The Royal College of Pathologists
Pathology: the science behind the cure

Guidelines on veterinary necropsy practice

Post-mortem examination of animals having received chemotherapeutic or radioactive agents

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Foreword

Guidelines published by the Royal College of Pathologists are generally systematically developed statements to assist pathologists to provide a high standard of care for patients. Guidelines for veterinary pathologists also assist pathologists to advise veterinarians and the owners or keepers of animals about appropriate treatment for specific clinical circumstances. This Guideline is somewhat different in that it is intended to protect the health of the pathologists themselves while carrying out their work.

This document has been developed to cover most common circumstances, but it is recognised that guidelines cannot anticipate every pathological specimen type and clinical scenario. The guidelines themselves constitute the tools for dissemination and implementation of good practice, although occasional variation from the practice recommended may therefore be required to ensure the safety of personnel in particular circumstances.

Post-mortem examinations (PMEs) are a vital tool in helping us understand disease, how best to treat it and in developing and refining those treatments. This, coupled with significant advances in both veterinary and human oncology and medical practice has led to an increase in the use of chemotherapeutic and radioactive agents to combat disease in animals. While this has resulted in increased survival and quality of life for those treated, these agents can pose a risk to those who undertake PMEs. That risk may be related directly to the health of the practitioner or be more amorphous and relate to reputational risk around how to dispose of the materials or which are the relevant regulations to follow. This document, produced by recognised experts in the field of veterinary pathology, provides clear, simple and easy to follow guidance, which covers all the areas likely to cause concern from the types of materials one is likely to encounter, to suitable personal protective equipment, to disposal and relevant regulations. As such, it is hugely helpful to all practitioners who might be involved in animal post mortems.

The following stakeholders were consulted for this document:

- European College of Veterinary Internal Medicine
- European College of Veterinary Pathologists.

No major organisational changes or cost implications have been identified that would hinder the implementation of the guideline.

As the primary aim of these guidelines is to ensure the health and safety of personnel and therefore legislation and sources of official guidance published by the Health and Safety Executive and the International Atomic Energy Agency were searched and reviewed. Further information used to develop this clinical guideline was obtained by undertaking a systematic search using PubMed. Key terms searched included cytotoxic drugs, chemotherapy, radioactive source, ionising radiation, brachytherapy, autopsy and post mortem. As there is a relative paucity of evidence concerning the risks associated with exposure to hazardous agents in tissues and cadavers, literature from the last 20 years to March 2023 was accessed. Much of the content of the document represents custom and practice and is based on the substantial clinical experience of the stakeholders and other experts consulted. Consensus of evidence was achieved by expert review. Gaps in the evidence will be identified by College members via feedback received during consultation

Published evidence was evaluated using modified SIGN guidance (see Appendix A). The sections of this autopsy guideline that indicate compliance with each of the AGREE II standards are indicated in Appendix B.

A formal revision cycle for all guidelines takes place on a 5-year cycle. The College will ask the authors of the guideline to consider whether or not the guideline needs to be revised. A full consultation process will be undertaken if major revisions are required. If minor revisions or changes are required, a short note of the proposed changes will be placed on the College website for two weeks for members' attention. If members do not object to the changes, the changes will be incorporated into the guideline and the full revised version (incorporating the changes) will replace the existing version on the College website.

The guideline has been reviewed by the Death Investigation Committee, the Veterinary Pathology Specialty Advisory Committee (SAC) and Professional Guidelines team and will be placed on the College website for consultation with the membership from 31 July to 28 August 2023. All comments received from the membership will be addressed by the authors to the satisfaction of the Clinical Lead for Guideline Review.

The guideline was developed without external funding to the writing group. The College requires the authors of guidelines to provide a list of potential conflicts of interest; these are monitored by the Professional Guidelines team and are available on request. The authors of this document have declared that there are no conflicts of interest.

1 Introduction

This document has been prepared by the Veterinary Pathology SAC to provide guidance on safe practice when carrying out post-mortem examinations (PMEs) of animals that have been administered chemotherapeutic or radioactive agents prior to their death.

By their very nature, chemotherapeutic substances damage or kill cells. Their action is rarely specific to tumour cells and normal cells are often damaged or killed. These agents are increasingly used in veterinary practice for therapeutic and diagnostic purposes; appropriate safety precautions must be taken to protect staff and owners from potential negative impacts on their health.

However, there is also a potential risk to those performing PMEs of animals that have undergone a procedure prior to death. Both cytotoxic drugs and radioactive agents can produce harm to those exposed to them, ranging from skin, eye and mucous membrane irritation and allergic reactions, through to more severe systemic tissue damage and carcinogenesis. There may also be negative impacts on fertility and pregnancy. Therefore, steps to protect the health and safety of all personnel are essential.

