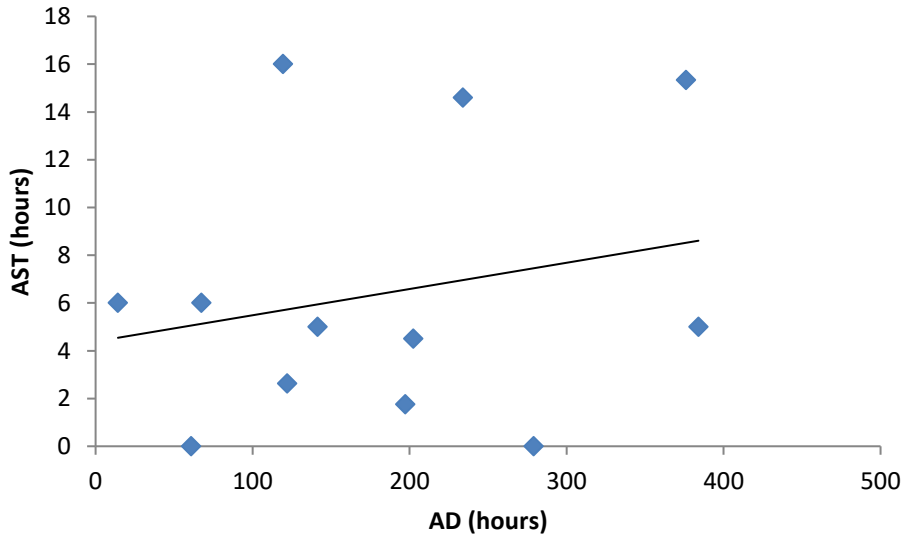
Line extensions: NCAs scientific staff (AD) and administrative staff (AST)

Figure-25: Average time spent (hours) for each NCA and EMA - All procedures phase I



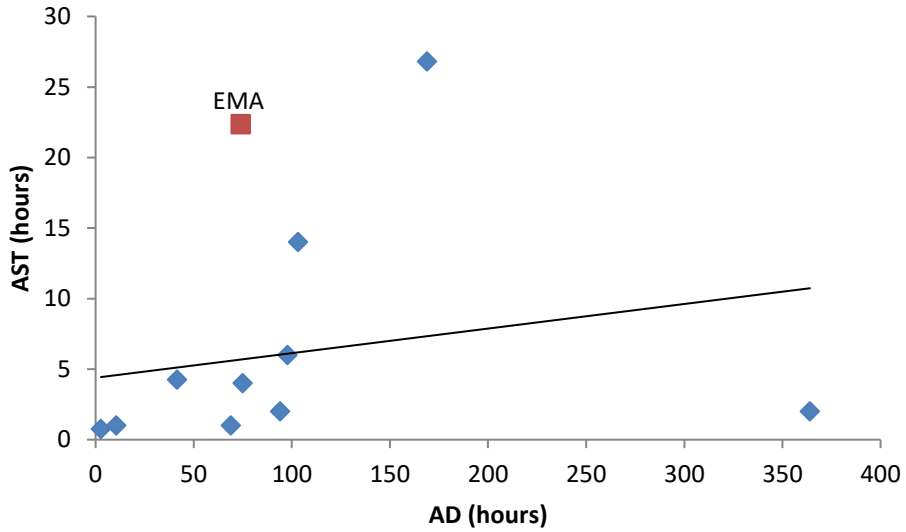
Note: Each point in the figure represents an individual NCA

Figure-26: Adjusted average time spent (hours) for each NCA - All procedures phase I



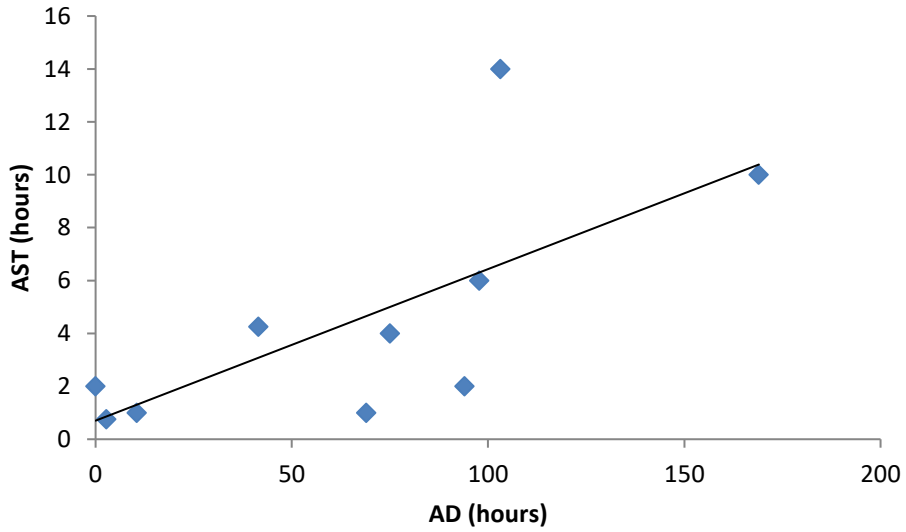
Note: Each point in the figure represents an individual NCA

Figure-27: Average time spent (hours) for each NCA and EMA - All procedures phase II



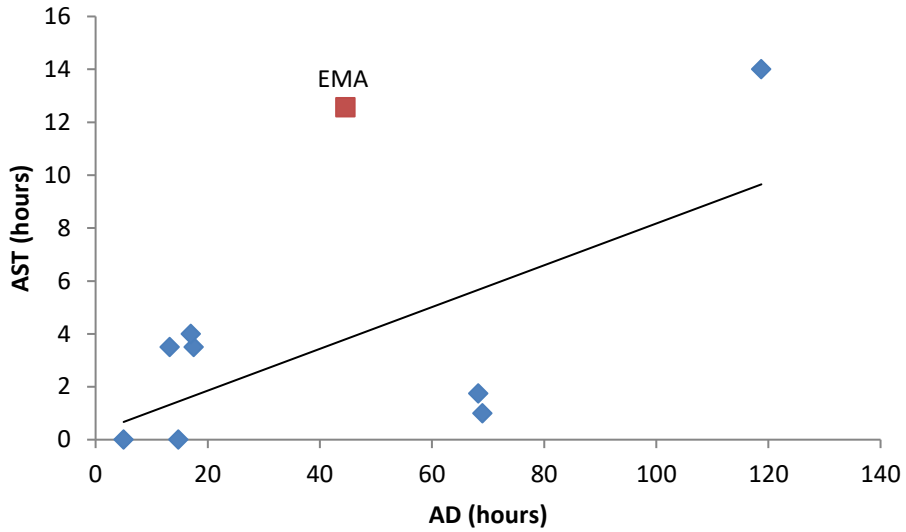
Note: Each point in the figure represents an individual NCA

Figure-28: Adjusted average time spent (hours) for each NCA - All procedures phase II



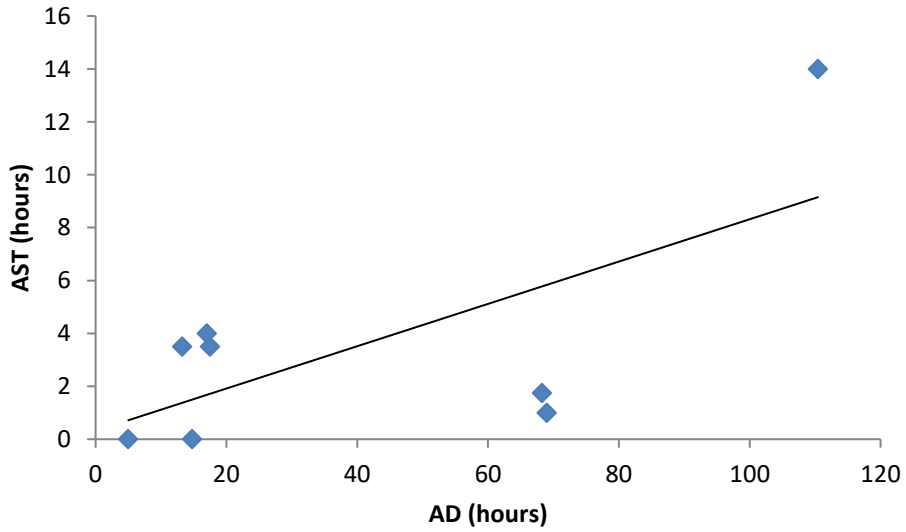
Note: Each point in the figure represents an individual NCA

Figure-29: Average time spent (hours) for each NCA and EMA - All procedures phase III



Note: Each point in the figure represents an individual NCA

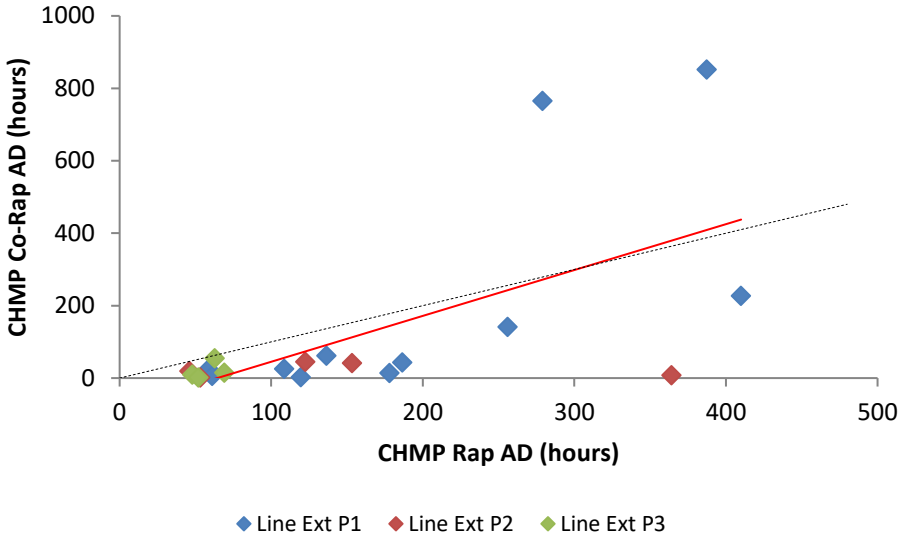
Figure-30: Adjusted average time spent (hours) for each NCA - All procedures phase I



Note: Each point in the figure represents an individual NCA

Line Extensions: Rap and Co-Rap

Figure-31: Time spent (hours) by CHMP Rap and Co-rap - All procedures



Note: Each point in the figure represents an individual procedure. The red line is the linear trendline. The dotted line is a 45 degree line.

Appendix 4. Data validation – Human medicines activities – Type II Variations

Table-11: Summary table for Type II Variations

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
Clinical	Jan'16 -Sep'16	110	8.83	4.45	92	44.66	2.44	10
Clinical indication	Jan'16 -Sep'16	19	75.70	11.36	14	391.00	6.66	2
Clinical safety	Jan'16 -Sep'16	135	9.78	4.51	116	42.50	3.25	15
Quality	Jan'16 -Sep'16	106	6.60	2.85	97	33.09	1.80	7

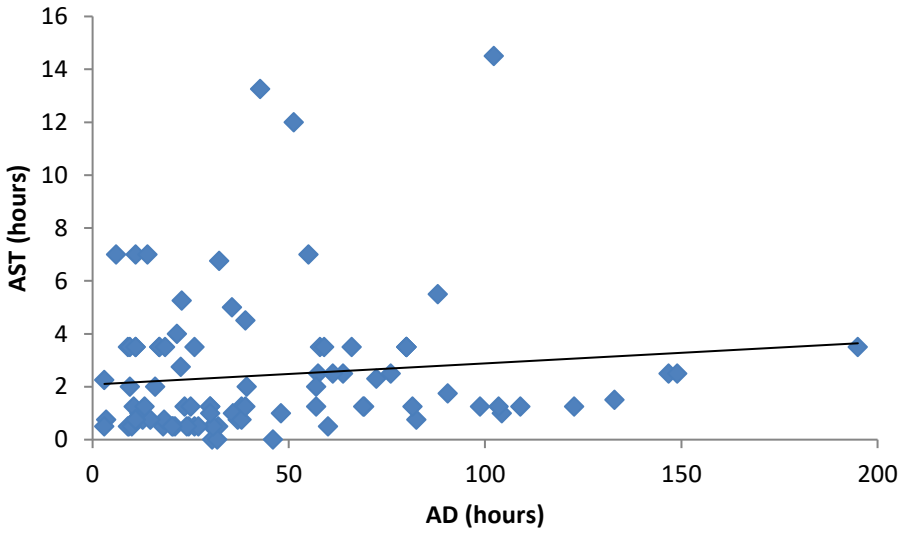
Table-12: Table-of outliers

Typ.	Product Name	CHMP Rap AD	CHMP Rap AST	PRAC Rap AD	PRAC Rap AST
C	000001	36.75	9.75		
C	000002	32.25	6.75		
C	000003			87.25	0.50
C	000004	122.75	1.25		
C	000005	43.25	6.75		
C	000006	125.00	2.50		
C	000007	34.00	6.25	68.25	8.25
C	000008	109.00	1.25		
C	000009	195.00	3.50		
CI	000010	489.00	19.75		
CI	000011			141.50	9.25
CS	000012	136.00	0.50		
CS	000001	11.25	8.25	1.75	42.25
CS	000013	103.00	8.00	103.00	8.00
CS	000014			50.50	42.25
CS	000015	31.00	9.00		
CS	000016			140.00	1.50
CS	000017	138.00	0.50		
CS	000018			115.00	
CS	000019	140.00	3.50		
CS	000020	140.00	3.50		
CS	000021	140.00	9.00		
CS	000022	48.50	6.00		
Q	000023	146.50	1.00		
Q	000024	112.25	0.75		
Q	000025	101.50	1.00		
Q	000026	134.50	1.00		
Q	000027	56.75	7.00		
Q	000028	124.00	1.00		
Q	000029	78.50	9.00		

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

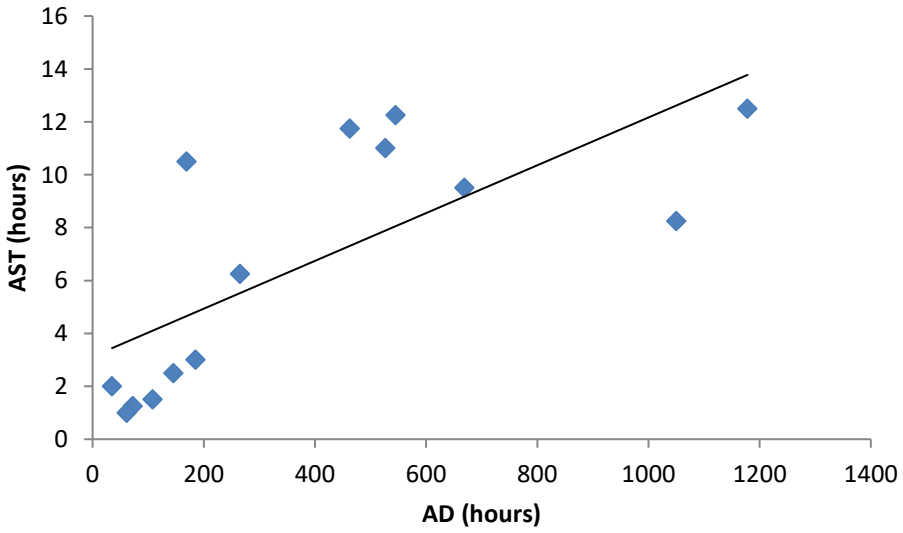
Type II variations: scientific staff (AD) and administrative staff (AST)

Figure-32: Total time spent (hours) by NCAs - all Clinical



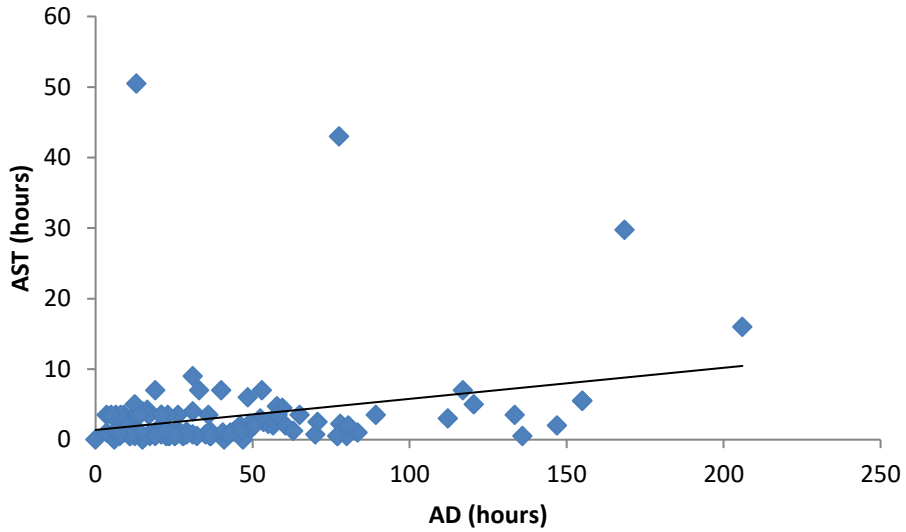
Note: Each point in the figure represents an individual procedure

Figure-33: Total time spent (hours) by NCAs - all Clinical Indication



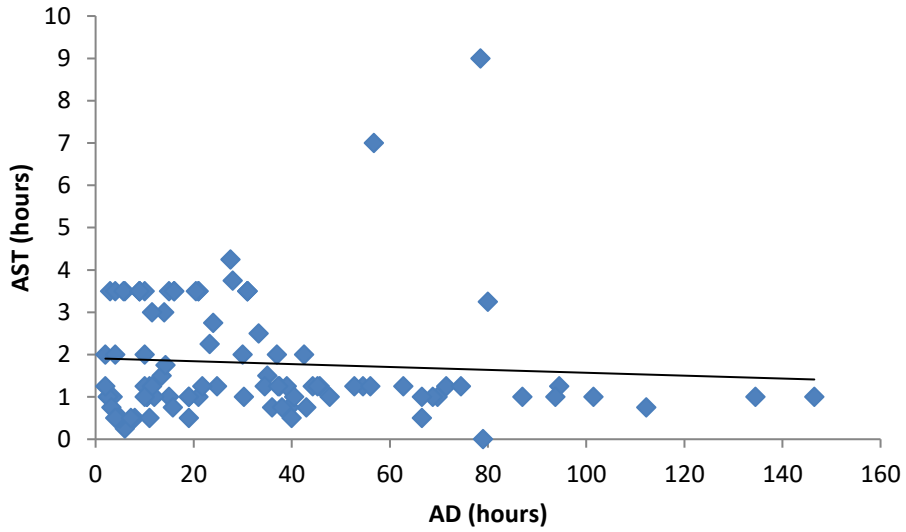
Note: Each point in the figure represents an individual procedure

Figure-34: Total time spent (hours) by NCAs - all Clinical Safety



Note: Each point in the figure represents an individual procedure

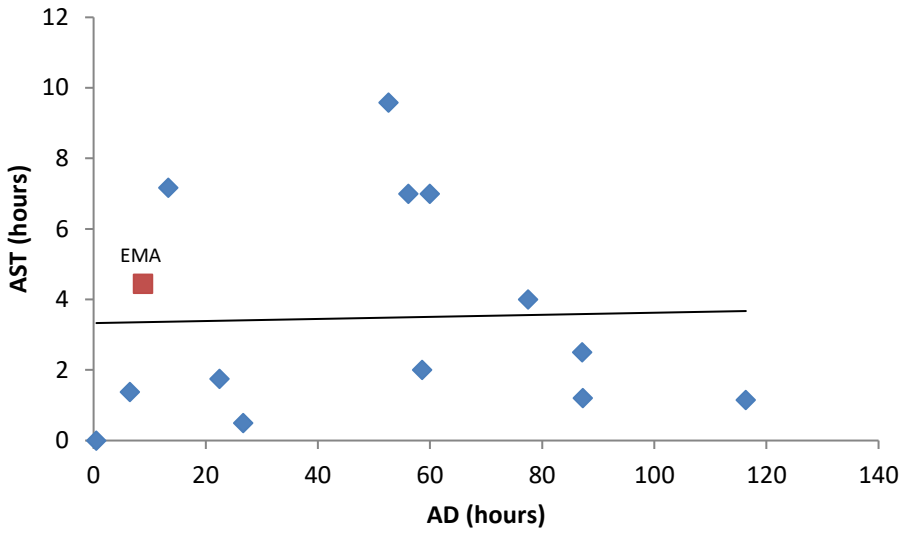
Figure-35: Total time spent (hours) by NCAs - all Quality



