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Accidental delivery of pigs for slaughter prior to end of withdrawal period for antimicrobial treatment - Ways of handling

Lis Alban [a,b,*], Boris Antunovic [c], Madalina Belous [d], Aivars Bērziņš [e,f], Silvia Bonardi [g], Rosa Maria García-Gimeno [h], Ian Jenson [i,j], Arja Helena Kautto [k], Michał Majewski [l], Derk Oorburg [m], Ioannis Sakaridis [n], Alexandrina Sirbu [o], Madalena Vieira-Pinto [p], Ivar Vågsholm [k], Jesper Valentin Petersen [a]

[a] Danish Agriculture & Food Council, Copenhagen, Denmark
[b] University of Copenhagen, Frederiksberg, Denmark
[c] University of J.J. Strossmayer, Faculty of Agrobiotechnical Sciences, Osijek, Croatia
[d] Faculty of Veterinary Medicine, Spiru Haret University, Bucharest, Romania
[e] Institute of Food Safety, Animal Health and Environment (BIOR), Riga, Latvia
[f] Faculty of Veterinary Medicine, Latvia University of Life Sciences and Technologies, Jelgava, Latvia
[g] University of Parma, Department of Veterinary Science, Parma, Italy
[h] Dept. Food Science and Technology, Universidad de Córdoba, Spain
[i] Centre for Food Safety and Innovation, University of Tasmania, Hobart, Tas, Australia
[j] FIRST Management Pty Ltd, North Parramatta, NSW, Australia
[k] Dept. Biomedical Sciences and Veterinary Public Health (BVF), Swedish University of Agricultural Sciences, Uppsala, Sweden
[l] Dept. of Animal Breeding and Product Quality Assessment, Poznan University of Life Sciences, Poland
[m] Vion Food Group, Boxtel, the Netherlands
[n] Veterinary Research Institute, Hellenic Agricultural Organization - Dimitra, Campus of Thermi, Thessaloniki, Greece
[o] FMMAE Ramnicu Valcea, Constantin Brancoveanu University of Pitesti, Romania
[p] Veterinary and Animal Research Centre, University of Trás-os-Montes and Alto Douro, Portugal

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ABSTRACT

Withdrawal periods after treatment with antimicrobials are set to minimise the frequency and concentration of residues in meat from treated pigs. Still, by mistake, pigs can be sent for slaughter too early. How should the abattoir respond when a pig producer contacts the abattoir to inform them of such a mistake? To address this, two questionnaire surveys were undertaken during spring of 2022, targeting the competent authority (CA) and the food business operator (FBO) from countries in- and outside the European Union. The results covering answers from 78 respondents from 27 countries show that most countries have procedures in place, but also various ways of responding, between CA and FBO, as well as between countries with a large export volume versus countries with a small export volume of pig meat. We developed a best practice model for handling such events, which covers stages before and after the pig is slaughtered and is subjected to official meat inspection and resulting decisions in accordance with relevant legislation. The model involves a quantitative exposure risk assessment, which should be undertaken by the FBO and verified by the CA. The assessment produces estimates of the concentrations of residues at the time of slaughter. If higher than the maximum residue limit, the expected use of the carcasses should be considered. Hereby, the consumer exposure risk can be assessed using the acceptable daily intake (ADI) value, and a risk-based management decision about the safe handling of the meat can be made. This approach would compensate for the huge variation in withdrawal periods for the same substances in force in the European countries.

* Corresponding author. Danish Agriculture & Food Council, Axeltorv 3, DK-1609, Copenhagen V, Denmark.
E-mail address: lia@lf.dk (L. Alban).

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1. Introduction

Even though many primary producers are aware of the importance of using antimicrobials (AM) wisely (European Parliament, 2017; Kirchhelle, 2018), AM residues exceeding the maximum residue limits (MRLs) are occasionally detected in monitoring programmes (EU Commission, 2010). In 2020, the official monitoring of residues of legal AMs in the European Union (EU) resulted in testing of 36,262 targeted samples from pigs, of which 42 (0.12%) were non-compliant. The non-compliant results were reported by 15 countries, and the detected substances consisted of tetracyclines, β-lactams, sulphonamides and fluoroquinolones (Brocca & Salvatore, 2022). Moreover, a survey on AM residues in meat commodities from the cross-border area between Spain and France detected residues in 3.5% of 5357 meat samples using biological screening methods, for which a subsequent chemical verification is needed to quantify exactly the concentration of the AM residue (Serrano et al., 2022).

In 2008, Pavlov et al. estimated that 80% of livestock were treated with AMs at least once in their lifetime (Pavlov et al., 2008). Since then, a remarkable change in AM consumption has been observed in the EU, where the overall consumption almost halved from 2011 to 2021 (European Medicines Agency, 2022). In pigs, the main use is in weaners for treatment of gastro-intestinal symptoms (Moura et al., 2023). Oral administration of AMs weeks or months before slaughter will not lead to the presence of residues in meat, because the AMs will have been metabolised and excreted from the body of the treated animal before the time of slaughter. In other cases, the AMs may not have been absorbed but work locally in the intestines, e.g., to treat diarrhoea in weaned piglets. For this reason, the use of injectables close to the time of slaughter poses the main risk for residues above MRL in meat, as also shown in own checks undertaken by Danish pig abattoirs (Alban et al., 2014).