The PME of an animal can be undertaken safely and in compliance with relevant legislative requirements by the implementation of relatively simple precautions following a risk assessment. This must consider not only direct exposure of personnel but the control of contamination, waste, the retention of samples and disposal of the cadaver. The risk assessment should be completed in consultation with an appropriately trained radiation protection advisor (RPA).

All facilities that perform veterinary PMEs should have standard operating procedures for encounters with expected and unexpected radioactive sources or chemotherapeutic agents. To minimise unexpected exposure to radioactive cases, good communication with submitting veterinarians is essential.

The aim of this document is to describe the hazardous agents commonly used in veterinary medicine, the circumstances in which they may be encountered when undertaking a veterinary PME in clinical practice or PME facility and what protocols and precautions should be employed to protect staff.

Procedures for the PME of animals involved in experimental or contract research or in clinical trials are not covered in this document because of their variable, potentially exceptional and specific nature.

1.1 Target users and health benefits of this guideline

The target primary users of this guideline are veterinary pathologists, veterinary clinicians, veterinary nurses and ancillary staff involved in the PME of animals in clinical veterinary practice and research. This will include veterinary pathology staff in specialist institutes, universities or companies, or veterinarians carrying out occasional PMEs in general practice. It includes staff performing gross PMEs or staff handling tissues for histological, cytological or microbiological investigations. The recommendations will also be of value to staff who clean the facilities and dispose of clinical waste and animal tissues after PMEs.

2 Regulations

The *Control of Substances Hazardous to Health Regulations 2002* (COSHH) are the overarching regulations pertinent to these guidelines. The current version of COSHH and the accompanying code of practice and guidance can be found on the Health and Safety Executive website.[1]

COSHH requires employers to control substances that are hazardous to health. This is achieved by:

- risk assessment to identify the potential hazards
- providing control measures and ensuring that they are used
- providing information, instruction and training
- providing monitoring and health surveillance
- planning for emergencies.

Work involving radioactive substances is also governed by the *Radioactive Substances Act 1993* and the *Ionising Radiations Regulations 2017*. The Health and Safety Executive (HSE) is the Government agency that regulates and enforces safety legislation, also acting as a source of advice.

3 Safety with potentially hazardous agents

Many of the measures necessary to protect personnel from harm from the hazardous agents covered by this guidance will already be part of the good practice processes adopted during PMEs. However, there are additional procedures that are required when handling the tissues from animals that have been treated with hazardous agents.

The basis of such safe practice is correct training, maintaining and following the correct procedures and possessing the necessary information concerning the history of the animals that are being examined.

Several agents administered to animals in clinical veterinary practice, whether in life or after death, may be hazardous to people encountering them. Guidance in this document applies to animals treated with chemotherapeutic agents and radioactive isotopes. There is clear guidance about handling these agents prior to administration and how treated animals should be handled by veterinary staff and owners during and after treatment, yet guidance for pathology staff is currently lacking.

3.1 Radioactive agents

PMEs involving animals retaining radioactive substances are fortunately rare but, when they occur, they can impose significant radiation safety and legal requirements.[2,3]

A variety of radioactive substances are employed for diagnosis or treatment in clinical veterinary practice. Such substances may be used in all species but they are more likely to be employed in companion animals and horses. The death of an animal soon after the administration of one of these agents will occur from time to time and the pathologist should be prepared for circumstances where these agents are encountered, whether expected or unexpected.[4]

While a cadaver may contain a retained radioactive substance, its presence does not necessarily require additional or greater precautions than those routinely adopted to prevent exposure to biological hazards. This will depend on its physical and biological half-life, the type of radiation emitted, the quantity retained and its physical form. When radioactive substances are administered, the amount retained will depend on the substance's physical half-life, but also on the rate at which it is excreted from the body (the biological half-life). The combination of these characteristics results in a shorter 'effective' half-life.[4] This is the most important parameter relevant to safety.

While alpha-emitting substances can be extremely harmful if ingested, they are rarely used in healthcare. Sources of beta-radiation are more frequently used in in the veterinary clinic; high energy beta-radiation presents a significant risk, both following ingestion or inhalation and externally. However, these risks can be controlled by conventional personal protective equipment (PPE), such as gloves and laboratory coats, simple decontamination procedures, the prevention of eating and drinking and conventional handwashing.

Agents emitting gamma radiation are also used in veterinary diagnosis and treatment, although, in the latter case, it is often the accompanying beta radiation that provides the therapeutic benefit. Gamma radiation is highly penetrative but the risk is greatly reduced by distance from the source or by effective shielding by substances such as lead.

For a risk assessment to be undertaken, the potential sources of ionising radiation, in terms of the isotopes and their physical or chemical forms that may be encountered, will need to be determined. Various forms of personal dosemeters can be worn to determine actual exposure.

Radioactive substances are used in 2 forms clinically:

- unsealed sources for diagnostic or therapeutic purposes
- sealed sources for therapeutic purposes (brachytherapy).

