10 October 2013
EMA/171117/2013
Veterinary Medicines Division

Overview of comments received on draft ESVAC reflection paper on collecting data on consumption of antimicrobial agents per animal species, on technical units of measurement and indicators for reporting consumption of antimicrobial agents in animals (EMA/286416/2012)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1	Pig Veterinary Society (UK)
2	LEI, part of Wageningen University and Research centre.
3	National Food institute, Technological University of Denmark.
4	Lic Zootechnie, BE
5	The Netherlands Veterinary Medicines Authority (SDa), Utrecht, The Netherlands.The Expert panel of the SDa
6	National Farmers Union of Scotland
7	FVE – Federation of Veterinarians of Europe
8	Ministry of Agriculture and Forestry, Finnish Food safety Authority (Evira), Finnish Medicines Agency (Fimea)
9	International Federation for Animal Health – Europe (IFAH-Europe)
10	IFIP - The French Institute for Pig and Pork industry
11	European farmers and European Agri-cooperatives (COPA-COGECA)
12	European Group for Generic Veterinary Products (EGGVP)
13	Bundesinstitut für Risikobewertung

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1. General comments – overview

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1	If primary aim is to measure use in animals, this data can only be collected at farm level. Veterinarians prescribe and supply but have no control over wastage (broken bottles, contaminated bottles, discards beyond 30 day breaching of bottles etc.) or of overestimates of expected usage – especially relevant to in feed medication supplied in compound feed. If data is to be collected it must be as accurate as possible.	The terms of reference from the European Commission request the ESVAC to collect estimates of consumption by species. Because of the variations in the already existing data collection systems established in the various MSs, it is agreed that the MSs should be allowed to select which data source they collect the data from as long as it provides reliable estimates. Data collection at the farm or veterinary level is the preferred methods and the closest to the actual use. However, the amount of delivered but not consumed antimicrobial agents is believed to be minimal in relation to the total consumption and therefore data collection based on delivery data or prescription data is considered to be relevant as well.
4	I welcome the initiative taken to collect data on the consumption of antibiotics. One should however not forget that there are already tools in place that may help you further. One of these tools is the Food Chain Information (FCI) that is in place since a couple of years in several Member States and provides help in both indication and use of several species. An link is provided to the EFSA "Scientific Opinion on the public health hazards to be covered by inspection of meat (poultry)" pointing out were the FCI can be most useful http://www.efsa.europa.eu/en/efsajournal/doc/2741.pdf Follows for your information parts of their abstract. Strengths identified were that Food Chain Information (FCI), as part of ante-mortem inspection, provides information related to disease	Thanks for the proposal. Regulation (EC) No 853/2004, Annex II, Section III, Point 3c indicates: "(c) veterinary medicinal products or other treatments administered to the animals within a relevant period and with a withdrawal period greater than zero, together with their dates of administration and withdrawal periods;" It is not required to e.g. give the dose and number of days at treatment and thus the data cannot be used to estimate the consumption, in weight of active ingredient. Moreover, relevant period is not standardised and might be defined differently by MSs. For broiler production this relevant period might be the whole production cycle whereas for other production systems it certainly is not the case.

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	occurrence during rearing and veterinary treatments, enabling a focused ante-mortem inspection on flocks with animal health concerns. In conclusion, for biological hazards it was assessed that a wider, more systematic and better focused use of the FCI will have positive impact on control of the main public health hazards associated with poultry meat. A series of recommendations were made regarding biological hazards on data collection…, and needs for research on optimal ways to use FCI and approaches for assessing the public health benefits.	Therefore this system would not allow complete data collection.
5	The Netherlands Veterinary Medicines Authority (SDa) wishes to congratulate the ESVAC drafting group for the very good quality of the reflection paper on consumption of antimicrobial agents. It provides a well-balanced overview of the different methods and purposes for collection of consumption data. It includes an analysis of strengths and weaknesses of different approaches chosen and facilitates a choice to be made for risk managers for a 'best' fitting system of data collection. The SDa fully endorses the choice of the Animal Defined Daily Dosage (or DDDA as used by ESVAC) is the unit of measurement of choice to quantify usage of antibiotics and exposure of animals to these drugs. Besides some minor comments on this reflection paper and a few suggestions for improvement to consider our major comments are aimed at the lack of harmonisation of both the numerator and the denominator for the calculation of the ADDD. We will provide more detailed comments on these topics below and provide suggestions for improvement. The SDa has the opinion that with regards to standardized quantification of antimicrobial usage on farms, there is no	Thanks for the support. Differences between the different data collection systems are shown in Table 2 of the reflection paper. The main

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	fundamental difference between cross-sectional, prospective or continuous data collection on farms. This is a matter of study design, but does not really affect the quantity that one wants to measure. It may change the time basis or averaging time over which one measure the DDD, and this element could be emphasized instead of the different study designs and contexts. We understand that for specific epidemiological studies additional data on usage can be important to collect. However, that is the responsibility of the individual research group and this does not require standardization and is not a matter of routine surveillance. Differences with regard to research and routine surveillance could also be emphasized.	difference between the study designs is the representativeness of data obtained. Thanks for the comment. Data for the assignment of DDDA and DCDA will not be collected at farm level but from the Summary of Products Characteristics (SPC).
	A general comment of Prof. dr. Johan Mouton, who is chair of the CRG in The Netherlands and actively involved in EUCAST. This reflection paper on the consumption of antimicrobial agents is of good quality, and is an important step in standardization and harmonization of approaches, terms and definitions across Europe. He made a few comments that may help to further improve the paper. These refer to definitions in particular. Importantly, across Europe, there should be a unified method of measurement; otherwise results will never make any sense. In that respect, ADDD is a good start. However, the main problem is exactly how these will be determined, what factors are taken into account and when this will be finalized. In the Netherlands we are currently evaluating and defining such a system (actually there is one, but is now being evaluated and validated, including rationale documents providing the background of the ADDD values). Such a harmonisation is of paramount importance; otherwise, as stated conclusions make no sense.	Thanks for the comment. Guidance on how to assign DDDA and DCDA will be developed as a next step.

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	Likewise, the definitions of numerator and denominator need to be very clear. Again, with agreement across Europe this will not make much sense. To compare with the EUCAST in the human antimicrobial arena, comparing resistance percentages between countries for resistance rates makes no sense at all if every country uses different breakpoints. Now that harmonisation is well on its way, the surveillance data are of much higher quality and decisions can be made on a more rational basis.	Thanks for the comment but this is outside the scope of this reflection paper.
6	NFU Scotland welcomes the opportunity to respond to this reflection paper on collecting data on consumption of antimicrobial agents by animals. Antimicrobial resistance is a growing concern within the medical profession and whilst the level of contribution from the veterinary sector remains unclear, the livestock sector recognises the need for clear data and strategies from all sectors to be able to tackle resistance.	Thanks for the support.
6	Any programme of data collection must deliver reliable, accurate information that is fit for purpose and meaningful. If data is to be used centrally across all Member States then it is vital that the data is consistent and comparable across those Member States. At the same time the system of data collection must be practical and cost effective with buy-in from those responsible for gathering and reporting the data. The more labour intensive the data collection process the greater chance for incomplete and inaccurate reports.	Accepted.
6	NFUS believes that since within the UK all veterinary antimicrobial products require a prescription this could provide a mechanism for monitoring the veterinary use of antimicrobial products. This may not entirely reflect the level of actually administered product but as a baseline it would still provide valuable information if recorded centrally with details relating to the type, class and number of	Thanks for the comment but because of the variations in the already existing data collection systems established in the various MSs, it is agreed that the MSs should be allowed to select which data source they collect the data from as long as it provides reliable estimates. We agree that data collection based on delivery data or prescription data may

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	animals the prescription covered. A basic cost effective system that could be used across Member States could: • Focus on a group of sentinel farms • Select farms to represent core production systems • Group antimicrobials based on shared pharmacological activity • Record on central database; system, number of livestock units, number of antimicrobial interventions, group of products used, volume of product used. • Recording should be at farm-gate level through veterinary dispensary or prescriptions issued.	provide relevant and reliable information.
6	Farmers do keep complete medicine records on farm but they are not recorded centrally. To use these records keepers would either need to start recording the data centrally or they would need to be gathered through on farm visits. Either of these options would be labouring intensive and unpopular and without some level of incentive they would be unlikely to get buy in and support. Keepers would be unwilling to get involved and there would be considerable bias involved in those choosing to volunteer unless there was incentive to do so.	See previous comments.
6	To deliver progress in recording system development and to optimise antimicrobial intervention the Commission must be proactive in supporting on farm activity. Pillar two CAP funding should be made available to incentivise the central recording of farm data, i.e. biological performance, episodes of disease, health status and both antimicrobial and vaccination interventions, as the foundation of	Thanks for the comment but this is outside the scope of the reflection paper.

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	science based progress. Benchmarking health performance in a standardised format can open the door to targeted system development and can demonstrate optimal therapeutic interventions that can provide templates for wider use.	
6	The paper proposes that through surveillance of antimicrobial consumption by animal species greater understanding of the development and occurrence of resistance can be gathered. It is not clear how this can be obtained simply through looking at the use of antimicrobials. Data on antimicrobial resistance must be gathered separately through veterinary feedback and sampling, not simply from looking at the amount of product used.	These proposals are part of the introduction which contains general considerations and not recommendations on collecting data by species for ESVAC. It is acknowledged that other factors may influence resistance development. The European Commission taking into account EFSA advice, has implemented an EU wide resistance data collection system. The consumption data at species level as proposed will provide very valuable information for the interpretation of the resistance data.
6	Data should be used to inform new veterinary strategies, it can also drive targeted system development by pinpointing areas where performance is suboptimal. NFUS has some concerns that the paper appears to already assume the data will be used to drive targeted intervention measures, such as legislative restrictions on use and setting targets for reduced consumption. The role veterinary antimicrobials play in human antimicrobial resistance remains unclear and without the proper data, this report seeks to gather, it is premature to be making such assumptions.	Thanks for the comment. ESVAC will collect data and maintain a database on consumption by species. It is for the MSs to decide how they will use the data at national level. The draft reflection paper line 137-143 gives examples on how data on consumption of antimicrobial agents can be used. These proposals are part of the introduction which contains general considerations and not on collecting data by species as such.
6	Antimicrobial products are vital for animal health, as they are for human health, and any strategy to tackle the problem of resistance must be based on sound science, not 'knee-jerk' reactions and using the precautionary principle as a regulatory base. This data gathering exercise, if carried out effectively, stands to deliver valuable data which, when combined with the proper science will aid development	These proposals are part of the introduction which contains general considerations and not on collecting data by species as such. The intention of the ESVAC project is precisely to gather data for risk analysis. The draft reflection paper, lines 137-143, gives examples on how data on consumption of antimicrobial agents can be used.