Low concentrations of AM residues in foods below MRL are not ascribable to any public health issues (Baynes et al., 2016), but the influence on the gut microbiota is understudied. According to Arsène et al. (2022), the toxic consequences of AM residues can be divided into two groups – direct and indirect. Direct consequences are related to toxic properties of substances (which are not likely for legal AMs) and the allergic reactions they can cause. Resistance to AMs is an indirect potential consequence of residues. In addition, residues of broad-spectrum AMs could influence the human microbiota of the gastrointestinal tract, as shown by Cabello (2006) in relation to consumption of farmed salmon. Moreover, inhibitory effects on fermentation can occur, e.g., when making dry-cured sausages such as chorizo (Arsène et al., 2022). However, as professional sausage producers use the decline in pH as an indicator of adequate fermentation, sausages with AM residues above the MRLs are not placed on the market.

In Europe, negative human health consequences related to AM residues after consumption of contaminated meat or products thereof are rarely reported. This could be because of the low concentrations of the AMs in the raw meat. The case reports found in the literature deal mainly with allergies due to the presence of ß-lactam residues in meat as shown by Baptista et al. (2010). The last reported case in the EU dates to 2001 and refers to a person who had eaten beef and subsequently developed anaphylactic shock. This was likely a reaction to a penicillin treatment of the animal (Raison-Peyron et al., 2001). Another case deals with a German butcher, who knew he was allergic to penicillin and who developed allergic reactions after consumption of meat from a pig that was subjected to emergency slaughter (Tscheuschner, 1972). Confirmed cases of allergic reactions related to residues of other legal AMs in meat have not been described so far. Thermal processes, like cooking, roasting or boiling, lead to changes in the properties of proteins, fats and water content, and reduce the food safety risk related to the AM residues by decreasing their concentration, as well as modifying their chemical structure or solubility (Almashhadany, 2020; Rana et al., 2019).

Withdrawal times have been defined to minimise residues of legal AMs in meat, and monitoring is in place to verify compliance with the withdrawal times. Usually, a pig producer would know when a batch of pigs has reached slaughter weight and would be ready to be shipped to the abattoir. In this case, any choice of AM treatment must consider the withdrawal period to ensure compliance with the existing rules. For sows, the time of slaughter may not be known in advance, as it is a multi-criteria decision. Correct individual marking and registration of AM treatment make it easy to ensure that treated sows are not delivered for slaughter prior to the end of the withdrawal period. Still, finishing pigs and sows can be sent to slaughter by mistake before the end of the withdrawal period, as shown by Alban et al. (2014) and Baptista et al. (2012).

In this situation, the pig producer may contact the abattoir after the delivery of the animals for slaughter to report the unintentional shipment of treated animals. If the animals have not yet been slaughtered, they will be identified, kept aside and handled by the authorities in accordance with the Regulation 2019/2090 (EU Commission, 2019). It is impossible to send the animals back to the farm of origin due to biosecurity and management issues. Most abattoirs have some capacity for keeping live pigs, but only for a limited period (Alban et al., 2023), in line with the legal requirement for slaughter of animals without undue delay (EU Council, 2009). This implies that the pigs will be euthanised and the carcasses disposed of, if the withdrawal period of the AM left at the time of slaughter is too long. In the EU, before 2019, it was possible to slaughter such animals and subject them to testing using a free-testing regime. According to Article 3 (5) in Regulation (EU) 2019/2090, this is no longer allowed when the suspicion deals with legal AM, but allowed if the suspicion deals with illegal treatment (EU Commission, 2019). Hereby, the current legislation may create a disincentive for pig producers to contact the abattoir, if their animals have been delivered within the withdrawal period by mistake.

If slaughter has taken place, the question is how the carcass and by-products of a treated pig should be handled and by whom, e.g., the competent authority (CA) or the food business operator (FBO). Regulation (EU) 2019/2090 does not give guidance for that situation (EU Commission, 2019). This makes it possible for the countries to deal with such cases in different ways. Concerning the meat and by-products originating from the slaughtered animals, several scenarios are possible. The treated carcasses could have been approved by the official veterinarian (OV) before information about non-compliance with the withdrawal period became available. The half-carcasses could further have been divided, cut, deboned, packed or cold-stored, depending on how long a time has passed since slaughter. A decision by either the OV or the FBO is therefore required: is the violation of the rules so grave that the meat and by-products should be condemned? Could a quantitative risk assessment help to identify how the carcasses and by-products might be used in a safe way? Similarly, for products placed on the market, do they have to be recalled and condemned and if, who is legally responsible for acting? A condemnation policy simply based on a pig producer's information about erroneous delivery of animals for slaughter could lead to excessive food waste perhaps without any real need to protect consumer safety, among others because withdrawal periods for the same substance vary between countries. This would contradict the EU policy of reducing food waste as outlined by the European Parliament Resolution (European Parliament, 2017) to reduce food waste in the EU by 30% and 50% by 2025 and 2030, respectively.

Any policy should ensure that the legislation in force is complied with. Moreover, large abattoirs can have additional concerns regarding their export requirements. Hereto, the large abattoir's production system with fast throughputs in large quantities, requires a high degree of predictability and clarity in the decision process, i.e., agreed procedures between FBO and CA. Preferably, guidance is in place to help the OV to come to a defendable and structured decision as suggested by Kahneman et al. (2021). In line with the EU General Food Law (Regulation (EC) 178/2002), all such decisions should involve risk assessment, and all risk management activities, including mitigating measures, should be

proportionate to the risk identified (EU Commission, 2002) and in line with the sustainable goals specified in the European Green Deal (EU Commission, 2022).