3.1.1 Unsealed sources

Most diagnostic applications involve intravenous injection of radioactive materials with a relatively short half-life. The short half-life of these substances reduces the risk of significant exposure to personnel carrying out PMEs. For example, the commonly used technetium-99m (^{99m}Tc) has a half-life of 6 hours. Therefore, 24 hours after administration, the activity level is reduced to 6% and then drops to less than 0.05% after 48 hours.[4] ^{99m}Tc is commonly used for gamma-scintigraphy in horses for conditions that often result in euthanasia and submission for PMEs; this, coupled with the quantity of the agent administered, should be seriously considered by the pathologist.

Therapeutic administration of unsealed agents usually involves the use of material with a longer half-life and may utilise a variety of different routes, including intravenous, oral or injection into body cavities.

The radioisotopes used in this form may include those given in Table 1.

Table 1: Unsealed radioisotopes used therapeutically or for diagnostic investigation.

Used therapeutically	Used for diagnostic tests
Iodine-131	Technetium-99m
Yttrium-90	Indium-111
Phosphorous-32	Iodine-123
Strontium-89	Fluorine-18
Samarium-153	

Iodine-131 (^{131}I) is the most-used therapeutic agent for the treatment of diseases of the thyroid. Although it is very effective in this regard, gamma and beta radiation combine with a long physical and effective half-life to present a significant radiation risk, particularly to persons coming into direct contact with organs and bodily fluids in which iodine has been concentrated. With these characteristics and common usage, it is likely to present the greatest risk to staff involved with veterinary PMEs.

Although the administration of beta emitting isotopes, such as strontium-89 (^{89}Sr), yttrium-90 and phosphorous-32, rarely requires specific external radiation protection precautions, this may not be the case for direct contact with internal organs or bodily fluids encountered during PME. In such cases, high skin doses can be received without the implementation of suitable precautions. It is preferable to delay a PME to allow sufficient radioactive decay, but this may be impractical given the long effective half-lives of some of these isotopes. For example, the physical half-life of ^{89}Sr is 51 days, rendering it impractical to delay PME for sufficient time for radioactive decay to reduce emissions significantly; appropriate precautions will need to be employed to reduce the dose received. If appropriate, it may be possible to refrigerate or freeze the cadaver until such time that sufficient radioactive decay has rendered the body safe to handle.

3.1.2 Sealed sources

Radioactive sources used in interstitial brachytherapy, such as seeds, needles, tubes, or wires, may be surgically inserted directly into or immediately adjacent to diseased tissues. They are used to treat cancers of accessible sites, like the prostate, intra-oral cancers and superficial tumours, particularly in small animals and horses.[5]

In intracavitary therapy, radioactive sources are introduced into the body cavity in a form-fitting applicator to irradiate the cavity walls and any lesion therein. The common cancers treated are those of the cervix, uterus, vagina, rectum, nasopharynx and oesophagus.

Radioisotopes emitting gamma rays are usually employed in brachytherapy as they have good penetrating power, although the sources are encapsulated in a metal film to absorb any unwanted beta-radiation. In other cases, beta-emitters may be used.[6]

Some of these sources are intended to remain permanently implanted and some are applied temporarily to be removed after an appropriate period. Many of the agents used, whether permanently or temporarily implanted, have long physical half-lives, making it impractical to delay PME for sufficient radioactive decay to significantly reduce emissions. Temporarily implanted, sealed radioactive sources and organs in which radioactive sources are permanently implanted should, therefore, be removed prior to PME if possible.

The radioisotopes used in this form may include those given in Table 2.

Table 2: Implanted sealed radioisotope sources.

Yttrium-90
Caesium-137
Iridium-192
Strontium-90
Rubidium-106
Iodine-125
Phosphorous-32
Gold-198
Cobalt-60

3.1.3 Specific risk to personnel

Persons who may encounter radioactive emissions during their work are subject to dose limits specifying the maximum exposure allowed; it is an offence to exceed these limits.[7] The limits are specified by Schedule 3 of the Ionising Radiations Regulations 2017.[8] The risk assessment concerning any radiation hazard should consider the potential exposure an individual may receive during their work (including accidental exposures), consulting an RPA as necessary.[9] This will help identify whether staff should be subject to personal dose monitoring.

There are different limits set for different categories of staff and visitors but, for most employees, the limit on total effective dose is 20 mSv and 500 mSv for the extremities in a calendar year. The dose limit for persons under the age of 18 or pregnant women are lower. It should be noted that, in normal veterinary pathology practice, these dose levels are unlikely to be approached.[10]

On most occasions, the deaths of animals to which radioactive substances have been administered will be notified to the pathologist. However, it must also be expected that these agents may be encountered without warning if the clinical history or handover accompanying the cadaver is inadequate. Staff should be aware of these risks and of the necessary actions to be taken if suspected implanted sources are discovered or notice of administration of an unsealed source is received after the PME has commenced.

