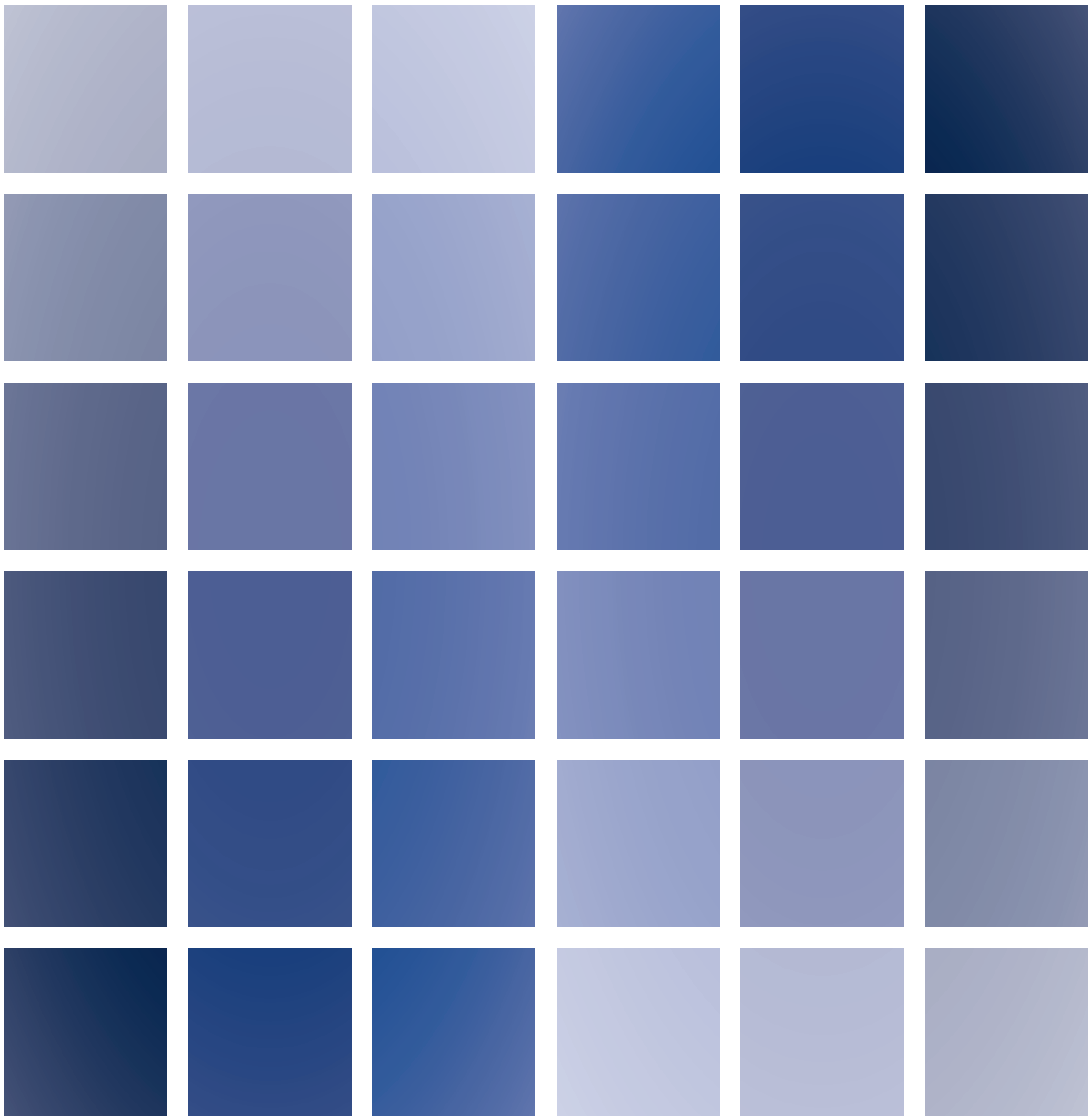
Use of Prussian Blue (Ferric Hexacyanoferrate) for Decorporation of Radiocaesium

Advice from the Health Protection Agency



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This paper from the Health Protection Agency reflects understanding and evaluation of the current scientific evidence as presented and referenced in this document.

Abstract

This document provides advice on the use of Prussian Blue (ferric hexacyanoferrate) as a decorporation agent in the event of poisoning with radiocaesium. It has been developed by the Health Protection Agency in partnership with a number of organisations using the scientific evidence available and advice from other countries.

The advice covers how radiocaesium contamination would be detected in the population and requirements for triage, dose assessment and monitoring, including timing and guidelines for the internal contamination levels at which treatment is advised. It also covers doses for adults and children, side-effects, duration of treatment and on-treatment monitoring. There is an appendix with draft public information leaflets for use in a contamination event, based on the proposed triage, monitoring and treatment guidelines.

Prussian Blue is a medical treatment, not suitable for mass distribution. The advice does not cover the logistics of arranging for prescription of this treatment in the NHS nor the use of Prussian Blue as an antidote for thallium poisoning.

Summary of Advice

1 Purpose of this document

This document provides advice on the use of Prussian Blue as a decorporation agent for people internally contaminated with radiocaesium following an accident or incident. It has been developed by the Health Protection Agency in partnership with a number of organisations using the scientific evidence available and advice from other countries. It also contains draft public and patient information leaflets that could be tailored to a specific incident. This summary of the advice incorporates the information of greatest use to treating clinicians.

2 How Prussian Blue works

Prussian Blue is not a treatment for the acute radiation syndrome or radiation burns. It increases excretion of all caesium isotopes to reduce the committed dose following an intake (ingestion, inhalation or through a wound). Radiation doses can also occur from intakes of other radionuclides, direct irradiation or external contamination from radiocaesium or other radionuclides. Prussian Blue is ineffective against these types of exposure and therefore internal contamination with radiocaesium should be positively identified before considering treatment with Prussian Blue. It is also used in the treatment of thallium poisoning.

3 Rationale for the use of Prussian Blue

After intake, caesium becomes evenly distributed in the body and is excreted slowly, primarily by the liver and gastrointestinal tract but also in urine and sweat. Prussian Blue can reduce the whole-body committed radiation dose by up to two-thirds. It is a safe and effective drug, but requires a long course of treatment under medical supervision. If treatment is truncated, the dose reduction achieved will be reduced.

4 Detection of the problem

In an incident it is important to determine as soon as possible if there has been external contamination of individuals, as prompt decontamination can reduce external radiation doses and limit the ongoing potential for intakes.

There are a number of isotopes of caesium. Many of these have only short half-lives (days or less). Two isotopes of radiocaesium, caesium-134 and caesium-137, are of interest in the context of Prussian Blue due to their use in industry and medicine, and their relatively long half-lives (approximately two and 30 years, respectively). Both caesium-134 and caesium-137 emit beta and gamma radiation in their decay chains. Caesium-137 is of primary concern since it has both industrial and medical applications.

The initiation of an incident will typically be either an indication of abnormal conditions in a situation where a radiation source is managed, or – in circumstances where there is no prior assumption that a source is there – an indication that a radiation source is or has been present. There are a number of

indicators that may lead to the discovery that a radiation source is, or may have been, present. These include:

a effects on human health, such as radiation sickness or radiation burns,

b visual identification – for example, radiation warning signs on radiation sources or vehicles used to transport radioactive materials,

c detection through environmental radiation monitoring – for example, at ports or other locations.

Such alerts would trigger radiation emergency response plans for public protection and initiation of the analysis and identification of the radionuclide. Once discovered, environmental radiation monitoring would be used to define hazardous locations and thus guide triage of members of the public for monitoring. Where criminal intent is suspected, intelligence information may support the use of, or focus on, some of these indicators.

5 Triage and dose assessment

In line with current UK guidance, lifesaving treatment should always take priority over decontamination and monitoring. Intakes of caesium-137 that could cause deterministic injuries (tissue reactions, acute radiation syndrome and radiation burns) should be identified as soon as possible in order to initiate medical surveillance and specific treatment. This would require whole-body monitoring but rapid screening using immediately available instruments may be sufficient to make early treatment decisions. It is also important to detect external contamination so that it can be removed as soon as possible. In emergency situations decontamination could be done on a presumptive basis.

The magnitude of an intake of caesium-137 can be assessed, and hence the health implications predicted, by measuring the rate of excretion in urine and/or faeces. However, direct measurement of the amount present in the body using one or more gamma-ray detectors (*in vivo* monitoring) has several advantages over excreta monitoring (or use of nasal wipes or swabs). As a direct (rather than indirect) measurement it is more reliable, the result is obtained almost immediately, and less effort is needed. The HPA transportable body monitor can make measurements close to the site of an incident. However, most body monitoring facilities are fixed and require the patient to travel to them.

6 Selection of people for monitoring and possible treatment

People should be selected for monitoring using a triage system that gives priority to those who are likely to have had higher intakes of radiocaesium (see below). Detailed triage criteria will depend on the specific incident. Guidelines on establishing a practicable triage process have been published in the TMT (Triage, Monitoring and Treatment) Handbook, which was developed for incidents involving the malevolent release of radiation*.

* The TMT project was funded under the European Union 6th Framework Programme and the HPA was a major contributor. The TMT Handbook is available at www.tmthandbook.org, where more detailed guidance is available (Rojas-Palmer et al, 2009).

7 Speed of monitoring

Triage procedures should not be so time consuming that treatment with Prussian Blue is delayed for people with potentially large radiation doses (hundreds of millisievert and above) from radiocaesium intakes while they wait for detailed assessments.

In the event that intakes for some individuals are large enough to give rise to deterministic health effects, then whole-body monitoring of the most highly exposed individuals would need to be carried out within 24–48 hours of the intake to enable timely decisions on medical management. If intakes are lower, where health risks are stochastic (risk of cancer induction in the future), then the main function of monitoring is to provide information to allow decisions to be made on Prussian Blue treatment, but will also provide information on doses and risks to individuals. In these circumstances it would be sufficient to carry out monitoring within seven days.

If very large numbers of people require monitoring, then it would be acceptable to delay measurements of people with lower estimated risks for up to 28 days. Although earlier treatment allows a larger proportional decrease in committed dose, Prussian Blue is still effective if treatment is started within 28 days of the intake. In a significant incident it is also expected that a large number of people would wish to be monitored for reassurance purposes.

Whole-body monitoring is the 'gold standard' in determining the body burden of internal contaminants such as radiocaesium. However, the relative scarcity of whole-body monitoring capacity, particularly in the early post-incident stages, may militate in favour of a more pragmatic approach to starting treatment. If treatment is started before whole-body monitoring then, although monitoring is desirable as soon as practicable, priority should be given to people in whom a change in clinical management is the likely outcome of the whole-body monitoring.

8 Criteria for selecting people for whole-body monitoring in an incident where radiocaesium contamination has been confirmed

Criteria will usually include physical injury, clinical signs and symptoms, proximity to a point source dispersal incident and dose assessments based on the results of rapid screening measurements.

Physical injury

Lifesaving treatment should always take priority over decontamination and monitoring. However, people with physical injuries related to the exposure event may well be among the most highly contaminated (externally as well as internally), and so may have the most urgent need for individual monitoring, decontamination and treatment.