The question is how to handle the situation when a farmer reports the accidental delivery of one or more treated pigs to the abattoir prior to the end of the withdrawal period of the legal drugs used. Moreover, would it be possible to develop a set of best practices based on the surveillance objective of individual countries? Aiming to address these issues, the EU COST Action network called RIBMINS (Risk-based meat inspection and meat safety assurance system – for more information please see: http://ribmins.com) decided to undertake and analyse a survey that collected information about current ways of handling pigs delivered for slaughter prior the end of the AM withdrawal period or meat from such pigs in countries inside and outside the EU.

2. Materials and methods

A questionnaire was developed by a project group within RIBMINS. The first parts dealt with routine detection and handling of AM residues in pigs delivered to the abattoir. That work is published separately (Alban et al., 2023). Moreover, the questionnaire dealt with the situation that occurs when a pig producer contacts the abattoir because one or more pigs have been sent for slaughter by mistake before the end of the withdrawal period of the legal drugs used.

The survey was conducted via two versions of a questionnaire, one targeting the CA and the other the FBO. Access to both versions was through a link on the RIBMINS website (https://ribmins.com/survey-on-residues-of-antimicrobials-in-pigs/). The link was open from 29 March to 5 July 2022. Respondents were informed that the data would be analysed by the RIBMINS working group and processed in accordance with the EU data protection law. This implied that all answers were anonymised. Approval of the questionnaire was received from the Research Ethics Committee of Science and Health at the University of Copenhagen on March 29, 2022 - Journal number 504-0308/22-5000. For a more detailed description of how the survey was undertaken, please see Alban et al. (2023).

It was explained to the respondents that the theoretical case they were to consider dealt with a pig producer who had provided Food Chain Information (FCI) indicating compliance with the withdrawal periods of all drug treatments. However, the pig producer later informed the abattoir that one or more pigs had been sent before the end of the withdrawal period. The respondents were asked seven questions regarding ways of handling the situation, depending upon the time interval between the moment the animals were treated with AM and the moment the animals were slaughtered (Fig. 1).

Two hypotheses were investigated. The first dealt with the potential difference in views between the CA and the FBO. The second dealt with the potential difference between countries with a large and major part of their pig meat being traded or exported and countries with minor exports of pig meat. To investigate the second hypothesis, data describing pig meat production and export figures were collected. The countries were divided according to the volume of the pig meat exported, where a major exporter was a country that exported more than 250,000 tons of pig meat per year, and this volume accounted for more than 25% of the pig meat produced in the country. All other countries were considered as minor exporters. Further details are presented in Table S1. Chi square test and Fisher's exact test were used to assess whether the groups differed statistically. For these analyses, the respondents answering "I do not know" were excluded.

3. Results and discussion

In total, 78 persons representing 27 countries provided answers to the questionnaire. Of these, 42 represented a CA and 36 represented an FBO. Likewise, 36 represented countries which were major pig meat exporters and 42 represented countries which were minor pig meat exporters. Please see Table S1 for an overview of the 27 countries included and their division into major and minor exporters.

3.1. Current practices

The first question dealt with the existence of procedures to handle such a situation and who should manage the case (Table S2). Overall, there was a significant difference between CA and FBO ($P_{Fisher} = 0.002$). Most CA respondents (71%) claimed that they would manage the case. In contrast, among the FBOs, an equal part (42%) stated that either the

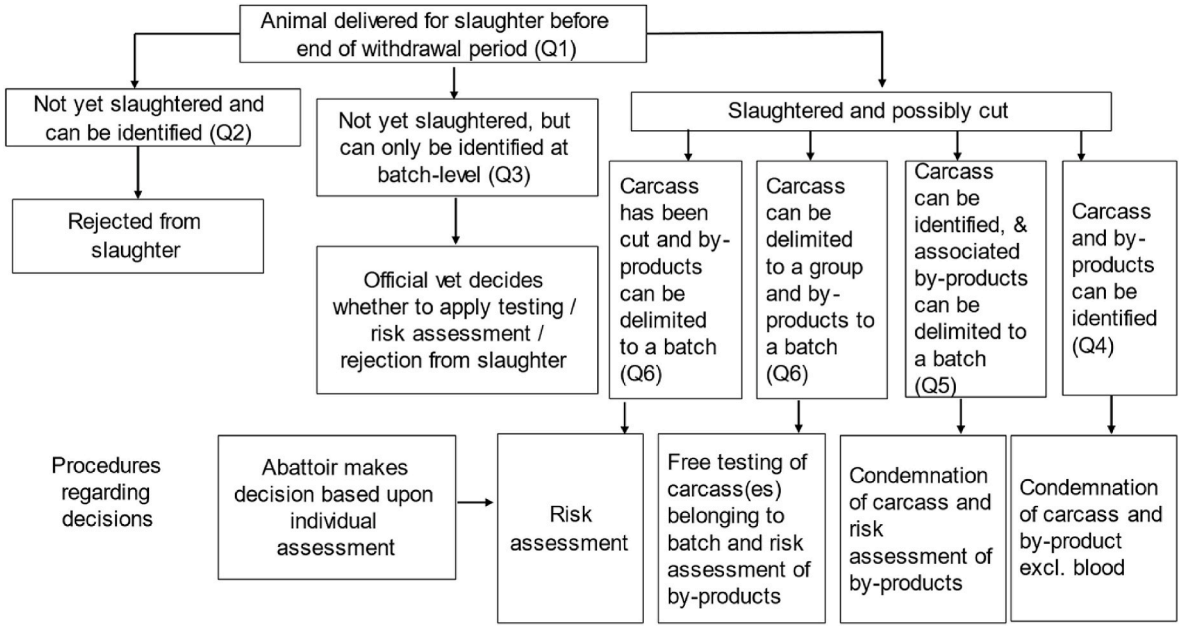

Fig. 1. Description of different possible scenarios covering the slaughter and cutting stages of relevance for a situation where a pig producer contacts an abattoir to inform them of an accidental delivery of one or more pigs for slaughter prior to the end of the withdrawal period related to the legal drugs used. The Q numbers refer to the survey questions asked to competent authorities and food business operators, 2022.