The risk of significant exposure to ionising radiation is dependent on the activity of the agent, how it was administered, its physical and effective half-lives, the time since administration, whether it was concentrated in a particular organ or body fluid and whether these came into close contact with associated personnel. It is, therefore, not possible to generalise about the hazard posed by individual agents, but rather the risks associated with each case must be individually assessed.

3.1.4 Specific precautions to be taken

Knowledge that a cadaver contains an unsealed radioactive substance can only be gained by the disclosure of the submitting veterinarian and enquiries made by the acting pathologist. If there is prior knowledge, a specific risk assessment must be made in consultation with an RPA and the need for additional radiation protection controls determined in accordance with appropriate regulations. It may be appropriate to monitor whole-body and skin/hand radiation doses received by the most-exposed staff using suitable dosemeters.

A cadaver containing sealed radioactive sources is unlikely to pose a significant risk prior to examination; these can be removed prior to PME. However, cadavers retaining recently administered unsealed sources, such as ^{131}I, may present both an internal and external risk and so they should only be handled, when necessary, by personnel wearing gloves and an impervious gown or apron. Ideally, a primary radiation protective garment, such as a lead apron, would be utilised. The cadaver must be contained to prevent the spillage of body fluids and any contaminated bedding secured in a leak-proof bag.

Some unsealed agents may concentrate in a particular cavity or organ, such as ^{131}I in the thyroid gland(s). Sealed sources will have been deposited in a restricted location. Drainage of the cavity or excision of the relevant organ will reduce exposure if undertaken at the start of the PME. Material should be safely removed and stored for a suitable period to allow radioactive decay to render it safe.

Where removal of radioactive material is not practical, the PME can be undertaken using normal standard precautions supplemented by radiation-specific measures under the guidance of the RPA.

It is not possible, and indeed unwise, to quote specific time periods after which it is safe to undertake the PME after administration of a radioactive substance. This is because of the multiple factors involved, such as the administered and retained dose, the length and proximity of exposure, the number of such PMEs performed by pathology staff, individual susceptibility of personnel and the physical and effective half-lives of the radioisotope used.

Radiation exposure can be reduced by delaying the PME, perhaps by refrigerated storage, but this may not be practicable depending on the rate of radioactive decay. In situations where radioactive material has been localised but not removed, care should be taken to minimise the length of time spent handling radioactive material and by increasing the distance between personnel and the source.

The risk of skin contamination and exposure of skin and hands to beta radiation can be reduced by wearing two pairs of latex or nitrile gloves, with the outer pair being renewed following work on the more highly radioactive regions. If gloves are cut or torn during the examination and the skin is broken and/or a wound is sustained, the injury and any skin contamination should be irrigated immediately with soap and water. Exposure to airborne material can be prevented by wearing eye protection and a face mask, shield or visor.

In situations where more frequent exposure to radioactive material may be expected or where higher doses may be encountered, the wearing of a portable dosemeter and real-time measurement and recording of radioactivity prior to and during the PME in cases suspected of posing a radiation hazard is to be recommended.

Samples collected for further testing may retain a proportion of the administered radioactivity; however, the sample activity will usually be low, owing to a combination of low sample volume, radioactive decay, dilution and excretion. A risk assessment must be completed to determine whether additional precautions to those normally employed in pathology laboratories will be necessary.

All persons leaving the area should discard their protective clothing and thoroughly wash any exposed skin. In the case of unsealed sources, all equipment and surfaces should be washed to dilute any residual activity. Where sealed sources have been used, great care must be used to prevent solid radioactive material from entering the drainage system.

Any retained material should be stored safely and appropriately until radioactive decay has rendered the material safe and disposal is permitted under legislation including the *Radioactive Substances Act 1993*.[11,12] Any such storage must be recorded and an RPA must be consulted to ensure compliance. Similar considerations should apply if the cadaver is to be incinerated.

Occasionally, sealed brachytherapy sources incorporating iridium-192 (^{192}Ir) and caesium-137 (^{137}Cs) or sources used for strontium-90 plesiotherapy may be employed in veterinary patients. These sources are usually implanted or applied for very short periods and so are extremely unlikely to be encountered in a PME. However, these agents have very long physical half-lives and represent a particular hazard. Complete recovery and expert removal of the source into a shielded container under the direction of a person trained to handle such sources is essential.[4]

3.2 Chemotherapeutic agents

The use of cytotoxic chemotherapeutic drugs in veterinary practice is becoming increasingly common. It is inevitable that some animals will die soon after their administration; these cases may be presented for PME.