Clinical signs and symptoms

Any person with nausea, vomiting or diarrhoea should be assumed to be highly contaminated until rapid screening measurements of external and internal contamination are carried out. Such measurements are required urgently. However, these symptoms may have other causes, such as stress or anxiety.

Proximity to a point source dispersal incident

Those who were close to, or in contact with, the source of contamination (eg affected people in the immediate vicinity, first-responders not wearing respiratory personal protective equipment (PPE) or people within the Hot Zone) will have a greater likelihood of internal contamination than those who were further away, outside the cordon. There may be upwind dispersion in complex urban environments. It is reasonable to assume intakes by unprotected people near the incident in the absence of evidence to the contrary.

Dose assessments based on the results of rapid screening measurements

Rapid screening measurements could include:

- **a** measurements of contamination of skin and clothing with hand-held beta-contamination probes including the radiation monitoring equipment (RAM-GENE™ *) held by NHS emergency departments,
- **b** measurements of internal contamination in the torso using hand-held gamma probes,
- **c** measurements of internal/external contamination with portal radiation monitors,
- **d** measurements of internal contamination with portable high resolution spectrometry systems.

Rapid dose assessments based on these measurements would be carried out using generic assumptions and standardised methodology.

People selected for monitoring by the triage process should be prioritised according to the likelihood and magnitude of their potential exposure. Guidelines are given in TMT Handbook. More accurate whole-body monitoring should be carried out on these people, and clinical decisions to start Prussian Blue treatment should be made using information about the committed effective dose computed from these measurements compared with the guidance levels below. These dose assessments could make use of specific information on exposure conditions; the HPA has the necessary facilities and expertise to carry out the calculations required.

9 Whole-body monitoring

Whole-body monitoring measurements could be carried out using the HPA transportable body monitor (maximum throughput ten people per hour) and the HPA laboratory body monitoring facilities (maximum throughput six people per hour). If necessary, five other sites across the UK that have appropriate facilities, normally used for monitoring workers, could be requested to carry out laboratory body monitoring measurements on members of the public, with the HPA coordinating their efforts. It is assumed that each site could monitor three people per hour. However, availability of these facilities would depend on the ability of the other organisations to respond during the incident and, possibly, on security considerations.

* The RAM-GENE monitor is designed to measure dose rates and to check for external radioactive contamination. It would not have the sensitivity to detect contamination within the human body reliably at the lowest levels for which Prussian Blue treatment might be initiated. Other simple hand-held monitors do have the required sensitivity. The HPA can advise on the choice of instruments.

Logistical challenges that may reduce throughput include the provision of transport and welfare (including food and drink) for people who are to be monitored, provision of ancillary services such as laundry and modesty gowns, and the practicalities of asking people to be monitored during the night.

The first 24 hours are likely to be taken up with readying equipment and putting arrangements into place. Subsequently, a theoretical maximum daily throughput would be several hundred measurements per day if all the facilities are fully utilised. However, this is unlikely to be achieved in practice. Over the first three days, with suitable logistical support, the HPA could monitor at least 200 people, and subsequently could achieve a throughput of about 100 people per day.

10 Pre-absorption and prophylactic use of Prussian Blue

Prophylactic use of Prussian Blue is not currently recommended. If protection of workers is required in the aftermath of an incident, other countermeasures such as the use of personal protective equipment, limiting time spent in the affected area, sheltering or distancing would minimise doses from any radionuclide involved.

11 Guidance levels for treatment with Prussian Blue

Guidance levels for Prussian Blue should be set to reflect the relative balance of harms and benefits. In setting guidance levels the HPA has considered both existing ionising radiation Emergency Reference Levels (ERLs) of dose (NRPB, 1997) and the levels of risk at which other public health interventions are usually considered.

It is recommended that guidance levels of 30 mSv (lower threshold) and 300 mSv (upper threshold) projected effective dose be adopted. These levels ensure comparability with other emergency radiological protection advice and recognise additional protection from other countermeasures, such as sheltering, evacuation and decontamination, that would be adopted in practice. In particular, these guidance levels are comparable with existing ERLs for 'disruptive' countermeasures, eg evacuation. They are set at the level of risk at which other public health measures are taken. This recognises that the lower guidance level would be aspired to in practice, the upper one applying if there were other considerations of national capability. These guidance levels should apply equally to accidental or deliberate scenarios.

At the lower guidance level, 30 mSv, the radiation health benefit to the patient would be generally small, but for some patients, the discomfort and disruption of the treatment might be far outweighed by the reassurance provided, and so should be considered. At the upper guidance level, 300 mSv, the overall benefit to the patient would be expected to be significant. Only in exceptional circumstances (eg advanced age) would it be reasonable to consider not treating a patient with a projected dose at this level.

While Prussian Blue can be effective in reducing doses from intakes of radiocaesium, this should not detract from the role of other countermeasures in emergency plans and responses, such as sheltering, evacuation or foodchain intervention for the public and the use of appropriate personal protective equipment (PPE) for emergency responders.

12 Initiation and duration of treatment

After an intake, the amount of caesium in the body decreases naturally through excretion. Prussian Blue treatment enhances the rate of loss, each day's treatment expelling a small proportion of the caesium still in the body. Repeat measurements and associated dose assessments will inform the decision by clinician and patient about whether to continue or stop treatment.

Prussian Blue treatment is best started within about seven days of intake, but will still deliver a useful dose saving if treatment commences within 28 days. Any radiation exposure should be reduced to as low as reasonably achievable, and so treatment should continue until it is no longer providing a significant reduction in committed effective dose. Usually, this will indicate a treatment duration of three to six months. Reduction in doses to 40–55% of those expected in the absence of treatment may be achievable. If the patient is treated for just a month, only about half of this dose saving would be achieved. Another factor to consider is the absolute value of additional dose saved from continuing treatment. The HPA advises that little benefit would be gained when further dose reductions from Prussian Blue treatment are comparable with annual background radiation doses in the UK – typically around 2 mSv or so.

Prussian Blue has been shown to have low levels and severity of side-effects. However, if there were adverse reactions, the prescribing clinician may review the benefits and drawbacks of continuing treatment.

13 Dosage of Prussian Blue

The recommended dosage for Prussian Blue Antidotum Thallii-Heyl® (UK) [equivalent to Radiogardase® (USA)] 500 mg insoluble Prussian Blue per capsule is:

a **adults and adolescents*:** 1 g (two capsules) orally three times daily (total of 3 g per day),

b **children (1–12 year olds):** 0.5 g (one capsule) orally three times daily (total of 1.5 g per day), noting that this dose has little evidence base,

c **under 1 year olds:** there are variations in the developmental maturity of the biliary system and gastrointestinal tract of neonates and infants (0–1 year olds). The dose-related adverse effects of insoluble Prussian Blue on an immature gastrointestinal tract are not known. There may be more absorption of Prussian Blue into the body but the effects of this are unknown. Dosing in infants and neonates has not been established. In the absence of other guidance a dose per body mass extrapolated from the children's guidance above and under strict medical and radiological supervision would be indicated.

If patients cannot tolerate swallowing large numbers of capsules, the capsules may be opened and mixed with food or liquids. This may result in blue discolouration of the mouth and teeth.

* In reviewing the evidence we have found ambiguity in the recommended dose in manufacturers' instructions, some US guidance and some US websites. However, the scientific evidence supports the adult doses defined above. There is evidence that higher doses do not increase the effectiveness of the treatment and cause more side-effects (Lipsztein et al, 1991a,b). Similarly, it is unclear why some of the international guidance extends infancy up to two years of age for the purposes of dose calculation.

14 Special considerations

Treatment of deterministic health effects

The diagnosis and treatment of deterministic health effects is not within the scope of this review. The HPA independent Advisory Group on Ionising Radiation has recently reviewed this topic and provided links to numerous other sources of advice (AGIR, 2009).

Pregnancy

Comprehensive animal reproductive studies have not been conducted with Prussian Blue. However, whilst caesium-137 is known to cross the placenta, Prussian Blue should not, since it is not absorbed from the mother's gut. The risk to a fetus from radiation-related adverse health effects of intakes of caesium-137 is therefore expected to be greater than any fetal toxic risk from Prussian Blue. Therefore pregnant women should be considered for treatment at doses near the lower guideline level (30 mSv).

Breast-feeding

Caesium is transmitted from the mother to infant in breast milk. Prussian Blue does not enter the circulation and thus does not enter breast milk. The committed effective dose to an infant resulting from an intake of radiocaesium by the mother would be no greater than about 30% of the dose to the mother. The risk of adverse health effects for the infant is therefore not expected to exceed that for the mother, even though the risk per unit dose is somewhat higher for an infant than for an adult.

For mothers who have received intakes of radiocaesium resulting in committed effective doses less than the lower guidance level (30 mSv), the benefits of breast-feeding are presumed to outweigh the radiation risk and so the mother should be advised that there is no need to stop breast-feeding.

For mothers with committed effective doses greater than the lower guidance level, Prussian Blue treatment is recommended. In these cases, it is also recommended that doses and risks to the infant should be individually assessed to inform advice to the mother on whether to stop breast-feeding.

Foreign travel

Many airports and other ports now monitor passengers for radiation with instruments that can pick up low levels of radiocaesium. Therefore passengers with low levels of internal contamination may be stopped and subject to questioning. It may be prudent to warn patients about this and suggest they take documentary proof that they have been contaminated with radiocaesium in order to speed passage through ports in the same way as cards are issued to those who have undergone brachytherapy radiation treatment.

15 Patient monitoring to determine effectiveness of treatment

The effectiveness of treatment should be assessed by determining the cumulative dose saved as treatment proceeds. This would ensure that unnecessary continuation of an individual's treatment can be avoided. A series of laboratory whole-body monitoring measurements could be conducted to establish the biological half-life of caesium during the period of Prussian Blue treatment, and the biological half-life after treatment ceases. Because the caesium biological half-life is known to be quite variable between

individuals, the half-lives would ideally be established for each individual treated. The frequency of such monitoring could be limited by the number of people who are undergoing treatment. The HPA would carry out the required measurements and provide assessments of the effectiveness of treatment. If whole-body monitoring capacity is limited or other logistical issues arise, other monitoring techniques such as urine monitoring may be considered.

In general, the dose of Prussian Blue should not be decreased as the body burden of caesium-137 falls. However, under medical supervision it may be considered in order to control side-effects, with account taken of the effect on caesium elimination.

16 Contraindications, side-effects and physiological monitoring

Prussian Blue is well tolerated by the human body. Constipation and coloured stool are the only consistently reported side-effects. Constipation can be treated by co-administration of a laxative or increasing the amount of fibre in the diet. Because of its tendency to produce constipation it has been suggested that Prussian Blue should be used cautiously in those with gastrointestinal motility disorders. With high doses given over a prolonged period non-specific gastrointestinal distress is also a feature. In one source the incidence of constipation in patients treated with Prussian Blue was reported as 24% (Drugs.com, 2008).