CA would manage the case or that a quality assurance (QA) programme is in place, describing the procedure. Only a few respondents indicated that the abattoir has no procedure for such a situation (10–11% for both CA and FBO). There was also a significant difference between the responses from major and minor exporting countries ($P_{Fisher} = 0.037$). Most minor exporters (69%) claimed that the CA would manage the case. On the contrary, among the major exporters, the most common answer (44%) was that either the CA would manage the case or that the FBO's fit-for-purpose quality assurance programme is in place and used (31%). Only a few CA respondents indicated that the abattoir has no procedure for such a situation (minor: 5%), whereas this was the case for 17% of the respondents from countries with a major part of their pig meat being exported.

Question 2 dealt with the situation where the individual animal has not yet been slaughtered and can be identified easily (Table S3). Here, it was of interest to know what happens at the beginning when the abattoir informs the OV. There was a significant difference in responses between CA and FBO ($P_{Fisher}<0.0001$). The most common answer among CA respondents (48%) was that the abattoir would inform the OV, who would then reject the animal from slaughter. In contrast, the most common answer from the FBOs (37%) was that the abattoir would make their own decision on rejection from slaughter or inform the OV about this decision. Detaining and housing of animals rejected from slaughter until the expiry of the withdrawal period were mentioned by 17% of the CA respondents but only by 3% of the FBOs. Overall, there was no significant difference between the responses from the major and the minor exporting countries ($P_{Fisher} = 0.78$). The most common answer among respondents representing the major exporting countries (43%) was that the abattoir would inform the OV, who would then reject the animal from slaughter. This was also the most common answer from the respondents representing the minor exporting countries (31%).

Question 3 dealt with the situation where the animal has not yet been slaughtered, but it cannot be identified individually as it is part of a batch (Table S4). Overall, there was a significant difference in answers from the CAs and FBOs ($P = 0.039$). Most CAs (55%) and FBOs (64%) responded that the OV would decide what to do. The OV's decision could be based on a risk assessment (CA: 31% and FBO: 28%), could be to house the animals until expiry of the withdrawal period (CA:21% and FBO: 17%) or to carry out testing to check for presence of residues (free-testing) (CA: 40%, but only 11% for FBO) (Table S4). There was no significant difference between the major and minor exporting countries ($P = 0.99$). Most major exporting countries (64%) and minor exporting countries (55%) responded that the OV would decide what to do. It could be a decision based on a risk assessment (major: 33% and minor 33%), could be to house the animals until expiry of the withdrawal period (major: 19% and minor: 19%) or to carry out free-testing (major: 25%, and minor: 29%).

Question 4 dealt with the situation where the animal has been slaughtered and the carcass cut, deboned and packed (Table S5). Hence, traceability has been reduced to a lot, but the products have not left the abattoir. Here, there was a significant difference between the answers from CAs and FBOs ($P_{Fisher} = 0.005$). A common view (CA: 29% and FBO: 40%) was that the case would be reported to the OV, who would decide how to handle the specific case. Moreover, the OV would order the abattoir to trace and subsequently treat the carcass and all parts thereof as Category 2 by-products, for which pressure sterilisation is required according to EU legislation (CA: 33% and FBO: 29%). Use of risk assessment as a basis for the decision was also commonly mentioned by the FBOs (29% regarding the abattoir's decision and 29% regarding the OV's decision) whereas these answers were less common among the CA respondents (0% and 14%, respectively). Use of test results was mentioned by 5% of the CA respondents and 26% of the FBO respondents. There was no significant difference between the major and minor exporting countries ($P_{Fisher} = 0.83$). A common view (major: 34% and minor: 33%) was that the case would be reported to the OV, who would decide how to handle the specific case. Another common answer was that the OV would order the abattoir to trace and subsequently treat the carcass and all parts thereof as category 2 by-products (major: 26% and minor: 36%). Moreover, use of risk assessment as a basis for decision was not commonly reported, regardless of whether it would be undertaken by the CA (major: 23% and minor: 19%) or by the abattoir (major: 17% and minor: 10%). Likewise, use of test results was only reported infrequently (major: 11% and minor: 17%).

Question 5 dealt with the situation where the traceability has been reduced to a lot, and edible parts have left the abattoir and been placed on the market (Table S6). Overall, there was a significant difference between answers from the CAs and FBOs ($P_{Fisher} = 0.045$). The most common view was that the decision regarding recall would be pending the outcome of a risk assessment made by the OV (CA: 46% and FBO: 44%), or the FBO (CA: 7% and FBO: 36%). This was followed by a recall of the edible parts from the market (CA: 39% and FBO: 42%). Hence, there was a discrepancy between FBOs and CAs on who would conduct the risk assessment, but both parties claimed that a recall from the market would take place or that the decision to recall is pending on outcome of a risk assessment. Overall, there was no significant difference between respondents from major or minor exporting countries ($P_{Fisher} = 0.27$). The most common view was that the decision regarding recall would be pending the outcome of a risk assessment made by the OV (major: 47% and minor: 44%) or the FBO (major: 28% and minor 15%). This was followed by a recall of the edible parts from the market (major: 33% and minor: 46%), reflecting stronger incentives for decisions by FBOs in major exporting countries compared to minor exporting countries.