3.2.1 Specific risk to personnel

Most veterinary drugs do not pose a major hazard to the person handling an animal treated with them. Cytotoxic chemotherapeutic agents are the exception. These are a group of medicines that are toxic to cells by preventing their replication or growth and are used to treat cancer and some other diseases. However, their toxicity is not specific to cancer cells and they can present significant risks to people who are exposed to them. Routes of exposure can include skin contact, inhalation, ingestion and needle stick injuries. Furthermore, exposure can come through handling animals to which these drugs have been administered. The effect on those exposed may be acute – e.g. contact dermatitis, local allergic reactions, vomiting, abdominal pain and hepatitis – or chronic, e.g. carcinogenesis, myelosuppression, foetal loss, teratogenesis in pregnancy and increased risk of stillbirth.[13]

Human healthcare workers handling chemotherapeutics have frequently been found to have higher levels of chromosomal aberrations, as well as an incremental increased risk of infertility and early pregnancy loss compared to the general population.[14]

Staff handling the supply and administration of these drugs should be specifically trained, must follow strict protocols and are subject to exacting regulation.[14,15] Treated animals should only be discharged into the care of their owners when it is safe to do so and only after they have been instructed in safe handling of them and their excretion products.

These agents may also be encountered by staff performing PMEs; consequently, staff should be made aware of the risks and protected. Employers have a legal obligation to assess the risks and take suitable actions to protect their staff, including providing adequate training and safety equipment under the COSHH Regulations 2002. Guidelines are available for safe handling of cytotoxic drugs from the Health and Safety Executive,[13] with more general advice being given by the COSHH Approved Code of Practice.[16] The risk assessment should account for the agents likely to be encountered and their potential toxic effects and evaluate the likely risk of exposure. Such risk assessments and written protocols should take account of all workers who may encounter treated animals, their tissues and waste products. Concern should be applied for more susceptible personnel. Workers who are immunocompromised, pregnant, breastfeeding or attempting to conceive should avoid exposure altogether or decrease exposure to as low a level as reasonably practicable.

Protocols should aim to control exposure at source by using enclosed systems where practical, adequate extraction systems and appropriate PPE. Consideration should be made toward the number of personnel and the duration of exposure. Good hygiene practice, including the prohibition of eating and drinking in the vicinity of the hazard, must be enforced.

Chemotherapy agents are administered systemically and will therefore be found throughout the body, in bodily fluids and in excreta for a varying time after administration. As there are no known safe levels of any of the agents used in veterinary practice, the aim should be for exposure to be as low as reasonably achievable (using the ‘As low as reasonably achievable’ [ALARA] principle in radiation safety). Moreover, apart from acute exposure, repeated exposure to much smaller doses may result in little-understood chronic effects.

Moreover, most drugs are metabolised before being excreted and, in many cases, the metabolites are also potentially toxic, thereby extending the effective elimination time, during which exposure poses a risk to personnel.

A few studies in dogs and extrapolation from human studies allow the estimation of indicative times for the elimination of commonly used cytotoxic agents after their therapeutic administration. Surprisingly, different studies have not suggested different elimination times. As it is not possible to accurately specify safe periods, the precautionary principle demands taking account of the indicative times suggested in Table 3, but also adding a safety margin where possible.[17–19] Obviously, the death of an animal within the periods indicated will result in the cessation of excretion and metabolism to some extent; therefore, the hazardous agent must be assumed to remain in the tissues for a much longer period. Drugs are excreted via a variety of routes and, therefore, toxic compounds may be present in urine, faeces, saliva, vomitus and sebum. Moreover, orally administered drugs may be retained for even longer periods, owing to differences in bioavailability.

Table 3: Common cytotoxic agents and period of detection after last administration.

Drug	**Major excretion routes**	**Days detected post-administration**
5-Fluorouracil	Faeces	3
Carboplatin	Urine	5 (21*)
Chlorambucil	Largely metabolised by the liver	2
Cisplatin	Urine	8
Cyclophosphamide	Urine	4
Cytarabine	Urine	3
Doxorubicin	Urine/faeces	7 (21*)
Gemcitabine	Urine	7
Lomustine	Urine	3
Mitoxantrone	Faeces	8
Vincristine	Faeces	3 (7*)
Vinblastine	Faeces	3 (14*)
*Figures in brackets indicate suggestions that metabolites can be detected at longer intervals.		

Despite the listing of these indicative elimination times, it is clearly difficult to be precise. This is especially notable given the range of species and medical conditions, the paucity of evidence in published research, the fact that metabolites may also be toxic and the individual variations in bioavailability. Moreover, since the metabolism and excretion of these agents is an active process, the death of an animal before excretion is complete must surely extend the period during which these agents remain in the body. Therefore, the default position should be to always avoid direct exposure to tissues, bodily fluids,

excreta and aerosols from animals that have received cytotoxic chemotherapy using appropriate containment or PPE.

3.2.2 Specific precautions to be taken

The sections that follow describe actions that are needed to protect personnel who may be at risk from exposure to hazardous agents that may have been administered to and remain in animals. Many of these actions will already be in place as part of PME procedures and, therefore, must be incorporated into those already in place.