Prussian Blue has the potential to bind to other elements (such as potassium and sodium) and cause an electrolyte or other nutritional imbalance. Serial monitoring of electrolytes has shown mild hypokalaemia in a few treated individuals (7%) (Drugs.com, 2008). This was rapidly reversed by potassium replacement. This may, however, indicate that patients with pre-existing electrolyte imbalance or cardiac arrhythmias are a sensitive subgroup and Prussian Blue should be used with caution in this group. Baseline levels of serum electrolytes should be measured and the subsequent monitoring frequency determined by clinical considerations. As a minimum, an on-treatment measurement of electrolytes should be made in the first week of treatment.

Since Prussian Blue is not systemically bioavailable and does not rely upon renal elimination or hepatic metabolism, its use is not specifically contraindicated in patients with impaired renal or liver function. It may be less effective in patients with impaired bile secretion due to liver or gall bladder disease because that is the route by which caesium in the body re-enters the gastrointestinal tract. Draft US FDA guidance (US FDA, 2003) suggested that patients with disorders associated with hypersecretory states, eg gastrinaemia and Zollinger-Ellison Syndrome, may find that Prussian Blue is ineffective and they may be at risk of cyanide poisoning because Prussian Blue dissociates and may release cyanide in very acidic environments (eg pH 0–1). Updated evidence, US FDA guidance and manufacturers' information, has removed this precaution (US FDA, 2004, 2008; Yang et al, 2007).

Drug interactions are possible and the literature contains anecdotal reports of decreased bioavailability of oral tetracycline. Therefore blood levels or clinical responses should be carefully monitored. There is no evidence in the literature about the effect of Prussian Blue on effectiveness of the oral contraceptive pill. The package insert for the Radiogardase® preparation suggests that measurements of iron and ferritin may also be appropriate during the first four days of a course of treatment but there is no reference to support the need for this (REAC/TS, 2009).

17 Radiological protection issues for patients undergoing treatment

Patients should be informed about the urinary and faecal excretion of caesium to enable them to minimise radiation exposure to themselves or others. Precautions include using a toilet instead of a urinal, flushing several times after use, cleaning up spilled urine or faeces completely and washing hands thoroughly. Healthcare professionals should also follow appropriate radiological protection advice to avoid unnecessary exposure to themselves and the spread of contamination. Radiation risks to close contacts of people with large intakes may need to be considered by the treating clinician and specific advice given to protect household contacts.

18 Termination of therapy

The decision to terminate therapy must be made by the patient based on advice from the prescribing clinician. Therapy should be continued until the whole-body concentration of radiocaesium is reduced substantially, based on the principle that any radiation exposure should be reduced to as low as is reasonably achievable. Other important factors include the rate of elimination with Prussian Blue treatment compared to natural elimination and the absolute value of additional dose saved from continuing therapy. If the dose averted by continued therapy is negligible, with negligible being an individual committed effective dose of 2 mSv (equivalent to background radiation levels and conferring a fatal cancer risk of about 1 in 10,000), then, with consideration, treatment can be stopped.

The following are also criteria for termination of therapy:

a no further reduction in the radiocaesium concentration in the body is observed in serial whole-body counting or excreta sampling beyond what would happen without treatment,

b concern about adverse reactions with continuing administration.

19 Status of Prussian Blue as a medical treatment, UK formulation

Prussian Blue is a medical treatment and patients will require medical prescription and medical follow-up. It is not currently licensed for use in the UK so prescription would need to be on a named-patient basis. UK stocks are obtained from Germany. The formulation used in the UK is Prussian Blue Antidotum Thallii-Heyl® (UK) [equivalent to Radiogardase® (USA)]. Currently supplies can be restocked in about three months, although this may lengthen if there was a surge in demand worldwide. Prussian Blue should be stored as any other hard gelatin capsule.

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1 Introduction

Radioactive caesium (radiocaesium) is a product of nuclear fission that is used in radiation sources for industry and medicine. Exposure of the public to radiocaesium could occur following a nuclear reactor accident or accidental or deliberate exposure to a caesium source. There are a number of isotopes of caesium, many of which have only short half-lives (days or less). Two isotopes of radiocaesium, caesium-134 and caesium-137, are of interest in the context of Prussian Blue due to their use in industry and medicine, their relatively long half-lives (approximately two and 30 years, respectively), and their radiation emissions. Caesium-137 is of primary concern since it has industrial and medical applications.

The caesium-137 used in radiation sources is often in the form of caesium chloride, a powdery salt, which, if it makes its way into the environment, can be easily dispersed. Caesium chloride and most other caesium compounds are soluble and readily absorbed from the gastrointestinal tract, lungs and wounds. Caesium salts behave like potassium in the body. Around 80% of caesium is excreted through the kidneys and 20% in the faeces. Caesium is excreted into the digestive tract in bile. Caesium-137 (with a physical half-life of 30 years) emits beta and gamma radiation in its decay chain; its biological half-life is between 50 and 150 days. Therefore internal contamination of the body with radiocaesium causes whole-body irradiation. The specific activity of caesium-137 is 3.2 TBq g^{-1}. Therefore significant doses from a radiological point of view can occur from intakes of very small volumes of contaminated material. The quantity of caesium-137 ingested following any accident or incident scenario would be insufficient to cause chemical toxicological problems. A comprehensive review of the toxicology, including radiotoxicology, of caesium has been published by the US Agency for Toxic Substances and Disease Registry (US DHHS, 2004).

Prussian Blue increases excretion of caesium-137 and can significantly reduce the whole-body committed effective radiation dose by a factor of two or three. It is a safe and effective drug, although a course of daily treatment over a number of months may be required. Prussian Blue is also used in the treatment of thallium poisoning. Prussian Blue is ineffective in the treatment of contamination by any other radioactive elements.

Other measures to decrease peak absorption of caesium following ingestion or shorten caesium transit time in the alimentary tract have been described (see US DHHS, 2004), including cathartics, gastric lavage and the administration of potassium. These measures have not been evaluated as thoroughly as Prussian Blue and are not discussed further in this document. In the Goiânia radiation incident diuretics and increased ingestion of water were used, but found not to be effective (de Oliveira et al, 2001). An overview of the international guidance for the use of Prussian Blue for treatment of intakes of radiocaesium is given in Appendix A.

Whilst Prussian Blue is effective as an agent of decorporation for soluble caesium compounds, it is important to remember that it is not a treatment for acute radiation syndrome, nor effective as a decorporation agent for other radionuclides. Acute radiation syndrome can also occur from intakes of other radionuclides or external exposure to radiation, without contamination or the need for decorporation treatment.

This document reviews the evidence about use of Prussian Blue as a decorporation agent for radiocaesium and provides guidance on detection, triage, guideline treatment thresholds, dosage, side-effects and patient monitoring given a range of exposure scenarios. Draft public information leaflets for use in a contamination event, based on the proposed triage, monitoring and treatment guidelines, are given in Appendix B.

2 Effectiveness of Prussian Blue for Reducing Doses from Intakes of Radiocaesium

2.1 Introduction

Prussian Blue (ferric hexacyanoferrate) binds caesium in the gastrointestinal tract after it has been inhaled, ingested or excreted into the bile by the liver. It forms an insoluble complex, by ion exchange, thereby reducing both the primary uptake and gastrointestinal reabsorption of caesium.

Prussian Blue is the substance most widely recommended for decorporation of caesium (Gerber and Thomas, 1992; Hengé-Napoli et al, 2000; US DHS, 2003; US FDA, 2003, 2008). The efficacy of Prussian Blue and other ion exchangers has been demonstrated in both humans and animals (Hengé-Napoli et al, 2000). After ingestion, Prussian Blue does not cross the intestinal barrier but forms an insoluble complex by ion exchange when it encounters certain metal cations such as caesium in the lumen. This reaction inhibits the absorption of caesium from the gastrointestinal tract, and breaks the natural cycle of secretion–absorption. After the systemic uptake of caesium, the reduction in committed effective dose is unlikely to exceed two- or three-fold even with protracted treatment. In 2003 Prussian Blue was approved for administration to members of the public by the US Food and Drug Administration (US FDA, 2003).

The efficacy of other hexacyanoferrates has been investigated in humans and animals, but despite reports of greater efficacy for the ammonium and potassium salts, most of the guidance and experience in accidental and occupational intakes is with Prussian Blue.

Although Prussian Blue is most effective when administered before or within 24 hours of the ingestion or inhalation of radiocaesium, studies show that it retains most of its effectiveness if treatment is started up to seven days after the intake. Prussian Blue can still make significant reductions to committed radiation dose if treatment is started up to 28 days after the intake.

The efficacy of Prussian Blue has been demonstrated in animals and in humans, notably after the Goiânia incident (Melo et al, 1994; IAEA, 1998; US DHS, 2003). In the Goiânia incident the dosage of Prussian Blue used varied between 1 and 3 g per day for children and between 3 and 10 g per day for adults, with no observed medical side-effects after several months of treatment. Study of the *in vivo* monitoring data from the individuals in the Goiânia incident, concluded that elimination of caesium followed first-order kinetics, both with and without Prussian Blue treatment. The caesium biological half-lives for both sexes were influenced mainly by the weight of the individual. On average, Prussian Blue reduced the half-life by 68%. The results suggested that there was an optimum dosage for a certain weight range to achieve this reduction in half-life, but more data were required to prove this assumption statistically (Lipsztein et al, 1991a,b).

In 46 patients, the committed effective dose, E_{50}, was reduced by factors between 1.7 and 6.2, with a median value of 2.1, after several months of treatment (Melo et al, 1994; IAEA, 1998).

The objective of the short study reported below was to determine the amount of dose reduction that would be obtained by administering Prussian Blue commencing at various times after an intake of caesium-137, for different durations.

2.2 Method

Calculations were performed using the International Commission on Radiological Protection Publication 30 biokinetic model, which describes the systemic behaviour of caesium following uptake to body fluids (ICRP, 1979). In this model, 10% of the uptake is retained with a half-life of two days, and the remaining 90% is retained with a half-life of 110 days. The model is a simplification of the retention behaviour found in the general population. In particular, the half-life of the long-term retention component is known to be quite variable, with typical values in the range 50–150 days.

For the purposes of this study, the systemic model provides an adequate description of the biokinetics of caesium after either ingestion or inhalation of soluble (Type F) material, which is the ICRP default assumption for caesium compounds. For materials ingested or inhaled in a less soluble form, more complex modelling would be needed.