Question 6 dealt with the situation where the animal by-products belonging to a lot, including blood, have already been placed on the market (Table S7). Here, there was no overall significant difference between the CA and FBO responses ($P_{Fisher} = 0.28$). The most common answer (45%) among the CAs was to base the decision regarding downgrading the by-products on a risk assessment. However, the second most common CA answer (33%) was that a risk assessment is never performed because of limitations in the EU legislation. The majority of the FBO respondents stated that the decision is based upon a risk assessment – made either by the FBO (29%) or the OV (29%) – and 20% of FBOs stated a risk assessment cannot be conducted because of EU legislation. The two CAs who responded that the case is not considered relevant gave further explanations. The first stated that the specific by-products cannot be located after leaving the abattoir, and that no cases of AM residues in pigs had been detected over the last 10 years. The other CA stated that the OV will make a risk assessment. There were no comments from the three FBO respondents who also responded that the case is not considered relevant. Overall, there was no significant difference between the respondents from major or minor exporting countries ($P_{Fisher} = 0.69$). The most common answer was to base the decision regarding downgrading these by-products on a risk assessment (major: 47% and minor: 29%). However, the second most common answer from both groups of respondents was that a risk assessment is never performed because of limitations in the EU legislation (major: 28% and minor: 27%). Around one-fifth of the respondents indicated that the FBO of the receiving plant would base a decision regarding whether to downgrade from animal by-product category 3, for which there is no requirement for heat treatment to category 2, which requires pressure sterilisation) on a risk assessment (major: 19% and minor: 24%).

Question 7 dealt with when the meat or a meat product is placed on a market (Table S8). The answers did not differ statistically between CA and FBO ($P = 0.79$). Most respondents indicated that "placing on the market" means when the meat has left the abattoir and is no longer under the responsibility of the FBO (CA:46% and FBO:64%), followed by "when a health mark has been given" (CA: 32% and FBO: 28%), and then by "left abattoir but under FBO responsibility" (CA. 27% and FBO: 28%). If another approach was used, one CA respondent stated: "basically available for human consumption". No comments were received from the FBOs. Overall, there was no significant difference between the

respondents from major and minor exporting countries ($P_{Fisher} = 0.068$). Regarding differences between major and minor exporting countries, most respondents indicated that "placing on the market" is when the meat has left the abattoir and is no longer under the responsibility of the FBO (major: 69% and minor: 41%), followed by "when a health mark has been applied on the carcass" (major: 25% and minor: 54%) and then by "left abattoir but under FBO responsibility (major: 28% and minor: 27%).

In summary, when a pig producer contacts the abattoir regarding delivery of pigs prior to the end of the withdrawal period of a legal drug treatment, the erroneously-delivered pigs can be still alive or can already be slaughtered and have been subjected to official controls that have resulted in a positive meat inspection decision and health marking in accordance with relevant legislation. If slaughtered and health marked, the carcass is usually cut into the ham, the middle piece and the front end. On the same day or the day after, the three pieces are cut into more pieces and deboned as described in Fig. 1. Moreover, from each slaughter batch of pigs slaughtered at the same time or day, the blood and the other by-products are each combined. Hence, the longer the time is between the delivery of the pigs and the pig producer contacting the abattoir, the more complicated the situation becomes. The results of our survey show that most respondents have a procedure to handle such a case. For those who have no procedures, this will likely make it more difficult to handle these cases in a systematic way. This lack of specified procedure could also reflect that the pig producers in some countries are not in the habit of contacting the abattoir when an error regarding AM withdrawal period has occurred. The majority of CAs expect to handle these cases. In contrast, the FBOs believe their QA programmes would be the best way to handle the issue. This discrepancy in answers shows that both CA and FBO are taking responsibility when these cases arise, reflecting uncertainty on responsibility and legal rights depending on the specific scenario. It should be highlighted that where the official control has not been carried out and the health mark not applied on the carcass, it is up to the CA to handle the case. Likewise, it may be argued that when the official control has been carried out and the health mark has been applied on the carcass, the FBO should handle the case.

The answers found in our survey show that there is some disagreement both within and between CA and FBO respondents as to what the EU legislation allows regarding use of risk assessment and testing for the AM residues. Some CAs treat the pigs in the same way as before the legislative change that came into force in 2019 and that deleted the possibility of testing for drug residues. Hence, when the pig producer reports that legal AMs have been used, those CAs still order testing to be undertaken post slaughter and before the final meat inspection decision is made. We hypothesise that this could occur for cases where the withdrawal period has almost been complied with. This would mean those OVs are focused on animal welfare, and therefore, are following the regulations for killing without undue delay (EU Council, 2009). The major exporting countries allow larger roles for the FBO's QA programmes than the minor exporting countries. At many abattoirs, detaining and housing of animals rejected from slaughter until the expiry of the AM withdrawal period may not be feasible or even illegal (EU Council, 2009), because specific pens must be used. The lairage area at the abattoir may not approved for longer animal stays. Still, housing the pigs and testing for AM residues was chosen by 17% of the CAs, whereas only 3% of the FBOs. This difference could be related to the difference between theory and practice, and because the FBO, not the CA, would have the responsibility for these animals.