Note: Each point in the figure represents an individual procedure

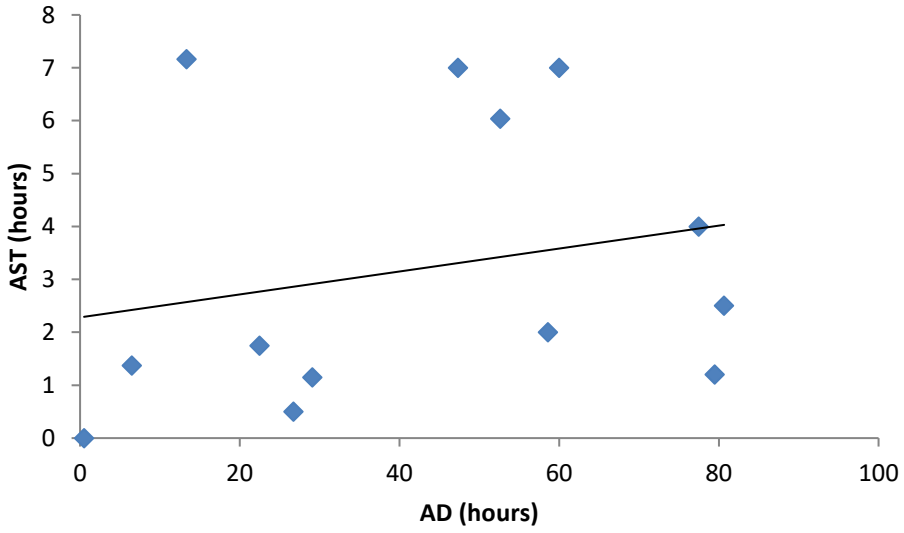
Type II Initial variations: NCAs scientific staff (AD) and administrative staff (AST)

Figure-36: Average time spent (hours) for each NCA and EMA – clinical



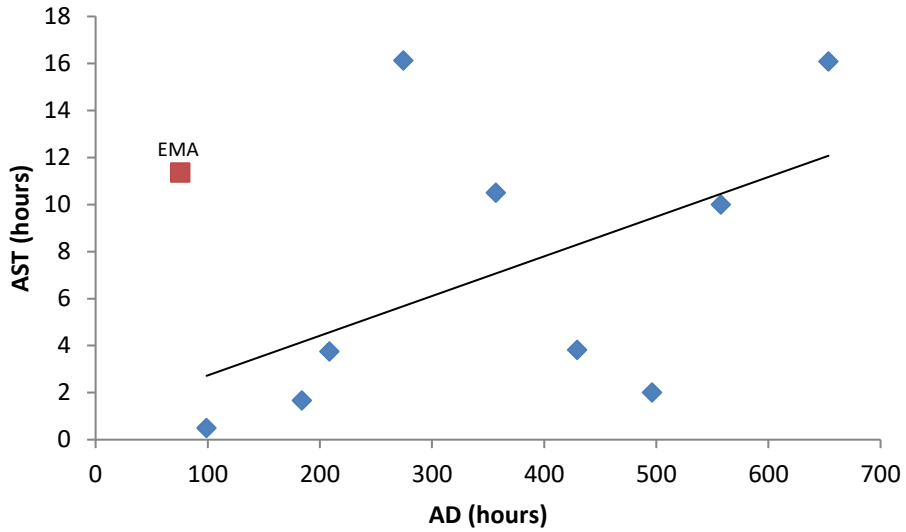
Note: Each point in the figure represents an individual NCA

Figure-37: Adjusted average time spent (hours) for each NCA – clinical



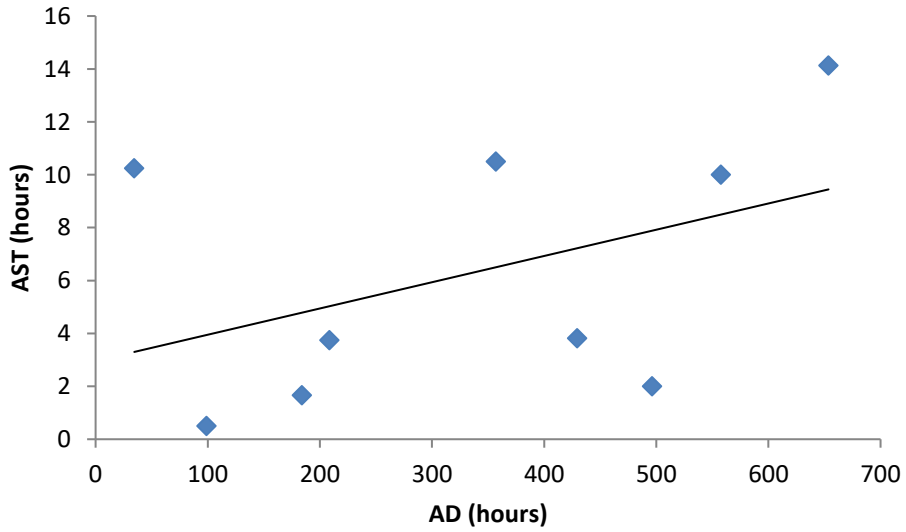
Note: Each point in the figure represents an individual NCA

Figure-38: Average time spent (hours) for each NCA and EMA - clinical indication



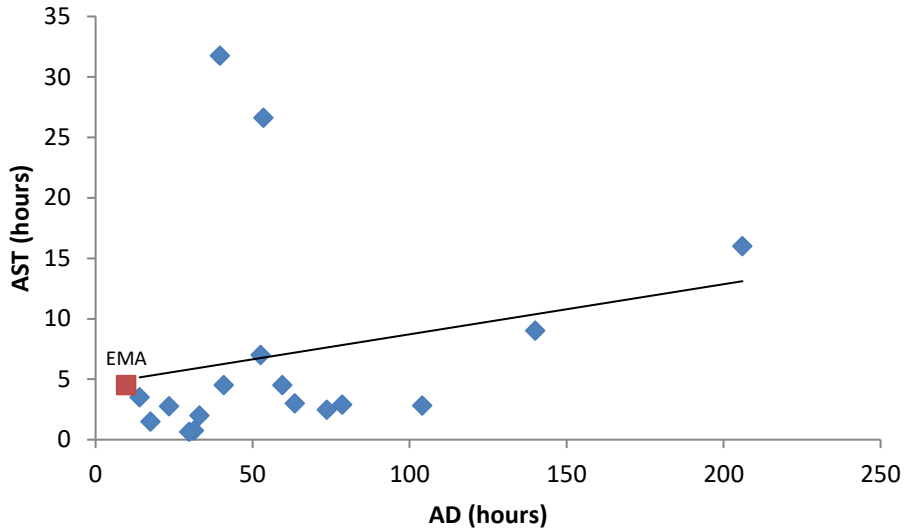
Note: Each point in the figure represents an individual NCA

Figure-39: Adjusted average time spent (hours) for each NCA - clinical indication



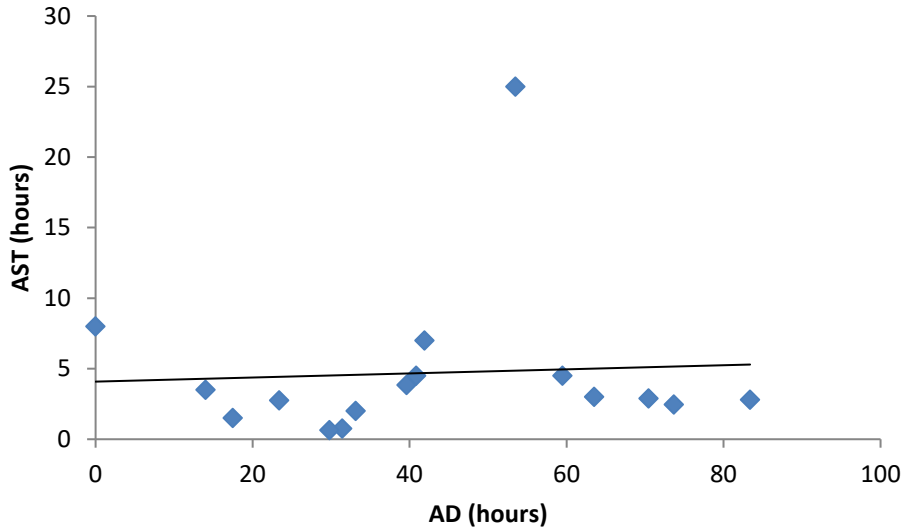
Note: Each point in the figure represents an individual NCA

Figure-40: Average time spent (hours) for each NCA and EMA - clinical safety



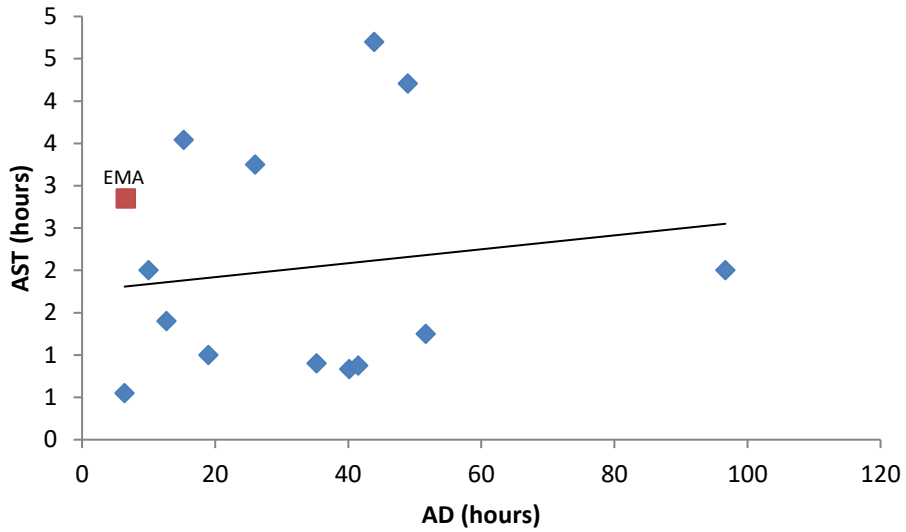
Note: Each point in the figure represents an individual NCA

Figure-41: Adjusted Average time spent (hours) for each NCA - clinical safety



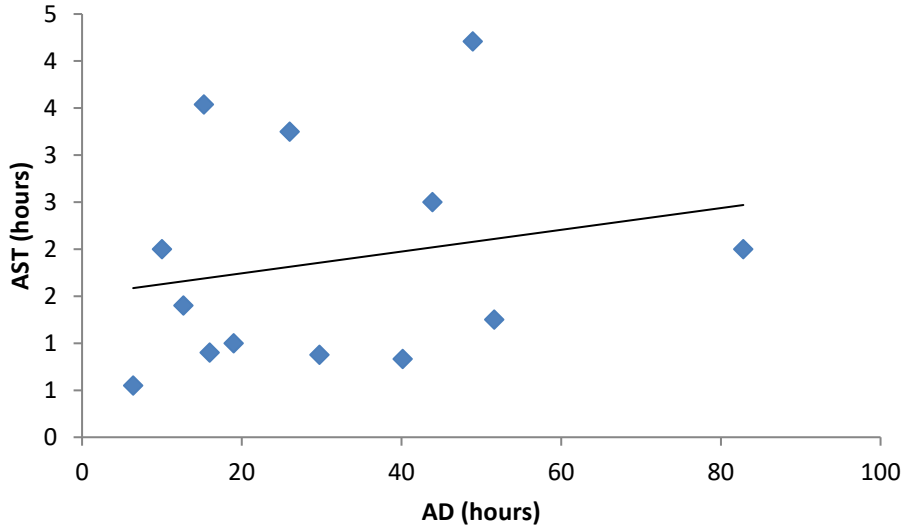
Note: Each point in the figure represents an individual NCA

Figure-42: Average time spent (hours) for each NCA and EMA – Quality



Note: Each point in the figure represents an individual NCA

Figure-43: Adjusted Average time spent for each NCA and EMA – Quality



Note: Each point in the figure represents an individual NCA

Appendix 5. Data validation – Human medicines activities – Type IB variations

Table-13: Summary table for Type IB variations – MBDG 2016 Report

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
Red	Jul'16	51	0.63	4.19	42	9.04	1.91	2
Amber	Jul'16	17	1.07	6.43	13	4.12	1.48	1
Green	Jul'16	24	0.29	4.76	-	-	-	

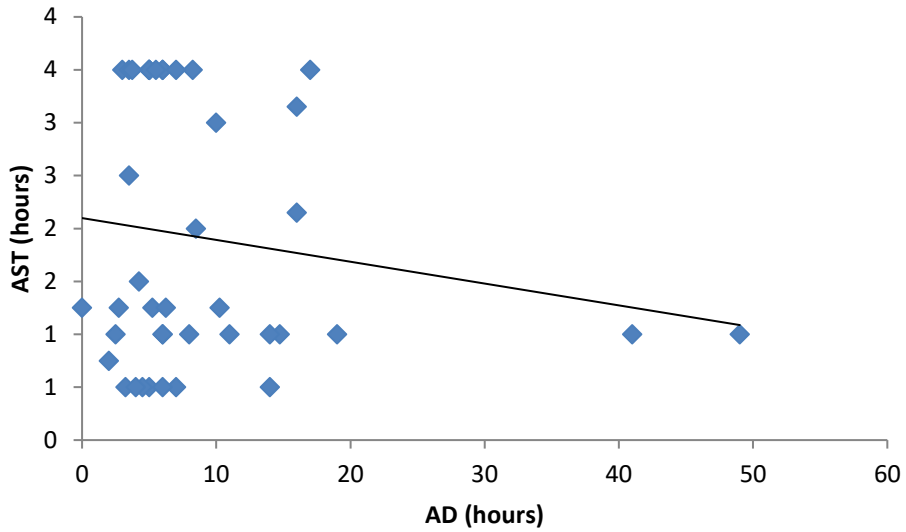
Table-14: Table-of outliers

Typ.	Product Name	Rapp AD	Rapp AST
Red	EMEA/H/X/000000/IB/0001	41.00	1.00
Red	EMEA/H/X/000000/IB/0002	49.00	1.00
Amber	EMEA/H/X/000000/IB/0003	12.00	0.50

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

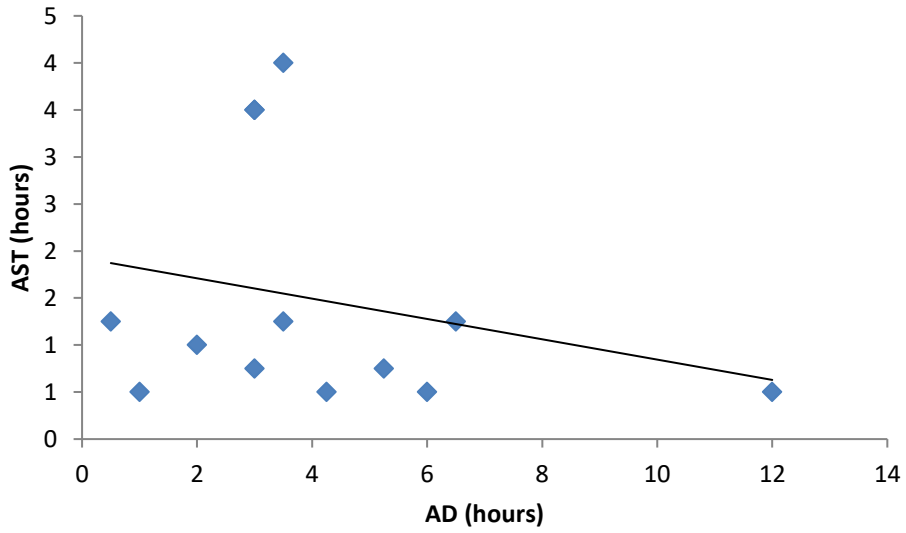
Type IB variations: scientific staff (AD) and administrative staff (AST)

Figure-44: Total time spent (hours) by NCAs - All Red variations



Note: Each point in the figure represents an individual procedure

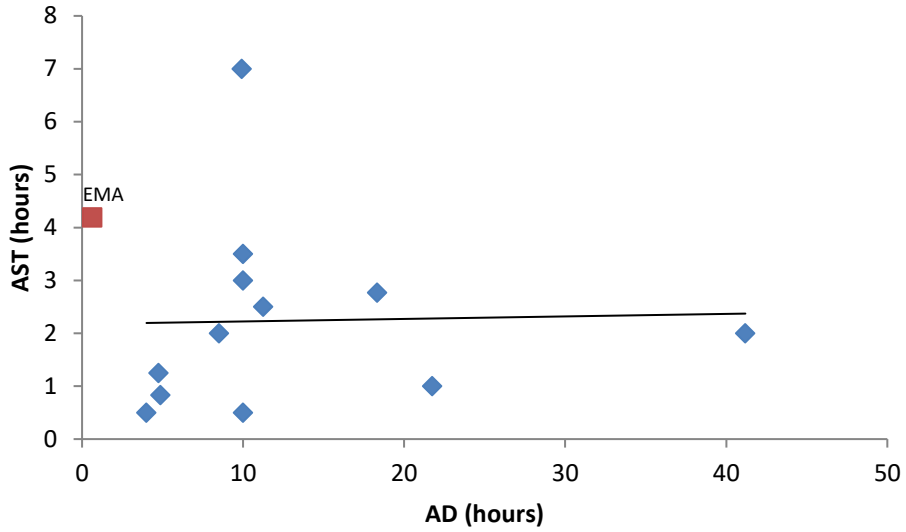
Figure-45: Total time spent (hours) by NCAs - All Amber variations



Note: Each point in the figure represents an individual procedure

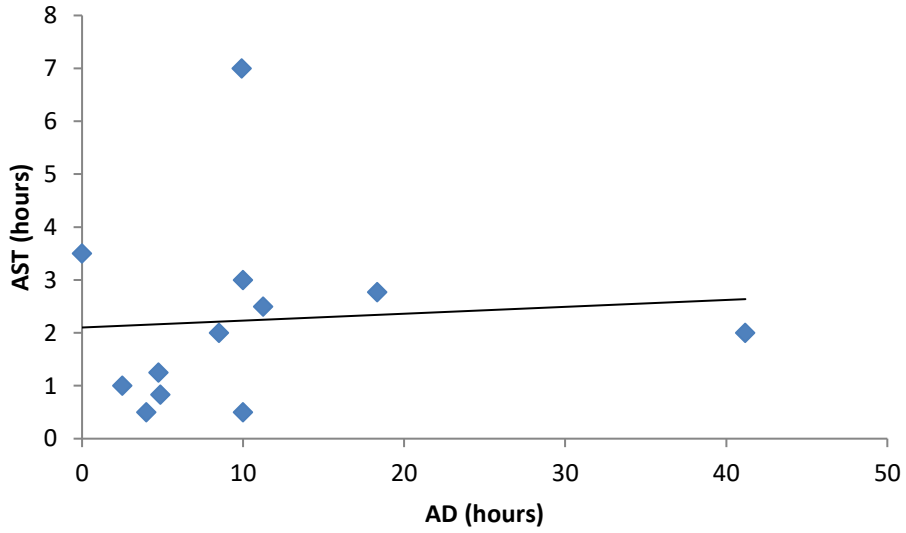
Type IB variations: NCAs scientific staff (AD) and administrative staff (AST)

Figure-46: Average time spent (hours) for each NCA and EMA - red variations



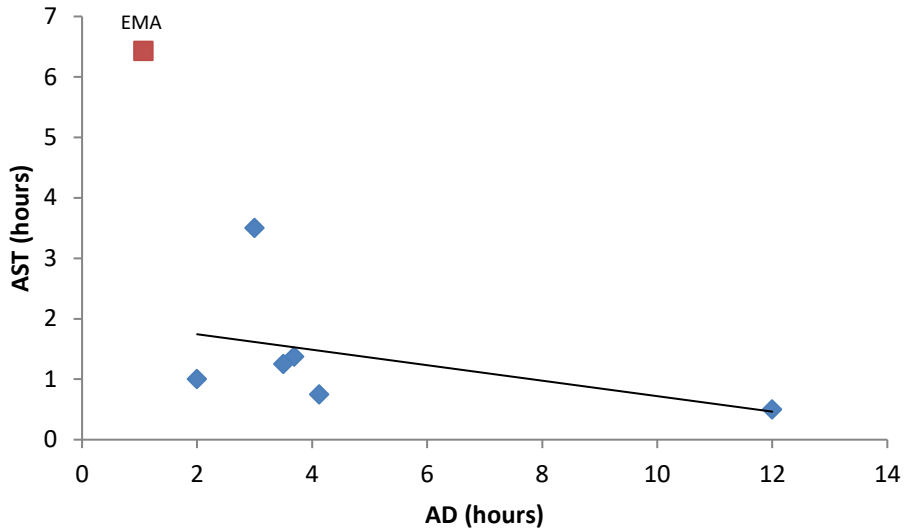
Note: Each point in the figure represents an individual NCA

Figure-47: Adjusted average time spent (hours) for each NCA - red variations



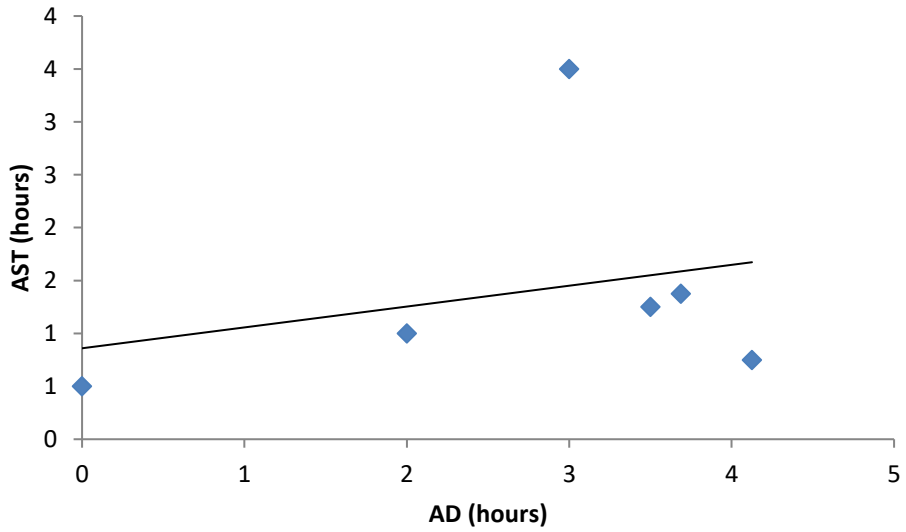
Note: Each point in the figure represents an individual NCA