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	of targeted strategies, strategies which can only be developed once the data has been considered.	
7	FVE welcomes and support the development of a European wide system for monitoring the consumption of antimicrobials in Europe. Although we are very pleased with this effort, we would like to express some further points for consideration. - The system to be developed should be simple, reliable, and robust - The system should be practical and easy to use by farmers or veterinarians; - In not every country the veterinary practice regularly is automatized. A new system should also have a non-digital format. - Prescription and distribution mechanisms are different in the European countries. Therefore in order to be able to first receive and then analyze the data different systems will be required in practice, in the different EU countries. - In some EU countries, veterinarian is not the only one qualified profession to provide antimicrobials i.e. French integrators in agriculture, UK para vets/technicians, etc. The system should ensure that all channels in the country are included in the data collection system. - Monitoring of the consumption data on medicated feed shall be included in the system. - Internet pharmacies already exist in certain EU countries. The system shall ensure that data from Internet sales of the veterinary medicinal products are collected as well.	Accepted. Accepted. See previous comments. Accepted. This is why every country will have to develop a data collection system adapted to the local situation. Accepted. This is why every country will have to develop a data collection system adapted to the local situation. Thanks for the comment. It is “automatically” included in the ATCvet codes in Table 5 but will be highlighted in the revised reflection paper Thanks for the comment but the aim for the reflection paper is not to describe how to collect sales data but data on consumption at farm level or from veterinarians. Throughout the EU veterinary antimicrobials agents are prescription only. Therefore, for every sold antimicrobial there should be at least a prescription which can be used as a source of information. All legal sales of veterinary antimicrobial agents

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		should be covered by the proposed systems of collection of data.
	- The system shall respect data protection according to the national law of each EU country.	Accepted
	- There is obviously muddled thinking about species in this document. This needs to be expressed clearly and accurately to avoid causing confusion and rendering the data less useful. For instance, different species of poultry (domestic chickens, turkeys, geese, ducks …) may be kept under very different forms of husbandry with different antimicrobial needs and uses.	Accepted. This is clarified in Table 4 of the reflection paper but will be highlighted throughout the document as appropriate.
	- Although FVE agrees on poultry, pigs, and cattle being the first target groups of species to be monitored, the system shall soon be extended and include other ones like horses, small ruminants, fish and companion animals.	Accepted.
	- The impact of the use of antimicrobials both in humans as in animals on the development of antimicrobial resistance to both human and animal side shall be appropriately assessed (by using the same breakpoints) in the different EU countries.	Thanks for the comment this is outside the scope of the reflection paper.
8	We welcome the initiative by the European Commission to collect data on the consumption of veterinary antimicrobials by animal species. Furthermore, we appreciate the effort the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project has done in preparing the draft reflection paper.	Thanks for the support.
	Finland would like to express its willingness to participate the pilot project. We are currently developing a system to collect data on the actual use of antimicrobials in pig and cattle herds and poultry flocks. The data will cover the animal species, age groups and indications.	Accepted.
	We consider it very important to build up our national system to be compatible with the ESVAC system. Therefore, Finland suggests that	Thanks for the comment. We agree that consumption data in relation to indications are very valuable for national use

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	also data collection at indication level could be considered to be included in the ESVAC project to provide that possibility for the countries able and willing to collect such data.	and support each country that is able and willing to collect such detailed data for use at national level.
9	IFAH-Europe welcomes the opportunity to comment on this reflection paper. This document is complex to understand and it includes major issues whose resolution is not yet determined (*i.e*. "detailed protocol on how to standardize the assignment of DDDAs and DCDAs should be developed"). In this respect, we would welcome work on the harmonization of these units of measurement per species across Europe at the earliest opportunity, at least for the countries involved in the pilot study.	Thanks for the comment. See previous comments.
9	**Electronic Data collection**: The electronic collection of data at the farm level is advised by the reflection paper as the preferred method. Whilst this would be ideal and continuous automated data collection is already in place or under development in some countries (i.e. Belgium, Denmark, Finland, Netherlands, Norway and Sweden); care must be taken with a wider implementation to ensure cost efficiency. Steps should also be taken to ensure the quality of the data collected and a uniform interpretation of the data to be entered.	Thanks for the comment. Note that this is acknowledged in lines 75-78 in the draft reflection paper
9	**Units of Measurement:** The report proposes using the concept of defined daily doses for animals (DDDAs) as one unit of measurement. Whilst the equivalent is used in the human equivalent ESAC, there are a number of issues with DDDAs: • There are differences in terms of dosing amongst the SPCs across Europe; using an average DDDA for all of Europe is a compromise that needs to be checked against reality to	Thanks for the comment. This is also the case for DDDs used in human medicine that is an international accepted system for the analysis and reporting of consumption data.

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	ensure valid comparisons between countries.	See previous comments
	• DDDAs (and DCDAs) make the assumption that products are used in accordance with the SPC and as acknowledged in the reflection paper this is not always the case.	Thanks for the comment. DDDA and DCDA are technical units of measurement only (a compromise) and are not regarded as the real daily dose and cure dose used.
	• DDDAs were created to account for the differences in potency between different products of the same class, but they do not adjust for the differences in duration.	Thanks for the comment. This is the reason why is proposed to use the defined course dose (DCDA) which takes into account the treatment duration.
	• It is questionable to advise the collection of data at the farm level which would allow the use of PDDA or UDDAs and then merge the data into DDDAs. IFAH-Europe would prefer the use of PDDDAs or UDDDAs.	Thanks for the comment. In human medicine an identical unit of measurement is used and ESVAC is asked to harmonize with ESAC-Net. DCDA will be used in addition to DDDA. Used daily dose animal (UDDA) is a unit to express the real dose administered in the observed animals it is not possible to standardise this unit across EU. This is also the case for prescribed daily dose animal (PDDA). Nevertheless, countries that are willing and able to collect more detailed data are encouraged to do so since this will provide them with valuable insights.
	The other proposed measure of consumption is the DCDA. The use of the DCDA compensates for some of the problems arising from the use of DDDAs and is therefore a good measure to use that should be the leading indicator. It may be argued that the number of exposures (DCDAs) is more relevant than duration of exposure (DDDAs) but it is probably premature to say which measure is more relevant for antibiotic resistance.	Thanks for the comment. Both DDDA and DCDA are of interest and provide different information. It cannot be determined which one is more important than the other and therefore there is no leading indicator.

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9	**Comparison of data with Humans:** Data on human and animal usage should not be "compared" but analysed. There is no relation between the antibiotic requirements of a broiler during its lifespan of 40 days and that of a human over their lifespan. The paper correctly mentions that these data are ratios with a numerator and a denominator. When the denominators are so different direct comparisons are fraught with difficulties and are not justifiable. Data collection in the veterinary sector should not be driven by a wish to make comparisons with the human sector but rather should be fit for purpose.	Accepted. It is changed to "analysed" together with data from human medicine.
9	**Species data to be collected:** We agree that priority should be given to pigs and poultry. With regards to cattle, we would suggest focussing on veal, given the low consumption of antibiotics in the dairy and beef sectors. However, it is important that the collection is eventually done for all species produced in the EU to ensure we have a full picture.	Accepted. If there is a need to make further priorities this will be taken into account when developing project.
9	**Animal Live Weights:** The live weights proposed for use are debatable. For instance, the proposed weight for pig weaners is 7kg; the range for this production type is normally 7-20 kg. Likewise for finishers the proposed weight is 35 kg whereas the range is normally 20-110 kg. See also the proposals in the specific comments section.	Accepted. The weights are revised according to the comments received (see table in revised reflection paper) For the calculation of the number of DDDA's based on the amount of antimicrobial agents used (nominator) for a group of animals (denominator) an average weight at treatment needs to be determined. A range would not be possible. Therefore a compromise average at treatment is proposed in the Table 4 in the revised reflection paper.
9	**Groups of therapeutic products to be included:** IFAH-Europe agrees with the proposed groups to be included.	
9	**Combination Products:**	

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	This proposal appears to count a combination as several treatments by the individual active ingredients. This will artificially increase the general exposure although it more accurately indicates exposure to an individual active ingredient. The argument that each active ingredient should be followed individually is open to debate as with a combination product there should be a synergistic effect resulting in the better control of resistance.	Thanks for the comment. A combination product exerts a selection pressure by each of the ingredient includes and may also select for multi-resistant strains. Therefore it is sensible to count exposure to each of the antimicrobial agents included in a combination product.
9	**Long Acting products:** It is unclear how DDDAs should be defined for long acting products. There is insufficient evidence for differential selection pressures associated with various durations of activity, which would vary by antibiotic and bacterial species. DCDAs are to be preferred.	Thanks for the comment. Will be addressed when developing the guidance on how to assign DDDA and DCDA. We would argue that there is insufficient understanding rather than insufficient proof of the difference of selection pressure associated with various durations of activity. Therefore it is of interest to include the treatment duration as a relevant variable.
9	**Pilot Project:** IFAH-Europe agrees with the principle of a pilot project. However, costs need to be controlled.	Accepted.
9	**Contextual Data:** It is important that contextual data (*e.g.* disease prevalence, major changes to farming practices) are collected in order to allow the interpretation of changes in antibiotic usage.	Thanks for the comment, but is not the aim of ESVAC to collect those data. When reporting the data by ESVAC such interpretation will have to be provided by the MSs based on national data. Member States that are able and willing to collect this data as well as data on indications of use for their own analysis are encouraged to do so.
11	Improving antimicrobial use requires transparency and responsibility among all key stakeholders along the food chain, including farmers. Copa-Cogeca welcomes ESVAC's aim to establish a system for	

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	collection of reliable and standardised data on consumption of antimicrobial agents by animal species.	
	2. Copa-Cogeca believes that this system of collection of data should be done in a practical and cost-effective manner which, in the end, can deliver reliable and accurate information both on the use of antimicrobials and on antimicrobial resistance across all EU Member States.	Accepted
	3. Public authorities play an important role to implement strict but practical programmes to monitor antimicrobial use and resistance. They should be able to carry out checks and suppress illegal practices when necessary.	Thanks for the comment but this is outside the scope of the reflection paper
	4. Given that some EU countries have not yet put in place effective monitoring and surveillance programmes, Copa-Cogeca believes it is necessary to encourage every Member State to do so. It is particularly important that monitoring programmes are developed in line with national surveillance programmes, involving control authorities, farmers' organisations, veterinarians and the pharmaceutical industry in their development. This would help to reduce additional costs at farm level and to prevent abusive use of products.	Accepted. Thanks for the comment but the involvement of the different stakeholders is a matter within the MSs.
	5. It is of paramount importance to have a harmonised system for collecting data from all EU Member States, given that this constitutes the first step towards accurate risk assessment on the use of antimicrobials. If the objectives and expected outcomes were harmonised, the tools for achieving such results might be better targeted to the characteristics of individual Member States (e.g. production systems).	See previous comments.