Risk assessment

All facilities where the PME of veterinary patients is conducted should provide a specific risk assessment highlighting and assessing the risks associated with the PME of animals to which hazardous agents have been administered. Such risk assessments should include a consideration of the range of personnel that might be exposed, including any with greater susceptibility through age or pregnancy. It should also assess the frequency of submission of such animals and the agents that may have been administered, together with their toxicity.[13,20]

Safety measures

Control measures to minimise the risk of exposure to harmful agents administered to animals undergoing PME should be a combination of training, procedures, supervision, equipment, health surveillance and possession of the necessary information concerning the history of the animals that are being examined. All of these are necessary to provide a safe working environment.[13]

Communication

When animals are submitted for PME, usually from practising veterinary surgeons, they must be accompanied by information concerning any specific hazard that may be posed by the submission. This may be infection with hazardous organisms or, in this context, hazardous agents that may have been administered to and be contained within the body.

The provision of such necessary information should be mandated and facilitated using submission forms with specific questions concerning the underlying disease being investigated, the investigation and/or treatment carried out, the potentially hazardous agents employed and the date and time of administration. Further questioning of the referring veterinary surgeon as to the therapeutics administered in the submitted case may be warranted. The PME should not proceed unless the pathologist is certain whether

hazardous agents have or have not been administered to the animal to reduce or mitigate potential risks.

Training

Training appropriate to the role of the staff member and consistent with the risk assessment should be provided and reviewed and/or refreshed at least on an annual basis or whenever new information becomes available. Training should be recorded in the staff member's training record.[20]

Health surveillance

Health surveillance programmes are necessary for all workers employed in situations where hazards encountered at work can impact workers' health. Health surveillance is required by law if hazards to health remain, even after controls have been put in place. Therefore, if a risk assessment determines that there is a risk of exposure to hazardous agents in the bodies of animals submitted for PME, a health surveillance scheme should be established in consultation with an appropriately qualified occupational health doctor.[21] Only those personnel who are exposed to the hazards should be included and they should be consulted and informed of the nature of the health surveillance programme and the hazards that it is intended to mitigate. It must be clear who is to lead and manage the scheme; other roles, responsibilities and communication arrangements must be clear.

Employees should be encouraged to come forward with any concerns. An open culture should be encouraged, whereby those that are medically vulnerable can seek further advice and guidance of working with veterinary cases treated with radioactive or chemotherapeutic agents. Women must be able to notify their supervisors if they are actively attempting to become pregnant, are pregnant or are lactating. Consultation with consideration for alternative duties on the advice of their physician may also be warranted.

It must be clear what action will be taken if health surveillance highlights ill health that may have arisen because of exposure in the workplace and how this might result in actions necessary to prevent further harm. It must be complemented by training that highlights the potential effects that exposure to the hazardous agents might induce and what symptoms should be reported to their doctor.

When deemed necessary by the risk assessment, appropriate personnel should wear whole-body dosemeters to measure cumulative exposure to ionising radiation so that this can be considered in the periodic health assessment.

Records of the outcome of health surveillance must be comprehensive and kept for at least the period specified under the regulations, for example 40 years under COSHH.[21] Medical records should be retained by the occupational health doctor.

Limit exposure

Many of the necessary actions for dealing with an animal that contains a hazardous agent will already be used for protection from pathogens. Any additional specific actions required should be incorporated into the existing safe practice protocols.

The first action that is necessary is to limit the number of people encountering the animals that contain the hazardous agent. Those that do should minimise their time of exposure and maximise the distance, particularly where radioactive agents are suspected or known to have been used. Pregnant or breastfeeding women, men or women attempting to conceive or any visitors or staff who have not been fully trained should be kept out of the area where the PME is being performed. As detailed in the sections above, where possible and depending on the radioactive isotope employed, the PME should be delayed for radioactive activity to diminish to a safe level. If possible, the PME or handling of harvested samples should be performed in some form of containment or safety cabinet.

If the hazardous agent is known to be concentrated in a particular organ or body fluid after systemic administration (e.g. ^{131}I in the thyroid gland), or in the case of sealed radioactive implants, the contaminated material should be removed using forceps to shielded containers before the rest of the PME is completed.

In the extremely rare instances when a ^{137}Cs or ^{192}Ir source is discovered, it must be completely removed to a shielded container using precautions determined by a case-specific risk assessment and under the direction of a person trained to handle such sources.[23]

Appropriate PPE and its use should be determined after a risk assessment. However, in many circumstances, disposable impervious gowns made of polyethylene-coated polypropylene or other laminate materials with back closure offer the best protection. Eye, face and respiratory protection in the form of goggles or visors with an FFP2 or FFP3 mask should be worn when there is any risk of aerosolisation. 2 pairs of latex or nitrile chemotherapy gloves must be used with a cut resistant glove worn in between these. The inner 2 gloves must be worn under and the outer glove worn over the cuff of the gown.[14,22,23] If deemed necessary by the risk assessment, dosemeters can be worn on the fingers or hands to measure the doses received by the skin in real time, if close contact is

made with organs or body fluids retaining significant radioactivity. PPE should be removed carefully and in a specific order to avoid touching the contaminated parts.