Figure-48: Average time spent (hours) for each NCA and EMA - amber variations



Note: Each point in the figure represents an individual NCA

Figure-49: Adjusted average time spent (hours) for each NCA - amber variations



Note: Each point in the figure represents an individual NCA

Appendix 6. Data validation – Human medicines activities – Renewals

Table-15: Summary table for Renewals – MBDG 2016 Report

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
Renewals	Jul'16	33	19.77	12.45	22	47.44	10.17	6

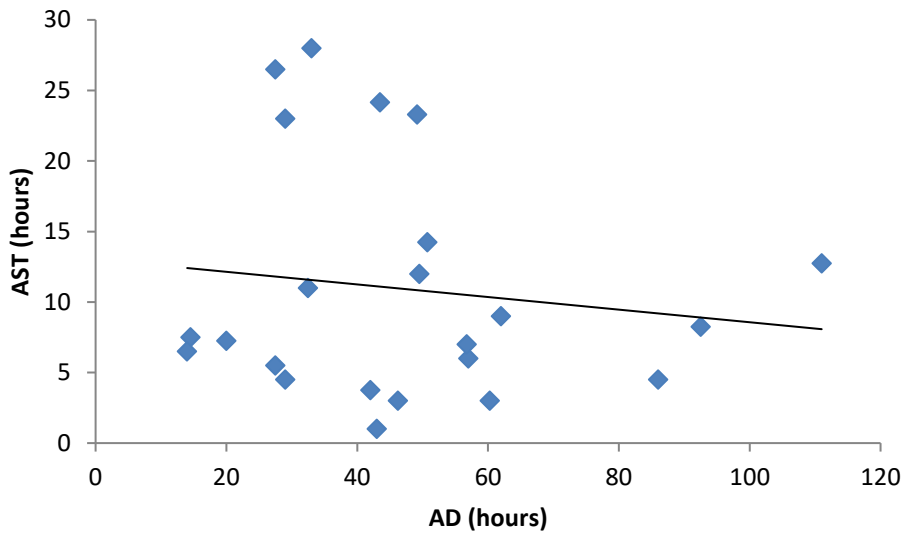
Table-16: Table-of outliers

Proc number	CHMP Rap AD	CHMP Rap AST	CHMP Co-Rap AD	CHMP Co-Rap AST	PRAC Rap AD	PRAC Rap AST
EMEA/H/C/000000/R/0001			27.00	5.75		
EMEA/H/C/000000/R/0002	15.00	20.75				
EMEA/H/C/000000/R/0003					70.00	2.00
EMEA/H/C/000000/R/0004	86.00	4.00				
EMEA/H/C/000000/R/0005	64.00	9.00				
EMEA/H/C/000000/R/0006			51.25	0.75		

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

Renewals: scientific staff (AD) and administrative staff (AST)

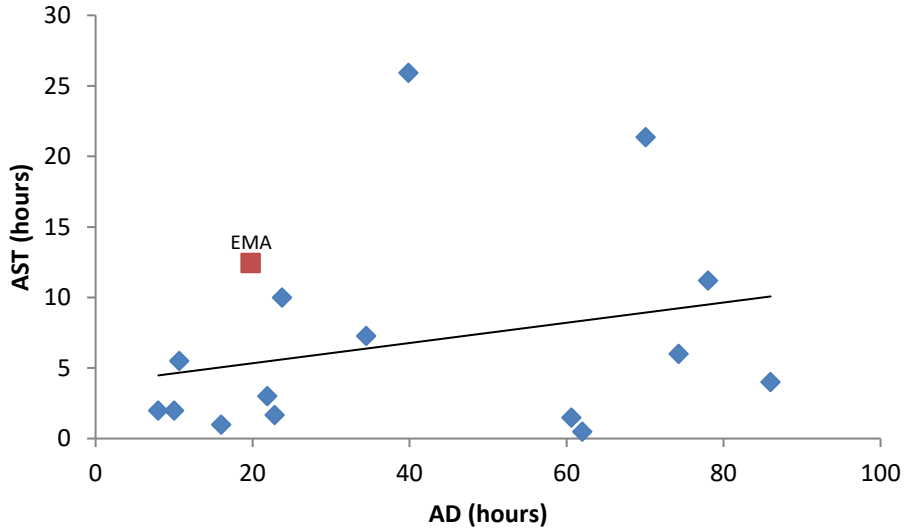
Figure-50: Total time spent (hours) by NCAs - All renewals



Note: Each point in the figure represents an individual procedure

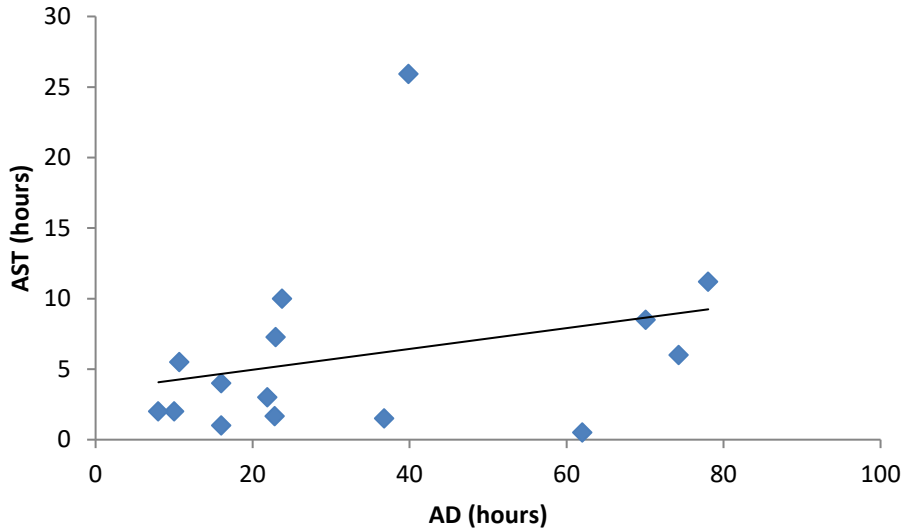
Renewals: NCAs scientific staff (AD) and administrative staff (AST)

Figure-51: Average time spent (hours) for each NCA and EMA



Note: Each point in the figure represents an individual NCA

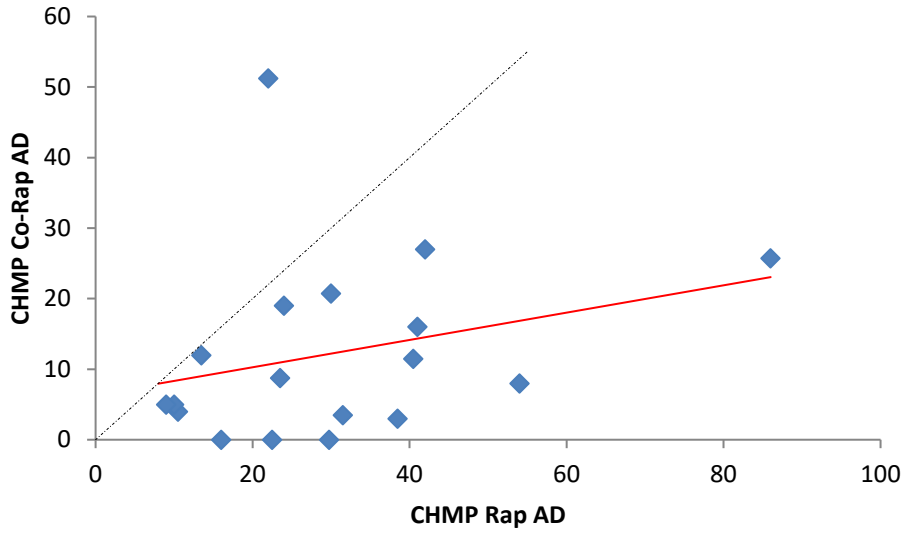
Figure-52: Adjusted average time spent (hours) for each NCA



Note: Each point in the figure represents an individual NCA

Renewals: Rap and Co-Rap

Figure-53: Time spent (hours) in CHMP Rap and Co-rap - All procedures



Note: Each point in the figure represents an individual procedure. The red line is the linear trendline. The dotted line is a 45 degree line.

Appendix 7. Data validation – Human medicines activities – Paediatrics

Table-17: Summary table for Paediatric – MBDG 2016 Report

	Sampling period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
Compliance Check	Mar'16 – Sep'16	12	9.36	4.23	9	11.50	0.64	1
PIP Modification	Mar'16 – Sep'16	33	15.06	5.96	20	19.05	1.24	3
Waiver	Mar'16 – Sep'16	10	15.26	7.23	10	24.33	1.10	2
New PIPs P1	Mar'16 – Sep'16	26	17.81	10.68	25	34.07	1.67	2
New PIPs P2	Mar'16 – Sep'16	19	25.85	6.01	10	24.15	1.15	2

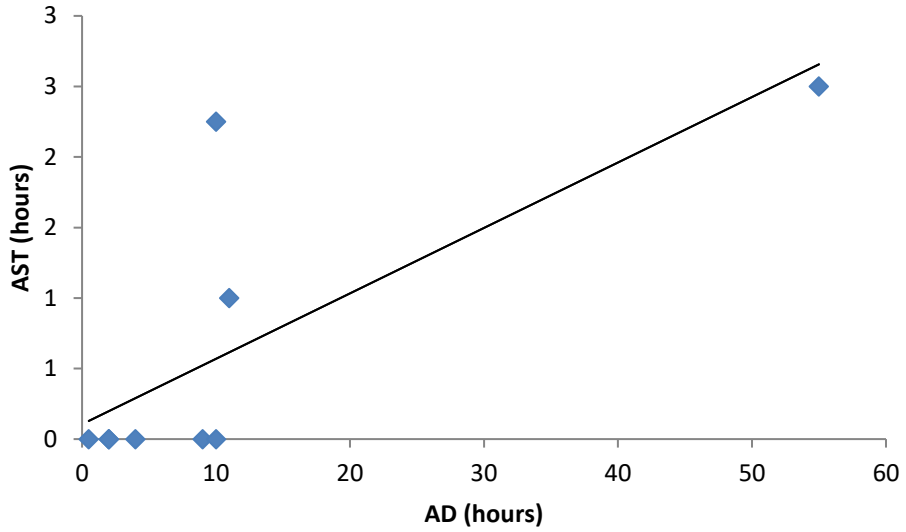
Table-18: Table-of outliers

Type	Ref Code	Rapporteur AD	Rapporteur AST	Peer Reviewer AD	Peer Reviewer AST
Compl. Ch.	HP0000-01	55.00	2.50		
PIP Mod.	HP0000-02	41.25	1.25		
PIP Mod.	HP0000-03			31.00	1.25
PIP Mod.	HP0000-04	17.00	2.25	37.50	1.50
Waiver	HP0000-05	40.00	2.50		
Waiver	HP0000-06	40.00	2.50		
New PIP	HP0000-07	38.00		45.00	
New PIP	HP0000-08	53.50	1.25		
PIP Rest.	HP0000-09	54.50	5.25		
PIP Rest.	HP0000-10			42.00	2.50

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

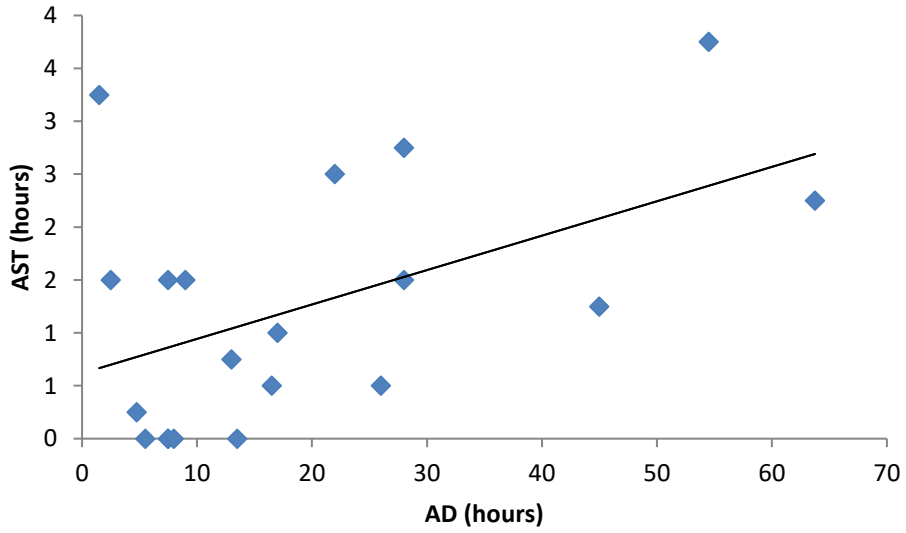
Scientific staff (AD) and administrative staff (AST)

Figure-54: Total time spent (hours) by NCAs – All Paediatric Compliance check



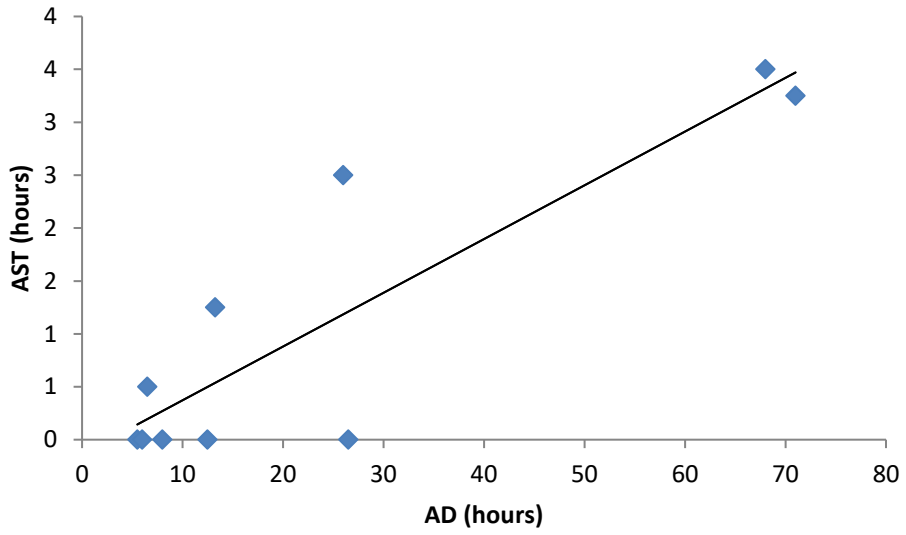
Note: Each point in the figure represents an individual procedure

Figure-55: Total time spent (hours) by NCAs – All Paediatric PIP modification



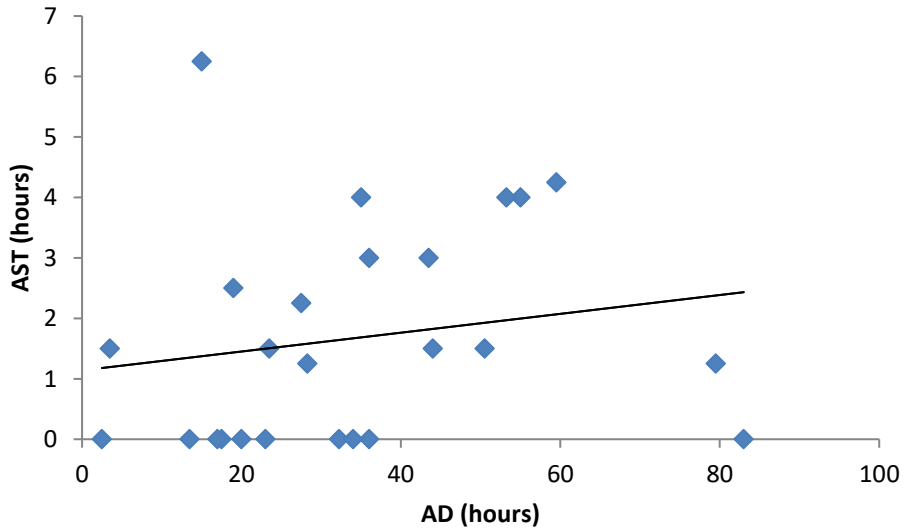
Note: Each point in the figure represents an individual procedure

Figure-56: Total time spent (hours) by NCAs – All Paediatric Waiver



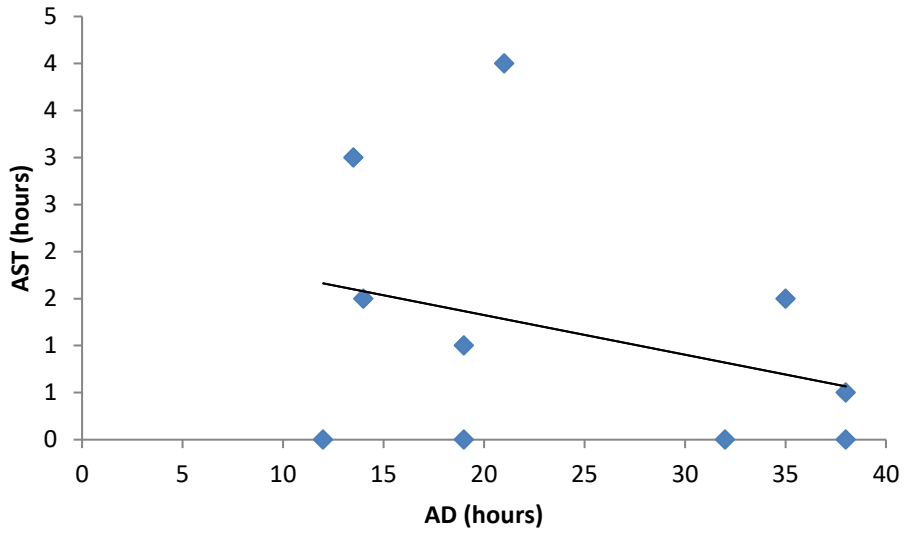
Note: Each point in the figure represents an individual procedure

Figure-57: Total time spent (hours) by NCAs – All New PIPs Phase I



Note: Each point in the figure represents an individual procedure

Figure-58: Total time spent (hours) by NCAs – All New PIPs Phase II



Note: Each point in the figure represents an individual procedure

Appendix 8. Data validation – Human medicines activities – Orphan designations

Table-19: Summary table for Orphan designation – MBDG 2016 Report

	Sampling period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
Compliance Check	Mar'16 – Sep'16	87	21.93	9.00	61	12.16	0.37	3

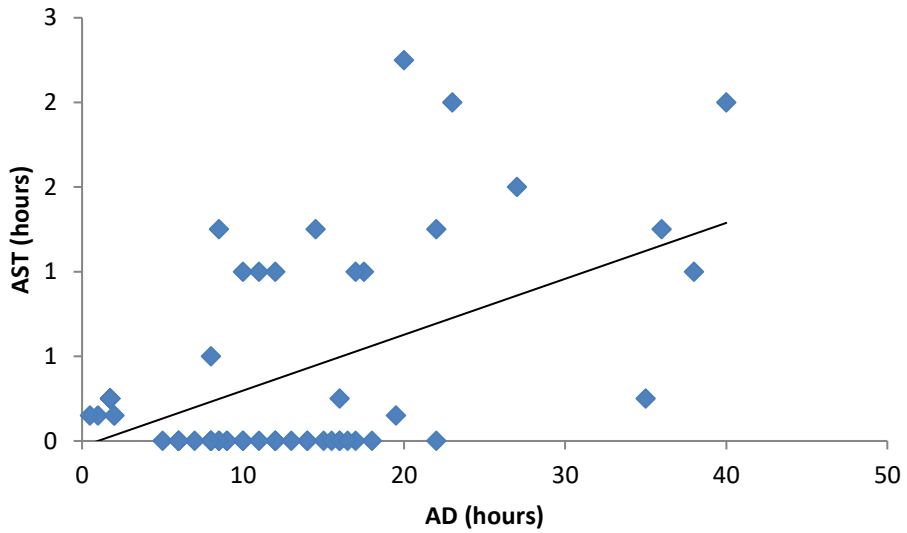
Table-20: Table-of outliers

Ref Code	Coordinator 1 AD	Coordinator 1 AST
H1-OD-001	23.00	2.00
H1-OD-002	40.00	2.00

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

Scientific staff (AD) and administrative staff (AST)