In the calculations presented here, it is assumed that Prussian Blue has the effect of reducing the biological half-life of the long-term retention component by a factor of three during the period over

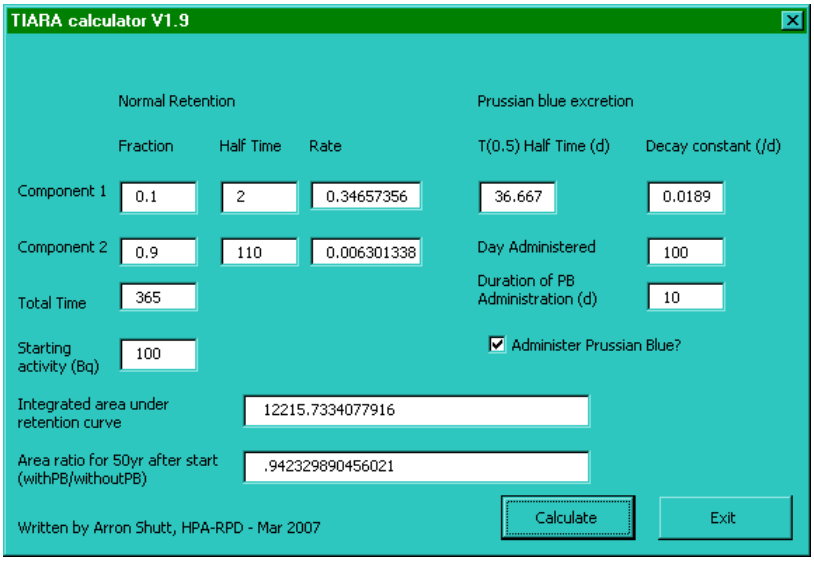

FIGURE 2.1 User interface of the TIARA-CALC Microsoft Excel macro, which allows easy alteration of model parameter values and displays the dose reduction factor

which it is administered, while the short-term component remains unchanged. When Prussian Blue administration stops, the half-life is assumed to return immediately to its normal value.

A Microsoft Excel spreadsheet macro produced by the HPA (TIARA-CALC) was used to carry out these calculations (Figure 2.1). The user can specify the start time of administration of Prussian Blue after an acute intake of caesium-137, the duration of its administration, the retention fractions and retention half-lives in the absence of such treatment, and the half-life of the long-term retention component during Prussian Blue administration. The number of nuclear disintegrations in the body is determined from the area under the retention curve over the time interval 0–50 years. The macro displays the dose reduction factor, which is defined here as the committed effective dose, E_{50}, after treatment with Prussian Blue, divided by the E_{50} if no Prussian Blue treatment was carried out. This factor is quantified by dividing the area under the retention curve after administration of Prussian Blue by the area under the retention curve without Prussian Blue administration.

2.3 Results and Discussion

An example of the effect of Prussian Blue treatment on caesium-137 whole-body retention is shown in Figure 2.2. Here, administration of Prussian Blue starts at 28 days, and continues for a further 28 days. For comparison, retention without Prussian Blue treatment is also shown.

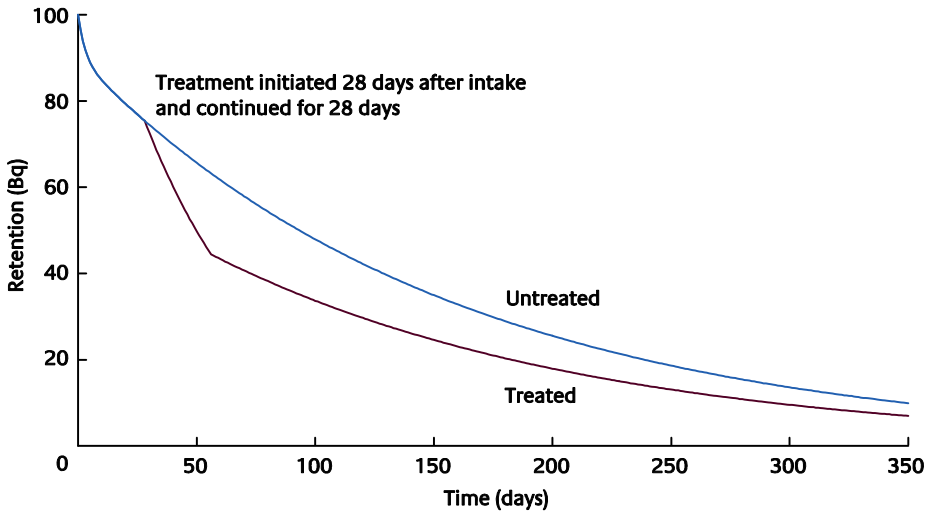

FIGURE 2.2 Output from TIARA-CALC showing whole-body retention of caesium with and without Prussian Blue treatment

Values for the dose reduction factor are given in Table 2.1 for Prussian Blue administration starting at 0, 7, 14, 28, 84 and 168 days after intake of caesium-137, with durations of 28, 84, 168, 252, 365 and 3000 days.

TABLE 2.1 Dose reduction factors – lower factors correspond to more effective treatment regimes

Treatment duration (days)	Treatment start time after intake (days)					
	0	7	14	28	84	168
0	1	–	–	–	–	–
28	0.730	0.744	0.755	0.776	0.843	0.907
84	0.472	0.500	0.521	0.562	0.692	0.819
168	0.363	0.396	0.422	0.471	0.628	0.781
252	0.340	0.375	0.402	0.452	0.615	0.773
365	0.335	0.370	0.397	0.448	0.612	0.772
3000	0.335	0.369	0.397	0.448	0.612	0.771

Figure 2.3 shows the dose saving resulting from each day's Prussian Blue treatment when treatment starts at the time of the exposure. The calculation is performed by

a calculating the committed effective dose when Prussian Blue treatment starts immediately and ends after a set number of days, T',

b repeating the calculation with treatment ending at day $T' - 1$,

c subtracting the doses to determine the dose saving from Prussian Blue administered on day T'.

The dose saving is expressed as a percentage of the total dose saving obtained when treatment continues for 365 days.

Figure 2.4 shows the corresponding cumulative dose saving, when treatment starts at the time of exposure and ends at a time T' between 0 and 365 days.

Figures 2.5 and 2.6 show the corresponding figures when the start of treatment is delayed by 28 days and ends at 365 days.

The longest period of Prussian Blue treatment likely to be encountered would correspond to the situation where treatment commences on the same day as the exposure, and continues for 180 days. In most realistic scenarios, however, treatment would be unlikely to start until several days after exposure.

Figures 2.7 and 2.8 demonstrate the consequences for dose saving of delaying commencement of Prussian Blue treatment. Figure 7 shows the cumulative dose saving when Prussian Blue treatment commences seven days after exposure, expressed as a percentage of the dose saving when treatment starts immediately and continues for 180 days. Figure 8 shows similar data for the case where Prussian Blue treatment commences 28 days after exposure.

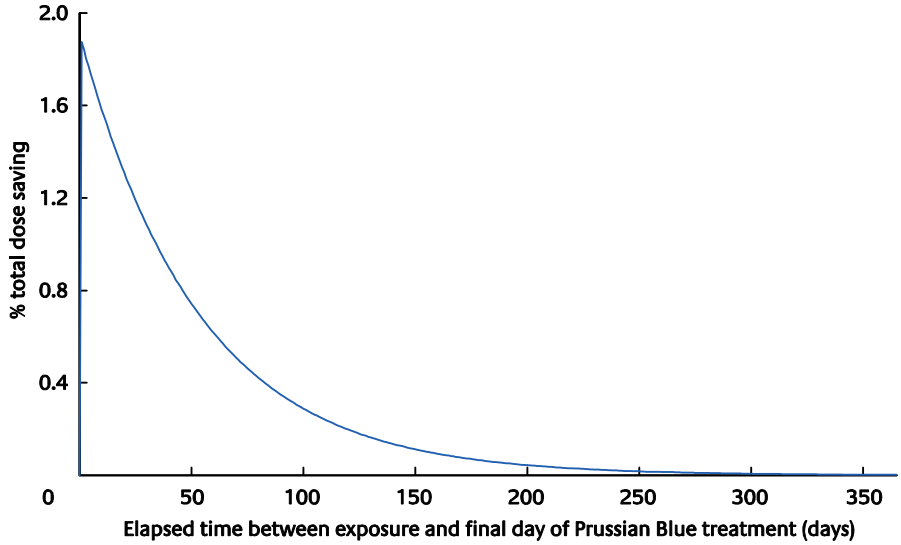

FIGURE 2.3 Dose saving resulting from each day of Prussian Blue treatment, which starts at the time of exposure. Dose saving expressed as a percentage of the dose saved when treatment is continued for 365 days

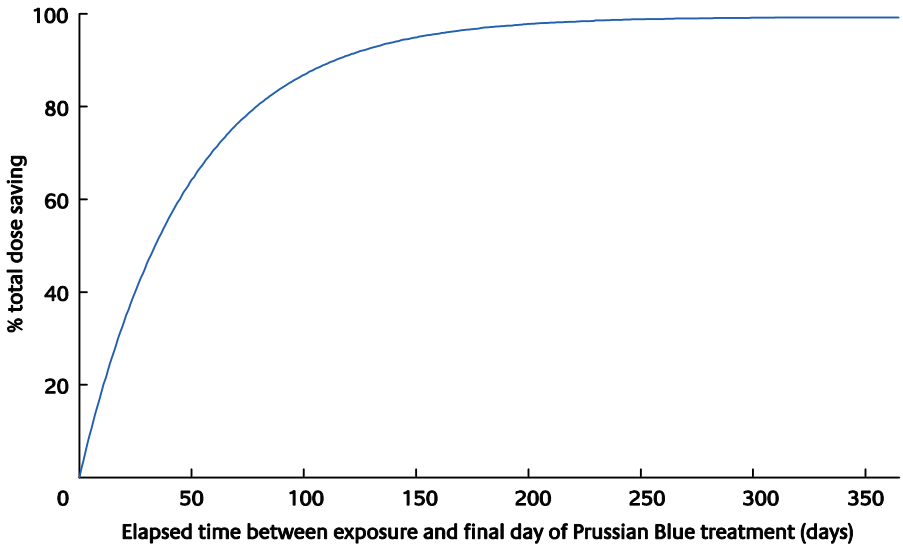

FIGURE 2.4 Cumulative dose saving with increasing duration of Prussian Blue treatment, which starts at the time of exposure, and ends at time *T*. Dose saving expressed as a percentage of the dose saved when treatment is continued for 365 days

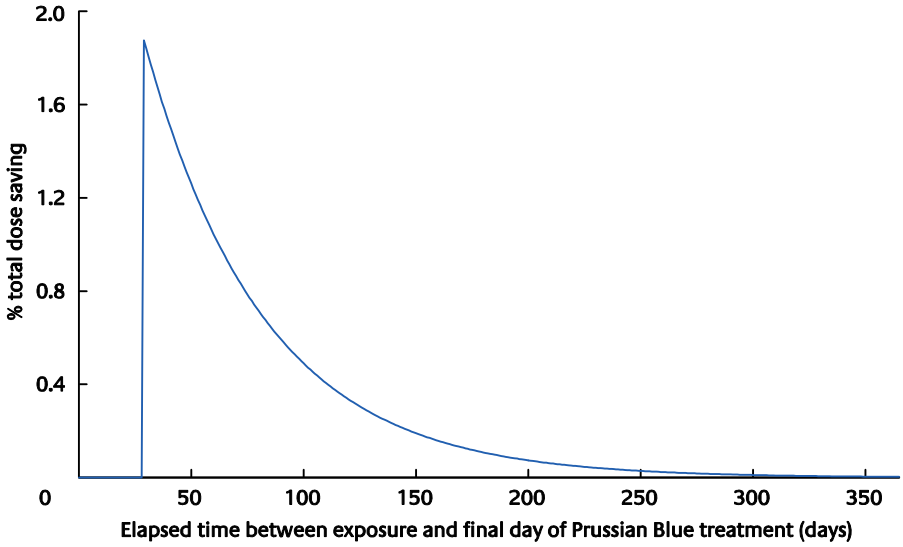

FIGURE 2.5 Dose saving resulting from each day of Prussian Blue treatment, which starts 28 days after exposure. Dose saving expressed as a percentage of the dose saved when treatment is continued until 365 days after exposure