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	6. Copa-Cogeca believes that the collection of information for epidemiological surveillance of antimicrobial use should be carried out on a more aggregated level, between veterinarians and pharmacists, within each Member State.	Thanks for the comment but veterinary antimicrobial agents are dispensed by pharmacies in only a few countries therefore the reflection paper focuses on collection of data on farms or veterinarians. In those countries where distribution through pharmacists is important this should be included in the data collection system as relevant.
	Given that a veterinary prescription is a precondition for antimicrobial use at farm level, Copa-Cogeca believes that veterinarians and pharmacists should play a key role in providing relevant information for the official monitoring programme at Member State level.	See previous comments.
	Aggregated data collection would preserve a certain degree of data accuracy and would facilitate a risk assessment procedure across EU Member States.	Accepted.
	7. Farmers are, however, obliged to record all treatments on farm in order to facilitate evaluation and allow for possible adjustments to future treatments. Copa-Cogeca believes however that this information should be made available only for on-farm controls.	Thanks for the comment but this is outside the scope of this reflection paper.
	8. Copa-Cogeca considers that information provided on antimicrobial use at farm level must be treated confidentially and only made available upon official request. Consequent trade restrictions must be avoided.	Thanks for the comment but ESVAC will not collect data from individual farms but aggregated by species and year. Confidentiality policy is therefore a matter between each MS and the farmers and/or veterinarians
12	EGGVP welcomes this reflection paper and supports and encourages the work of ESVAC on the species and dose related issues, as those contribute to reach the ultimate goal which is obtaining real data on use (attitudes and practices) in the field of veterinary antimicrobials.	Thanks for the support.

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	EGGVP believes that the collection of sales data at the level of the MAH or distributor is too limited (many factors needed to interpret data correctly and to make conclusions on use by animal owners / farmers and on how prudently veterinarians prescribe antimicrobials) and it should not be seen as an indicator of use. Sales data can be however very valuable for other purposes (e.g. validation) and thus EGGVP supports its collection because, in combination with other data, it improves transparency and is a fundamental step to perform risk assessment.	
13	Overall, the reflection paper provides a good starting point for harmonization of the data collection on antimicrobial use in livestock. The approach of running a pilot followed by a baseline survey is welcome as this approach provides the basis for a realistic system that is already partially established in the MS when routine collection is meant to commence. However, from a risk assessment perspective a number of questions remain. For example, the inclusion of animal species in the priority list needs to be refined. Throughout the document it should be clarified that the 'animal species' 'poultry' includes broilers and turkeys and that data need to be recorded and analysed separately for the two species. There is some inconsistency throughout the document as to whether the data should be recorded, stored and provided from all farms or a subset only. This needs clarification. Furthermore, the word 'surveillance' should be replaced by	Thanks for the support. Thanks for the comment but methodology/use of the data for risk assessment is not the aim of the reflection paper Thanks for the comment. The reference to poultry is clarified in the revised reflection paper. Thanks for the comment but it depends on the methodology used for the monitoring at MS level – i.e. whether data are collected from all farms/veterinarians or a selection of farms/veterinarians. MSs will decide the most convenient system to implement. Thanks for the comment but surveillance is used in ESVAC in

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	'monitoring' as defined by directive 2003/99/EC. Surveillance should only be used, if immediate action is planned which is not the case in this situation. From our national experience, we would recommend to focus on or at least to implement an additional technical unit of measurement 'number of applications' and indicator 'number of UDDs per 1000 animals' which reflects from our experience most valid the real consumption patterns and which is comparable across animal species, age groups, regions and years.	order to harmonise with terms applied by the counterpart in human medicine – i.e. ESAC-Net at ECDC Nonetheless we agree with the comment and regret the confusing terminology. This is addressed in the revised reflection paper. See previous comments. Used daily dose animal (UDDA) is a unit to express the real dose administered in the observed animals it is not possible to standardise this unit across EU. However countries that want to go more in detail and collect the necessary data to calculate the UDDA as well for use at national level are encouraged to do so.

2. Specific comments on text

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
Line 351	1	Comment: DDDA PDDA will be very inaccurate due to wide variation in dose rates applied both under SPCs (many Abs have different dosages for different disease treatments) and by veterinarians under cascade provisions. Greatest inaccuracy is in in-feed. Also tendency to overdose very young pigs due to small volumes needed. Single bottle supplied can be prescribed for use in more than one class of pigs on a farm.	Thanks for the comment these proposals are part of the introduction which contains general considerations. As mentioned before, as a next step guidelines will be developed on how to establish an overall DDDA list. Similar to human medicine the DDDA (or DCDA) are technical units of measurement and should not be considered as a “correct dose” but as a compromise.
Lines 439-445	1	Comment: Agree with in principle but be aware many farmers are still not computer literate/ do not have internet connections; still major problems in rural areas of UK with broadband supply and mobile telephone networks.	See previous comments.
Line 481		Comment: weights need to be expressed as ranges but within the categories listed there are vast ranges E.g. piglets 1.5 kg -8 kg Weaners 8-30 kg Finishers 30-100 kg (or even greater within European markets e.g. 150 kg in Italy) Adults 130-300 kg (more for mature boars) If using a single weight figure for each class this will need to be a median or average figure – not the lightest weight in the class.	See previous comments and the revised Table 4 in the revised reflection paper.

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Line 492	1	Comment: Be aware that some Abs will be used to cover more than one condition within a population e.g. Tylosin is active against Mycoplasma (respiratory/systemic) and Lawsonia (Intestinal).	Thanks for the comment but this is out of scope for the reflection paper.
Lines 499-440	1	Comment: On farm usage is highly variable especially re in feed AB use which provides majority of total use. Great care is required in extrapolation with many different farm types, sizes and health status/standard.	Accepted. The draft reflection paper already addresses the issue of representativeness, but is highlighted in the revised reflection paper.
Line 519	1	Comment: Continuous data collection from 100% of users is the only way to achieve accurate figures of national use. Any other method can only be an estimate and risks error. This is critically important if regulation/restriction follows.	Thanks for the comment. We agree that collection of data of 100% of users is the preferred system but do not agree that this is the only way to achieve accurate figures and it may not be possible for all countries to implement this.
Line 593	1	Comment: Practical issues; With in-water medication with continuous flow, duration of treatment can be prolonged with ever decreasing dilution rate. In feed – for one off treatments, un-medicated feed is often added to feed bin before medicated feed has finished. As bins empty from the centre, progressive dilution occurs extending treatment periods.	Thanks for the comment but this is outside the scope for the reflection paper.
Line 609	1	Comment: See comments above re weight ranges within categories.	See previous comments and revised Table 4 in the revised reflection paper.
Line 644	1	Comment: See comments 351 above re variability of SPC dose rates for single products.	Thanks for the comment but similar to human medicine the DDDA (or DCDA) are technical units of measurement and

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
			should not be considered as a “correct dose” but as a compromise.
Line 688	1	Comment: Sales do not equal use.	Accepted.
Line 709	1	Comment: To repeat comments above, variability within SPCs for dose and duration plus individual VS variation in prescribing practice make DDDA and DCDA assumptions very unreliable.	See previous comment.
Lines 75-83	2	It is important to take into account all relevant pro’s and con’s of population data versus sample surveys. Detailed comments: 1) Regarding representativeness and accuracy: A sample survey has a possible problem: selection bias. However, to reduce bias, random sampling can be used. Extrapolation from sample to population always implies an estimation error (sampling error). Through stratified sampling, as in the Farm Accountancy Data Network (FADN) sample survey, the sampling error can be reduced. In the Netherlands LEI Wageningen UR monitored veterinary antibiotic use for the national government, using the existing FADN network, which led to valuable use data on species level. These experiences during more than 10 years of monitoring might be used in other EU countries as well. 2) Regarding quality of the data - If the registration for a central database has a legal basis, then the data quality will be guaranteed, to	See previous comment. Thanks for the comment. Each MS will develop its data collection system in agreement with the local situation and

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		some extent. This legal basis should apply for all crucial data, i.e., both the animal numbers and the antibiotic use data. However, still population data may also contain errors and inaccuracies, e.g. errors in unit (gram-milligram), errors in animal numbers. - In a sample survey, data quality is generally higher. Especially when the FADN system is used. The FADN researchers know all farms in the sample, and they can easily check if registration errors occur. - In a sample survey you run the risk of having a bias, especially when the majority of participants are farmers with low antibiotic use. However, this risk is much lower if the collection of antibiotic use data is only a small part of the sample survey, as it is in the FADN monitoring in the Netherlands.	the available data sources. We agree that avoiding bias and assuring accurate data is of paramount importance as mentioned several places in the reflection paper.
		3) Regarding possibilities for further research, relating use data to other data: - The FADN sample makes it possible to relate the antibiotic use data to other socio-economic and sustainability indicators (e.g., farm size, income, feed price, animal welfare etc.). This connection is important for further investigation, for example, to understand the impact of reduction of antibiotic use on production costs and the farmers' income, or the reasons for the medicine use.	Thanks for the comment but this is out of scope for the reflection paper.
		4) Regarding other advantages - Central registration enables governmental supervision on every individual farm and veterinarian,	Thanks for the comment but this is out of scope for the reflection paper.

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		and it offers considerable opportunities for benchmarking. - Sample surveys are valuable to validate and verify the central database's data. 5) Regarding costs of the surveillance: - Costs of central registration are substantially higher than costs of sample survey, especially if the sample survey can be based on existing FADN infrastructure - Central database with use data can also be used for sample surveys.	Thanks for the comment, but this is already described in the reflection paper.
Line 75-83	2	In our opinion, the ideal situation is central data collection from farmers' or veterinarians' records, combined with a high quality sample survey, preferably using the FADN infrastructure.	See previous comments.
Lines 266-267	2	The reflection paper suggests a stratification of overall national sales data to gain insight into the use on species level. This is probably the most economical of all options. However, it will be difficult to collect reliable use data per species, unless use data per species are available from high quality sample surveys.	Thanks for the comment this is also described in the reflection paper.
Line 479	2	Comments regarding Table 4: The assumptions for the weights at treatment probably remain rough estimates, because the true weights will differ between countries and may also fluctuate through time. It is recommended that ESVAC makes clear what general assumptions were used to estimate the weights at treatment. Furthermore, it is	Accepted. See previous comments and Table 4 in the revised reflection paper.

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		recommended that ESVAC not only mentions the name of the animal category and the proposed weight at treatment (e.g. “meat cattle (beef)” and “500 kg”), but also clearly indicates the corresponding production period, age and start/end weight (e.g., for meat cattle (beef): birth weight 45 kg to slaughter weight of 650 kg at 18 months). Detailed comments: - Piglets 2 kg. Estimated average weight is 4 or 5 kg, because the piglets grow from approximately 1.5 kg to about 8 kg at weaning. However, the much lower estimated weight of 2 kg is justifiable; if the general assumption is that the animals receive treatment mostly in the first part of the period. - Weaners 7 kg. In the Netherlands, the weight at weaning is even higher than 7 kg (about 8 kg). Estimated average weight is 16 or 17 kg because the weaners grow from approximately 8 kg to about 25 kg (or even 30 kg) at delivering to the finishing farm. - Sows bears 220 kg: OK. - Finishers 35 kg. Estimated average weight is 70 kg because the fattening pigs grow from approximately 25 kg to about 110-115 kg at delivering to the slaughter house. In Denmark an average of 50 kg is used, which is probably closer to the average weight during treatment. - Veal 170 kg: this is average weight of veal calves. However, from the sample survey in the Netherlands, we know that the true weight at treatment is much	See previous comments.