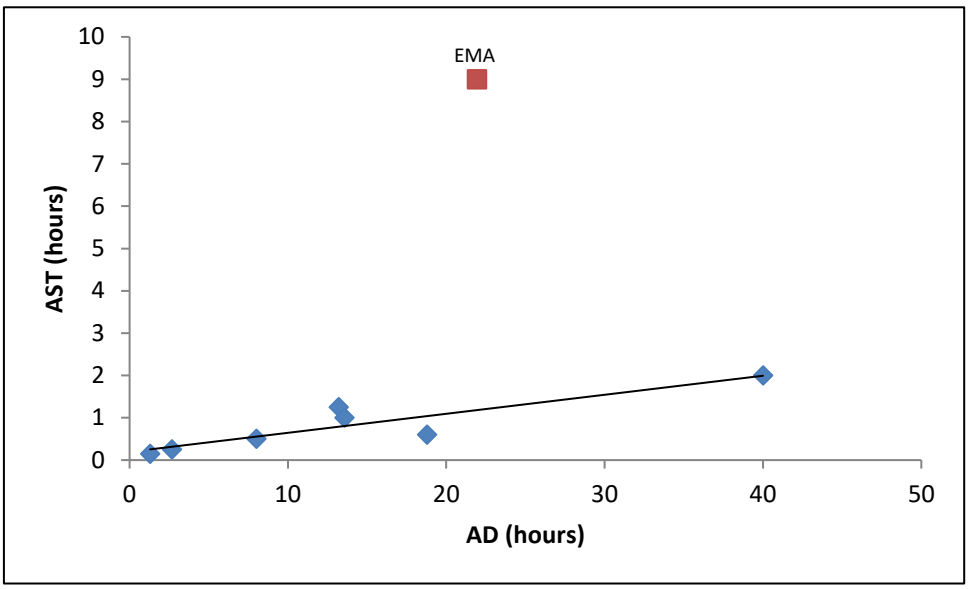
Figure-59: Total time spent (hours) by NCAs – All Orphan designations



Note: Each point in the figure represents an individual procedure

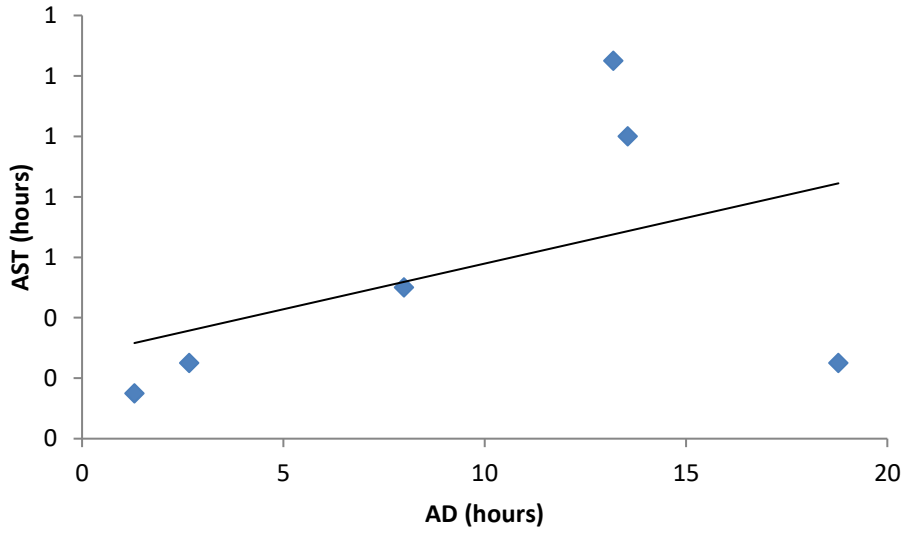
Orphan designation: NCAs scientific staff (AD) and administrative staff (AST)

Figure-60: Average time spent (hours) for each NCA and EMA



Note: Each point in the figure represents an individual NCA

Figure-61: Adjusted average time spent (hours) for each NCA



Note: Each point in the figure represents an individual NCA

Appendix 9. Data validation – Human medicines activities – Inspections

Table-21: Summary table for inspections – MBDG 2016 Report

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Travel	Number of outliers
PhV inspections	Jan '16 – Oct '16	1	31.10	28.35	1	102.00	26.00	34.00	-
GCP inspections	Jan '16 – Oct '16	6	56.21	14.62	6	616.50	66.83	162.01	2
GMP inspections	Jan '16 – Oct '16	8	15.59	0.81	8	81.63	3.50	47.71	1

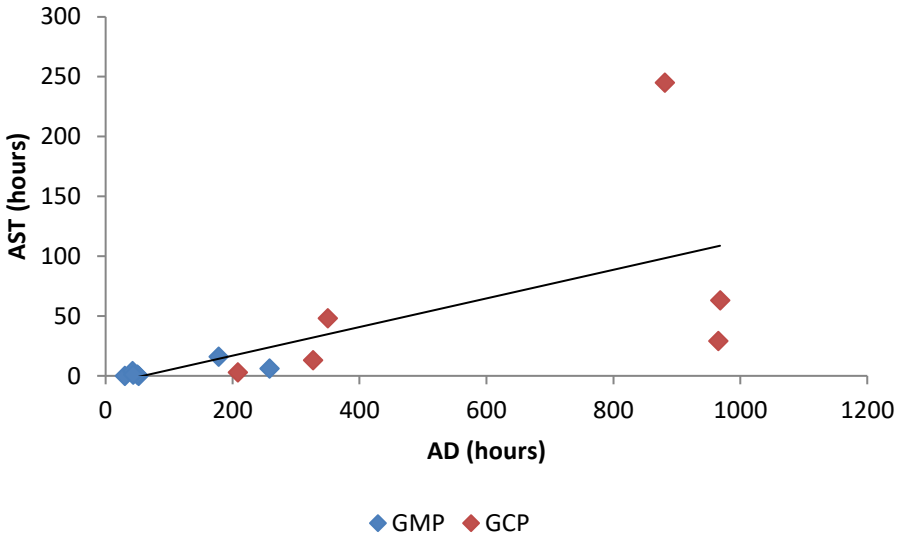
Table-22: Table-of outliers

	Ref Code	Inspector 1 AD	Inspector 1 AST	Travel	Inspector 2 AD	Inspector 2 AST	Travel
GCP	EMEA/H/C/000001	536.25	132.00	20.00	194.25	108.00	20.00
GCP	EMEA/H/C/000002	350.00	3.00	160.00	332.50	30.00	180.40
GMP	EMEA/H/C/000003	178.00	16.00	90.00			

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

Scientific staff (AD) and administrative staff (AST)

Figure-62: Total time spent (hours) by NCAs – All GMP and GCP inspections



Note: Each point in the figure represents an individual procedure

Appendix 10. Data validation – Human medicines activities – Scientific advice

Table-23: Summary table Scientific Advice – MBDG 2016 Report (Pilot Exercise)

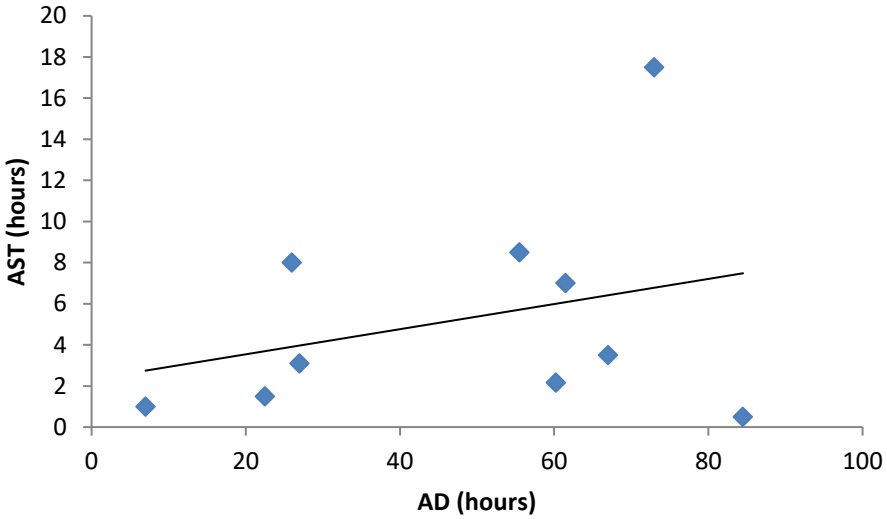
	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
Initial SA Level I	Feb'15-Jun`15	10	29	30.9	10	48.4	5.3	-
Initial SA Level II	Feb'15-Jun`15	27	42.9	31.2	27	79.2	4.7	3
Initial SA Level III	Feb'15-Jun`15	37	47.2	32.4	37	122.3	4.2	5
Follow Up SA – L I	Feb'15-Jun`15	5	30.3	31.6	5	83.1	7	-
Follow Up SA – L II	Feb'15-Jun`15	18	40.7	31.2	18	81.1	4.3	4
Follow Up SA – L III	Feb'15-Jun`15	5	38.4	32.5	5	163.5	6.2	-

Table-24: Table-of outliers

Procedure number	Fee level	SAWP coord-inator_1	SAWP AST_1	SAWP coord-inator_2	SAWP AST_2
EMEA/H/SA/00001/0/2015/II	II	125	6		
EMEA/H/SA/00002/0/2015/II	II	90.75	7		
EMEA/H/SA/00003/0/2015/II	II			96.75	
EMEA/H/SA/00004/0/2015/III	III			195	
EMEA/H/SA/00005/0/2015/III	III			150.5	
EMEA/H/SA/00006/0/2015/III	III	221.5			
EMEA/H/SA/00007/0/2015/III	III	308.25			
EMEA/H/SA/00008/0/2015/III	III			168.75	
EMEA/H/SA/00009/0/2015/II	II	32	13		
EMEA/H/SA/00010/0/2015/II	II	112.5	6.5	172.33	7

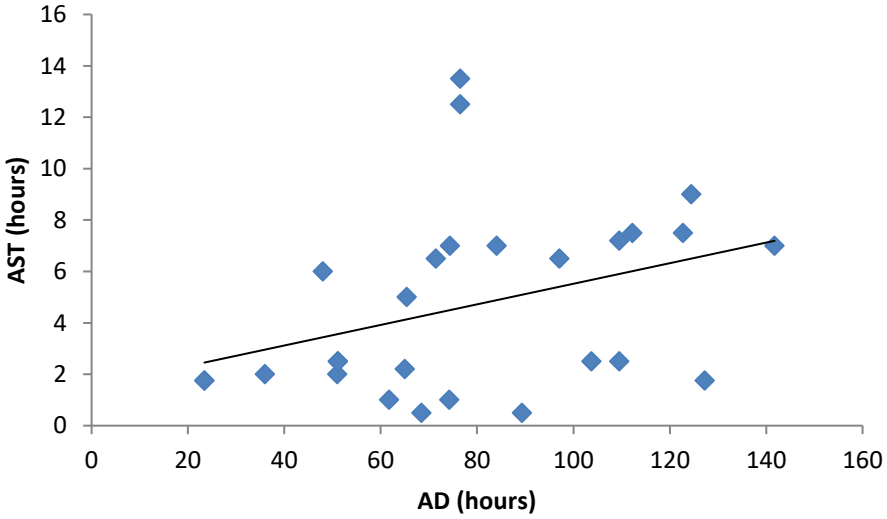
Scientific advice: Scientific staff (AD) and administrative staff (AST)

Figure-63: Total time spent (hours) by NCAs – All Initial Scientific Advice Level I



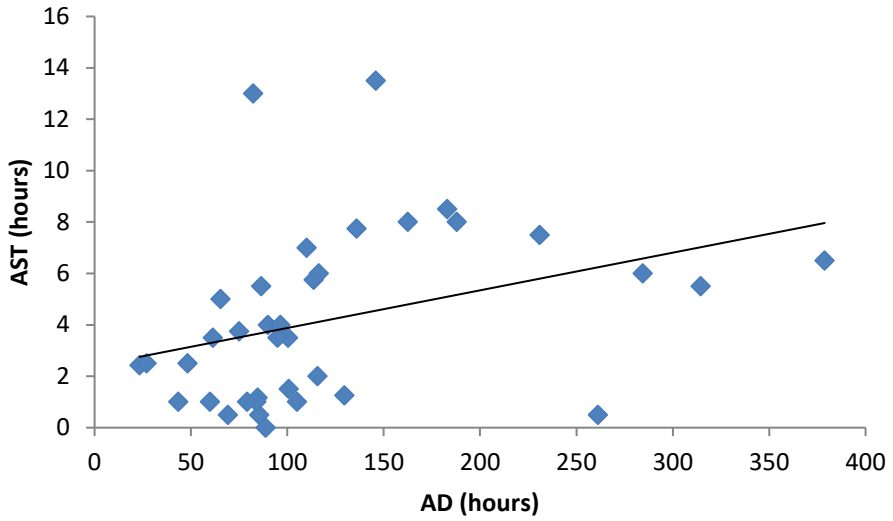
Note: Each point in the figure represents an individual procedure

Figure-64: Total time spent (hours) by NCAs – All Initial Scientific Advice Level II



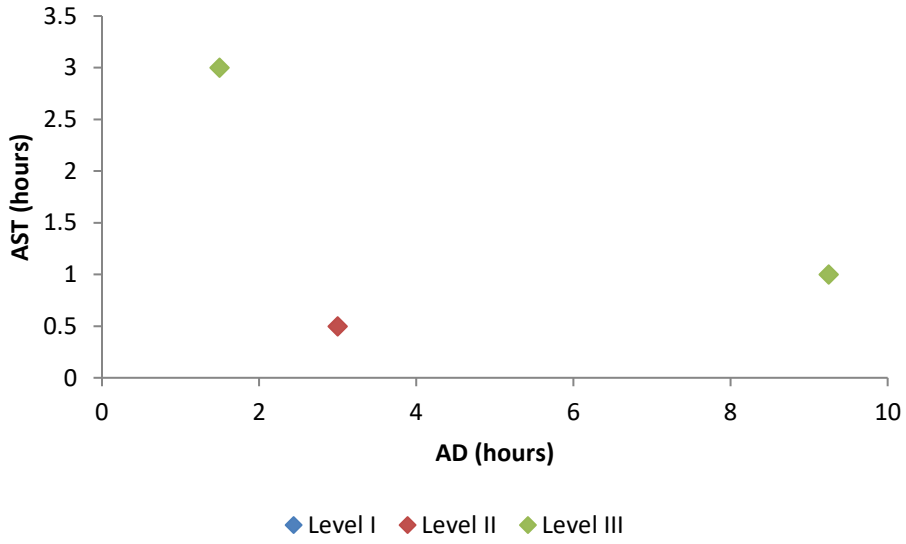
Note: Each point in the figure represents an individual procedure

Figure-65: Total time spent (hours) by NCAs – All Initial Scientific Advice Level III



Note: Each point in the figure represents an individual procedure

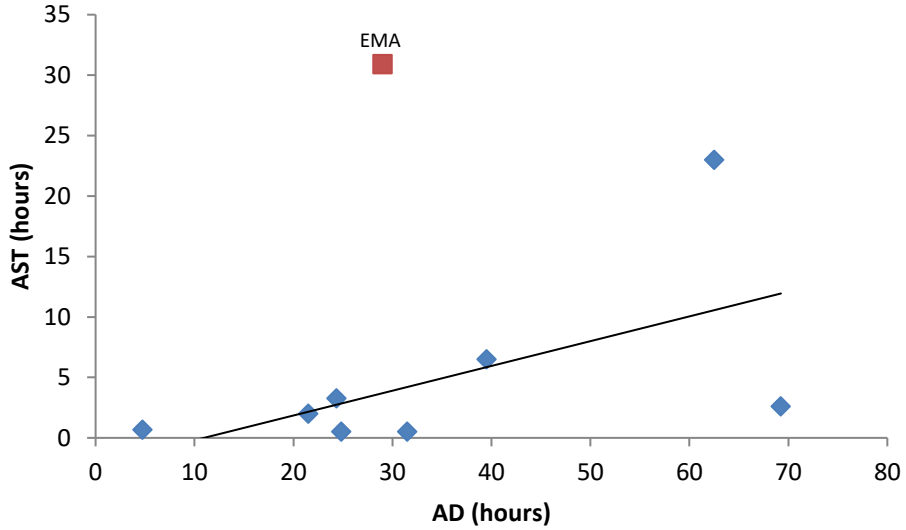
Figure-66: Total time spent (hours) by NCAs – All Scientific Advice Follow Up



Note: Each point in the figure represents an individual procedure

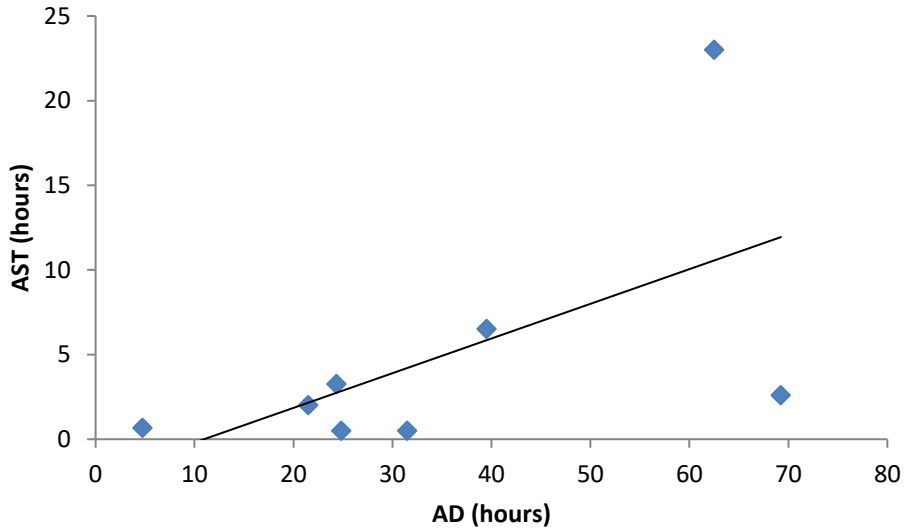
Scientific Advice: NCAs scientific staff (AD) and administrative staff (AST)

Figure-67: Average time spent (hours) for each NCA and EMA – Initial Scientific Advice Level I



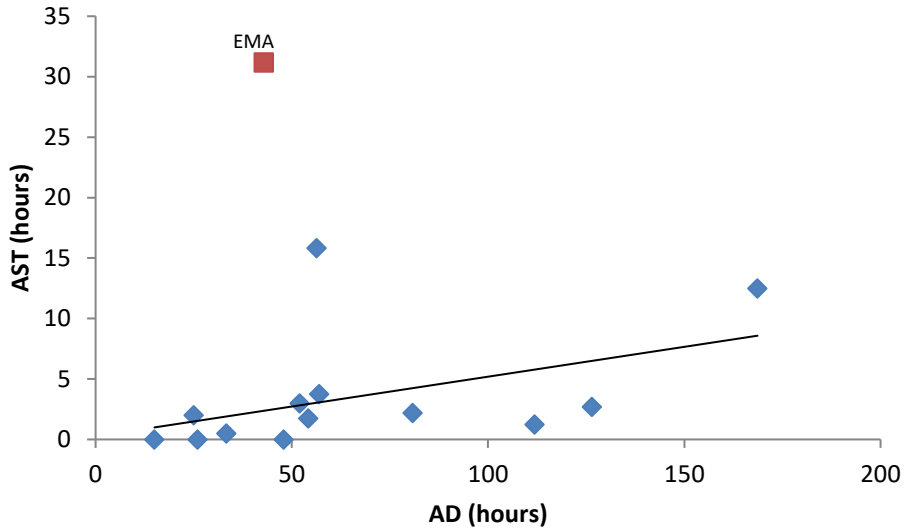
Note: Each point in the figure represents an individual NCA

Figure-68: Adjusted Average time spent (hours) for each NCA– Initial Scientific Advice Level I



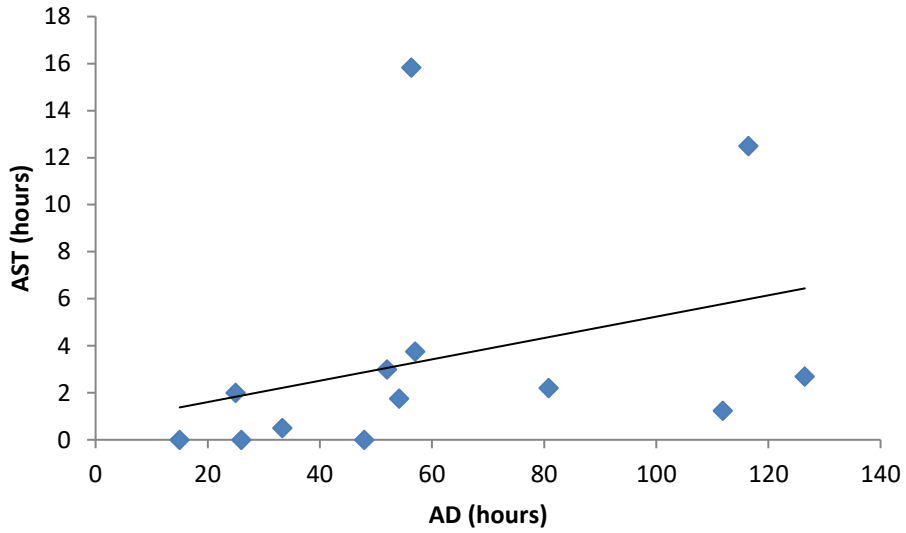
Note: Each point in the figure represents an individual NCA

Figure-69: Average time spent (hours) for each NCA and EMA – Initial Scientific Advice Level II