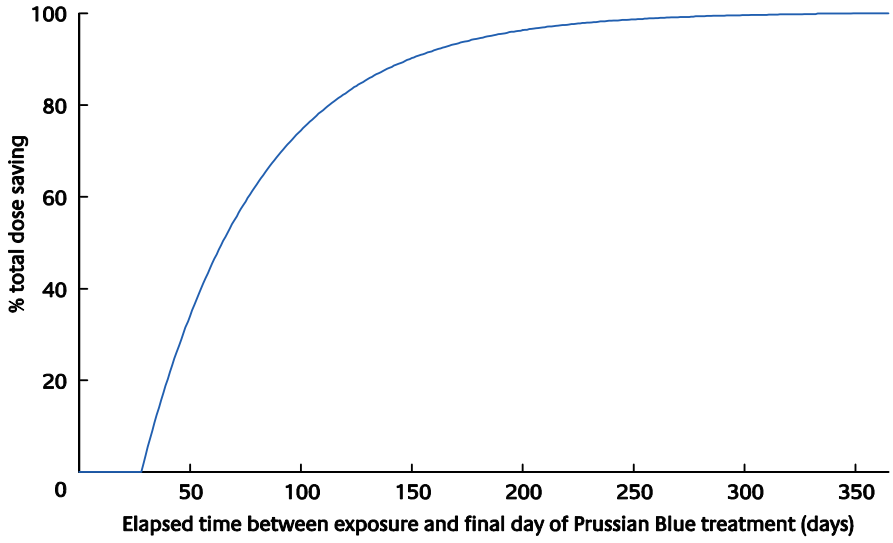

FIGURE 2.6 Cumulative dose saving with increasing duration of Prussian Blue treatment, which starts 28 days after exposure, and ends at time *T*′. Dose saving expressed as a percentage of the dose saved when treatment is continued until 365 days after exposure

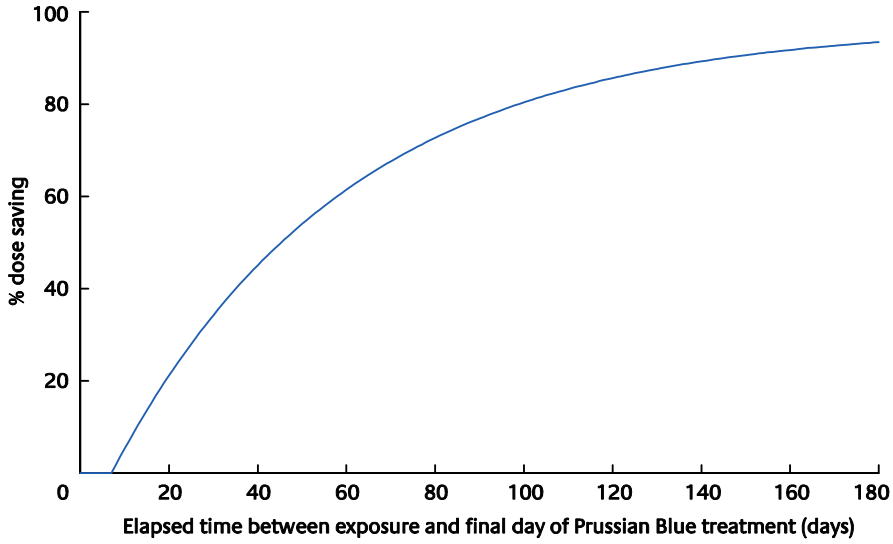

FIGURE 2.7 Cumulative dose saving with increasing duration of Prussian Blue treatment, which starts 7 days after exposure, and ends at time *T*′. Dose saving expressed as a percentage of the dose saved when treatment starts immediately after exposure and continues until 180 days after exposure

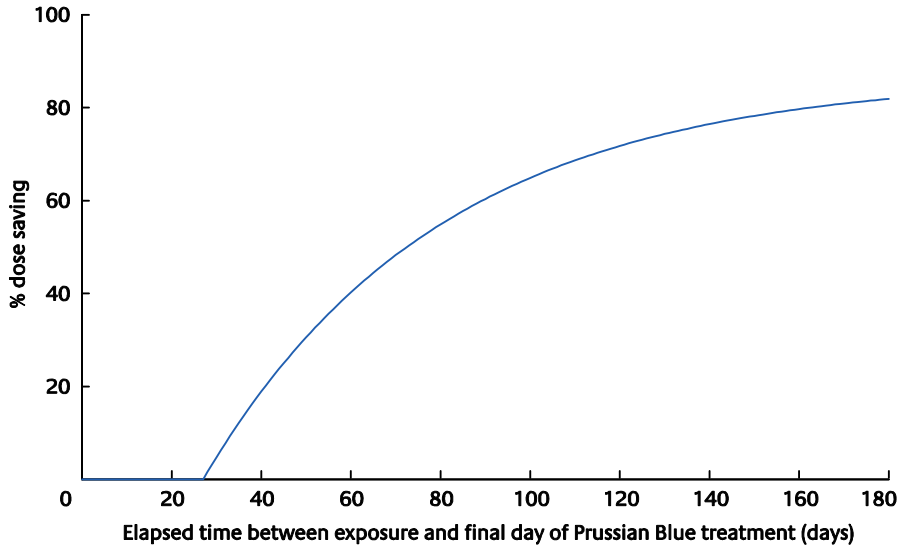

FIGURE 2.8 Cumulative dose saving with increasing duration of Prussian Blue treatment, which starts 28 days after exposure, and ends at time *T*′. Dose saving expressed as a percentage of the dose saved when treatment starts immediately after exposure and continues until 180 days after exposure

Unsurprisingly, the best attainable dose saving is achieved by initiating treatment as soon as possible after exposure and continuing treatment indefinitely. The dose could then be reduced to one-third of the value that would result if no Prussian Blue treatment was employed. The results show that only minor further reductions in dose are achieved by extending treatment beyond about 180 days. Figures 2.4 and 2.6 show that the dose saved with this duration of treatment is greater than 95% of the dose that would be saved if treatment was prolonged indefinitely. The corresponding figure when treatment is prolonged for 90 days is about 80%. Figures 2.7 and 2.8 show that the dose saved is reduced by about 6% when treatment is delayed until seven days post-exposure, and by about 18% when delayed until 28 days post-exposure, assuming that treatment continues until 180 days post-exposure.

2.4 Conclusions

Delaying commencement of treatment with Prussian Blue for seven days after intake would not significantly decrease its efficacy. However, treatment should commence within about 28 days. Such a delay would be acceptable for people with lower estimated risks if very large numbers of people require monitoring. From a consideration of dose saving, treatment should continue until at least three months post-exposure. No significant benefit is obtained by extending treatment duration beyond about six months. Reduction in doses to 40–55% of the doses expected in the absence of Prussian Blue treatment would then appear to be achievable. If treatment extends only over one month, only about half of this dose saving is achieved.

3 Detecting and Identifying Radiocaesium Contamination in the Environment

This chapter describes the radioisotopes of caesium for which Prussian Blue treatment may be relevant. It presents information on the operational means by which abnormal radiation levels and radiocaesium are likely to be detected and identified when incidents have occurred. These mechanisms are illustrated by reference to a range of scenarios that might involve radiocaesium.

3.1 Caesium Radioisotopes of Interest

There are over 30 radioisotopes of caesium and one stable isotope (caesium-133). Most of the radioisotopes have short half-lives (days or less). One isotope, caesium-135, has a very long half-life (approximately two million years) but is rarely encountered and is not considered further here. Two isotopes of radiocaesium, caesium-134 and caesium-137, are of interest in the context of Prussian Blue due to their use in industry and medicine, their relatively long half-lives (approximately two and 30 years, respectively) and their radiation emissions.

Both caesium-134 and caesium-137 undergo radioactive decay which results in the emission of energetic beta and gamma radiation. Caesium-137 undergoes beta decay without gamma emission but its decay product is barium-137m, which has a half-life of only a few minutes and has a significant gamma-ray emission. Appendix C shows details of the relevant radiation energies.

Both isotopes are created in nuclear reactors during the fission process and build up in nuclear fuel as fission products. Caesium-137 is generally more abundant in spent nuclear fuel and persists longer owing to its much longer half-life. It is used in a range of medical applications, including the irradiation of blood products and radiotherapy (teletherapy and brachytherapy). In industry, caesium-137 is used for applications that include food sterilisation and as level gauges in production environments.

Caesium-137 sources can range in activity up to thousands of terabecquerels (several kilograms of caesium) for major irradiation facilities but many sources are orders of magnitude smaller than this, with consequently much lower masses of caesium. In some sources, the caesium-137 is in a powdered salt form such as caesium chloride. A source of this type this would generally be encapsulated in metal to prevent dispersion of the caesium but still allow the radiation to penetrate. Further information on typical uses and activities of radiocaesium in radiation sources may be found in the International Atomic Energy Agency (IAEA) report on source categorisation (IAEA, 2005).

3.2 Detection of Radiation Sources and their Effects

This section describes the means by which the effects of radiation are detected and how the radiocaesium itself may be identified. The initiation of an incident will typically take one of two forms.

There may be an indication of abnormal conditions in a situation where a radiation source is managed. In this case, it would be reasonable, in the UK at least, to assume that the main characteristics of sources being managed are known and hence the potential for radiocaesium being involved should be known prior to the incident taking place.

The second scenario is where there is no prior assumption that a radiation source is present but there are indications that one is or may have been present. The indications may be clinical effects, labelling or similar visual clues, or unusual radiation monitoring results. In these cases, the indications may be fortuitous and, on their own, are unlikely to provide conclusive evidence that there is a radiation source present and that it is radiocaesium. However, they may be a trigger to initiate other radiation-specific response arrangements.

3.2.1 Detection by clinical effects

Following short duration exposure to ionising radiation above certain thresholds, clinical effects can be observed. Beta and gamma radiation emitted by radiocaesium, and many other radionuclides, can cause observable effects such as erythema or radiation burns associated with skin exposure, or symptoms of acute radiation syndrome associated with broader 'whole-body' exposure such as nausea, vomiting and diarrhoea. These effects are dose dependent and may be delayed in onset.

By observing these symptoms, a clinician may suspect or diagnose acute radiation exposure. However, without prior information suggesting radiation as a possible cause of illness, diagnosis may be delayed because many more common conditions have similar symptoms and signs. Information regarding recognition and diagnosis of unusual illnesses has been published (HPA, 2007), which includes effects of radiation exposure. Clinical effects are not specific to radiocaesium exposure. Hence, even if radiation exposure is recognised, identification of radiocaesium, as opposed to other radionuclides, would not be possible by observing clinical effects.

In the Goiânia incident in Brazil in 1987, a disused caesium-137 teletherapy source was unwittingly dismantled and handled. There was a significant delay in determining that the unexplained medical conditions were caused by internal radiation exposure (IAEA, 1988).