Our survey showed there is great uncertainty and disagreement on the definition of when a product is placed on the market. This was regardless of whether the response came from CA or FBO or from a major or a minor exporting country. This question is crucial for both FBO and CA regarding responsibilities, rights and duties in handling cases, when a pig producer erroneously has delivered a pig prior to the end of the withdrawal period. According to Regulation (EC) 853/2004, the FBO shall not "place on the market" a product of animal origin handled in an establishment "unless it has a health mark applied" in accordance with the regulation. The question is when is a product of animal origin 'placed on the market'? According to the EU General Food Law (Regulation (EC) No 178/2002), the definition of "placing on the market of food and feed" is meaning "the holding of food or feed for the purpose of sale, including offering for sale or any other form of transfer, whether free of charge or not, and the sale, distribution, and other forms of transfer themselves" (EU Commission, 2002). It is important to notice that this definition does not require the relevant food or feed to be subject of "an offer or agreement for transfer of rights" (supply) to be placed on the market. Further, the term "holding of food or feed for the purpose of sale" (in stock at a warehouse) reflects the fact that "the food chain can involve long production cycles and certain goods are held in storage for long period". It means that meat, i.e., the carcass cut into half or the half in three parts, from slaughtered pigs, should be deemed "legally placed on the EU-market" at the moment it has been subject to an official control and has been health marked in accordance with relevant legislation.

3.2. Best practice model

We developed a best practice model, which can be used both when the delivered and treated pig is still alive and when it has been slaughtered, and the carcass is health marked. The best practice model is summarised in Fig. 2 and involves a quantitative exposure risk assessment, to be undertaken by the FBO and verified by the CA. As noted in the answers to the seven questions, risk assessment is commonly used by the responding CAs and FBOs. As we did not specify what was precisely was meant by risk assessment, respondents could have had differing interpretations and mainly had generic risk assessment instead of a quantitative approach in mind. To harmonise this, we suggest using an approach that is scientifically sound, yet feasible to undertake in one day. The approach consists of quantitative estimations of the concentration of AMs in the meat at the time of slaughter and of the amounts in a serving. The model consists of the elements listed in Table 1, and it can be found on the website of RIBMINS.

First, the relevant information about the treated pig(s) is collected, i.e., the weight in kg of the live or slaughtered pig(s). This information is used to calculate the weight of the carcass(es) without bones. The slaughter weight excludes the animal by-products and the edible by-products, and here a value of 86.4 kg was used in Table 1, representing the average of finishing pigs slaughtered in Denmark during 4 weeks in spring 2023 (n = 985.380) (Personal communication H. Christensen). The edible part of a slaughtered pig was set to 85% based upon a report from Danish Meat Research Institute (Danish Meat Research Institute, 1992). Next, information about the drug(s) used, the concentrations and the dosages is retrieved from the pig producer, along with the day and hour that the treatments took place. Thereafter, information about the day and hour of the slaughter is retrieved from the abattoir.

Information about the half-life of each drug used is collected from a reliable source such as a national medicine agency or the European Medicine Agency. Examples of this is provided in the Supplementary materials. Based upon this, the number of half-life periods that have passed between treatment and slaughter is then calculated. These figures are used to calculate the reduction factors – one for each drug – corresponding to the proportion (%) of the remaining amounts of drugs left in the carcass. These reduction factors are multiplied by the initial amounts of drugs used for treatment to derive the amounts of residues (in μg) present in the carcass at the time of slaughter, while assuming equal distribution of the residues in the part of the carcass that is edible (excluding the bones). Thereafter, the resulting theoretical concentration of residues can be calculated in μg per kg, followed by the amount in μg, which can be present in a serving. Although ordinary portion sizes of pig meat are around 125 g (Government of Canada, 2022), we use 200 g of meat as a conservative choice. The calculated concentration is then compared with the MRL, and the amount in a serving is compared with the acceptable daily intake (ADI), which is the estimate of the residue,

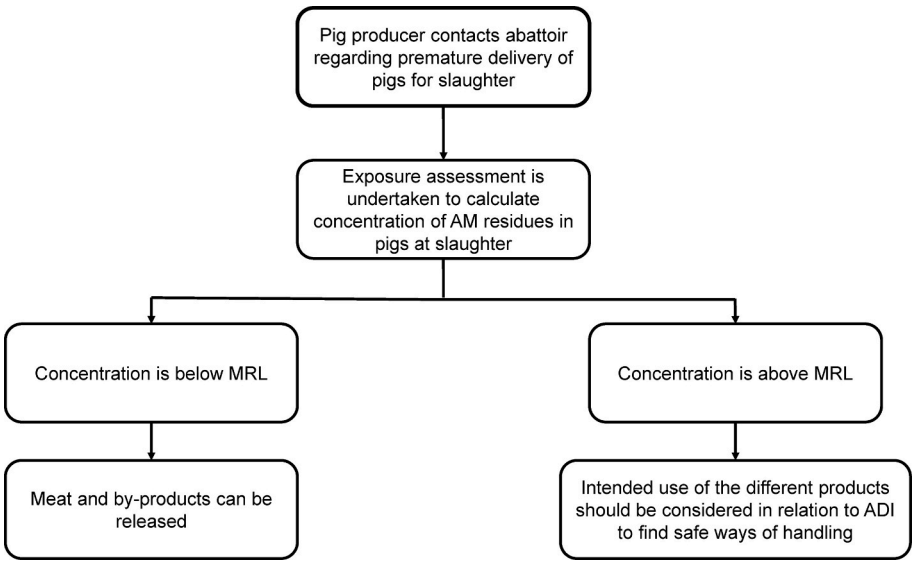

Fig. 2. Graphical description of best practice model involving use of a quantitative exposure assessment as a way to identify safe ways of handling pigs sent prematurely for slaughter in relation to the withdrawal period after antimicrobials treatment. MRL: Maximum residue limit. ADI: Acceptable daily intake.

expressed in terms of micrograms or milligrams per kilogram of bodyweight, that can be ingested daily over a lifetime without any appreciable health risk (European Medicines Agency, 2012). Like for half-life, the MRL and the ADI values can be found on different websites of public agencies. Please see the Supplementary materials for examples of this. A user-friendly version of the excel model showing the calculations of the individual steps of the model can be found on the RIBMINS website (https://ribmins.com/survey-on-residues-of-antimicrobials-in-pigs/).