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		lower. Bondt et al (PVM paper, 2012) assume 86 kg for (white) veal calves, as average weight during treatment (http://dx.doi.org/10.1016/j.prevetmed.2012.07.009)! The now proposed high weight of 170 kg for veal calves is inconsistent with the much lower weights that are assumed for pigs. - Dairy 500 kg: low weight for an average dairy cow in the Netherlands, but possibly OK as an EU average. However, for beef cattle, an average weight of 200 or 300 kg would be more logical. - Broilers 1 kg: OK. This was the true average weight and also average weight at treatment in the Netherlands for many years, but in the last few years, the weight at treatment has dropped to approximately 0.7 kg. This makes clear that any estimate remains unsure, might differ between countries and might considerably fluctuate through time. - Turkey 10 kg: quite low as an average weight. However, the same comment as for veal calves: an estimated weight at treatment of 5 or 6 kg seems more logical, and more consistent with the assumed low weights for pigs.	
Lines 171-172	3	Comment: A differentiation between prevalence and incidence is given. However, the two examples given are both amount prescribed for a population (subpopulation) of animals within a given time period (the first example being a year or life production cycle?). Thus, both examples are incidence estimates.	Accepted, in both cases the incidence of treatments are estimated. This has been modified in the reflection paper as follows: *"Such estimates may either refer to all animals at risk, regardless of when they started to use the antimicrobial*

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		Proposed change (if any):	*agents or focus on animals that were given antimicrobial agents within a defined period. The collection of data is most meaningful when they form part of a continuous evaluation system"*
Lines 177-183	3	Comment: Full national surveillance data are not needed for research in the association between antimicrobial use and resistance (line 177-181). However, national data on species level are necessary to determine resistance containment strategies, i.e. evaluate the expected outcome from the regulation of antimicrobial use, as a support to decision makers (related to statement, line 181-183) Proposed change (if any):	Thanks for the comment but it does not read that full national surveillance data are needed for research
Lines 306	3	Comment: Some products for parenteral use are approved only for pet animals (specifically Convenia). Such products should be considered used in pet animals Proposed change: the data on overall sales are split into products which are almost solely used in pets (including tablets and products approved for use in pets only) and all other pharmaceutical forms that are mainly used in food producing animals.	Thanks for the comment. This refers to a methodology used in the current ESVAC data collection at national level and is not the focus of this paper where the data collection at animal species level is discussed. See previous comments.
Lines 347-350	3	For a specific formulation and active compound, the approved dose may vary considerably between products (depending on the company, approved indication and time of approval). It is therefore important that the DDDA is defined for the formulation	Accepted. Guidance on how to determine DDDA and DCDA will be developed as the next step.

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		and active compound, NOT individually for the specific product.	
Line 360-64	3	It is important to clearly define “population at risk” as one of the following: 1) In principle all domestic animals are “at risk” (of becoming sick and being treated) – Thus, the population at risk may be the (biomass of) all domestic animals. This is in parallel to what is used in human pharmaco-epidemiology (inhabitant-days)	Thanks for the comment but no disagreement is identified. It is important that the population at risk is defined at the same level as the data collection is performed. If data are collected at the national level the total numbers of animals in a country are to be used as the population at risk. If the treatment data are collected at herd level the number of animals in the herds (if necessary further subdivided in the different production stages) included in the study is to be taken as the population at risk.
		2) Population “at risk” may be defined as the number of animals or biomass of the age-groups that are frequently treated (e.g. weaning pigs). This would correspond to the measure “per bed-days”. However, it underestimates the total population at risk.	Thanks for the comment but all animals are in principle at risk but some have a higher risk.
		3) Weight of animals slaughtered/dead. This is a proxy for the population, which may be used to measure changes in population (production). It is not a measure of the population size, because it does not take into account the lifespan of the animals. Therefore it underestimates the population size of long-lived subpopulations (e.g. humans, pets and	Thanks for the comment but this part describes systems currently in use in MSs.

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		dairy cows) and overestimates the population of slaughter pigs and particularly of poultry. It is not statistically robust for comparison of selection pressure between populations, but may be used to follow trends in selection pressure within meat production.	
Line 364	3	The wording “stable” may refer either to the collection of data or whether the measure is statistically robust (i.e. not imposing bias into the analysis, when changes in the population occurs)	Thanks for the comment; it refers to statistically robust.
Line 386	3	Batches and flocks also represent a production cycle, so why do you mention this as something different from a production cycle?	Thanks for the comment; we have made a change in the text accordingly.
Line 409-412	3	It is important in this type of study to be aware that there may be important seasonal variation in the AM use. Thus, using just one production cycle in one season will create bias.	Accepted
Line 438	3	Farms with continuous electronic data collection may not be representative to all farms, i.e. this method may cause selection bias.	The automated data collection systems referred to here is a nationwide data collection system and not a system only implemented in a selection of the farms. This has been clarified in the revised reflection paper: “If **nationwide** automated data collection systems…”
Line 468	3	EFSA also monitor resistance in turkey. As the resistance level in turkey is generally very high, it is important to monitor the use in turkeys as well.	Accepted. (Poultry includes turkeys).

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Line 479, Table 4	3	Weight of weaners: 7 kg is the approximate weight at weaning, but they are on average treated at a much higher weight (between the weights of 7 kg at 4 weeks to 30 kg at 11-12 weeks of age). Assuming that they are treated the first two weeks only, would give an average weight of treatment at app.12 kg. However, it must be decided whether the biomass should represent all animals at risk (app 18 kg/pig for weaners) or the average weight at treatment (somewhere between 10-19 kg depending on the treatment incidence in the weaning-pig-population). As the latter varies significantly between countries, I believe it is better to use the total population at risk (i.e. for weaners the average weight of all weaner pigs= app. 18 kg). In accordance, the “total population at risk” seems to be the suggested measure for broilers and turkey in Table 4. Regarding veal calves: it is necessary to differentiate between two populations (production types): 170 kg can be used as the average weight (of total population at risk) in the “young beef” production. As opposed, the veal calves in NL are slaughtered at app. 160 kg, thus the average weight is around 80 kg. As mentioned, “total population at risk” is the measure used in human pharmaco-epidemiology:	See previous comments and Table 4 in the revised reflection paper.
Line 572	3	“the animal population at risk of being treated” :	Thanks for the comment. This terminology refers to the group

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		again, any domestic animal is at risk (cf. comment to line 360-62). The only exception is risk of treatment with specific products aimed at specific age groups, e.g. Intramammary devices or dosage pumps for piglets.	of animals where the consumption data are collected. This will be taken into account when reporting the data
Line 607 and line 677	3	Yes, the standard dose should be defined for active ingredient and formulation. Note: as the dose the daily maintenance dose, the dosage should be calculated depending on the frequency of treatment within a cure: i.e. meant for products that are given twice a day, the standard dose equals two singular doses. Correspondingly, for products with prolonged effect, the standard dose should be calculated as the singular dose divided by number of days with clinical effect of one dose.	Thanks for the comments. Guidance on how to assign the technical units of measurement will be developed as a next step
Line 632	3	Mg active ingredient sold per 1000 animals *within production type/species*	Accepted.
Line 125	4	Comment: All use of antimicrobial agents …promotes the selection and dissemination This statement is too broad and lacks proof that all antimicrobial agents will do this Proposed change (if any): The use of antimicrobial agents …may promote the selection	Thanks for the comment but the proposed sentence is too weak.
Line 130	4	Comment: direct contact from animal to animal keeper and from person to person	Accepted.

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		Proposed change (if any): add: through direct contact, the food chain…	
Line 133	4	Comment: reducing unnecessary use: unfortunately nowhere in the rest of the document “unnecessary use” is been explained, nor tackled. The proposal is therefor to add “indications” to the parameters to be taken in the collection of the data Proposed change (if any):add indications to the parameters on antibiotic use	Thanks for the comment. At this stage, the collection of data on the indications is not a requirement; the MSs will need to decide if they want to collect such data. Countries that are willing and able to collect this information in an accurate and standardized way are encouraged to do so.
Line 249	4	Comment: Table 1 gives an overview of different data in different European countries. However it should be mentioned that some of these 30 countries are not member of the E.U.	Noted.
Line 266	4	Comment: table 2: data collected cross sectional studies and prospective studies …from logbook, on-farm documents, etc. although enclosed in the etc. a major document available is the FCI Food Chain Information document that should be present at every slaughtering Proposed change (if any): add Food Chain Information document	Thanks for the comment but this part describes current systems in place in various MSs.
Line 297-298	4	Comment: Not only the variation can be detected between herds but also the use patterns and preference of the prescribing veterinarian, the broiler integration e.g. and not the least emerging diseases if	Thanks for the comment but this is out of scope of the reflection paper.

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		combined with the indication for use	
Lines 299-303	4	Comment: However, such studies are usually expensive and time consuming and as a result information on only a sample of the herds is obtained. Often the sampled herds are selected based on the willingness of the 300 farmer to cooperate and inherently include the risk of bias. The Food Chain Information document these data are readily available for the entire life in case of broilers (poultry for fattening) and the last 2 months for fattening pigs. Collection of these data cost about one man day per 5 million broilers	See previous comments.
Lines 382-407	4	Comment: again the use of the existing document FCI has been overlooked	Thanks for the comment but this part describes current systems in place in various MSs.
Lines 417-419	4	Comment: “Unless the data are collected continuously, prospective longitudinal studies should usually be conducted in a selected number of study farms that are representative for the study region in order to minimise the workload” If done in a farm that is “representative for the study region” the chances are that one may miss seasonal influences, farmer and veterinary preferences and disease incidences in neighbouring farms. This variation may lead to misinterpretation of the data when generalizing towards the region.	Thanks for the comment but the issue of representativeness is addressed in the reflection paper.
Lines 421-	4	Comment: Missing in this is the accurate data provided	Thanks for the comment. At this stage, the collection of data

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423		by the identified prescribing veterinarian and the indication for the therapy. Proposed change (if any): add prescribing veterinarian and disease indication	on the indications is not a requirement; the MSs will need to decide if they want to collect such data. Countries that are willing and able to collect this information in an accurate and standardized way are encouraged to do so. Collection of data from veterinarians is now highlighted in the revised reflection paper.
Line 450	4	Comment: made for each country depending on the distribution system for antimicrobial agents… Proposed change (if any): add; including the antimicrobials administered in the feed	Accepted.
Lines 459-460	4	Comment: in order draw valid conclusions one should crosscheck with other available data that are species and indication specific, such as pig pumps, intrauterine boluses, intramammaries… Proposed change (if any): the data need to be crosschecked with other available data such as sales figures on specific target species related/ registered products	Accepted.
Line 467	4	Comment: poultry (Gallus gallus) is too broad and should be divided up in subcategories, broilers, replacement pullets layers and breeders. Of those broilers (chickens for fattening) is most likely to be a “heavy” user. Similarly in pigs weaned piglets and growers are likely to be “heavy” users Proposed change (if any): divided by species subcategories like chickens for fattening, suckling piglets, weaned piglets…as can be found in the technical guidance on tolerance and efficacy studies in target animals of EFSA; appendix B. http://www.efsa.europa.eu/en/efsajournal/pub/2175.h	Accepted. See previous comments

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Lines 476-477 table 4	4	Comment: within the Member States, there might be a great variation in animal production category, e.g. Bacon pigs UK end weight 70 kg Italian fattening pigs up to 170 kg life weight chickens for fattening 5 weeks (Germany) to 20 weeks for "label rouge" France. Turkeys can range from 6 kg life weight to 10 kg for the hens and 16 kg for the toms. Further the age group and proposed reference weight in the table does not correspond with the appendix B "Categories and definitions of target animals" and should be made uniform. Proposed change (if any):bring in accordance with the common practice and present legislation	See previous comments and Table 4 in the revised reflection paper. One common average weight at treatment valid for all EU countries needs to be established for each production stage.
Lines 490-491 table 5	4	Comment: intestinal use: oral route instead of intestinal use? Proposed change (if any): oral route or intestinal disorders	Thanks for the comments but these terms are used in the ATCvet system applied by ESVAC and harmonized with ESAC-Net (ATC system).
Lines 506-507 table 6	4	Comment: under item 2 data to collect on each farm, since in country or EU registration numbers are unique, would it not be wise to mention the registration number also? Under item 6 animal species and age. Missing in this is the indication for the use of the antimicrobial agent, the start and end date of the antimicrobial use, the birth date of the animals. Under item 8 animal weights at treatment. For animals of different age and weight this may induce a variation. E.g. fattening pigs from 40 to 80 kg that	Thanks for the comment but this is a list of minimum set of variables needed to provide the data to ESVAC. The MSs are encouraged to collect information of e.g. indication for use at the national level See previous comments.