3.2.2 Detection by appearance and labelling of a radiation source

Legislation requires that radiation sources are managed securely and appropriately labelled. It is possible that a radiation source out of management control may be identified by this labelling or, if in transit, through accompanying signage and documentation. If a radiation hazard is suspected, a person with

relevant experience, such as a trained emergency responder or radiation specialist, may recognise the visible physical characteristics of a source or its housing. These characteristics may provide clues to the presence or absence of radiocaesium. The use of the familiar radiation trefoil symbol may also alert non-specialists that a radiation source may be present.

The presence of radioactive material or a specific radionuclide cannot be conclusively established through labelling alone. It is likely to provide contributory evidence that can be coupled with radiation monitoring results. Labelling on radiation sources and their containers is often the primary means by which incidents involving lost sources are recognised.

The presence of radiation may also be suspected through other less likely phenomena, including shading of photographic film, unusual images on X-ray security scanners (such as those at airports) and, at very high radiation intensities and under particular circumstances, a characteristic blue glow (the Cerenkov effect).

3.2.3 Detection through radiation monitoring

Ionising radiation can be detected through the use of radiation monitoring equipment. The radiations emitted by relevant radiocaesium isotopes are at energies and intensities that are within the operating range of most general-purpose beta and gamma monitors.

Radiation monitors can be portable or static. Static devices are often configured to trigger an alarm when dose rates exceed certain thresholds and may be connected to a computer system that monitors the dose rates of many monitors simultaneously. Examples include the emergency plume gamma monitoring systems used on the boundary of most nuclear sites and the UK Radioactive Incident Monitoring Network (RIMNET, maintained by Defra) which provides a national network of gamma monitors.

Portable devices take a range of forms, most often used to measure ambient dose rate or to measure levels of surface contamination. These devices are used in a range of locations, including hospitals, industry, research, defence and nuclear power environments. In circumstances where radiation monitoring is undertaken routinely, it is usual for operators to know the normal background levels and their fluctuation. It is therefore likely that, in such an environment, significant and sustained abnormal radiation levels will be recognised and investigated. Appendix D shows the types of hand-held radiation monitoring equipment that would be suitable for use with radiocaesium.

A number of incidents have been first recognised from high readings observed on radiation monitoring instruments. This includes fortuitous discovery of radiation or contamination from sources not related to the primary purpose of the monitoring. Examples include the initial detection in Sweden of abnormal radiation and contamination levels caused by activity that had been released during the Chernobyl nuclear plant accident in 1986 and an incident in Mexico in 1984 involving steel heavily contaminated with cobalt-60 that was discovered when a lorry load of the contaminated steel triggered boundary radiation alarms at a US nuclear site.

3.3 Identification of Radiocaesium through Analytical Techniques

Explicit identification of radiocaesium can only be performed by using specific radiation analysis techniques and equipment or by tracing the source of the radiation to the original source container.

Gamma rays emitted during radioactive decay have characteristic energies. Gamma spectrometers may be used to measure the energy of gamma rays emitted from the source or a contaminated sample. The measured energies may then be compared with a library of known gamma energies emitted by specific radionuclides. The presence of individual radionuclides, including caesium-134 or caesium-137, can thus be confirmed.

When this is undertaken in an environment of controlled geometry and other constraints, the number of gamma rays at a particular energy can be used with information about detection efficiencies to quantify the activity levels in a sample.

Since caesium-134 and caesium-137 are commonly encountered radionuclides and their gamma energies fall within the usual operating range of spectrometers, it is likely that most gamma spectrometry equipment used in typical environments will have these radionuclides in their data libraries and will be able to identify them.

Hand-held spectrometers are used in operational environments where there is a need to identify which radionuclides are present but not to determine their activity levels. These devices often have a limited data library of radionuclides and may have limited capabilities in situations where multiple radionuclides may be present. However, caesium-137, the most commonly encountered caesium radioisotope, is almost always included in data libraries. Caesium-134 is less generally included.

Laboratory analysis is generally used to provide quantitative measures of the activity levels of specific radionuclides in an environmental or biological sample. Gamma spectrometry is used in whole-body monitors to determine the presence and levels of radionuclides within people. Human bioassay samples such as urine, faeces and nose-blows can also be analysed. Environmental materials that are commonly analysed in this way include air, soil, grass, water and foodstuffs.

Laboratory techniques are often able to identify the presence of radionuclides at levels that may not be achievable with more portable equipment used in the wider environment.

3.4 Incidents which might involve Radiocaesium

A variety of scenarios and operational arrangements might lead to the release and detection of abnormal radiation levels and/or the presence of radiocaesium. These are outlined below.

3.4.1 Incidents involving legitimate, managed sources

Radiocaesium sources that are under proper management could suffer an incident. This section describes the relevant controls that are in place in the UK and the situations that could lead to an incident involving radiocaesium.

A range of legislation covers the acquisition, disposal, security and safety matters associated with holding radioactive material:

a Radioactive Substances Act 1993,

b Radiation (Emergency Preparedness and Public Information) Regulations 2001,

c Ionising Radiations Regulations 1999,

d Nuclear Installations Act 1965,

e High Activity and Sealed Radioactive Sources and Orphan Sources Regulations 2005.

In addition, there are legislative, safety and labelling requirements for the transport of radioactive material by road, rail, air, etc.

These legal requirements place different requirements for record keeping, assessment and monitoring of hazard potential, maintenance of contingency or emergency plans, and provision of protection advice. A significant incident involving radiocaesium associated with a legitimate enterprise, as described below, is likely to be identified quickly.

3.4.1.1 Nuclear site accident

Nuclear sites have the means to identify a release of radioactive material. This includes fixed radiation monitoring systems within and around the plant. Response arrangements for such an event include environmental monitoring and the identification of radionuclides released, supported by prior assessment of the characteristics of potential incidents.

3.4.1.2 Sources used in industry, medicine or research

Most industrial, research or medical holdings of radioactive material in the UK are not sufficiently active, under the Radiation (Emergency Preparedness and Public Information) Regulations (REPPIR) 2001, to require the levels of emergency planning carried at a major nuclear site. However, legislation still requires that the material is kept safely and securely, monitored appropriately, that contingency plans are in place and that the appropriate authorities are notified of any suspected loss. Individual organisations and locations are expected to have good records and knowledge of the radiation sources and specific radionuclides that they hold.

3.4.1.3 Incidents occurring overseas

Radiocaesium from overseas incidents may affect the UK either directly (eg airborne dispersion of activity released from an overseas nuclear reactor) or indirectly (eg exposure of UK citizens abroad).

UK authorities would be made aware of radiation incidents overseas, and the nuclide(s) involved, through a range of mechanisms. Bilateral notification arrangements are in place with a number of European countries. Arrangements are in place covering EU member states and many member states of the IAEA (including the UK) have signed a convention on early notification in the event of nuclear or radiological incidents. The UK can also be alerted in real-time to elevated radiation levels detected by RIMNET. A range of specialist organisations, including the HPA, can provide RIMNET with more detailed information, including results of gamma spectrometric analysis that would identify whether radiocaesium is present.

Individuals returning from abroad who have been affected by an overseas incident could be monitored, if needed, by the HPA or other organisations on return to the UK. Some equipment is spectrometric and could identify individual radiocaesium isotopes. It is worth noting that for some scenarios, such as a reactor release, there may be caesium present but it may be a minority constituent compared with other radionuclides.

3.4.2 Incidents involving sources out of proper management control

While many incidents could arise from legitimate, managed radiation sources with surveillance, monitoring and specific response plans, there is also the potential for incidents to arise through circumstances which do not have the existing source-related management. These situations are outlined below together with information about the means by which the presence of radiation and radiocaesium would be recognised.

3.4.2.1 Suspected terrorist or criminal use of radiation sources

The UK emergency services have CBRN (chemical, biological, radiological and nuclear) specialists, a range of detection, identification and monitoring equipment and related response arrangements (Cabinet Office, 2010). This is supported by intelligence-related work regarding intended or potential malicious activities. Details are not placed in the public domain.

3.4.2.2 Programme Cyclamen

Programme Cyclamen aims to detect movements of illicit radioactive material into the UK. The equipment used can identify a wide variety of gamma-emitting radionuclides. If an illicit source is suspected or found, standard arrangements provide for police and public health involvement where this is needed.

3.4.2.3 Metals recycling industry

The national and international trade in recycling metals can act as a sink for radiation sources that have fallen out of management control. Within the UK, many metals recycling locations operate portal radiation monitors that alarm when significant radiation is detected in incoming shipments. The portal monitors do not generally indicate the type of radionuclide that is causing the elevated radiation levels.

3.4.2.4 NAIR scheme

In cases where a radiation incident is suspected but there is not a pre-determined plan to provide a response, the longstanding NAIR scheme – the National Arrangements for Incidents involving Radioactivity (McColl and Kruse, 2002) – can be used by the police to obtain radiological protection expertise to protect the public. The NAIR scheme provides appropriate radiation expertise voluntarily from a range of organisations, mostly NHS medical physics departments and nuclear establishments. The NAIR scheme, coordinated by the HPA, operates at two stages: stage one provides a more local (hence more rapidly available) but generally simpler response; stage two (based on UK nuclear sites) provides a greater range of capability. The stage two responders will have access to spectroscopic equipment that can identify radiocaesium.

3.5 Conclusions

The identification of an incident involving radiocaesium in the environment typically involves the following sequence:

a suspicion that radiation or radioactive material may be or may have been present,

b initiation of a response involving radiation monitoring equipment,

c specific identification of radiocaesium.

Within the UK and many other countries, regulatory control of radiation sources means that an incident involving a legitimately owned source should be noticed and promptly reported.

In other circumstances, such as the loss or theft of a source, there are a number of ways by which an incident might be recognised. In these cases there may be a delay before an incident is properly recognised.

4 Exposure Scenarios

Exposures to radiocaesium can potentially occur from a wide range of originating events, both accidental and malicious. These include nuclear site accidents, unplanned releases from operating or shutdown reactors or other parts of nuclear licensed sites, lost sources, deliberate contamination of food and water, and deliberate dispersion.

The magnitude of the caesium-137 intake that would be needed over a short period of time to cause deterministic effects is given in Table 4.1.

TABLE 4.1 Quantities of caesium-137 ingested to produce deterministic effects (based on NRPB, 1996)

Deterministic effect	Intake giving threshold dose [a]		Intake giving LD_{50}/ED_{50} [b]		Time at which threshold effect occurs [c]
	Bq	g	Bq	g	
Non-fatal – vomiting	$2\ 10^{9}$	$6.3\ 10^{-4}$	$5\ 10^{9}$	$1.6\ 10^{-3}$	Some months
Fatal – bone marrow syndrome	$1\ 10^{9}$	$3.1\ 10^{-4}$	$2\ 10^{9}$	$6.3\ 10^{-4}$	Some months to years

Notes

(a) Threshold dose: the dose that will give rise to an effect in 1% of the exposed population.

(b) LD_{50}/ ED_{50}: the dose that will give rise to death/an effect in 50% of the exposed population.