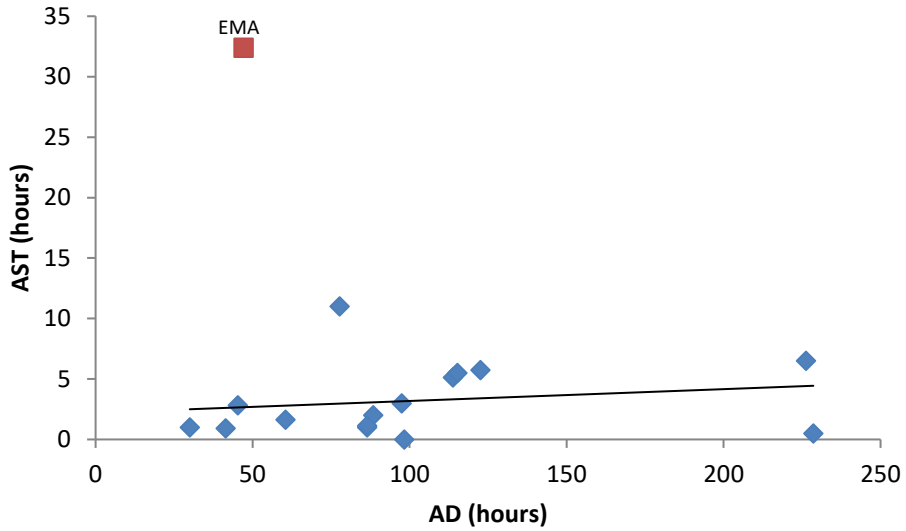
Note: Each point in the figure represents an individual NCA

Figure-70: Adjusted Average time spent (hours) for each NCA– Initial Scientific Advice Level II



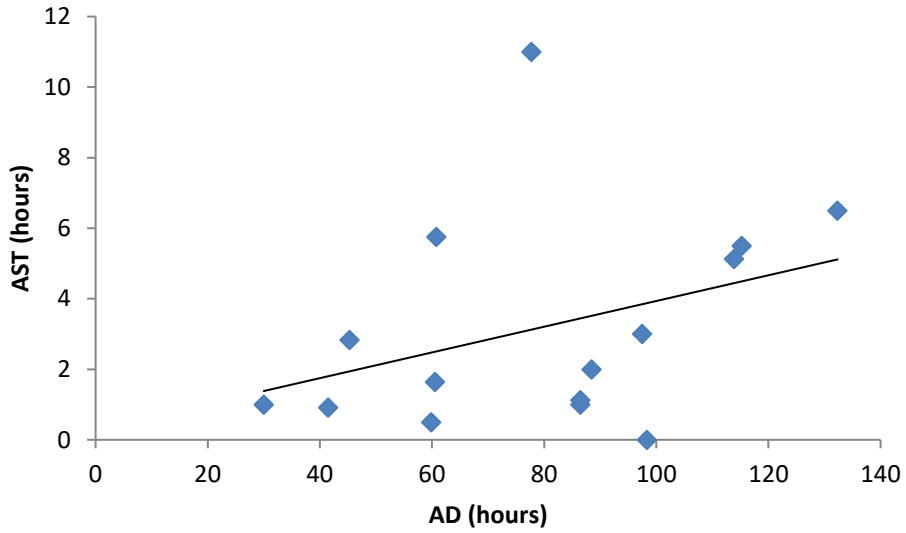
Note: Each point in the figure represents an individual NCA

Figure-71: Average time spent (hours) for each NCA and EMA – Initial Scientific Advice Level III



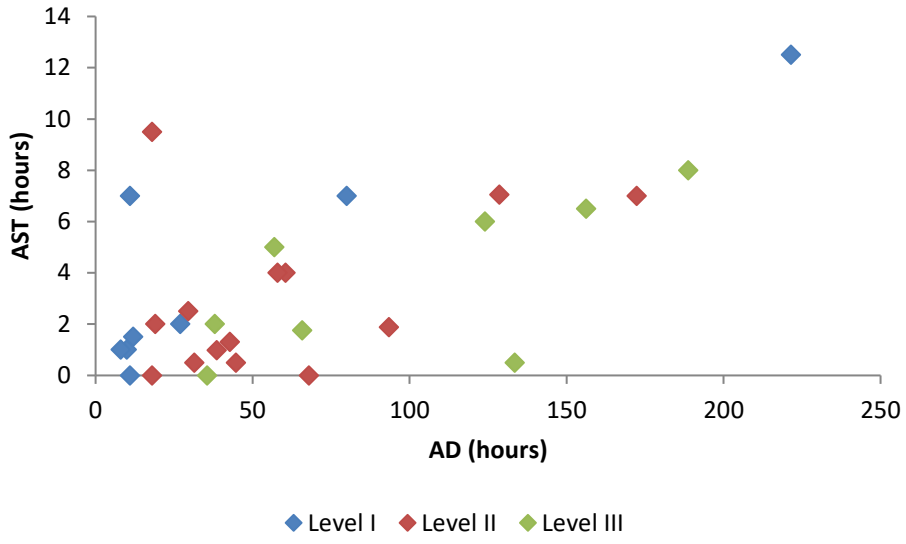
Note: Each point in the figure represents an individual NCA

Figure-72: Adjusted Average time spent (hours) for each NCA– Initial Scientific Advice Level III



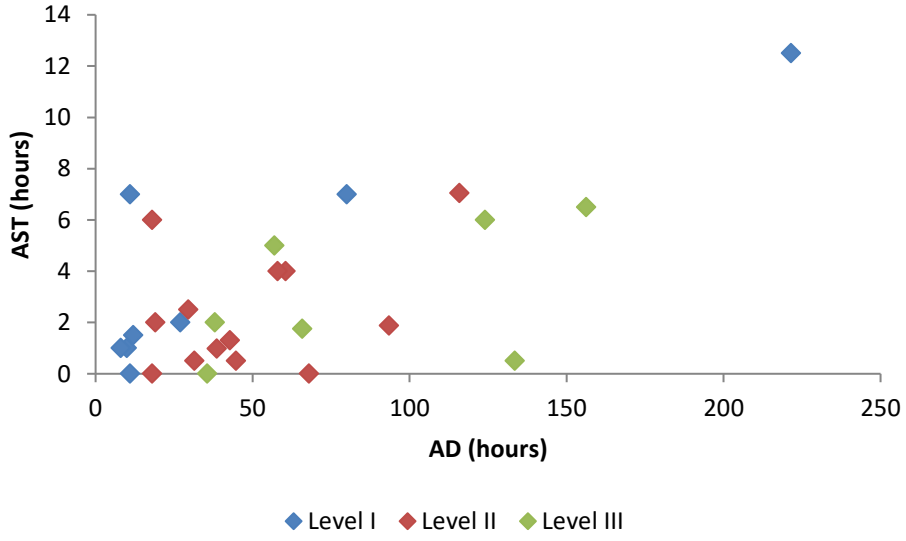
Note: Each point in the figure represents an individual NCA

Figure-73: Average time spent (hours) for each NCA and – Follow Up Scientific Advice



Note: Each point in the figure represents an individual NCA

Figure-74: Adjusted Average time spent (hours) for each NCA– Follow Up Scientific Advice



Note: Each point in the figure represents an individual NCA

Appendix 11. Data validation – Human medicines activities – Scientific committees

Table-25: Scientific Committees Summary Table-– 2016 MBDG Report

	Sampling Period	EMA Sample	EMA Total	NCA Sample	NCA Total	Number of outliers
CHMP	Sep – Oct '16	31	1016.50	31	3508.50	6
PRAC	Sep – Oct '16	28	777.16	28	2902.75	5
CAT	Sep – Oct '16	26	382.92	26	835.88	4
HMPC	Sep – Oct '16	20	276.54	20	887.00	3

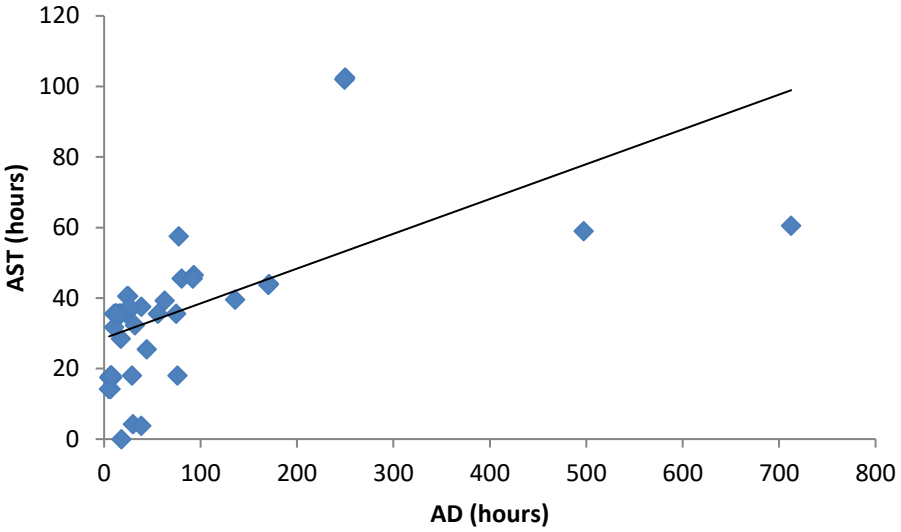
Table-26: Table-of outliers

	WORKLOAD		
Agency	**Member**	**AD Support**	**AST Support**
CHMP_01	220.00	26.00	8.00
CHMP_02	241.00	1160.00	50.00
CHMP_02	165.00	806.00	47.00
CHMP_03	80.00	416.00	134.00
CHMP_03	80.00	415.00	133.00
CHMP_03	80.00	415.00	133.00
PRAC_04	175.00	111.25	401.25
PRAC_05	260.00	32.00	0.00
PRAC_06	216.00	378.00	23.00
PRAC_07	160.00	477.00	153.00
PRAC_07	195.00	583.00	187.00
CAT_08	179.00	20.00	7.00
CAT_09	85.00	61.50	8.25
CAT_09	144.00	61.50	8.25
CAT_10	193.00	49.00	10.00
HMPC_11	350.00	100.00	0.00
HMPC_12	98.75	15.75	25.50
HMPC_12	98.75	15.00	25.00

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

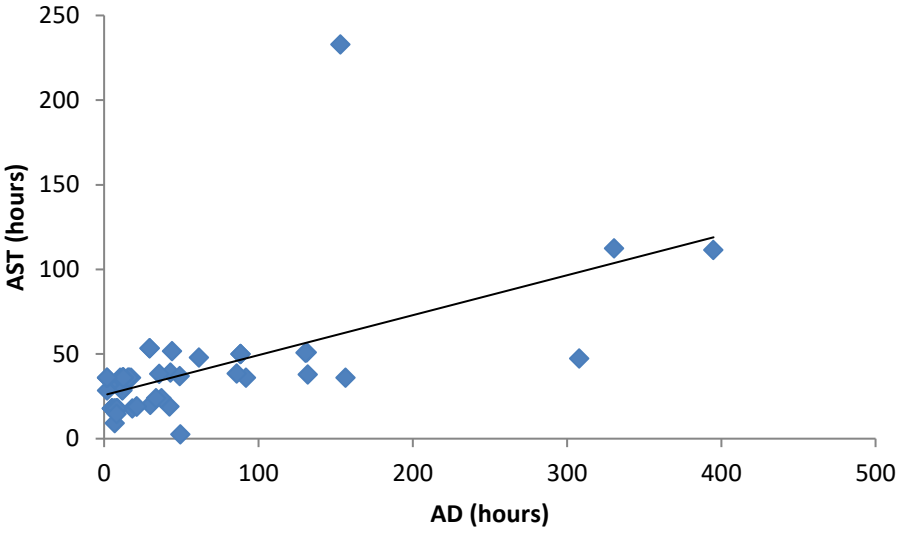
Committees: scientific staff (AD) and administrative staff (AST)

Figure-75: Total time spent (hours) by NCAs – all CHMP



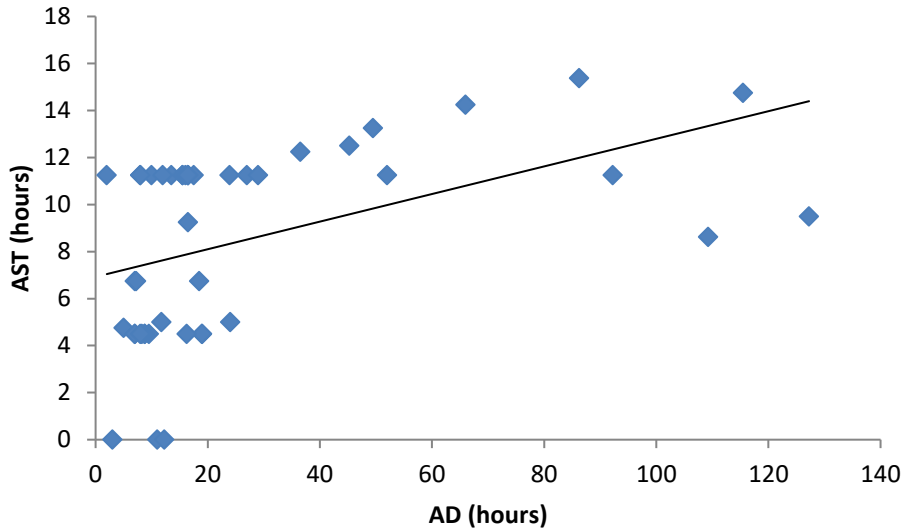
Note: Each point in the figure represents an individual procedure

Figure-76: Total time spent (hours) by NCAs – all PRAC



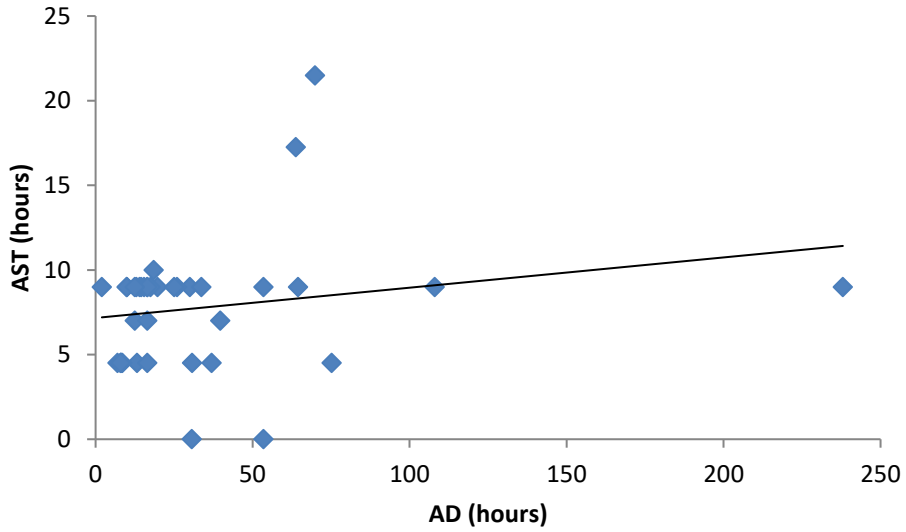
Note: Each point in the figure represents an individual procedure

Figure-77: Total time spent (hours) by NCAs – all CAT



Note: Each point in the figure represents an individual NCA

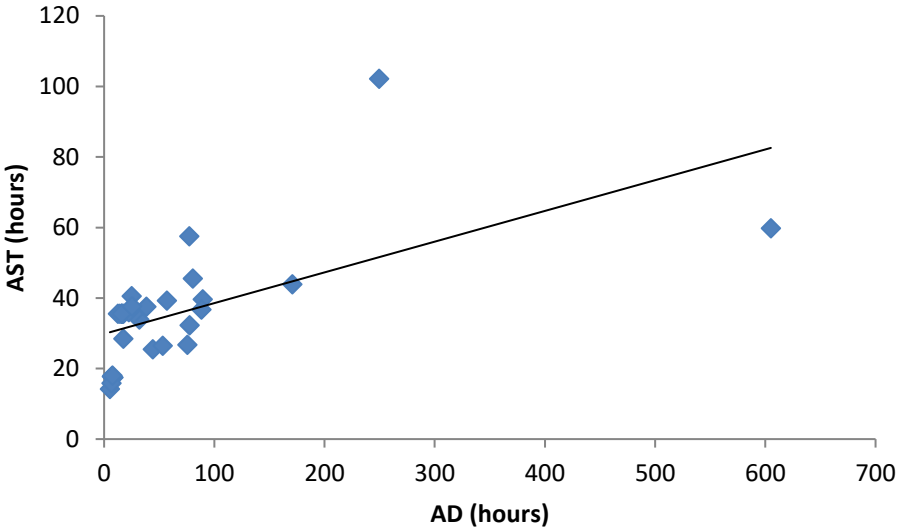
Figure-78: Total time spent (hours) by NCAs – all HMPC



Note: Each point in the figure represents an individual NCA

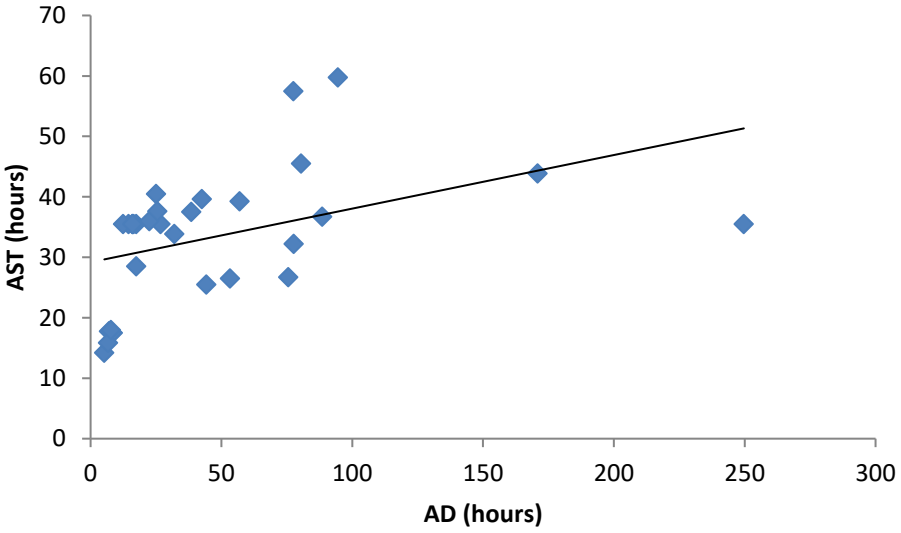
Committees: NCAs scientific staff (AD) and administrative staff (AST)

Figure-79: Average time spent (hours) for each NCA – CHMP



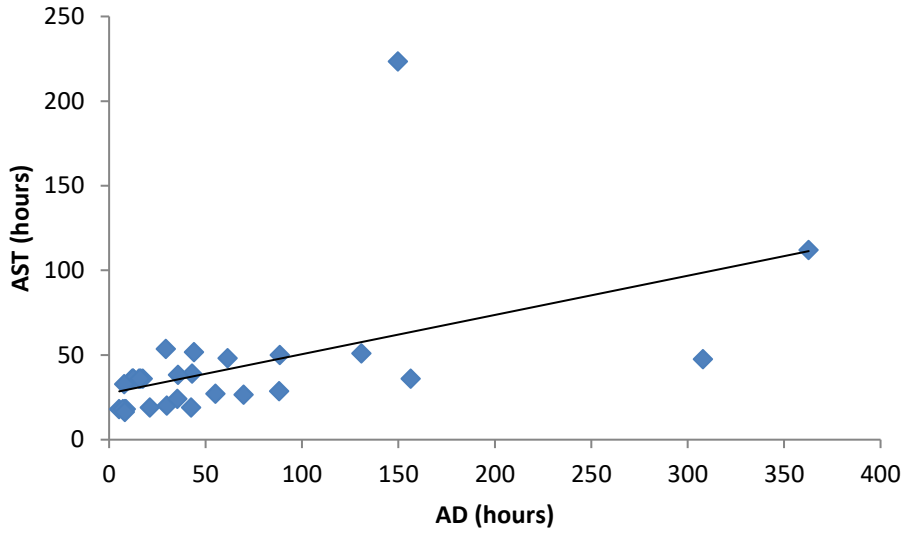
Note: Each point in the figure represents an individual NCA

Figure-80: Adjusted Average time spent (hours) for each NCA – CHMP



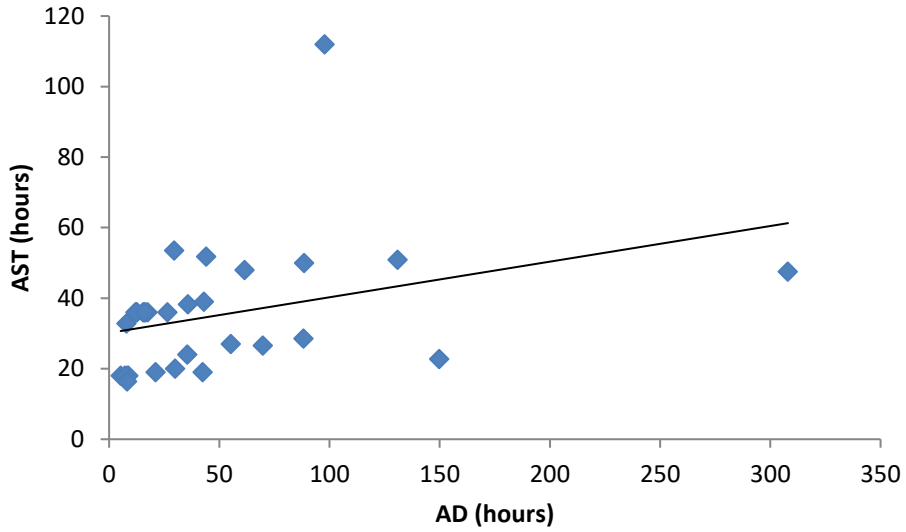
Note: Each point in the figure represents an individual NCA