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		have to be group treated via the feed or water. Item 9 daily dose, it will be better to calculate the daily dose from the amount of product given, the animal weight, and the nb of animals treated. Item 10 number of days treated can be calculated from the difference between end date minus start date. Proposed change (if any): include the data that are readily available at farm level and calculate from it the daily doses. The indication for the use of the antimicrobial is a very valuable parameter that has to be taken into account for further follow up investigations and decisions.	Thanks for the comment but data for the assignment of DDDA and DCDA will not be collected at farm level but from Special Products Characteristics. See previous comments.
Line 516	4	Comment: non inclusion of indications Proposed change (if any): If possible include them.	See previous comments.
Line 544	4	Comment: figure 1 - no of treatments x amount used… this is ok for individual treatment regimens (parenteral dosage, pig pump, bolus) but mass medication by feed or water treatment (major antimicrobial use) cannot be made this way. - - Amount sold in tons per age group. Is the amount the active ingredient or the product as such. Also by nature kg is a better measurement than ton (metric ton) - Antimicrobials bought per age group: What to do on a mixed farm, e.g. pigs and poultry,	Thanks for the comment but calculations according to Figure 1 can be used for oral mass medication as well. Thanks for the comment but if expressed in kg it can result in a very high numbers. However, if during the pilot phase it is identified that it is better to use kg this will be changed when implementing the system in the MSs. Thanks for the comment but every antimicrobial product bought is based on a veterinary prescription that needs to

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		most of the antimicrobials can be bought for different age groups and more than one species. - Finally the estimation of the amount sold in the national population can only give a temporary picture taken at a certain time, it does not take into account emerging diseases, an epidemic outbreak needing massive medication. Therefore the collection of the indication for the use of the antibiotic gives that extra information.	specify where the antimicrobial agents should be used for (animal species, age group etc.) Thanks for the comment but for ESVAC estimates on consumption by species and weight group per year will be collected. Events such as epidemics of diseases that are to be treated with antimicrobial agents will influence these data and some MSs might want to collect them for use at national level – e.g. to interpret the consumption data.
Line 555	4	Comment: overall sales in tonnes: it is better to use Kg as measurement since Kg is international more accepted as standard unit, tonnes may be denominated as metric tonnes and are well possible that some of the agents by species and age class are e.g. 50 Kg and would require then fractions of tonnes. Proposed change (if any): use Kg as measuring unit	See previous comments.
Line 94 as first line in which this abbreviation is used	5	Comment: DDDA, DCDA etc. Proposed change (if any): In our opinion the correct abbreviation should be ADDD or ADCD, because Animal Defined Daily Dosage is correct English grammar and Defined Daily Dosage Animals not (derived from French). Moreover, ADD has been used as an abbreviation in publications	Thanks for the comment. ADD is a term frequently used at national level and is not standardized across countries whereas DDDA will be a standardized term across countries and publicly available value. Thus, the name has to be different.
Line 97	5	Comment: 'it could be reasonable to compare the consumption between the human and animal sector' is	Accepted. This has been changed in the revised reflection paper.

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		in our opinion only a partial purpose of implementing DDDA (or ADDD) and 'reasonable' is not a correct statement. Moreover, the purpose or advantage is much wider than a comparison with human usage only. Proposed change (if any): change 'it could be reasonable to compare' to 'facilitates the comparison of consumption between humans and animals, between farms of one production type and between countries'	
Line 252 onwards	5	Although the total amount does provide some insight in how much is used in general, it cannot easily serve more purposes. Not taking into account when, how much, etc. is meaningless. An example: more animals in a country just mean more usage. In other words everything is relative and this could be more emphasized. If ADDD is taken in, you will run in the same problem at one level lower. It is only within certain (!!) species that a comparison could be useful. But in general combining does more harm than good. Thus, more specification is required.	Thanks for the comment but this part describes systems currently in use in MSs.
Line 261	5	Comment: 'validation' implies a hierarchy (which is the gold standard?) or at least a certain level of agreement between DDDA and sales data. This has and probably cannot be unambiguously established since sales data are based on many in principle different sources of information including parallel-imported drugs or	Accepted.

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		drugs that need to be excluded from the statistics like exported drugs, usage in all kind of animal species in which no DDDA's are recorded etc. Proposed change (if any): change to 'can be compared with data collected by species'	
Table 2: Comparison with resistance, 2nd column	5	Comment: 'Yes, but only on ecological level', is difficult to understand or even without true meaning Proposed changes: +/- (depends on specification of sales by animal species and antibiotic class)	Accepted.
Line 339: DDD has not been developed for veterinary medicine	5	Comments: without a standardised DDD assigned to antimicrobials through an ATCvet-code it is very difficult to standardise the numerator. The SDa misses this aspect in the document. Countries that apply the ADD methodology (DK, NL) have standardised this themselves. Proposed action: For optimum harmonisation we suggest that ESVAC adds to the ATCvet-code table a defined daily dosage (DDD) for each antimicrobial listed, for each animal species and each administration route. It should include the number of KG's animal by species that can be treated with such a dosage. This will take into account the pharmacokinetic properties of long acting versus short acting formularies of identical drugs (e.g. Excenel versus Naxcel) and will facilitate the determination of the exposure of animals	Thanks for the comment but since DDDA and DCDA is proposed to be assigned separately for each ingredient for combination products link to the ATCvet code is not always applicable. DDDA and DCDA can also be assigned for antimicrobial agents and form which is the main principle for assignment of technical units of measurement and can be done without any link to the ATCvet system. Accepted. We have included injection longacting (INJ-LA) as form to be reported.

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		to antibiotics accurately. There is a need for a harmonized and evidence based approach to obtain the DDD for each antimicrobial. This is an area where further work is urgently needed. Additional comments of prof. Mouton: A standardised ADDD assigned to antimicrobials through an ATCvet-code (that should and could be used throughout Europe!!) is a requirement here, see also general comment. Of note, not all codes are available in software systems in every country. This should be a first requirement. As noted in the general comment, ADDD are currently being defined in the Netherlands, taking into account not only dose itself, but also duration of activity as based on pharmacokinetic properties (long acting vs. short acting).	Thanks for the comment. DDDA and DCDA values will be assigned from SPC information Guidance on how to assign DDDA and DCDA will be developed as the next step. Thank you for the comment but this is outside the scope of this reflection paper Thanks for the comment but it is suggested to also use DCDA that takes into account the length of the treatment. The issue of long acting products is addressed in chapter 6.3.
Line 359 onwards	5	This is a crucial paragraph. At present, it just states current practice and a short suggestion how this could be improved. Yet many of the conclusions that will be drawn are based on assumptions and definitions of the denominator. This paragraph needs extension to describe the shortcomings of the present system and in what direction this needs to be going or a reference there to. There is a reference later on, including a table with reference weights, but the table is relatively crude.	Thanks for the comment but this part describes current systems in place.
Table 4 with	5	Comments: The SDa understands that a limited	See previous comments and Table 4 in the revised reflection

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reference weights		number of age groups should be chosen, but the composition of the current table is not complete and will result in no DDDA to be calculated for many farm types. Because of that reason we in NL have defined more age groups and productions types. Such a table is highly relevant for adequate harmonisation of the denominator and needs in our opinion more detailed age groups and weights to be able to calculate DDDA's on e.g. different cattle type of farms, or different veal calf farms. This type of differentiation will be impossible based on the current table in the reflection paper. E.g. on dairy farms the usage in calves will be allocated to the adult animals of 500 kg. Therefore on farms with starters only, no DDDA can be calculated. We suggest that similar as done for pigs, average weights should be agreed upon for different age groups of calves, beef producing animals other than veal calves. The proposed weight for piglets or weaners is not the average weight of a young or weaned piglet but more the weight of these categories at the start. This is a not a uniform approach compared to e.g. broilers. The average weight of a piglet will be around 4 – 5 kg and of a weaner around 17.5 kg. I have added a table with all average animal weights used in NL by the SDa to be able to calculate an average animal weight per farm type of relevance Proposed change: The SDa suggests that ESVAC reconsiders this table and after this consultation period	paper.

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		starts an inquiry in MS's that apply these weight groups to define the most appropriate average weight of animal categories present at different farm types to be able to calculate the most appropriate denominator for all farm types of relevance. The SDa can share its experience on this item and the choices that are made in NL. We understand that for European standardisation purposes, choices need to be made. However, the rationale behind these choices needs to be fully transparent.	
Table 5	5	The SDa considers type 1 data redundant for an EU-wide reflection paper on standardisation of antibiotic use measurement. This type of data can be applicable for detailed epidemiological studies. However, the question to be answered in these studies will affect the level of detail required on usage data. This should not be standardized and has no added value to the report. Factors like treatment duration and numbers of animals the drugs are prescribed for are not relevant for this document. The report should solely focus at standardized units of measurement for sales data and continuous collection of data on antibiotics at farms.	See previous comments.
Line 604	5	'defined cure dose' should be 'defined course dose'	Accepted.
Line 629/631	5	In these lines the following statement is made: 'In the ESVAC project, the indicators for consumption of veterinary antimicrobial agents should be numbers of	

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		DDDA or DCDA consumed by age group divided by the number of animals species produced...' The reference to the denominator in this statement seems incorrect. The SDa believes that ESVAC intended to state the following: 'consumed by age group divided by the number of animals per species....'.	Accepted.
Line 112-113	5	Comment: On page 5 for the reporting of data by species three different indicators are suggested to be used: Of which the first suggestion in lines 112 en 113 is in our opinion inappropriate. "Weight of active ingredient consumed per 1000 animals and age group/production type per year (mg/1000 animals per year) by country" By relating the amount of antibiotics solely to numbers of animals and not include the weight of these animals, the data cannot be used for any accurate comparisons. Moreover, the weight of antibiotics is a poor indicator of exposure, given the variation of administration routes and dosages used. Besides for comparisons of national sales data related to an appropriate denominator, usage of the weight of active ingredients is a poor indicator of exposure of animals and has no added value to ADDD's. Proposed change (if any): We advise to delete this option.	Thanks for the comments but several indicators can be used to express the consumption in order to enable various type of analysis. Accepted. The indicator to be used is weight of active ingredient consumed per weight class per 1000 animal produced per year See previous comments.