Table 1 contains an example from real life, where a pig producer contacted the abattoir regarding the erroneous delivery of one pig for slaughter. The pig had been treated with two different antimicrobial products based on lincomycin and benzylpenicillin as well as a pain killer based on meloxicam. The withdrawal periods in the country of the case were 6 days for the products based on lincomycin and meloxicam, and 5 days for the product based on benzylpenicillin. The pig was delivered 2 days after treatment, and hence, the withdrawal periods for all three treatments had not been observed. Despite this, the calculations in Table 1 show that the amounts of residues present in the meat at the time of slaughter were below the MRLs, and that a serving of 200 g meat from the treated pigs would have contained levels of AMs much lower than the ADI: 10.6 μg lincomycin as well as minute levels of benzylpenicillin and meloxicam. Hence, the food safety risk from consumption of products from the treated pig would have been considered negligible. Relying on the violation of the withdrawal period alone would have led to total condemnation. The discrepancy arises because safety factors are included when deciding the withdrawal period. The details is the calculations are shown in the excel sheet, which can be found in: https://ribmins.com/survey-on-residues-of-antimicrobials-in-pigs/.

3.3. Limitations and further work

According to the EU legislation, any animal sent for slaughter must be accompanied by a declaration from the primary producer that guarantees the animal complies with the withdrawal period before slaughter if treated with veterinary medicinal products (EU Parliament and Council, 2004). This information is part of the FCI. Similarly, the abattoir must ensure that animals received for slaughter are accompanied by relevant FCI, which includes the guarantees that the animals comply with the withdrawal periods before slaughter. Any animal that does not comply with the FCI-requirements cannot be allowed to enter the abattoir (EU Parliament and Council, 2004). Hence, a system is in place to limit the number of occasions that animals erroneously leave the production premises before the end of the withdrawal period.

The EU legislation is based on MRLs, but MRLs are not the same in all countries around the world (Léger et al., 2019). Likewise, withdrawal periods differ. In the EU, withdrawal periods can be defined at national or EU level. For AMs licensed decades ago, most withdrawal periods were defined at national levels, whereas for newer AMs, an EU licence has been the norm. This can create major differences between the withdrawal period in force in one country compared to that in another. An example is the oxytetracycline AM, Engemycin 100 mg/ml, for which the withdrawal period after intramuscular injection is 30 days in Denmark (https://xnet.dkma.dk/indlaegsseddel/PdfFileServlet?formulationid=4322&lang=da), 10–14 days in the United Kingdom (https://www.farmacy.co.uk/engemycin-10-dd-injection-100ml/p230) and 8 days in Austria (https://www.msd-tiergesundheit.at/produkte/engemycin-100-mg-ml/). As explained by Lund et al. (under revision), such variations are not science-based, but a result of the presumably different approaches in place at the national CAs over several decades, where different safety factors could have been applied. When some veterinary products are lacking on the national market, the clinical veterinarians are supposed to use products existing in other EU Member States instead of the ones they are used to. But which rules should they then be applied? Although recommendations are given in the new EU Regulation on veterinary medicinal products (The European Parliament and the EU Council, 2019), the answers are not always clear.

To counteract the confusion that could arise from all these issues, our suggested best practice would be to calculate the concentration and amounts of residues present in the meat and other edible tissues at the time of slaughter, when a primary producer informs the abattoir of erroneous delivery within a withdrawal period of animals for slaughter. The calculation would make it possible to assess whether the non-compliant event (delivery before the end of the withdrawal period) has resulted in non-compliant levels of drugs in the meat. Moreover, we suggest focussing not just on the residual concentrations judged against the MRLs, but also, to consider the intended use of the carcass and organs using the ADI value when determining whether to allow them to enter the food or feed chain. This approach would minimise unnecessary condemnations in a safe way. The different elements of our exposure risk assessment model can be discussed, e.g., which serving size to operate with. In the examples given in Table 1, a serving size of 200 g was used, but other serving sizes could also be argued for. We have assumed that the AMs are present only in the edible part of the slaughtered animal. This is likely a worst-case scenario, which considers that some AMs have

Table 1
Description of elements of exposure risk assessment for residues of legal drugs potentially present in one or more pigs delivered to an abattoir before the end of the withdrawal period – two examples of antimicrobials are given as well as one pain killer.