Cleaning and waste management

In addition to normal cleaning practices following PME, additional procedures may be required following the handling of an animal containing hazardous agents, particularly radioactive agents. For animals treated with cytotoxic drugs, careful cleaning of surfaces with conventional cleaning agents followed by copious quantities of water are sufficient. Liquid waste can be disposed of via the normal PME room drainage.

For animals treated with radioactive agents, as far as possible, all excreta and other liquid waste should be contained and/or absorbed in absorbent material, which should be bagged and labelled. After the PME has been performed, the body and any tissues should also be carefully bagged and labelled. In line with the risk assessment and dependent on the source, this material should be stored for a suitable time prior to disposal or passed to a suitable contractor.[4]

4 Criteria for audit

As part of its Continuous Quality Improvement programme, the College promotes high quality clinical audit.[24] Clinical audit is a process that seeks to identify where improvements can be made within healthcare services by measuring them against evidence-based standards.

It is recognised that most pathologists will not regularly encounter cadavers or tissues that may contain residues of hazardous agents. Necessarily, the opportunity for audit is restricted and rely on more generalised criteria based on the quality of training, record keeping and use of PPE and dose monitoring equipment.

The following standards are suggested criteria based on these guidelines that might be used in periodic reviews to ensure that adequate procedures to protect the health and safety of all personnel.

- 100% of submissions are supported by documentation indicating the potential presence or absence of hazardous agents in submitted material.
- All staff in contact with cadavers or tissues have received appropriate training before exposure.
- Appropriate PPE and suitable dosemeters are available and in use.

- Equipment and consumables suitable for the safe collection and disposal of tissues and spillages must be readily available and in use.
- An RPA must be appointed and immediately available for advice.

5 References

1. The Health and Safety Executive. *Working with Substances Hazardous to Health: A Brief Guide to COSHH*. Accessed March 2023. Available at: https://www.hse.gov.uk/pubns/indg136.pdf
2. The International Atomic Energy Agency. *Radiation Protection and Safety in Veterinary Medicine Safety Reports Series No.104.* Vienna, Austria: International Atomic Energy Agency, 2021.
3. The Health and Safety Executive. *Working with Ionising Radiation: Ionising Radiations Regulations 2017, Approved Code of Practice and Guidance*. Accessed March 2023. Available at: https://www.hse.gov.uk/pubns/priced/l121.pdf
4. Singleton M, Start RD, Tindale W, Richardson C, Conway M. The radioactive autopsy: safe working practices. *Histopathology* 2017;51:289–304.
5. Advanced Veterinary Medical Imaging. *Brachytherapy.* Accessed March 2023. Available at: https://www.avmi.net/services/radiotherapy/brachytherapy/
6. Bakker CR, Lam GEH M, van Nimwegen SA, Rosenberg A, Nimwegan WF, Van Es RR *et al.* Intratumoral treatment with radioactive beta-emitting microparticles: a systematic review. *J Radiat Oncol* 2017;6:323–341.
7. The Health and Safety Executive. *Dose Monitoring, Assessment and Recording*. Accessed March 2023. Available at: https://www.hse.gov.uk/radiation/ionising/doses/index.htm
8. UK Government. *The Ionising Radiations Regulations 2017 (SI 2017/1075, Schedule 3)*. Accessed March 2023. Available at: https://www.legislation.gov.uk/uksi/2017/1075/schedule/3/made
9. The Health and Safety Executive. *Radiation Protection Advisors*. Accessed March 2023. Available at: https://www.hse.gov.uk/radiation/rpnews/rpa.htm
10. Greaves C, Tindale W. Radioiodine therapy: care of the helpless patient and handling of the radioactive corpse*. J Radiol Prot* 2001;4:381–392.
11. UK Government. *The Radioactive Substances Act 1993, c12.* Accessed March 2023. Available at: https://www.legislation.gov.uk/ukpga/1993/12/contents
12. Department for Environment, Food and Rural Affairs. *Radioactive Substances Regulation Guidance: Environmental Permitting Guidance Radioactive Substances*

Regulation For the Environmental Permitting (England and Wales) Regulations 2010 version 2.0. Accessed March 2023. Available at: https://www.gov.uk/government/publications/radioactive-substance-regulations-rsr-guidance

13. The Health and Safety Executive. *Safe Handling of Cytotoxic Drugs in the Workplace*. Accessed March 2023. Available at: https://www.hse.gov.uk/healthservices/safe-use-cytotoxic-drugs.htm

14. Smith AN, Klahn S, Phillips B, Parshley L, Bennett P, Flory A *et al*. ACVIM small animal consensus statement on safe use of cytotoxic chemotherapeutics in veterinary practice. *J Vet Intern Med* 2018;32:904–913.