(c) With a single intake, the dose is delivered over a period of months or years. The threshold dose for causing a tissue reaction depends on the dose rate; the lower the dose rate, the larger the total accumulated threshold dose. For caesium-137, there is only a factor of about two in dose between no effect and 50% effect. In estimating the time at which the effect occurs, it is assumed that the time at which symptoms might just appear is when the total accumulated dose exceeds the threshold dose. However, these doses are only 'ballpark' figures and are sensitive to assumptions; for example, if the assumed intake is doubled, the threshold is reached in half the time. In addition, the threshold itself decreases because the dose rate is increased, which drastically affects the time at which symptoms occur. The figures in the table correspond to the activities which provide the threshold dose, and the times are the times of onset of symptoms at the threshold; if the activity levels are increased then the time of onset will decrease.

The data in the table relate to adults. The information, even for adults, is very limited and there appear to be no data on deterministic effects from intakes of caesium-137 for children. However, it is thought that, overall, the intake level for a particular radionuclide for children would not differ from that for adults by more than around a factor of two.

The time at which deterministic effects occur, at the threshold level, is significant. The effects could be so protracted in time that they would not appear to be associated with a particular ingestion event, and would not be easily linked unless an exposure event was announced in advance. However, at levels of intake well above the threshold, the effects would appear proportionally earlier and may be more readily detected.

Table 4.2 provides an indication of the upper levels of numbers of people who might be exposed during a range of exposure scenarios given in this chapter. The significant uncertainties associated with these estimates must be emphasised, although the numbers given are thought to be more likely to be overestimates than underestimates.

TABLE 4.2 Upper levels of numbers of people who may be exposed to a given dose from caesium-137 during a number of scenarios

		Above 300 mSv effective dose		Above 30 mSv effective dose	
Scenario	**Deterministic effects**	**Without protective actions**	**With expected protective actions**	**Without protective actions**	**With expected protective actions**
Accidental release from nuclear site	Unlikely	100	Unlikely	10,000	100
Lost source	Few	10	N/A	100	N/A
Deliberate contamination of food/water	A few 10s	A few 100s	N/A	A few 1,000s	N/A
Malicious dispersion	Possibly a few	A few 10s	N/A	A few 100s	N/A

5 Detecting Internal Radiocaesium Contamination

5.1 General Principles of Triage and Selection for Prussian Blue Therapy

Triage is the use of simple procedures for rapidly sorting affected people into groups so as to expedite treatment and maximise the effective use of medical and monitoring resources. In the response to conventional incidents or accidents, triage is used to allocate medical treatment according to the severity of injuries. The process is intended to maximise the number of survivors and can be termed 'trauma triage'. Some but not all incidents considered in this report could require trauma triage to be carried out.

In the response to a radiological incident, triage also includes a group of actions that can be termed 'radiological triage'. Most major incidents involving external or internal contamination of people would require radiological triage to be carried out. Radiological triage actions are intended to sort people according to whether they have been exposed to radioactive material at a level that will definitely have an effect on their health (ie causing deterministic injuries); or whether they may have been exposed to radioactive material at lower levels that might impart a long-term health risk (ie stochastic health effects); or whether they are in the potentially large group of people whose exposures are very unlikely to have any effect on health, or who were not exposed at all. Once identified, the last group can be excluded from further consideration for medical treatment or monitoring, although measures aimed at providing general reassurance may be appropriate.

Where intakes of radiocaesium could be high enough to cause deterministic injuries (eg tissue reactions or acute radiation syndrome), these patients should be identified within 24–48 hours so that medical surveillance and specific treatment can be initiated. People with lower intakes may still be at risk of stochastic health effects (cancer induction in the future) and may need to be considered for treatment with Prussian Blue (Section 6.2). However, the process of identifying people in the latter group does not need to be carried out so urgently.

One of the main factors influencing decisions on treatment with Prussian Blue is the projected committed effective dose for an individual in the absence of treatment. Section 6.2 presents guidance levels for administration of Prussian Blue by projected dose. Ideally, the dose for each affected individual would be determined by whole-body monitoring, which provides a quantitative estimate of the amount of radiocaesium in the body at the time of measurement. If the time of intake is known, the committed effective dose can be determined from the measurement by applying standard biokinetic models.

A triage system for an incident resulting in exposure to radiocaesium is likely to have three main stages, which would be conducted sequentially for each individual:

a triage based on information on the potential for intake for each affected individual, taking into account factors such as proximity to a release, with the aim of identifying and prioritising people for rapid screening,

b triage based on the results of rapid screening measurements on individuals made using portable gamma-ray detectors, with the aim of identifying and prioritising people for more accurate whole-body monitoring measurements,

c triage based on the results of dose assessments derived from whole-body monitoring measurements, to select people for consideration for treatment with Prussian Blue.

Any triage system should be simple to implement, and should not be so time consuming that Prussian Blue treatment is delayed for people with potentially large radiation doses (hundreds of millisievert and above), while detailed assessments of radiocaesium intakes are awaited.

For all but the smallest incidents, whole-body monitoring is unlikely to become available within 24 hours of the incident. This is not a severe problem because (as explained in Chapter 2) it would be sufficient to carry out whole-body monitoring within seven days of an intake where the purpose is to enable decisions to be made on Prussian Blue treatment. If very large numbers of people require monitoring, then it would be acceptable to delay whole-body monitoring measurements of people with lower estimated risks for up to 28 days. Whilst earlier treatment allows a larger proportional decrease in committed dose, a useful level of efficacy is still obtained if treatment is started within 28 days of the intake.

It should be recognised that levels of public concern could result in a demand for more urgent monitoring than would be indicated by a purely objective consideration of the need for Prussian Blue treatment. For a large-scale incident where the demand for whole-body monitoring exceeds available capacity, the results of rapid screening measurements carried out with more immediately available instruments may be used to make early treatment decisions. Such measurements are intrinsically less accurate than whole-body monitoring, and guidance levels would need to be reduced accordingly. As a result, a larger fraction of the affected population could be selected for treatment than would otherwise be the case. If this strategy were to be adopted, then it should be ensured that stocks of Prussian Blue are not unnecessarily depleted as a result of treatment of cases at low risk.

After any significant incident, large numbers of people could wish to be monitored for reassurance. Any such monitoring should be allocated a lower priority than monitoring intended to facilitate decisions on Prussian Blue treatment.

Whole-body monitoring is the ‘gold standard’ for the determination of levels of internal contamination by radiocaesium. However, the relative scarcity of whole-body monitoring capacity in the early post-incident stages may militate in favour of a more pragmatic approach to starting treatment. If treatment is started before whole-body monitoring can be undertaken then, although monitoring is desirable as soon as practicable, priority should be given to people in whom a change in clinical management is the likely outcome of the whole-body monitoring.

5.2 Identification, Measurement and Quantification of Intakes of Radiocaesium

This section discusses first the triage procedures necessary to identify people who may have received significant intakes, and then the individual monitoring measurements needed to quantify committed effective dose with sufficient reliability to enable decisions to be made on Prussian Blue treatment. Such measurements range from simple ones with hand-held detectors to measurements with sophisticated laboratory body monitoring systems. In the early stages of the response to any incident, the measurements would be relatively simple but not as accurate as measurements made with laboratory monitoring systems. However, they could cope with large numbers of people being monitored rapidly, close to the site of the incident. Since throughput of laboratory body monitoring systems is relatively low, these simple 'screening' measurements would be used to select people for subsequent more accurate measurements in the laboratory. Ideally, the laboratory measurements would be used in the selection of people for treatment with Prussian Blue.

Much of the material in this section is taken from the TMT (Triage, Monitoring and Treatment) Handbook, downloadable from www.tmthandbook.org, where more detailed guidance is provided. The Handbook was produced under a European Union 6th Framework Programme project to which the HPA was a major contributor (Rojas-Palmer et al, 2009).

5.2.1 Initial triage

Various stages in the triage process can be identified, as described in Table 5.1. The early stages of triage are likely to be carried out before any results of individual monitoring become available. After 6–24 hours, the results of initial screening measurements would start to become available, and these results would be taken into account in the later stages of the triage process.

Trauma triage, if required, takes place in the first minutes and hours after an incident. Casualties are allocated to trauma triage categories (typically labelled *Immediate, Urgent* or *Delayed;* or *P1, P2* or *P3*) based on the urgency of their need for medical treatment. People allocated to these categories may well be among the most highly contaminated (externally as well as internally), and so may have the most urgent need for individual monitoring, decontamination and treatment.

Radiological triage based on information on location or proximity to the source of contamination is the first triage stage for people who are not physically injured. Following an incident in a major city or a location where large numbers of people have congregated, tens or hundreds of thousands of people could consider themselves to be contaminated. Such numbers would overwhelm any monitoring capability that could feasibly be brought to bear in the short term. One of the main purposes of this triage stage is to identify and exclude from further consideration the potentially large group of people who were not exposed, or who were exposed at an insignificant level.

TABLE 5.1 Stages in the triage process

Triage stage		Typical time period when triage decisions will be made	Information available
Trauma		0 – 12 hours	Severity of physical injuries to individuals
Radiological	Pre-monitoring	2 – 36 hours	Location, proximity, etc, at time of incident
		Up to 6 days	Clinical signs and symptoms and, in the later stages, the results of complete blood counts
	Post-monitoring	6 hours – 3 days	Results of initial screening measurements made at incident location
		12 hours – 6 days	Results of measurements made with transportable *in vivo* monitoring facilities close to incident location
		1 day – 6 days	Results of laboratory *in vivo* monitoring measurements
		3 days – 6 days	Results of laboratory *in vitro* measurements of biological samples (eg radionuclides in urine or cytogenetic measurements of blood)

Note: The results of radiological monitoring will continue to be received well beyond the end of the period where triage decisions are expected to be made. For some cases, the same will apply to the results of observations of clinical signs and symptoms.

The precise information on which to base triage decisions would depend on the circumstances of the incident, but the broad aims would be to identify the following groups of people to prioritise them for individual monitoring according to the likelihood or potential magnitude of their exposure:

a all who came into direct contact with debris, fumes or other material originating directly from the primary source (eg affected people in the immediate vicinity or first responders not wearing respiratory personal protective equipment, PPE),

b if the incident took place outdoors, then all those who were within an established Hot Zone (such people will have a greater likelihood of internal contamination than those further away outside the cordon; it should also be noted that upwind dispersal is possible in complex urban environments),

c if the incident took place indoors, then everyone within the same enclosed space (eg a building) at any time since the incident,

d if the source of contamination was mobile, then the same criteria should be applied to every point on the track of the source during the period when releases could have taken place,

e if the incident involved contamination of food or water, then all those who ate or drank contaminated material.

Radiological triage would need to make use of observations of clinical signs and symptoms if intakes of radiocaesium were large enough to give rise to early deterministic health effects. People exhibiting nausea, vomiting or diarrhoea and who could have been exposed should be identified, and referred for urgent medical assessment and monitoring. Since the dose received from internal contamination by radiocaesium is protracted over time, people encountering the onset of such symptoms during the weeks following an incident must also be identified. Whilst the symptoms may have other causes, such as stress or anxiety, the possibility that very high intakes may have taken place should not be discounted on these grounds.