	Kind of drug used for treatment of pig according to pig producer		
Variable	Lincomycin	Meloxicam	Benzylpenicillin
Live weight of slaughter pig (kg)		117.9 kg	
Slaughter weight (kg)		86.4 kg	
Estimated kg of edible part of carcass (85%)		73.4 kg	
Treatment dose	10 ml of 100 mg/ml	2 ml of 20 mg/ml	8 ml of 300 mg/ml
Time between last treatment and slaughter	2.0 days	2.0 days	2.0 days
If relevant, time between penultimate or previous treatments and slaughter	Not relevant	Not relevant	Not relevant
Halflife (worst case)	6 h	2.5 h	2.7 h
Number of half-lifes	2*24 h/6 h = 8	2*24 h/2.5 h = 19.2	2*24 h/2.7 h = 17.7
Reduction factor	$(0.5)^{8}$	$(0.5)^{19,2}$	$(0.5)^{17,7}$
Reduction factor multiplied with the treatment dose	$(0.5)^{8}$ * 10 ml * 100 mg/ml = 3.906 mg	$(0.5)^{19,2}$ * 2 ml * 20 mg/ml = $6.6*10^{-5}$ mg	$(0.5)^{17,7}$ * 8 ml * 300 mg/ml = 0.011 mg
Resulting amounts of residues (μg) at the time of slaughter	3906 μg	0.066 μg	11 μg
Concentration (μg/kg) in edible carcass	3906 μg/73.4 kg = 53.2 μg/kg	0.006 μg/73.4 kg = $8*10^{-5}$ μg/kg	11 μg/73.4 kg = 0.15 μg/kg
Residual amounts (μg) in serving size of 200 g	3,906 μg*200g/(73.4*1000g) = 10.6 μg	0.066 μg*200g/(73.4*1000g) = 0.0002 μg	11 μg*200g/(73.4*1000g) = 0.029 μg
ADI (Acceptable Daily Intake	<600 μg	<75 μg	<30 μg
MRL (μg/kg)	100 μg/kg	20 μg/kg	50 μg/kg

[a] If relevant, time between penultimate or previous treatments and slaughter should be considered.
[b] The most conservative half-life value should be chosen if more than one is indicated in the summary product specification.

a higher affinity to some tissues and organs than others. Again, this issue could be further refined in the exposure risk model.

The challenge for risk management of consumer exposures to AMs in the form of residues in meat can be referred to as a tip of the iceberg problem. We observe a phenomenon (tip of the iceberg) but extensive risk management e.g., in the form of extensive call-backs (based on detection of a positive sample in official monitoring or an FBO's own check) or condemnation of all meat from a slaughter day (because a pig producer has informed the abattoir of erroneous delivery of animals for slaughter), do not resolve the population issue of which the phenomenon is indicative. Instead, this should be interpreted as a representation of the population issue (the iceberg under water), where population-based risk management measures are needed. These could be, e.g., compliance on the farm with the pig producer's own check regarding use of AMs including ways of marking treated animals. In addition, the response given to the primary producer, who contacts the abattoir to report the erroneous delivery of pigs to slaughter, should be considered carefully using systems thinking (Anderson & Johnson, 1997). If the decision is to give the producer a fine, then it is doubtful that the producer will contact the abattoir again in a similar situation. Hence, a negative causal loop could be the result, where the lessons learnt for the pig producers in general would be to never contact the abattoir. Hence, it would be preferable if the abattoir could welcome the information, be able to perform a risk assessment, and take the necessary risk mitigating actions, without punishing the primary producer too much. Hence, this would allow the person or company to learn from the mistake.

Moreover, in line with Lund et al. (under revision), we recommended that the existing withdrawal periods are harmonised in the EU. The responsibility for this process lies with the pharmaceutical companies, which may have their reasons for not applying for new marketing authorisations. Among these reasons, new and costly studies would probably be required, with more narrow indications than applied decades ago.

4. Conclusion

Pigs may erroneously be delivered to slaughter before the end of the withdrawal period. In this situation, some pig producers may contact the abattoir to inform about this. How the situation is managed is important to the pig producer, FBO, CA and consumers. Our survey, undertaken among CAs and FBOs, provides evidence that there is no uniform approach in place among countries. There are different views regarding correct handling between CA and FBO and between countries with major and minor pig meat exports. OVs are frequently the decision-makers in this situation but left with little or diversified guidance. To harmonise this, we propose a risk-based best practice model, which can be used both when the animal is still alive and in case the animal has been slaughtered and health marked. The model consists of a quantitative exposure risk assessment that can estimate the actual risk, be performed within one day, and based on easily available data. Hereby, a decision can be reached, in a safe and defendable way, considering the information about the AM and other drugs used as well as the time that has passed between treatment and slaughter. This approach may lead to significant less food waste in the meat production, thus contributing to achieve some of the targets set by the European Green Deal. Finally, the current legislation regarding the placement of a product on the market is unclear. A feasible definition should be identified. This should ensure that meat that has been subject to an official control and has been health marked satisfies the requirements of the EU General Food Law (EU Regulation 178/2002) while considering that meat might occasionally contain AM residues in low levels, which is the reason for operating with MRL and ADI.

CRediT authorship contribution statement

Lis Alban : Conceptualization, Formal analysis, Writing - original draft, Writing - review & editing. **Jesper Valentin Petersen :** Formal analysis, Conceptualization.

Michał Majewski: Formal analysis, Writing - original draft, Writing - review & editing

Boris Antunovic, Madalina Belous, Aivars Bērziņš, Silvia Bonardi, Rosa Maria García-Gimeno, Ian Jenson, Arja Helena Kautto, Derk Oorburg, Ioannis Sakaridis, Alexandrina Sirbu, Madalena Vieira-Pinto, Ivar Vågsholm: Writing - original draft, Writing - review & editing.

Declaration of competing interest

We, the authors, declare that we have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Still, we would like to declare our affiliations, as we have done in the last part of the manuscript file:

LA and JP work for an organisation which gives advice to farmers and food-producing companies.

AS is a technical expert and acts as a freelance consultant in the food industry.

AHK is affiliated with the university while also working for the

Swedish Food Agency.

LA is also Adjunct Professor at the University of Copenhagen.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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