15. The British Small Animal Veterinary Association*. BSAVA Small Animal Formulary Part B: Exotic Pets*. Accessed March 2023. Available at: https://www.bsavalibrary.com/content/formulary/exotic-pets

16. The Health and Safety Executive. *Control of Substances Hazardous to Health: The Control of Substances Hazardous to Health Regulations 2002*. Accessed March 2023. Available at: https://www.hse.gov.uk/pubns/priced/l5.pdf

17. The European College of Veterinary Internal Medicine of Companion Animals*. Preventing Occupational and Environmental Exposure to Cytotoxic Drugs in Veterinary Medicine.* Accessed March 2023. Available at: https://www.ecvim-ca.org/images/downloads/guidelines/Guidelines_ECVIM_Hazards_Cytotoxic_drugs_2nd_version_July_2007.pdf

18. Knobloch A, Mohring S, Eberle N, Nolte I, Hamscher G, Simon D. Cytotoxic drug residues in urine of dogs receiving anticancer chemotherapy. *J Vet Int Med* 2015;24:384–390.

19. Hamscher G, Mohring A, Knobloch A, Eberle N, Nau H, Nolte I *et al*. Determination of drug residues in urine of dogs receiving anti-cancer chemotherapy by liquid chromatography-electrospray Ionization-tandem mass spectrometry: is there an environmental or occupational risk? *J Analytic Toxicol* 2010;34:142–148.

20. The Health and Safety Executive. *Work with Ionising Radiation: Ionising Radiations Regulations 2017.* Accessed March 2023. Available at: https://www.hse.gov.uk/pubns/priced/l121.pdf

21. The Health and Safety Executive. *Health Surveillance.* Accessed March 2023. Available at: https://www.hse.gov.uk/health-surveillance/overview.htm#article

22. The Health and Safety Executive*. COSHH Frequently Asked Questions.* Accessed March 2023. Available at: https://www.hse.gov.uk/coshh/faq.htm

23. Biller B, Berg J, Garrett L, Ruslander D, Wearing R, Abbott B *et al*. 2016 AAHA oncology guidelines for dogs and cats. *J Am Amin Hosp Assoc* 2016;52:181–204.

24. Royal College of Pathologists*. Conducting a Clinical Audit.* Accessed March 2023. Available at: https://www.rcpath.org/profession/patient-safety-and-quality-improvement/conducting-a-clinical-audit.html

Appendix A Summary table – Explanation of grades of evidence

(modified from Palmer K *et al. BMJ* 2008; 337:1832)

Grade (level) of evidence	**Nature of evidence**
Grade A	At least one high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target population or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Grade B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target population or Extrapolation evidence from studies described in A.
Grade C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high- quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target population or Extrapolation evidence from studies described in B.
Grade D	Non-analytic studies such as case reports, case series or expert opinion or Extrapolation evidence from studies described in C.
Good practice point (GPP)	Recommended best practice based on the clinical experience of the authors of the writing group.

Appendix B AGREE II guideline monitoring sheet

The autopsy guidelines of The Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. The sections of this autopsy guideline that indicate compliance with each of the AGREE II standards are indicated in the table.

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described	Introduction
2 The health question(s) covered by the guideline is (are) specifically described	Introduction
3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described	Foreword
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought	Foreword
6 The target users of the guideline are clearly defined	Introduction
Rigour of development	
7 Systematic methods were used to search for evidence	Foreword
8 The criteria for selecting the evidence are clearly described	Foreword
9 The strengths and limitations of the body of evidence are clearly described	Foreword
10 The methods for formulating the recommendations are clearly described	Foreword
11 The health benefits, side effects and risks have been considered in formulating the recommendations	Foreword and Introduction
12 There is an explicit link between the recommendations and the supporting evidence	2–3
13 The guideline has been externally reviewed by experts prior to its publication	Foreword
14 A procedure for updating the guideline is provided	Foreword
Clarity of presentation	
15 The recommendations are specific and unambiguous	2–3
16 The different options for management of the condition or health issue are clearly presented	2–3
17 Key recommendations are easily identifiable	2–3
Applicability	
18 The guideline describes facilitators and barriers to its application	Foreword
19 The guideline provides advice and/or tools on how the recommendations can be put into practice	2–3
20 The potential resource implications of applying the recommendations have been considered	Foreword
21 The guideline presents monitoring and/or auditing criteria	4
Editorial independence	
22 The views of the funding body have not influenced the content of the guideline	Foreword
23 Competing interest of guideline development group members have been recorded and addressed	Foreword