Figure-81: Average time spent (hours) for each NCA – PRAC



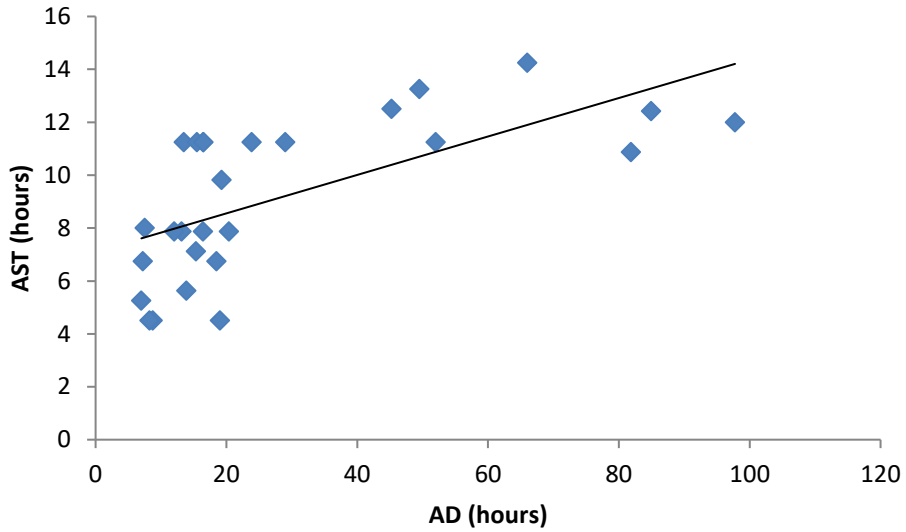
Note: Each point in the figure represents an individual NCA

Figure-82: Adjusted Average time spent (hours) for each NCA – PRAC



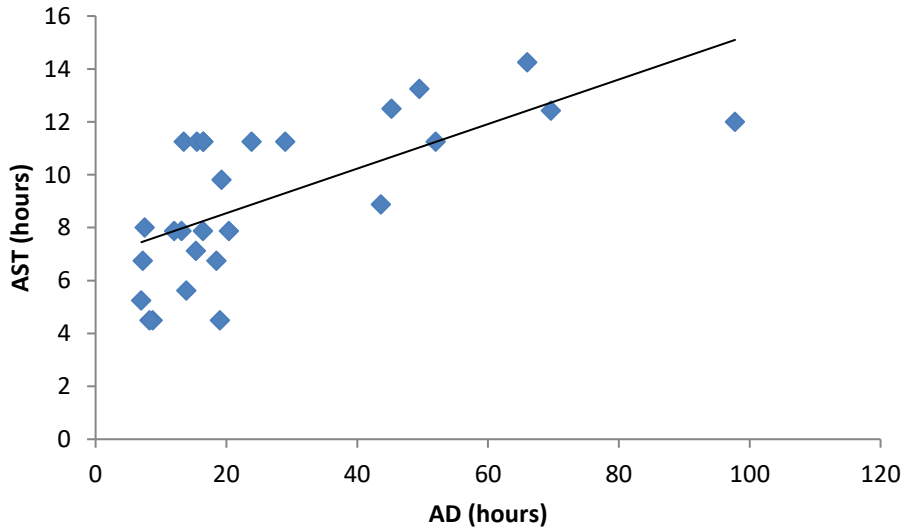
Note: Each point in the figure represents an individual NCA

Figure-83: Average time spent (hours) for each NCA – CAT



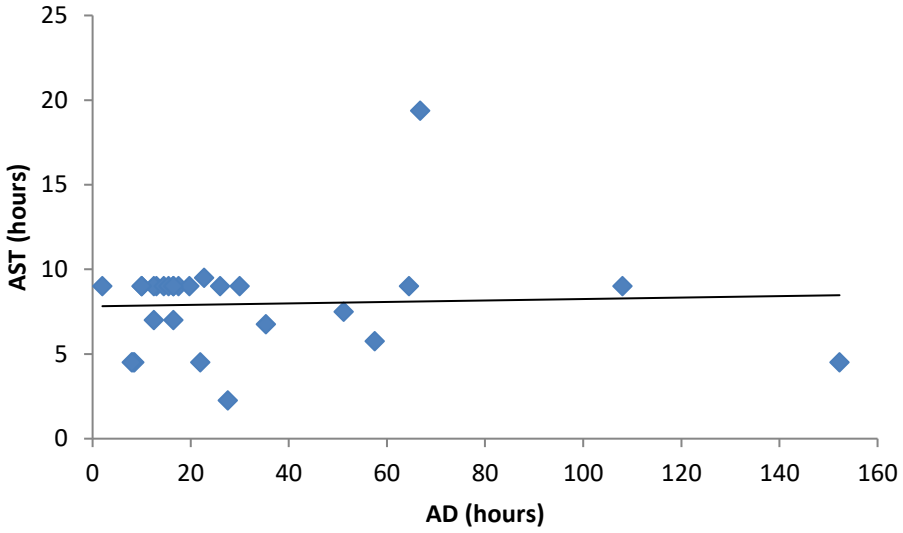
Note: Each point in the figure represents an individual NCA

Figure-84: Adjusted Average time spent (hours) for each NCA – CAT



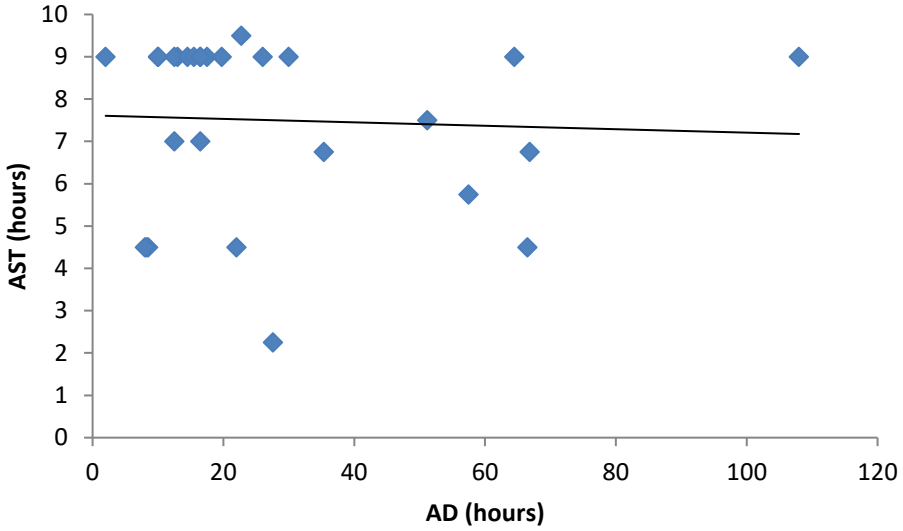
Note: Each point in the figure represents an individual NCA

Figure-85: Average time spent (hours) for each NCA – HMPC



Note: Each point in the figure represents an individual NCA

Figure-86: Adjusted Average time spent (hours) for each NCA – HMPC



Note: Each point in the figure represents an individual NCA

Appendix 12. Data validation – Veterinary medicines activities – Type IB variations

Table-27: Summary table for Type IB variations – MBDG 2016 Report

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
Type IB variations	May '16 – Aug'16	25	0.72	18.60	25	9.79	0.83	3

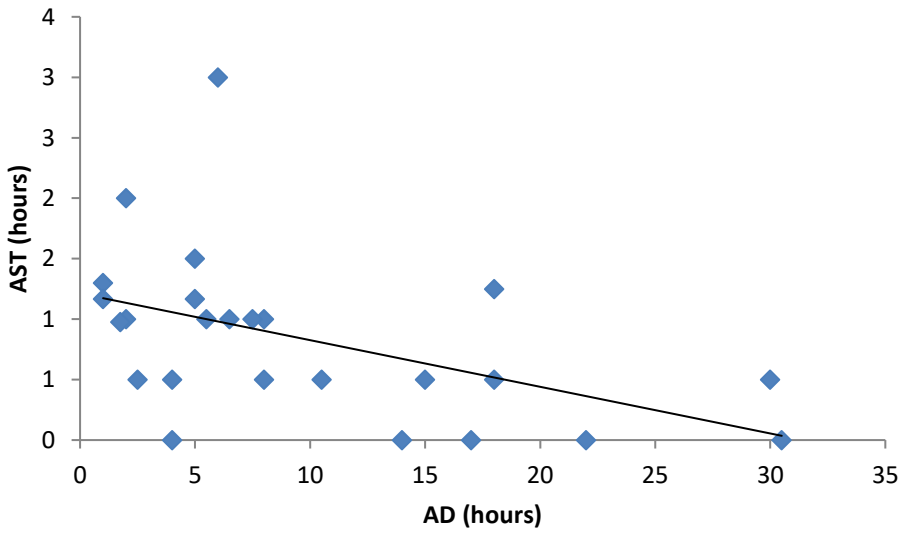
Table-28: Table-of outliers

Product Name	Rap AD	Rap AST
EMEA/V/C/000000/IB/0001	30.00	0.50
EMEA/V/C/000000/IB/0002	6.00	3.00
EMEA/V/C/000000/IB/0003	30.50	0.00

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

Type IB variations: scientific staff (AD) and administrative staff (AST)

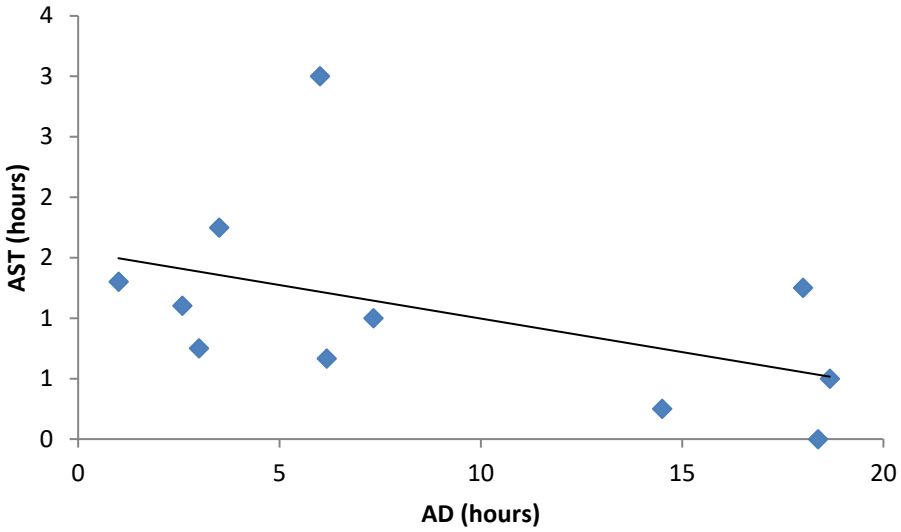
Figure-87: Total time spent (hours) by NCAs - All procedures



Note: Each point in the figure represents an individual procedure

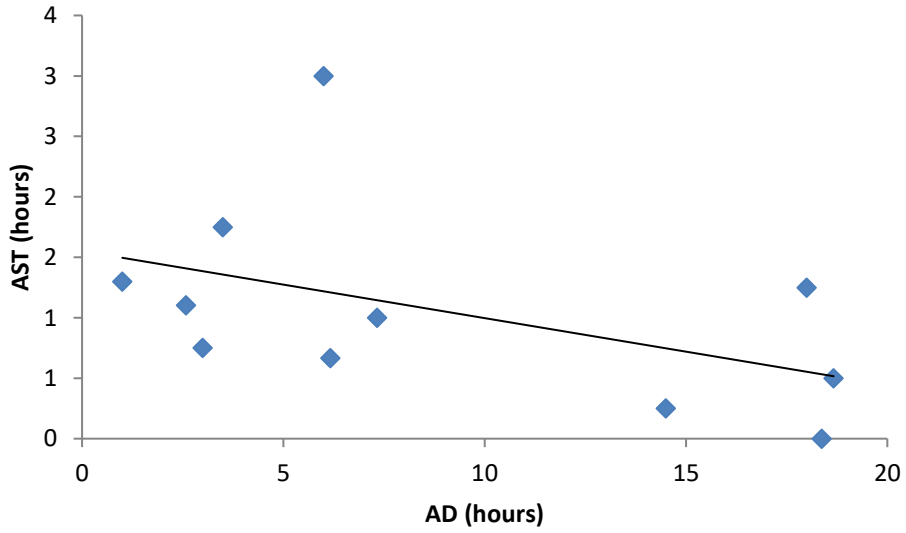
Type IB variations: NCAs scientific staff (AD) and administrative staff (AST)

Figure-88: Average time spent (hours) for each NCA



Note: Each point in the figure represents an individual NCA

Figure-89: Adjusted average time spent (hours) for each NCA



Note: Each point in the figure represents an individual NCA

Appendix 13. Data validation – Veterinary medicines activities – Initial marketing authorisations

Table-29: Summary table for Initial Marketing Authorisations – MBDG 2016 Report

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
New Active Substance	Jan'16 - Sep'16	25	292.23	105.50	25	1196.29	29.84	7
Known Active Substance	Jan'16 - Sep'16	4	265.77	75.44	4	970.13	19.68	-
Generic Application	Jan'16 - Sep'16	6	205.97	85.26	6	427.00	19.34	-

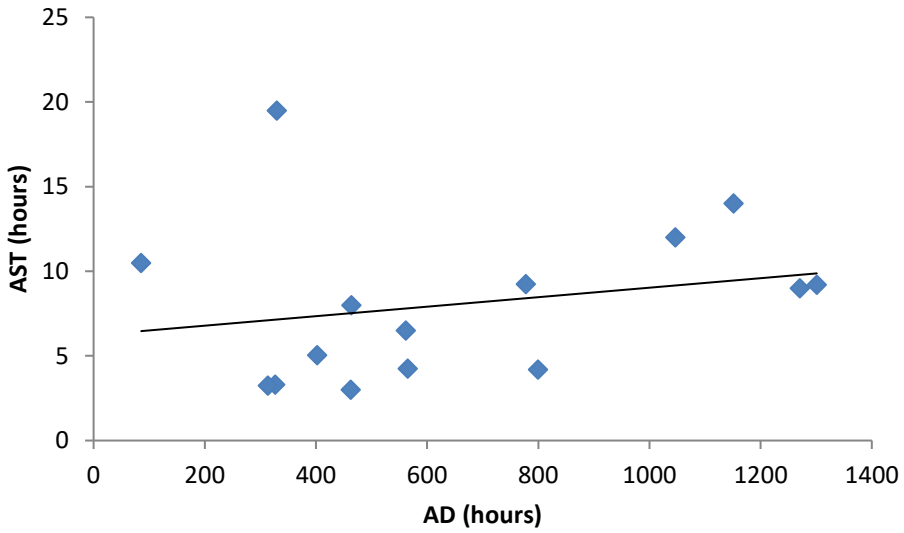
Table-30: Table-of outliers

Type	Proc number	Rap AD	Rap AST	Co-Rap AD	Co-Rap AST
NEW AS - Phase I	EMEA/V/C/000000/0001			544.00	0.00
NEW AS - Phase I	EMEA/V/C/000000/0002	429.00	6.00		
NEW AS - Phase II	EMEA/V/C/000000/0003			160.00	8.00
NEW AS - Phase II	EMEA/V/C/000000/0004			227.00	0.50
NEW AS - Phase III	EMEA/V/C/000000/0005	160.25	29.00		
NEW AS - Phase III	EMEA/V/C/000000/0006			146.75	1.25
NEW AS - Phase III	EMEA/V/C/000000/0007	286.00	0.00		

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

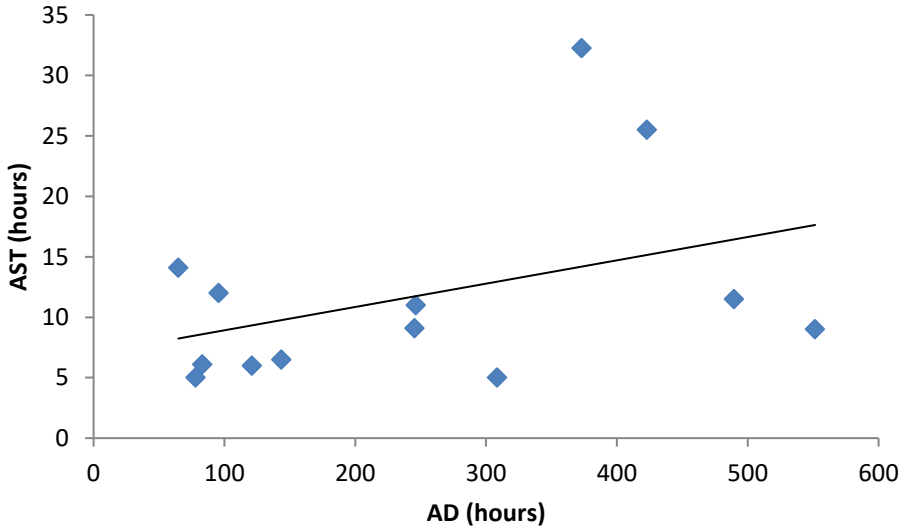
Initial marketing authorisations: scientific staff (AD) and administrative staff (AST)

Figure-90: Total time spent (hours) by NCAs - all procedures in phase 1



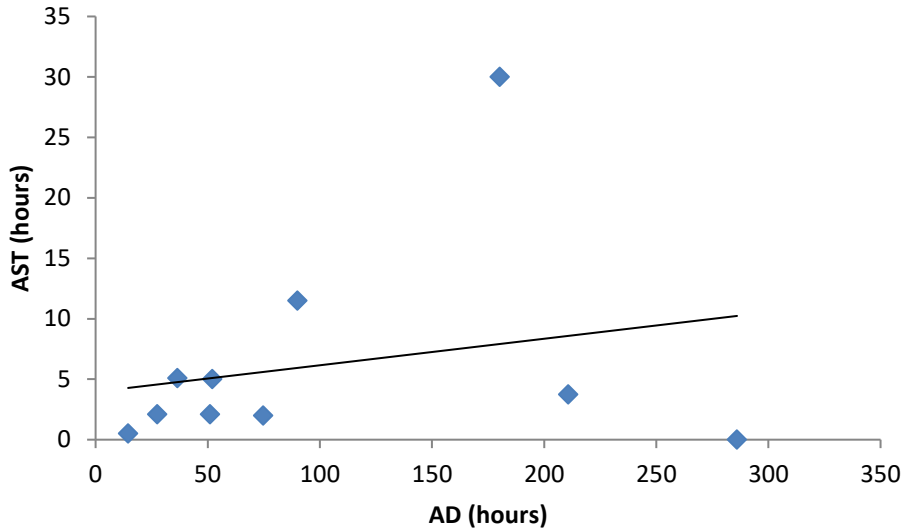
Note: Each point in the figure represents an individual procedure

Figure-91: Total time spent (hours) by NCAs - all procedures in phase 2



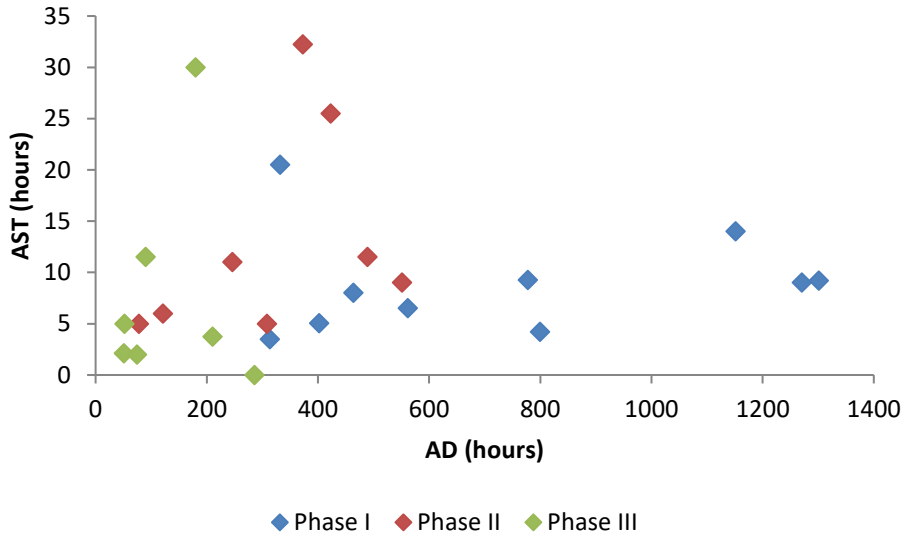
Note: Each point in the figure represents an individual procedure