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		If ESVAC decides to keep it in, the weight of the active ingredient should be related to an appropriate denominator: "Weight of active ingredient consumed per 1000 animal kilograms live weight/production type per year (mg/1000 animal kilograms per year) by country"	See previous comments.
Lines 73 -74	7	Comment: It is not specified which species amongst the groups of animals are to be selected for evaluation each year, e.g. will data for the two species, Bos taurus and Bos indicus be collected separately? There are of course many different species of poultry as indicated above (see general comments). The baseline study should probably limit itself to well-defined groups of animals and if "species" is used as the defining division (the text focuses strongly on species) then the specific species to be studied should be properly defined and named.	Thanks for the comment. This will be precised when starting the pilot.
Lines 311-312	7	Comment: Chevance's report does not specify species. The author refers to groups of animals of different types.	Thanks for the comment but this paper includes species or group of species.
Lines 438 - 439	7	Comment: Storage at farm level will not be of additional value, if electronic data have been already collected and kept. Try to make the system as simple as possible. Proposed change (if any): and storage at farm level	Accepted. Accepted.
Lines 461-476	7	Comment: Poultry are defined as Gallus gallus and the need to include other species such as rabbits and farmed fish is specified but, even if we ignore the fact	See previous comments.

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		that these additional groups may be multi-species, the limitation of studies of poultry to Gallus gallus is inappropriate.	
Lines 481	7	Comment: Subdividing per age, sex, etc. of targeted species needs to be well reflected. For example, why are laying hens not included in the table 4, and do we need 4 classes of pigs (is pigs, piglets not enough?)	See previous comment.
Lines 484-486	7	Comment: Antimicrobial drugs (not antiseptics) in all pharmaceutical forms (e.g. dermatological preparations, those for eye and ear and cutaneous spray) should be recorded, as we may need to be able to track the use of these substances in the future.	Thanks for the comment; the reflection paper provides an explanation why these forms are not included.
Lines 727-731	7	Comment: It would be wiser not to establish DDDA and DCD on a European level, in this phase, as it may create much confusion. Try to keep system as simple as possible.	Thank you for your comment but in order to harmonise the reporting of the consumption data across EU common DDDA and DCDA values have to be applied.
Line 276	8	Comment: minor change in the wording Proposed change underlined: "…or prescriptions and/or on data from farmers…"	Accepted.
Line 278	8	Comment: Data obtained from farm bookkeeping also includes detailed data on the dose used and duration of treatments, number of treated animals etc. Proposed change underlined: "…and for prescription data and data from farm bookkeeping this may also include…"	Thanks for the comment but this part describes systems currently in use in various MSs.
Lines 349-	8	Comment: DDDA assigned per kg animal is not useful	Thanks for the comment. It will be addressed when

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350		in case of intramammaries. It should be considered whether IMM-data should be separated to own tables and excluded from the DDDA/kg animal overall data. The same applies for intrauterine products. See also comments to section 6. Proposed change: Add sentence “For intramammaries and intrauterine products (that are not dosed on mg/kg basis) the DDDA should be based on actual dosing, for example, intramammaries - mg/quarter, uteritorias - mg/cow.	developing guidance on methodology on how to assign DDDA
Lines 476-482	8	Comment: Regulation 1165/2008 of EP and EC concerning livestock and meat statistics defines the various age groups that should be used for statistical purposes in the MSs. Suggested age groups in the reflection paper differs from those given in the regulation. It may be difficult to obtain exact number of animals in certain age groups as this information is not collected at national level. How will the number of animals in “the regulation based age groups” be used for the age groups suggested in table 4.? For example what data should be used for piglets? – piglets born alive? – piglets alive at 1 week of age? Is there reliable/comparable data on the number piglets available from all MSs? According to regulation 1165/2008 data is collected from pigs under 20 kg – shall this number be used for both piglets and weaners? Compared to cattle the lifecycle of pigs and poultry are relatively short. The national statistics on	See previous comments. Thanks for the comment. In the indicator, e.g. number of pigs slaughtered obtained from Eurostat and data from TRACES will be used as denominator. See previous comments.

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		number of live animals describes the situation at certain time point in the year in question. Is the same approach going to be used for farm level data? At national level an option is also to calculate the number of piglets based on the number of sows and production figures defining number of piglets born/per sow/year as well as piglet mortality. Instead of veal calves the data on usage should be collected on calves that are less than one year old. As regards calves, the same discussion is on-going in the frame of resistance monitoring and the same approach should be taken in the ESVAC in order to be able to compare resistance and usage data.	
Lines 497-500	8	Comment: In the continuous data collection systems that are under development the representativeness may not be 100%. E.g. in Finland our system will provide 98 % data coverage on pig production. With regards cattle the coverage will be substantially lower. Proposed change: Add information on how to handle data from data collection systems that are not yet 100% representative for example for a system that is still under development.	Accepted.
Lines 513-514	8	Comment: Age groups suggested in this document differ from those defined in the regulation 1165/2008. Shall this difference cause a problem for reporting MSs especially with the total number of animals at the national level?	See previous comments.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
Lines 527-528	8	Comment: Though calculations for both types I and II data are presented in the same chapter, in the results it should be clearly described that type I and II are not comparable. Preferably the data should be presented in separate tables (type I = used, type II = supposed/assumed use) Proposed change: The issue should be taken into consideration when reporting is developed.	Thanks for the comments. We agree that this have to be discussed when reporting the data.
Figure 1. on p.20	8	Comment: In the figure data from different sources (type I and II) are combined to 'Amount (A) sold, in tons, per age group in the study population'. It should be kept in mind that type I data is on actual use and II on supposed/assumed use. Proposed change underlined: 'Amount (A) sold/used (depending on the data source), in tons, per age group in the studied population' the same applies for the text in last box ('Estimation of the amount sold/used… '). Alternatively the textboxes could be divided into two for different type of data	See previous comments.
Figure 1. on p.20	8	Comment: It may be difficult to obtain R= 1 for national population. Given formula to extrapolate R<1 data to national consumption is very straight forward. Depending on the data collection method(s) used it should be considered whether such extrapolation provides accurate data. Using confidence interval as suggested in footnote is supported. Proposed change: Add to footnotes that prerequisites	Accepted.

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		for extrapolation should be given when guidance is developed.	
Table 7. on p.21 DATA COLLECTION METHOD	8	Comment: The proposed variables do not sufficiently differentiate between the actual data source i.e. data used, prescribed and overall sales data. It is suggested to add a new variable that precisely describes the data type. Proposed change: Add new variable 'DATA TYPE 'below Data collection method. Description of the variable: Used (U, data collected from farm bookkeeping), prescribed (P, data collected from pharmacies), sold (OS, data from overall sales) and other additional variable, if needed.	Accepted.
Lines 605-608	8	Comment: It is well known that there are several products on the market within the MSs with indications and dosing that are not in line with the current scientific requirements. The dosing used in the DDDA DCDA calculations should be harmonised in accordance with current scientific data.	Thanks for the comment but similar to in human medicine the DDDA (or DCDA) are technical units of measurement and should not be considered as a "correct dose" but as a compromise.
Figure 2. on p. 24 and section 5.8 (lines 628-633)	8	Comment: For animals with short production cycle (poultry) or certain age groups (calves, piglets, weaners) 'Proportion of animals treated should be considered as an alternative indicator. However this may require changes to the data collected.	Thanks for the comment. For ESVAC estimates on annual consumption by species/weight group/production type will be collected and reported by use of a denominator overall numbers of animals produced (or livestock) and transported (TRACEs data) in corresponding year.
Lines 646-647	8	Comment: For intramammary and intrauterine products it should be reconsidered whether it is advisable to assign the DDDA and DCDA by kg animal	Accepted. See previous comments.

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		species. It would more useful to indicator that is based in the actual dosing i.e. mg (or tubes) used per quarter (respectively for intrauterine products mg/cow or proportion of cows treated). Proposed change: To be taken into consideration already when next ESVAC report on 2011 sales data is prepared. Data on intramammaries and intrauterine products should be presented in own tables (as was done for tablets in ESVAC II report). Ideally the number of tubes/uteretoria sold / ATC class would be presented in proportion to the number of dairy cows.	Thanks for the comment but this is outside the scope of the reflection paper.
Chapter 6.3 on line 672-679	8	Comment: In order to facilitate analysing the sold/prescribed/used data it should be considered whether LA-products could be identified in the ESVAC-template. Proposed change: Consider adding a new variable to pharmaceutical forms: INJ-LA.	Accepted.
Lines 127 & 131	9	Comment: The term “transfer” would be preferable to “movements”	Accepted.
Line 132	9	Comment: The phrase “associated with” would be preferable to “promoted by”	Accepted.
Lines 186-187	9	Comment: Intervention measures are already described before any correlation has been made. We would suggest that the following should be deleted “such as restriction or ban of use of particular antimicrobial classes”	Thanks for the comment but this is a general consideration in the introduction part.

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Line 267	9	Comment: This table is very long and will inevitably be split over multiple pages, as a matter of course column headers should be repeated at the top of each page.	Accepted.
Lines 281, 367 & 563	9	Comment: Denominator: possible problems arise due to cross border trade in live animals e.g. animals are raised in country A, but just before slaughter, they are transported to a country B. This needs to be accounted for by the PCU concept.	Thanks for the comment but this part describes systems currently in use.
Line 347	9	Comment: It is important that DDDA is defined in a scientific and harmonised manner for long-acting products.	See previous comments.
Line 481	9	Comment: The proposed weight for weaners is low: 7kg. We would suggest using the Median of this production type: 7-20kg -> 13.5 kg. The proposed weight for finishers is low: 35kg. We would suggest using the Median of this production type: 20-110kg -> 65 kg. The weight chosen for Broilers is acceptable: 0.003kg -> 2.500kg: median is 1.25 kg instead of 1 kg. The classification for cattle seems arbitrary. The weight for veal calves is proposed as 170 kg. In fact, most antibiotic treatments are given to veal calves at the start of the production cycle, when they weight 70 kg or less. In terms of antibiotic use patterns, target ages would be <3 weeks (~50kg) for enteric infections, then BRD ~100 kg and BRD in conventional (beef) calves up to 6-9 months (~200-300 kg). Adult dairy or	See previous comments.