Figure-92: Total time spent (hours) by NCAs - all procedures in phase 3



Note: Each point in the figure represents an individual procedure

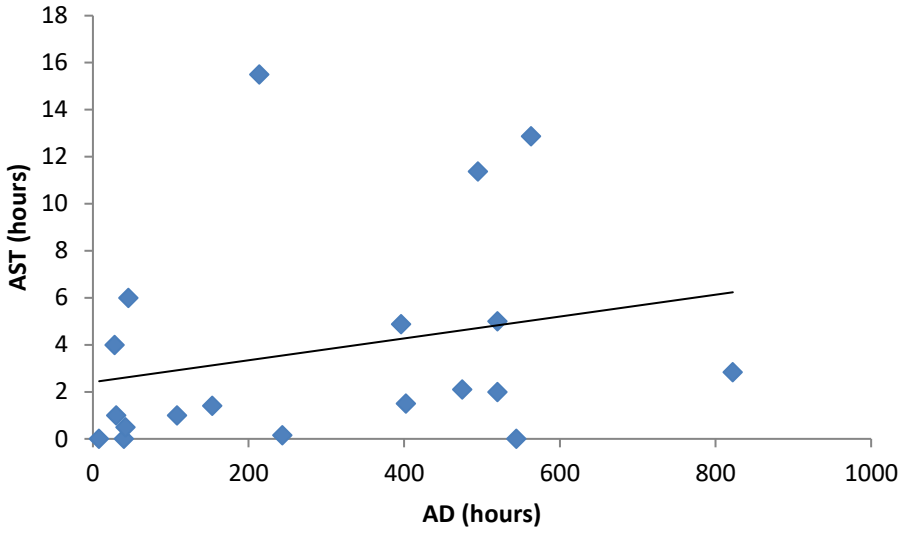
Figure-93: Total time spent (hours) by NCAs – all New Active Substance procedures



Note: Each point in the figure represents an individual procedure

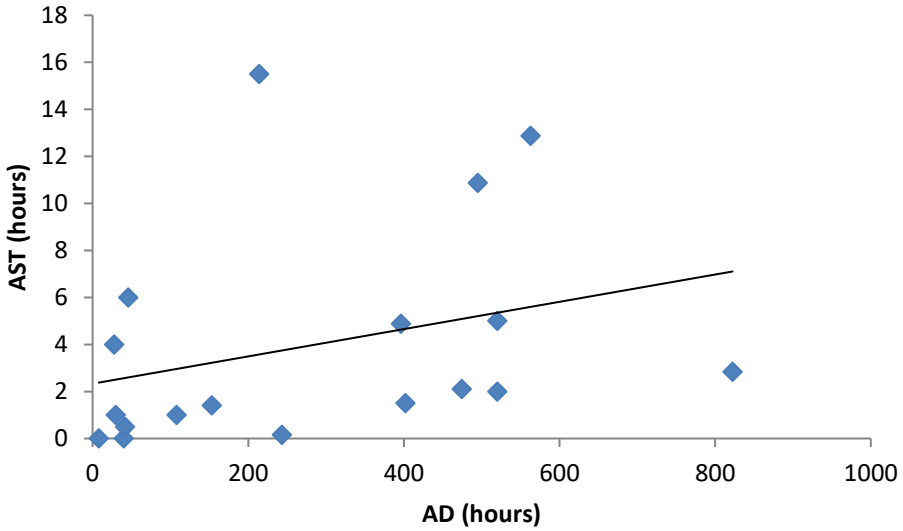
Initial marketing authorisations: NCAs scientific staff (AD) and administrative staff (AST)

Figure-94: Average[39] time spent (hours) for each NCA - All procedures phase 1



Note: Each point in the figure represents an individual NCA

Figure-95: Adjusted[40] average time spent (hours) for each NCA - All procedures phase 1

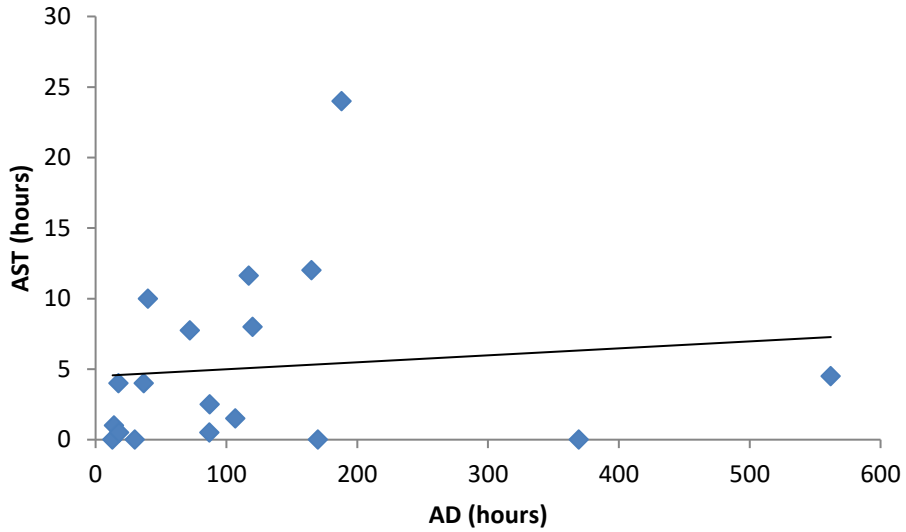


Note: Each point in the figure represents an individual NCA

[39] Average NCA1 = Average of CHMP Rap + Average of CHMP Co-Rap + Average of CHMP Peer Reviewer + Average of PRAC Rap + Average of PRAC Co-Rap

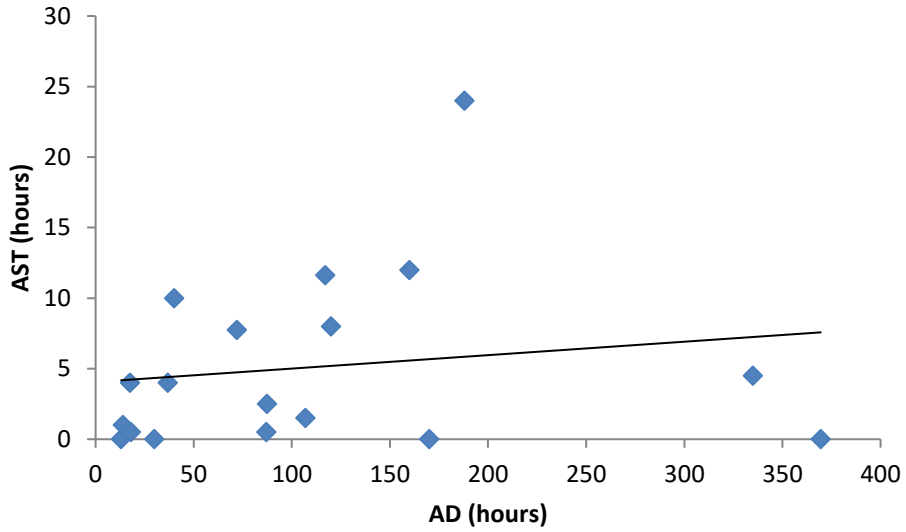
[40] Outliers excluded; outliers are defined as being more than 2 standard deviations from the mean.

Figure-96: Average time spent (hours) for each NCA - All procedures phase 2



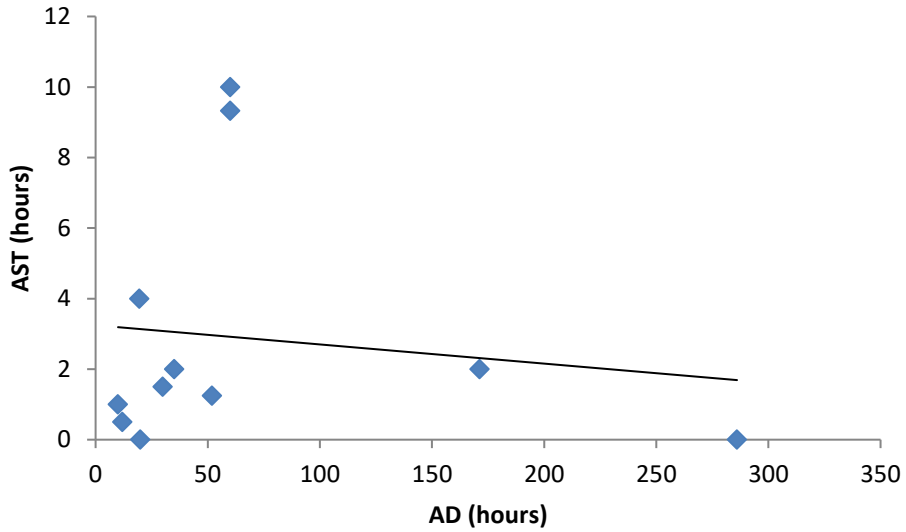
Note: Each point in the figure represents an individual NCA

Figure-97: Adjusted average time spent (hours) for each NCA - All procedures phase 2



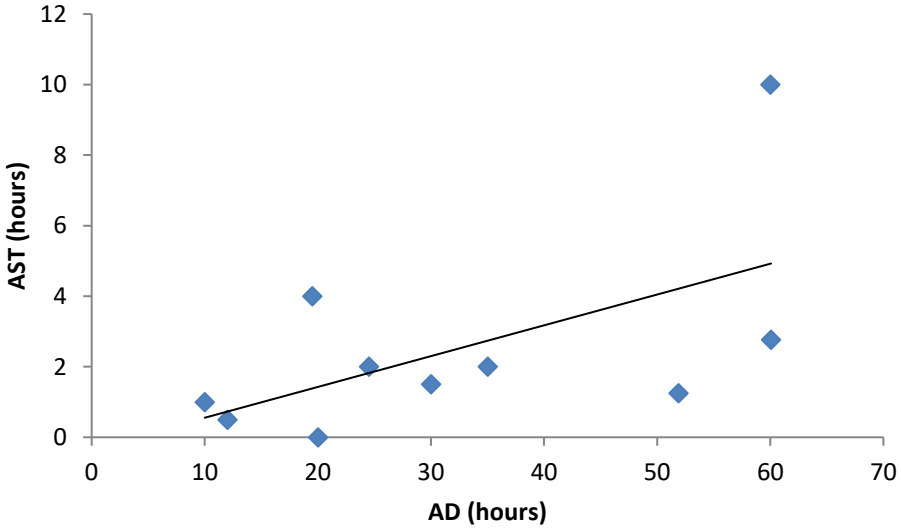
Note: Each point in the figure represents an individual NCA

Figure-98: Average time spent (hours) for each NCA - All procedures phase 3



Note: Each point in the figure represents an individual NCA

Figure-99: Adjusted average time spent (hours) for each NCA - All procedures phase 3



Note: Each point in the figure represents an individual NCA

Appendix 14. Data validation – Veterinary medicines activities – Line Extensions

Table-31: Summary table for line extension - MBDG 2016 Report

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST
Line extension Phase 1	Jan '16 – Nov '16	2	36.77	26.03	2	100.00	5.25
Line extension Phase 2	Jan '16 – Nov '16	2	25.39	13.16	2	56.00	4.38
Line extension Phase 3	Jan '16 – Nov '16	3	53.40	13.37	3	128.83	4.17
Line extension Re-examination	Jan '16 – Nov '16	2	237.27	66.91	2	94.25	0.75

Appendix 15. Data validation – Veterinary medicines activities – Maximum Residual Limit (MRL) applications

Table-32: Summary table for MRL - MBDG 2016 Report

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
MRL Phase 1	Jan '16 – Nov '16	6	65.30	15.53	6	184.58	17.06	1
MRL Phase 2	Jan '16 – Nov '16	3	47.20	7.23	3	41.17	2.57	-
MRL Phase 3	Jan '16 – Nov '16	1	27.42	7.40	1	25.00	0.50	-

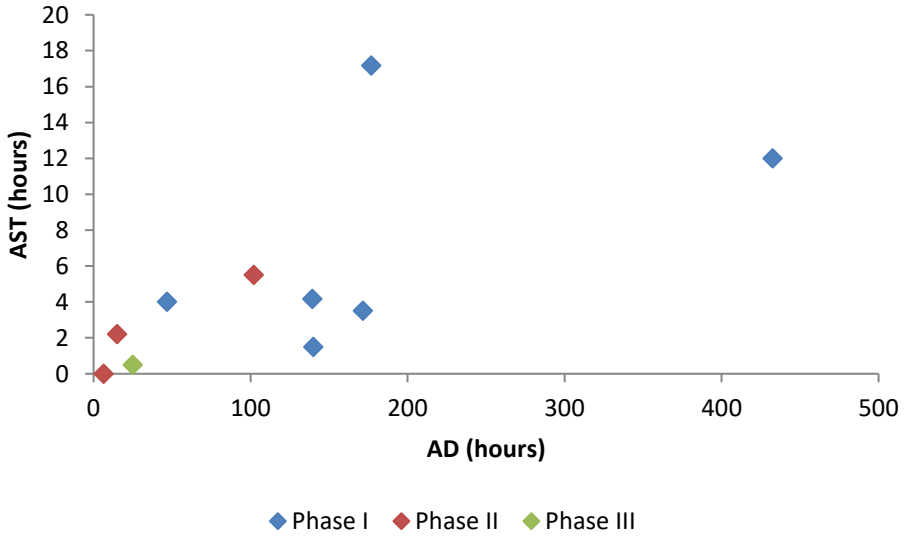
Table-33: Table-of outliers

Proc number	RAP AD	RAP AST
EMEA/X/MRL/00000/FULL/0001	300	7

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

MRL applications: scientific staff (AD) and administrative staff (AST)

Figure-100: Total time spent (hours) by NCAs – all MRL applications



Note: Each point in the figure represents an individual procedure

Appendix 16. Data validation – Veterinary medicines activities – Periodic Safety Update Reports (PSUR)

Table-34: Summary table for PSUR - MBDG 2016 Report

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
PSURs	Jan '16 – Oct '16	46	4.68	9.74	46	9.54	0.61	3

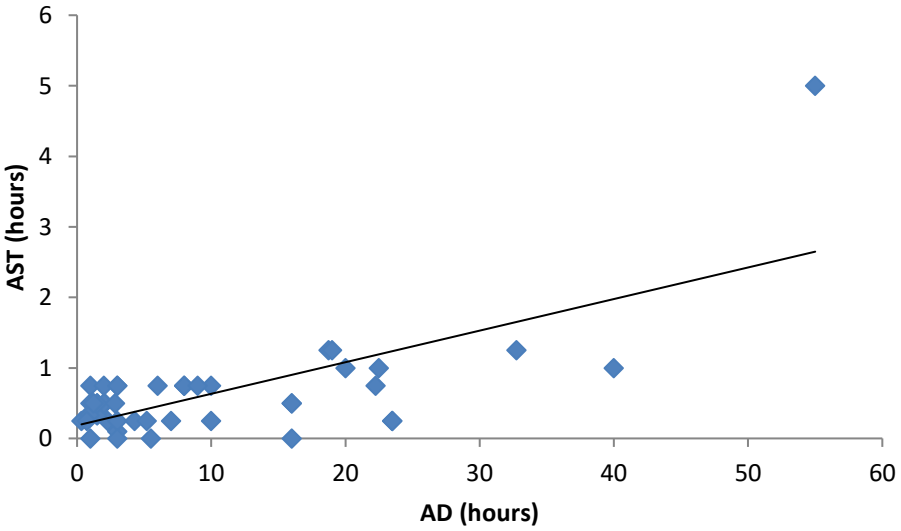
Table-35: Table-of outliers

Proc number	RAP AD	RAP AST
000000001	55.00	5.00
000000002	40.00	1.00

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

PSURs: scientific staff (AD) and administrative staff (AST)

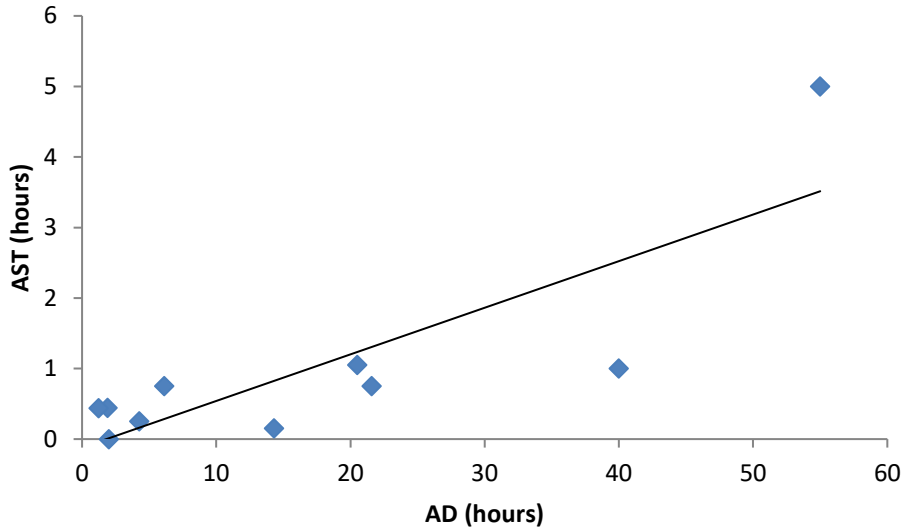
Figure-101: Total time spent (hours) by NCAs - all PSURs



Note: Each point in the figure represents an individual procedure

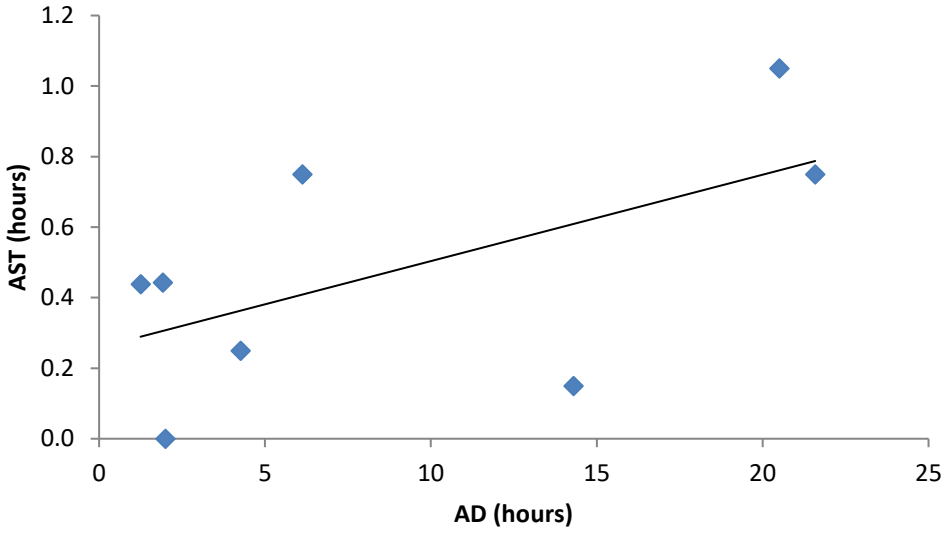
PSURs: NCAs scientific staff (AD) and administrative staff (AST)

Figure-102: Average time spent (hours) for each NCA - All PSURs



Note: Each point in the figure represents an individual NCA

Figure-103: Adjusted Average time spent (hours) for each NCA - All PSURs



Note: Each point in the figure represents an individual NCA

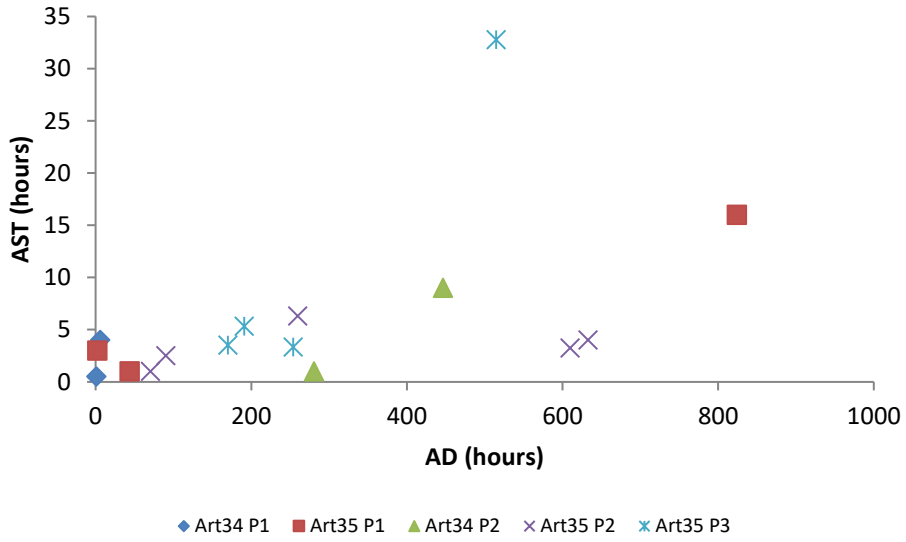
Appendix 17. Data validation – Veterinary medicines activities – Referrals

Table-36: Summary table for Referrals - MBDG 2016 Report

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST
Art 34 – Phase I	Mar '16 – Aug '16	2	67.49	16.55	2	5.00	0.75
Art 34 – Phase II	Mar '16 – Aug '16	2	123.20	11.80	2	363.75	5.00
Art 35 – Phase I	Mar '16 – Aug '16	3	36.78	14.63	3	290.17	6.67
Art 35 – Phase II	Mar '16 – Aug '16	5	73.92	14.05	5	257.75	3.26
Art 35 – Phase III	Mar '16 – Aug '16	4	153.35	27.99	4	282.50	11.23

Referrals: scientific staff (AD) and administrative staff (AST)

Figure-104: Total time spent (hours) by NCAs - all Referrals



Note: Each point in the figure represents an individual procedure

Appendix 18. Data validation – Veterinary medicines activities – Type II Variations

Table-37: Summary table for Type II Variations – MDBG report 2016

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
Quality	Jul '15 – Aug '16	16	11.96	36.94	16	23.38	1.09	3
Clinical	Jul '15 – Aug '16	7	42.41	72.41	7	87.89	2.42	1
Quality/clinical	Jul '15 – Aug '16	3	54.22	65.25	3	205.17	10.67	

Table-38: Table-of outliers

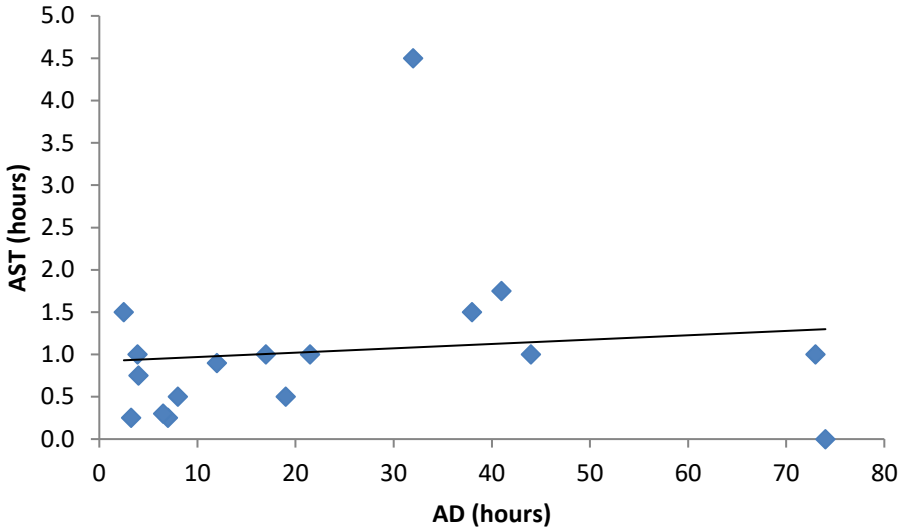
Procedure number	Fee Level	Area of advice	CVMP Rapporteur	CVMP coordinators - AST_1
EMEA/V/C/000000/II/0001/	II	Q	73	1
EMEA/V/C/000000/II/0002/	II	Q	74[41]	0
EMEA/V/C/000000/II/0003/	IV	Q	32	4.5
EMEA/V/C/000000/II/0004/	I	E	301	0.5

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff, and by NCAs. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

[41] Complex, due to the conversion of the dossier in a multristrain dossier and addition of a new serotype at the same time.