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		beef cows ~600kg.	
Line 492	9	Comment: “Intestinal” should be replaced with “oral”.	See previous comments.
Lines 666-669	9	Comment: The rationale for the combination of antimicrobial agents is to enlarge the spectrum of activity or to decrease the dose. This is not taken into account by the use of specific pressure of selection which would overestimate the risks.	Thanks for the comments but this will give information on exposure of the microbial flora to the various individual antimicrobial agents.
Line 672	9	Comment: It is unclear how DDDA for long acting products should be defined. Long-acting products should be reported like all other products, i.e. total dose in mg. There is insufficient evidence for differential selection pressures associated with various durations of activity, which in any case would be different for different individual antibiotics and different bacterial species.	Thanks for the comment. This will be addressed in the guidance on how to assign DDDAs.
Line 677	9	Comment: How will the “harmonised” duration of action be selected as different types of long acting products exist depending on the half-life of elimination of the active principle?	Thanks for the comment. This will be addressed in the guidance on how to assign DDDAs.
Lines 683-688	9	Comment: In all cases, collection needs to be done in a cost efficient manner.	Accepted.
Lines 689-695	9	Comment: DCDA represents the best technical unit of measurement as it takes the duration of treatment into account and not just the number of days of treatment as with the DDDA. This is particularly important when considering that treatments may be different across	See previous comments.

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		the EU.	
Line 701	9	Comment: The suggestion for the implementation should be representative of the different MSs and not only focused on those who already have a similar system in place. This would allow the overall feasibility of the recommendations to be evaluated.	See previous comments.
Line 709	9	Comment: Guidelines should be developed.	Thanks for the comment but the wording reflects the heading of the chapter – i.e. suggestions for implementation.
Lines 479-482	10	Comment: Thank you for giving us the opportunity to comment this consultation. Please, find below 2 remarks on the reference weights at treatment that are defined in table 4 for pigs, weaners and finishers. These weights appear to be low compared to weights at which animals can be treated in French Pig farms. Firstly, in France, pigs generally stay in post-weaning units from 6-8 kg until 30-35 kg. The mean weights at the beginning and at the end of the post-weaning period in 2011 were respectively 7.2 and 31.4 kg, according to the Technical and Economic French Database managed by IFIP (the French Institute for Pig and Pork Industry) and covering more than 1700 farrow-to-finish farms. Weaners can potentially be treated at one moment or another all along this period. Secondly, finishers can also be treated occasionally between 30-35kg and some days before abattoir (at 115 kg generally), in accordance with withdrawal times before the slaughter. However, most treatments take	See previous comments.

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		place during the first half of the fattening period. Proposed change (if any): Reference weights of 15 kg and 50 kg, respectively for weaners and finishers, would be better to represent the range of weights at which these animals can be treated.	
Lines 462-468	12	Comment: EGGVP agrees with prioritisation on pigs and poultry. Regarding bovines, we would propose excluding dairy cattle as this class of animals is “less exposed” (antimicrobials normally administered locally, for specific purposes, and for specific individuals).	See previous comments.
Lines 481-482	12	Comment: For the sake of harmonization and homogeneity of criteria, EGGVP suggests adopting bodyweights which are already available in current guidelines such as: - Eco-toxicity guidelines (EMEA/CVMP/ERA/418282/2005-Rev.1) - Pharmacovigilance guidelines (Volume 9B)	See previous comments.
Lines 681-688	12	Comment: EGGVP agrees with the ranking of preferred methods suggested in the reflection paper. Stratification by species based on overall sales data is the less accurate method because marketing authorization holders deliver data based on assumptions (estimation according to knowledge on the use of the drug in the different animal species and total number of animals per species in the country).	Accepted.
Lines 90-92	13	The suggested data described here to be provided to	Thank you for your comment but at this stage it is only

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		ESVAC do allow only a very rough estimate of the number of treatments in relation to the true animal population and husbandry system. Thus, an additional technical unit and indicator should be introduced which is based on the number of applications, treated animals and population under risk (e.g. number of UDDs (used daily doses per population, e.g. 1000 animals)).	feasible for most MSs to provide estimates on consumption See previous comments.
Lines 108-110	13	We agree that prioritising the animal species covered is needed and that the activity should focus on pigs, cattle and poultry. But the reason for starting data collection for this animal species should be due to public health relevance, and as monitoring of antimicrobial resistance is required by directive 2003/99/EC in these animal species.	Thanks for the comment but these describes for which species technical units of measurements should be prioritized to be developed.
Lines 112-113	13	We are not convinced that the 'weight of active ingredients consumed per 1000 animals' is of any relevance as these figures depend very much on the antimicrobials applied and the animal population by animal species. Thus, much misinterpretation will be the result of publishing such figures.	See previous comments.
Lines 114-119	13	The standardised definition of DDDA and DCDA is generally welcome. However, the calculations of the number of DDDA and DCDA used can only be made by real kg body weight (instead of standard body weights) because body weight changes rapidly in fast growing animals such as pigs, broilers and fattening turkeys. Using one single weight per category does not reflect this variation adequately. Moreover, it can be assumed that antimicrobial use differs between animals of	See previous comments.

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		different age, i.e. may be more pronounced in the early phase of the raising and fattening period. Ideally, the age of treated animals should be recorded to allow for a better estimation of their treatment. However, in currently applied documentation systems age of the treated animals is often not recorded, i. e. the information will also not be available. In poultry, where the weight of the animals increases by the factor 40 during a fattening period of one month errors from neglecting the weight of animals at treatment may be substantial, but even in pigs, a factor of 2 can be assumed if animals are treated way into the fattening period, e.g. for dysentery or an outbreak of respiratory disease.	
Lines 114-117	13	The calculation of number of DDDAs consumed should be done for each animal species, age group and production type. Furthermore, it is not clear at all in which way a standardised person (70kg) can be compared with a standardised animal or even different standardised animal species. We do not believe that this type of comparison is meaningful.	Accepted. Thanks for the comments but it is outside the scope of this reflection paper to describe how to perform such analysis
Lines 118-119	13	The calculation of number of DCDAs consumed should be done for each animal species, age group and production type.	Accepted.
Lines 125-127	13	This sentence is not correct. Selection of antimicrobial resistant bacteria is not only related to genetic mutations and gene movements. The sentence should read as follows: All use of antimicrobial agents – in	Accepted.

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		humans, animals and plants – promotes the selection and dissemination of antimicrobial resistant bacteria and resistance genes and the emergence of new resistant bacteria through genetic mutations and gene movements.	
Lines 129-131	13	In our understanding, exposure of humans via the food chain should not be considered an ecological contamination. We recommend rewording of the sentence.	Accepted.
Lines 131-133	13	The statement 'reducing unnecessary use' is not acceptable as usage of antimicrobials should be restricted to therapy of infectious diseases. Therefore, instead of 'reducing' it should be said 'prohibit unnecessary use'	Thanks for the comment but this is outside the scope of the reflection paper.
Lines 142-143	13	It is not clear at all, how from the pure knowledge of the consumption of antimicrobial agents the risk for resistance development can be predicted. This should be explained in more detail, especially which additional data are considered necessary.	Thanks for the comment. It reads "help to predict". This is the introduction part and describes possible use of the data. It does not aim to describe in details how to asses this including which additional data that are required.
Lines 240-245	13	In this sentence the word 'consumption' is used in two different ways, describing sales data or consumption data. For sales data, the word 'consumption' should be avoided.	Thanks for the comment. In the ESAC-Net and ESVAC consumption is part of the acronym. In the text it describes the various types of consumption data – i.e. sales and administered/prescribed amounts.
Lines 259-262	13	Some further limitations should be mentioned here: From sales data it is not known, whether these antimicrobials have been used for treatment of animals living in the same country, leading to an overestimate.	Accepted.

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		Furthermore, antimicrobials may be applied on animals in one country, but sold in another country, leading to an underestimate. Furthermore, for the individual countries, the figures may not be complete, e.g. as only antimicrobial sold to veterinarians, but not to feed mills are covered.	Thanks for the comment but ESVAC data on overall sales includes sales of premixes/sales of antimicrobials administered through feeding stuff.
Line 259-262 and Table 2	13	The document could be quite improved if more consistency would be ensured between table 1 and table 2. In table 1, focus is laid on 'continuous surveillance data', in Table 2 on 'continuous automated data collection'. The linkage between continuous and automated is not necessary; the difference to prospective studies is not clearly described. Furthermore, it is not clear whether the category 'continuous automated data collection' focus on continuous data collection covering all farmers or veterinarian records.	Accepted. Thanks for the comment but the tables do not deliver the same level of information (are independent).
		Line 'posology, duration': it is not clear what information is given in this line, as this covers two quite different meanings. Furthermore, we are not convinced that this information is available for systems based on stratification of national sales.	Thanks for the comment. Posology and duration is available from SPCs.
		Line 'proportion of animals, flocks, batches treated': Depending on the unit addressed, this is quite different information and it is not clear at all that this information will be available from all systems described. How can this information been deduced from stratified national sales?	Accepted. We agree that this cannot be deducted from national statistics and therefore we have changed this to "no".

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		Line 'variability between herds, flocks, batches: it is not clear at all that this information will be available from all systems described.	Thanks for the comment. We believe that with these systems it will be possible to describe the variability between herds, flocks and batches.
		Line 'time trends': Time trends can't necessarily been deduced from repeated surveys as this requires that surveys are performed in a comparable way (reflecting the same representative population).	Thanks for the comment. If the data is representative it should be comparable.
		Line 'comparison with resistance data': it is not clear how a comparison with resistance data can be performed other than on ecological level, if data are not collected in the same herds, farms etc. But this is not a requirement for the described study types. Please clarify.	Accepted. We agree with this comment, comparison with resistance data can be performed at an ecological level.
		Line 'sustainability': it is not clear what is depicted here. For the stratification sales approach, the availability of data for stratification is a prerequisite. This seems to be not ensured always. For the automated system, sustainability is only ensured, if it is compulsory by law.	It refers to the likelihood of sustainability of the described systems which will depend on external situations Accepted.
		Line 'feasibility': we agree that each of the systems is time and labour consuming when implementation is started. But all these systems can be developed in a way that they are not that demanding in the long run as all can apply automated data recording approaches.	See previous comments.
		Line 'advantages'. We can't consider it an advantage if major animal species are covered only as it is not clearing at all how detailed the information is.	Thanks for the comment but major species are on the first priorities.

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		Furthermore, this must be an absolute prerequisite.	
Line 270-272	13	Is should be clarified whether these systems cover all animal populations or only a subset. Germany can be mentioned in this sentence as well, as a system is under development currently (for details see attached paper published by Merle et al. 2012; further publications are in progress).	Accepted.
Line 346	13	It should be added 'for the individual active ingredients' to make more clearly what is the intention of that calculation. Furthermore, 'dosing' may be misleading, the work 'dose' might be more appropriate.	See previous comments.
Lines 347-350	13	We can't agree with this type of description. For human medicine, the DDD is related to an adult person (e.g. 70kg) and reflects a dose, and not to kg body weight and a dosage. As comparisons are envisaged, DDDA should also be related to the animal level. This makes it necessary, to define DDDA for all different animal species, age and production groups. For the suggested definition for a dosage, another abbreviation should be used, e.g. $DDDA_{kg}$.	Thanks for the comment but this part describes systems currently in use.
Lines 351-352	13	For the unit PDDA it should be included in the description whether it is related to kg bodyweight or an animal (see comments on DDDA).	See previous comments.
Lines 353-354	13	This term should be restricted to truly administered daily doses per animals. If this information is collected in a study, these are real figures and no estimates. For	Accepted.

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		calculations / estimates (e.g. from the amount applied divided true DDDA per animal), this term should not be used.	
Lines 356-358	13	The definition is not clear; especially it is not clear what the difference to DDDA (line 347-350) is and how the duration of treatment is taken into account. In this chapter, definitions are missing for the number of PDDAs and number of UDDA as these take into account the duration of treatments. Thus, at least an additional technical unit of measurement and indicator should be introduced which is based on the number of applications, treated animals and population under risk (e.g. number of UDDs (used daily doses per population, e.g. 1000 animals)).	Thanks for the comment but not relevant as this part describes units currently in use. Thanks for the comment but it reads in the text that PDDA and UDDA are prescribed daily dose and used daily dose, respectively. Thanks for the comment but this part describes systems currently in use and the denominator is addressed later.
Lines 374-376	13	From the text it is not clear whether a comparison between different animal species, age groups and indications (or formulations) is envisaged.	Thanks for the comment. How to perform such analysis is not within the scope of this reflection paper.
Lines 377-380	13	As explained in lines 229-238, there is already some legislation in place. Thus, in the paragraph it should be clarified which additional information should be recorded and stored. To be more specific, we are missing a requirement to record details on the number of treatments, the number of treated animals, the indication and the way of application.	Thanks for the comment. It is clear from Table 6 which information is needed to provide estimates on use to ESVAC. See previous comment

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		In addition, we are missing here a requirement as regards the collection of information on the population under risk, which is not part of records on treatments. Furthermore, the recommendation on the information which should be made available to ESVAC should be handled separately. It should not be the intention that raw data, as stored by a farmer or veterinarian, have to be made available to ESVAC.	Thanks for the comment but it reads ESVAC national contact points.
Lines 392-406	13	This paragraph is not in line with the legal requirements as described in section 4.1. As records have to be kept, the information should be collected exactly based in these requirements. For further details see comments on chapter 4. In addition, standardised group treatments are not in line with current legislation. Thus, in such a document it should not be described as an acceptable procedure.	Thanks for the comment but the data required in the current legislation do not fulfil the requirement for data in order to obtain estimates of consumption.
Lines 406-407	13	We do not fully agree with this statement. The importance of selecting representative farms should be highlighted. Furthermore, collecting information on single production cycles is not sufficient to calculate data for a fixed period of time, e.g. a one year period which is necessary to compare the situation between different animal species, age groups and production types. We are missing a paragraph dealing with the collection of data from veterinarians. The German study VetCAB has shown that quite valuable information can be collected and that the amount of information is much	Thanks for the comment but Figure 1 provide an example of extrapolation. Accepted.

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		higher compared to visiting individual farms.	
Lines 409-413	13	The first sentence is not clear, it reads like several visits are considered necessary within one production cycle. From our experience, one visit per year should be sufficient to collect all relevant information. The concerns regarding legal requirement to store information as addressed in the previous paragraph apply here too.	Thank you for the comment but production cycle is given as an example.
Lines 414-416	13	The same structure as in chapter 4.2.2 should be followed. Now, prospective studies and continuous automated systems (no studies but legal requirement?) are mixed. A chapter 5.1.3 dealing with continuous systems is missing.	Accepted.
Lines 421-425	13	These systems should also provide the number of animals treated as implemented in the German approach.	Accepted.
Lines 430-432	13	To ensure a representative sampling some selection and stratification criteria need to be considered. We do not understand why selection criteria such as herd size and geographical location may impair the representativeness. This needs clarification. If willingness to cooperate is considered a bias factor, only a legally binding system should be considered acceptable.	See previous comments. Thanks for the comment but this is outside the scope of the reflection paper.
Lines 438-439	13	It should be clarified that collection of information via veterinarians would be acceptable too. From our experience, this is much easier to implement.	Accepted.

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Lines 467-468	13	We do not agree with the recommendation that data collection should be focused within poultry on Gallus gallus. Furthermore, reference should be made to the legislation EFSAs activities are based on. Instead of poultry the term broilers should be used throughout. A category fattening turkeys should be added as the consumption of antimicrobials in this production system is substantial and the amount of turkey meat consumed is constantly increasing. Therefore, in the proposed baseline survey data on broilers (Gallus gallus) and turkeys may be collected during the same year but should be collected separately. The categories for cattle are not complete. Replacement stock in dairy herds and beef herds does not match the category „veal calves“, yet these animals may receive a considerable amount of antimicrobials in their early live (i.e. the first 6 months).	Accepted. Thanks for the comment but it refers to the report that reflects EFSA's activities Accepted Thanks for the comment but at this stage priority have to be made as indicated (line 72-74).
Lines 476-478	13	Throughout the document, always animal species, age group and production type should be addressed. The new wording 'production category' is not helpful.	Accepted.
Lines 479-482	13	In Table 4, details on the age groups and definition of the production types are missing. The proposed reference weights are not acceptable. Before suggesting details, the age groups and production types needs to be specified. Furthermore, please see	Accepted.

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		our general comments on this approach.	
Lines 495-500	13	This paragraph needs major revision as the document should deal with consumption data and not with sales data. Furthermore, as DDDA and DCDA are not well defined, and data sources are not specified, it is not clear at all which data will be published. As much extrapolation seems to be planned, the comparability of data between animal species and countries is questionable. The approach needs to be developed and discussed very thorough before the system can be implemented. In contrast, the proposed UDD would be easily comparable between animal species, age groups, production types and countries.	Accepted. Thanks for the comment but this is described in chapter 5.7. See previous comments.
Lines 506-511	13	As regards item 9, it should be clarified whether the dosage (expressed in mg/kg body weight) or the total amount (dose) should be reported. As regards item 11, it should be specified how this information should be collected, e.g. in systems with group-wise restocking of animals. We are missing the indication in this list of items to be collected.	Accepted See previous comments.
Lines 510-511	13	Footnote 3 is not clear. What is the relationship between the observation period and the route of administration?	Accepted
Line 515	13	There is some discrepancy to the content of table 6. There, daily dose (item9) and duration of treatment (item 10) is listed as information to be collected.	Thanks for the comments but these variables are needed to calculate the consumption
5.5.2.	13	5.5.2. Example on extrapolation to national level	Thanks for the comment but ESVAC will only collect data on

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		As already mentioned for the indicators to be calculated, a second indicator should be calculated for Type I data by just multiplying item (7) x (10) in step 1 which resembles the used daily doses and allows for calculation of number of UDDs per population.	estimated amounts used for each product, animal species and weight group. These will be analysed by use of DDDAs and DCDAs. Since UDD is the truly administered dose it does not make sense to calculate this for these aggregated data.
Line 555	13	The usage of the term 'sales' in this context is misleading; it should be changed to overall amount consumed.	Accepted.
Lines 557-560	13	In table 7, the term 'sales' should only be used if sales are considered and not the amount consumed. As regards the variables 'INGR', 'PRODRUG' it is not clear what has to be recorded her. From variable 'TONS USED' we take the information that all information provided should be related to the 'active ingredient'.	Accepted.
Lines 563-564	13	The population under risk is quite a crucial factor. A much more detailed description on the information needed which is really comparable between countries is necessary.	Accepted.
Lines 565-567	13	Before an Excel spread sheet for data collection is developed, clear definitions should be developed and agreed on.	Accepted.
Line 593	13	It is not clear why in this context the daily dose given is necessary. In our understanding, it is only used to calculate the number of treatments if detailed information is not recorded.	Thanks for the comment but it is necessary to calculate the amounts consumed.
Lines 603-608	13	As the two terms are not clearly defined (see comments to lines 347 to 358) it is difficult to	Thanks for the comment but these are described in chapter 4.3.2.

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		comment on this paragraph. It is difficult to understand why such a complicated estimate is to be made instead of recording the number of animals treated and treatment days.	Thanks for the comment. In order to report the data in a harmonized manner across EU taking into account differences in dosing it is vital to standardize DDDA and DCDA.
Line 614	13	From the indicators calculated, no valid estimate of the number of animals treated can be deduced. This would need some additional calculations on the average number of treatment days. It is not clear, why this simple information is not calculated directly from the information available.	Thanks for the comments. Use of DCDA will give an estimate of number of animals treated.
Lines 629-631	13	Calculation of such indicators can only be performed if valid data are available on the population under risk. As described in chapter 5.9., for most populations standardised data are not available. Furthermore, it needs to be addressed how data can be compared between age groups, production types and animal species.	Thanks for the comment. In ESVAC it is agreed to use Eurostat (and TRACES); these data are also used as denominator by EFSA. Thanks for the comment but how to perform such analysis is outside the scope of this reflection paper.
Lines 635-638	13	Calculation of such indicators can only be performed if valid data are available on the population under risk. A much more detailed description of the data necessary should be given in here.	See previous comments.
6.2.	13	**6.2. Combination products** Overall this chapter is difficult to understand as the human approach is not clearly described.	Thanks for the comment. Guidelines on how to assign DDDAs for such products will be developed as a next step.
Lines 666-669	13	We appreciate very much the approach that each individual antimicrobial agent is considered separately.	Accepted.

Line no.	Stakeholder no.	Comment and rationale; proposed changes	Outcome
Lines 677-678	13	We appreciate very much the approach to take into account the duration of action of such products. Details on how this will be established and considered in the calculations need to be included.	See previous comments.
Line 689	13	An additional unit of measurement should be the number of used daily doses.	See previous comments.
Line 696	13	An additional indicator should be the number of used daily doses per population.	See previous comments.
Line 700	13	Both the number of DDDA and DCDA should be calculated.	Accepted.
Lines 702-705	13	In addition to data collection, MS participating in this pilot study should be closely involved in the data analysis part. A baseline study should only be drafted after the pilot project is finalised and a report on the experiences is made available to all MS.	Accepted.
Line 725	13	The definition should be more precise stating that it is related to all applications at one day to a single animal.	Accepted.
Line 726	13	The definition should be more precise stating that these are the days with application of an antimicrobial agent or days with therapeutic concentrations of the antimicrobial at the site of effect. This difference is quite important when long acting products are considered.	Accepted.
Line 727	13	In the definition the word ‘assumed’ is misleading as it	Thanks for the comment but this definition are similar to the definition used in human medicine and indicates that this is

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		is calculated from published information in the SPCs.	not the real dose used but a compromise when dosing given in SPCs varies between countries and synonym products.
Lines 729-731	13	In this definition DDDA is defined differently from lines 727-728. Furthermore, it is not clear what the 'assumed duration of treatment' is. A definition for DCDA is missing.	Accepted. See previous comments. Thanks for the comment. A definition is included in line 727 but it lacks animals; this has been corrected in the revised reflection paper.
Lines 732-736	13	Is should be made clear that references to WHO refer to approaches in human medicine.	Accepted.