Type II variations: scientific staff (AD) and administrative staff (AST)

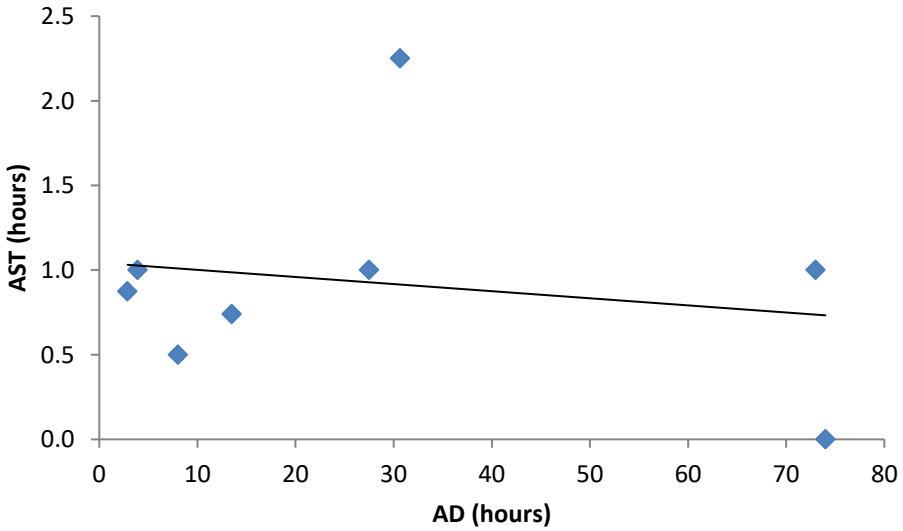
Figure-105: Total time spent (hours) by NCAs – all Quality



Note: Each point in the figure represents an individual procedure

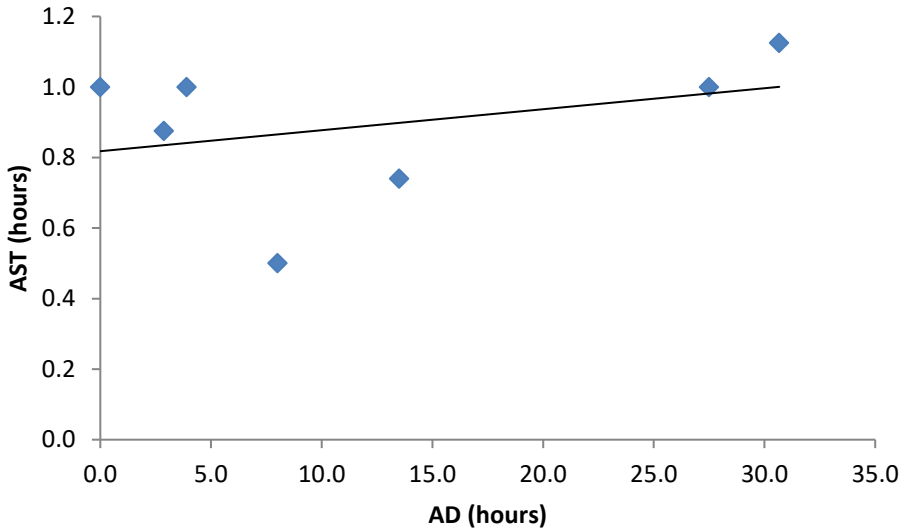
Type II variations: NCAs scientific staff (AD) and administrative staff (AST)

Figure-106: Average time spent (hours) for each NCA – Quality



Note: Each point in the figure represents an individual NCA

Figure-107: Adjusted average time spent (hours) for each NCA – Quality



Note: Each point in the figure represents an individual NCA

Appendix 19. Data validation – Veterinary medicines activities – Scientific Advice

Table-39: Summary table for Scientific Advice – MDBG 2016 Pilot Exercise

	Sampling Period	EMA Sample	EMA AD	EMA AST	NCA Sample	NCA AD	NCA AST	Number of outliers
Scientific Advice Level I	Jul '15 – Apr '16	8	20.08	22.64	8	69.38	0.46	-
Scientific Advice Level II	Jul '15 – Apr '16	6	18.38	21.94	6	61.21	0.76	-
Scientific Advice Level III	Jul '15 – Apr '16	9	19.01	22.36	10	32.33	1.14	1

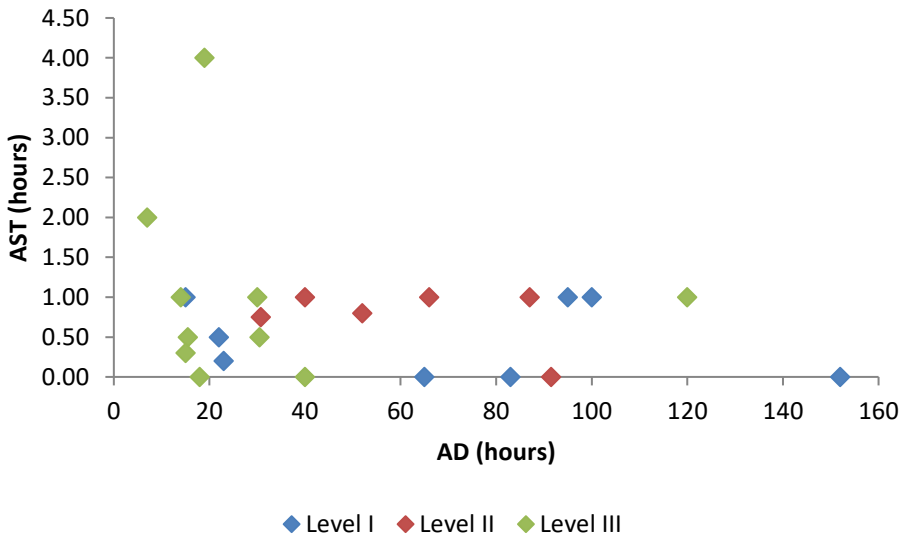
Table-40: Table-of outliers

Procedure number	Complexity Level	Initial vs. followup	NCA scientific	NCA AST
SA-0000-01-I	III	Initial	120.00[42]	1.00

The study team produced scatter plots to compare the allocation of time spent on activities by scientific and administrative staff. Each point in the scatter plots represents the total AD and AST hours for the entire procedure or the average for an individual NCA, therefore while the outliers are related to a specific role in the procedure, the points do not correspond to the outliers reported in the table above.

Scientific Advice: scientific staff (AD) and administrative staff (AST)

Figure-108: Total time spent (hours) by NCAs



Note: Each point in the figure represents an individual procedure

[42] EMA Comments on complexity: Complex long procedure with several discussions at CVMP

Appendix 20. EMA Data Summary and table of outliers

Table-41: Summary table for EMA HUMAN Data - MDBG report 2016

Activity	Sample	Mean AD	Mean AST	Number of outliers
InMA BiosimilarP1	8	112.84	47.84	0
InMA BiosimilarP2	6	61.25	7.14	0
InMA BiosimilarP3	8	101.42	43.91	0
InMA New ASP1	37	164.55	57.54	3
InMA New ASP2	31	87.84	27.14	5
InMA New ASP3	28	168.04	25.16	0
InMA GenericP1	16	73.71	34.60	1
InMA GenericP2	15	53.21	22.22	2
InMA GenericP3	12	62.48	31.53	0
InMA Known ASP1	6	168.15	54.79	0
InMA Known ASP2	1	100.25	5.50	0
InMA Known ASP3	6	144.96	26.58	0
InMA Fixed combin.P1	3	135.25	40.67	0
InMA Fixed combin.P2	2	73.88	7.13	0
InMA Fixed combin.P3	2	179.46	31.88	0
InMA HybridP1	3	103.83	28.14	0
InMA HybridP2	6	90.14	13.71	0
InMA HybridP3	4	122.54	9.69	0
InMA Well-established useP1	2	155.93	45.38	0
InMA Well-established useP2	1	116.66	8.00	0
InMA Well-established useP3	2	392.88	27.75	0
Line extension Phase 1	17	54.21	31.02	2
Line extension Phase 2	10	74.00	22.36	0
Line extension Phase 3	6	44.54	12.56	0
Type II - Clinical	110	8.83	4.45	12
Type II - CI&Q	19	75.70	11.36	1
Type II - CS	135	9.78	4.51	15
Type II - Quality	106	6.60	2.85	10
Type IB - Red	51	0.63	4.19	4
Type IB - Amber	17	1.07	6.43	1
Type IB - Green	24	0.29	4.76	2
Renewals	33	19.77	12.45	3
Initial SA Level I	10	29.00	30.90	1
Initial SA Level II	27	42.90	31.20	6
Initial SA Level III	37	47.20	32.40	2
Follow Up SA – L I	5	30.30	31.60	0
Follow Up SA – L II	18	40.70	31.20	2
Follow Up SA – L III	5	38.40	32.50	0
GMP	7	15.59	0.81	1
GCP	6	56.21	14.62	0

Activity	Sample	Mean AD	Mean AST	Number of outliers
GVP	1	31.10	28.35	0
Paediatrics Compl.Ch.	*14*	*9.36*	*4.23*	*1*
Paediatrics PIP Mod.	*38*	*15.06*	*5.96*	*3*
Paediatrics Waiver	*14*	*15.26*	*7.23*	*2*
Paediatrics New PIP	*32*	*17.81*	*10.68*	*2*
Paediatrics PIP Rest.	*23*	*25.85*	*6.01*	*2*
Orphan Designation	*87*	*21.93*	*9.00*	*3*

Table-42: Table-of outliers for EMA Human Activities

Activity	Type	Procedure	EMA AD	EMA AST
Initial MA	Generic	EMEA/H/C/000000/0001	160.75	34.25
Initial MA	New AS	EMEA/H/C/000000/0002	195.00	223.75
Initial MA	New AS	EMEA/H/C/000000/0003	297.50	40.75
Initial MA	New AS	EMEA/H/C/000000/0004	40.50	85.50
Initial MA	Generic	EMEA/H/C/000000/0005	39.50	79.00
Initial MA	Generic	EMEA/H/C/000000/0006	120.25	28.00
Initial MA	New AS	EMEA/H/C/000000/0007	89.25	98.50
Initial MA	New AS	EMEA/H/C/000000/0008	250.25	6.50
Initial MA	New AS	EMEA/H/C/000000/0009	89.75	105.00
Initial MA	New AS	EMEA/H/C/000000/0010	391.00	37.50
Initial MA	New AS	EMEA/H/C/000000/0011	74.17	64.84
Line Ext - Phase 1	New AS	EMEA/H/C/000000/X/0001	141.75	48.75
Line Ext - Phase 2	Generic	EMEA/H/C/000000/X/0002	112.75	78.25
Type II	C	EMEA/H/C/000000/II/0001	41.75	1.75
Type II	C	EMEA/H/C/000000/II/0002	26.00	12.50
Type II	C	EMEA/H/C/000000/II/0003	30.50	8.25
Type II	C	EMEA/H/C/000000/II/0004	0.50	17.25
Type II	C	EMEA/H/C/000000/II/0005	7.75	19.25
Type II	C	EMEA/H/C/000000/II/0006	24.75	5.50
Type II	C	EMEA/H/C/000000/II/0007	24.50	4.25
Type II	C	EMEA/H/C/000000/II/0008	13.00	11.25
Type II	C	EMEA/H/C/000000/II/0009	30.50	6.00
Type II	C	EMEA/H/C/000000/II/0010	25.25	7.50
Type II	C	EMEA/H/C/000000/II/0011	16.25	14.25
Type II	C	EMEA/H/C/000000/II/0012	26.00	10.00
Type II	CI&Q	EMEA/H/C/000000/II/0013	103.00	49.60
Type II	CS	EMEA/H/C/000000/II/0014	30.75	2.50
Type II	CS	EMEA/H/C/000000/II/0015	28.50	0.25
Type II	CS	EMEA/H/C/000000/II/0016	29.25	2.00
Type II	CS	EMEA/H/C/000000/II/0017	35.00	2.00
Type II	CS	EMEA/H/C/000000/II/0018	24.75	14.50
Type II	CS	EMEA/H/C/000000/II/0019	1.00	16.00

Activity	Type	Procedure	EMA AD	EMA AST
Type II	CS	EMEA/H/C/000000/II/0020	31.75	3.50
Type II	CS	EMEA/H/C/000000/II/0021	27.75	3.75
Type II	CS	EMEA/H/C/000000/II/0022	30.50	4.50
Type II	CS	EMEA/H/C/000000/II/0023	4.75	15.00
Type II	CS	EMEA/H/C/000000/II/0024	4.00	15.75
Type II	CS	EMEA/H/C/000000/II/0025	28.50	14.25
Type II	CS	EMEA/H/C/000000/II/0026	34.50	6.50
Type II	CS	EMEA/H/C/000000/II/0027	34.75	1.00
Type II	CS	EMEA/H/C/000000/II/0028	18.75	10.75
Type II	Q	EMEA/H/C/000000/II/0029	4.50	13.00
Type II	Q	EMEA/H/C/000000/II/0030	27.25	1.75
Type II	Q	EMEA/H/C/000000/II/0031	23.67	2.25
Type II	Q	EMEA/H/C/000000/II/0032	21.25	10.75
Type II	Q	EMEA/H/C/000000/II/0033	4.25	8.00
Type II	Q	EMEA/H/C/000000/II/0034	17.50	6.00
Type II	Q	EMEA/H/C/000000/II/0035	2.50	9.25
Type II	Q	EMEA/H/C/000000/II/0036	18.25	0.50
Type II	Q	EMEA/H/C/000000/II/0037	0.50	15.00
Type II	Q	EMEA/H/C/000000/II/0038	12.75	13.25
Type IB	Red	EMEA/H/C/000000/IB/0001	0.25	11.75
Type IB	Red	EMEA/H/C/000000/IB/0001	0.25	14.25
Type IB	Red	EMEA/H/C/000000/IB/0002	0.25	11.75
Type IB	Red	EMEA/H/C/000000/IB/0003	12.25	4.25
Type IB	Amber	EMEA/H/C/000000/IB/0004	3.75	2.00
Type IB	Green	EMEA/H/C/000000/IB/0005	0.25	16.75
Type IB	Green	EMEA/H/C/000000/IB/0006	0.75	11.25
Renewals	-	EMEA/H/C/000000/R/0001	62.25	7.50
Renewals	-	EMEA/H/C/000000/R/0002	11.00	26.25
Renewals	-	EMEA/H/C/000000/R/0003	29.50	34.50
Paediatrics	Compl. Ch.	HP0000-01	29.86	5.50
Paediatrics	PIP Mod.	HP0000-02	41.36	2.50
Paediatrics	PIP Mod.	HP0000-03	40.61	4.25
Paediatrics	PIP Mod.	HP0000-04		40.00
Paediatrics	Waiver	HP0000-05	57.86	3.00
Paediatrics	Waiver	HP0000-06		25.25
Paediatrics	New PIP	HP0000-07	51.36	10.00
Paediatrics	New PIP	HP0000-08	26.61	129.25
Paediatrics	PIP Rest.	HP0000-09	80.61	7.50
Paediatrics	PIP Rest.	HP0000-10	13.11	47.50
OD	-	H1-OD-001	43.77	6.94
OD	-	H1-OD-002	49.52	10.19
OD	-	H1-OD-003	46.02	9.44
GMP	-	EMEA/V/C/000001	30.19	0.5

Activity	Type	Procedure	EMA AD	EMA AST
Initial SA Level I	-	EMEA/H/SA/000001/I	23.9	36.7
Initial SA Level II	-	EMEA/H/SA/000002/II	87.20	30.20
Initial SA Level II	-	EMEA/H/SA/000004/II	33.70	36.70
Initial SA Level II	-	EMEA/H/SA/000005/II	43.70	35.20
Initial SA Level II	-	EMEA/H/SA/000006/II	41.90	35.00
Initial SA Level II	-	EMEA/H/SA/000007/II	90.20	30.20
Initial SA Level III	-	EMEA/H/SA/000008/II	31.70	42.70
Initial SA Level III	-	EMEA/H/SA/000009/II	90.70	30.20
Follow Up SA – L II	-	EMEA/H/SA/000010/FU	22.20	42.70
Follow Up SA – L II	-	EMEA/H/SA/000011/FU	86.40	30.20

Table-43: Summary table for EMA Veterinary Data - MDBG report 2016

Activity	Sample	Mean AD	Mean AST	Number of outliers
Type IB	25	0.72	18.6	2
MAA ph1 - Generics	2	78.46	45.57	0
MAA ph1 - Known AS	3	115.61	33.2	0
MAA ph1 - New AS	10	95.21	39.54	0
MAA ph2 - Generics	4	57.09	16.88	0
MAA ph2 - Known AS	1	41.84	5.82	0
MAA ph2 - New AS	8	88.7	29.54	0
MAA ph3 - Generics	3	70.42	22.82	0
MAA ph3 - New AS	7	108.32	36.42	0
Line Extensions Ph1	2	36.77	26.03	0
Line Extensions Ph2	2	25.39	13.16	0
Line Extensions Ph3	3	53.4	13.37	0
Line Extensions Re-ex.	2	237.27	66.91	0
MRL Ph1	6	65.3	15.53	0
MRL Ph2	3	47.2	7.23	0
MRL Ph3	1	27.42	7.4	0
PSURs	46	4.68	9.74	3
Art 34 – Phase I	2	67.49	16.55	0
Art 34 – Phase II	2	123.2	11.8	0
Art 35 – Phase I	3	36.78	14.63	0
Art 35 – Phase II	5	73.92	14.05	0
Art 35 – Phase III	4	153.35	27.99	0
Renewal	4	12.75	34	0
Type II - Quality	16	11.96	36.94	1
Type II - Clinical	7	42.41	72.41	0
Type II - Q/E	3	54.22	65.25	0
Scientific Advice Level I	8	20.08	22.64	1
Scientific Advice Level II	6	18.38	21.94	0
Scientific Advice Level III	9	19.01	22.36	1

Table-44: Table-of outliers for EMA Veterinary Activities

Activity	Type	Procedure	EMA AD	EMA AST
Type IB	3	EMEA/V/C/0000001/	7.00	25.5
Type IB	2	EMEA/V/C/0000002/	5.00	36.25
PSURs	-	0001	1.82	11.05
PSURs	-	0002	10.32	10.05
PSURs	-	0003	16.82	9.55
Type II - Q	-	WS0001	35.84	
Scientific Advice Level I	-	SA-000001-I	46.42	23.36
Scientific Advice Level III	-	SA-000002-I	35.67	23.86

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