Medical surveillance and treatment of people with deterministic effects is beyond the scope of this report, although administration of Prussian Blue would be an important part of any treatment programme. Confirmation of contamination levels that could give rise to deterministic effects in some people would probably increase the pressure for urgent individual monitoring for other groups.

5.2.2 Initial individual monitoring

The initial stages of triage should enable identification and prioritisation of people for rapid screening measurements according to the likelihood and magnitude of their potential exposure. For most incidents involving environmental spread of contamination, such measurements will probably be preceded by decontamination, which is now incorporated into emergency plans and is likely to be available before monitoring equipment can be brought to the scene.

There are a number of available options for initial rapid screening, as discussed below.

5.2.2.1 Measurements of contamination of skin and clothing with hand-held beta-contamination probes

Such measurements would be used to determine whether decontamination (or further decontamination) by means of washing or showering is necessary. Removal (or failing that, quantification) of external contamination on skin or clothing would also assist with interpretation of subsequent internal contamination measurements. External contamination must be removed before accurate measurements of internal contamination can be performed.

5.2.2.2 Measurements of internal contamination with hand-held gamma probes

Measurements made with suitable instruments have adequate sensitivity for rapid screening. The HPA has recently completed an evaluation of a number of hand-held instruments suitable for the rapid screening of people internally contaminated with radiocaesium (Scott and Youngman, 2008). Minimum detectable activities (MDAs) for a whole-body measurement of caesium-137 in an adult with a detector positioned 30 cm from the body ranged between 140 kBq and 2200 kBq, depending on the instrument, but were about 10 kBq for instruments where a measurement of the gamma spectrum could be made and the count rate in the caesium-137 photo-peak determined. The MDAs could be achieved using a 10 second count time for the non-spectrometric measurements, or a 60 second count time for spectrometric measurements. Committed effective doses for adults corresponding to these MDAs ranged

from 2 to 30 mSv, depending on the instrument, or about 0.15 mSv for an instrument capable of spectrometric measurements. These doses are determined assuming measurements take place 24 hours after exposure.

The instruments evaluated by Scott and Youngman are available at the HPA and some of them are also likely to be found in many NHS medical physics departments. If 20 such instruments were deployed, each with a throughput of three people per minute, then 30,000 people could be screened in a period of eight hours.

The RAM-GENE™ monitor, commonly found in NHS emergency departments, does not have the sensitivity to detect internal contamination at the lowest levels for which Prussian Blue treatment might be initiated. This instrument is designed primarily to measure gamma dose rates and to check for external radioactive contamination. Other simple hand-held monitors do have the required sensitivity and the HPA can advise on the choice of instruments.

5.2.2.3 Measurements with portal monitors

Portal monitors offer another approach to rapid screening. A number of portable portal monitors have been acquired by the HPA, and detailed evaluations of MDAs and corresponding measurement times are being carried out. An MDA for caesium-137 contamination levels in the region of 40 kBq is understood to be achievable. Throughputs for each instrument are likely to be in the region of three people per minute.

5.2.2.4 Measurements with portable high resolution spectrometry systems

Portable high resolution radionuclide detector systems have recently become available. Such systems can be used as improvised whole-body monitors, and the HPA has recently acquired and evaluated one such system for this purpose (Youngman, 2008). An MDA for caesium-137 in an adult of approximately 6 kBq is achievable for a five minute count time, corresponding to a committed effective dose well below 1 mSv. Such systems have the advantage that a positive identification of the contaminating radionuclide(s) can be made, and whole-body contents can be measured with accuracies in between those of hand-held instruments and laboratory body monitoring systems.

5.2.2.5 Initial internal dose assessment

Internal doses are usually determined from measurements of activity in the body using computer codes that implement the relevant ICRP biokinetic and dosimetric models. The HPA has developed a computer program (ERIDAS) specifically for use in the event of an accidental or deliberate release of radionuclides for the assessment of committed effective doses to individuals of various ages (Youngman et al, 2007). It is intended for use by personnel who may not be specialists in internal dosimetry.

ERIDAS does not provide assessments of absorbed doses to organs, since its primary aim is to allow dose assessment to be carried out rapidly for the large numbers of people with intakes that would be very unlikely to give rise to adverse health effects. However, the TMT Handbook contains tabulated data that allow absorbed doses to organs to be evaluated.

5.2.2.6 Action levels for initial individual monitoring measurements

Because of the uncertainties associated with the rapid initial screening measurements, these measurements do not provide a sufficiently accurate assessment of intake or committed effective dose. An action level is therefore required to indicate when more accurate whole-body measurements are required. The lowest projected committed effective dose at which Prussian Blue treatment would be considered is 30 mSv. Experience indicates that a conservative estimate of the uncertainty associated with a rapid measurement with a hand-held detector would be plus-or-minus a factor of five at the 95% confidence level. Thus, the action level should be set for a measured value corresponding to an indicated committed effective dose of 6 mSv. Action levels can be determined using the data presented by Scott and Youngman (2008).

A separate action level may be needed to identify those individuals who should be offered long-term follow-up measurements. The TMT Handbook proposes that such an action level should be set for a committed effective dose in the range 1–20 mSv, and should be chosen taking into account the numbers of people who may be identified for follow-up, and the available monitoring facilities. It is possible that such an action level could fall below the action level that would trigger more accurate whole-body monitoring for the purposes of Prussian Blue treatment, and so the initial decision on follow-up would need to be made on the basis of a rapid screening measurement. Consideration needs to be given to whether it is appropriate to offer long-term follow-up measurements to people who have not been identified for treatment with Prussian Blue.

People who received doses below these action levels may be directed to go home, with no other follow-up.

5.2.3 More accurate whole-body monitoring

The results of rapid screening measurements on individuals should be used to identify and prioritise people for more accurate whole-body monitoring measurements. The earliest such measurements are likely to be made using the HPA transportable body monitoring system. Later measurements could be provided by laboratory-based body monitoring systems.

5.2.3.1 HPA transportable body monitor

This system is described by Youngman (2003). It is designed so that it could be taken quickly to the location of an incident, and could be expected to deliver the first results within 24 hours, depending on the circumstances of the incident. An MDA for caesium-137 in an adult of approximately 500 Bq is achievable for a five minute count time, corresponding to a committed effective dose well below 1 mSv. A throughput of about ten people per hour is achievable with this count time. Somewhat higher throughputs could be achieved by reducing the count time, but this is eventually limited by the time taken to move people in and out of the seated measurement position. Uncertainties in measurements of whole-body activity are estimated to be no greater than plus-or-minus a factor of two at the 95% confidence level.

5.2.3.2 Laboratory monitoring systems

Two HPA systems situated at CRCE Chilton could be brought rapidly into operation. Typical count times are 15 minutes, and MDAs for caesium-137 equivalent to committed effective doses well below 1 mSv are achievable. A throughput of about six people per hour is feasible. This could probably not be improved significantly by reducing count times, because neither system is designed for rapid throughput of people. Uncertainties in measurements of whole-body activity made using laboratory monitoring systems are estimated to be no greater than plus-or-minus 20% at the 95% confidence level.

Five other sites in the UK operate whole-body monitors, normally for the purpose of monitoring workers. These are civil or military nuclear sites at locations ranging from Hampshire to Cumbria. No formal agreements exist, but it is expected that in an emergency, and for a short time, these organisations would be able to assist, with the HPA coordinating their efforts.

To estimate the capacity of this resource, it is assumed that each site could monitor three people per hour. However, the availability of these facilities would depend on the ability of other organisations to respond to a specific request at the time of an incident. The availability of non-HPA facilities may be constrained by their local operational requirements and security considerations.

5.2.3.3 Throughput of laboratory and transportable whole-body monitoring facilities

Logistical challenges that may reduce throughput include the provision of transport and welfare (including food and drink) for people who are to be monitored, provision of ancillary services such as laundry and modesty gowns, and the practicability of asking people to be monitored at night.

The first 24 hours are likely to be taken up with readying equipment and putting arrangements into place. Subsequently, a theoretical maximum daily throughput would be several hundred measurements per day if all transportable and laboratory facilities in the UK are fully utilised. However, this is unlikely to be achieved in practice. Over the first three days, with suitable logistical support, the HPA could monitor at least 200 people, and subsequently could achieve a throughput of about 100 per day.

Assuming 24-hour operation by all laboratories, a total UK capacity of 400 measurements per day might be achieved.

5.2.3.4 Bioassay sample monitoring

It is feasible to assess intakes of radiocaesium by measuring the rate of excretion in urine and/or faeces (although faecal monitoring is unlikely to be feasible as a mass monitoring technique in an emergency). Whole-body monitoring has several advantages over excreta monitoring, or the use of nasal wipes or swabs. It is a more reliable direct (rather than indirect) measurement; the result is obtained almost immediately, and less effort is needed. Nevertheless, urine bioassay and possibly faecal bioassay could usefully complement whole-body monitoring in some circumstances – for example, in an assessment of the *in vivo* solubility of the material inhaled or ingested, or in an assessment of the effectiveness of treatment.

5.2.3.5 Internal dose assessment based on the results of accurate whole-body monitoring

Clinical decisions to start Prussian Blue treatment should be made using information on the committed effective dose computed from whole-body measurement, compared with the guidance levels described in Section 6.2. Dose assessments could make use of specific information on exposure conditions; the HPA has the necessary facilities and expertise to carry out the calculations required.

5.3 Assessing the Effectiveness of Prussian Blue Treatment

Ideally, all patients treated with Prussian Blue should be offered long-term follow-up whole-body monitoring measurements. This would be to assess the effectiveness of treatment, and provide an accurate assessment of initial intake, committed effective dose and equivalent dose to organs and tissues arising from the exposure.

The effectiveness of treatment should be assessed by determining the cumulative dose saved as treatment proceeds. This would ensure that unnecessary continuation of an individual's treatment can be avoided. A series of laboratory whole-body monitoring measurements could be conducted to establish the biological half-life of caesium during the period of Prussian Blue treatment, and the biological half-life after treatment ceases. Because the caesium biological half-life is known to be quite variable between individuals, the half-lives would ideally be established for each individual treated. The frequency of such monitoring could be limited by the number of people who are undergoing treatment. The HPA would carry out the required measurements and provide assessments of the effectiveness of treatment. If whole-body monitoring capacity is limited or other logistical issues arise, other monitoring techniques such as urine monitoring may be considered.

6 Developing a Risk-based Intervention Level for Radiocaesium Ingestion or Inhalation

6.1 Pre-absorption and Prophylactic Use of Prussian Blue

Prophylactic use of Prussian Blue is not currently recommended. There is not enough known about absorption rates to define the effectiveness of this approach. If worker protection is required in the aftermath of an incident, other countermeasures such as the use of personal protective equipment, limiting time spent in the affected area, sheltering or distancing would serve to decrease doses from any radionuclide involved. Radiological monitoring of workers and scene management would also be important to decrease exposures. Prussian Blue is an unlicensed medical treatment and thus not suitable for mass distribution. There is scope for more research into absorption rates to explore the potential utility of this approach.

6.2 Guidance Levels for Administration of Prussian Blue

6.2.1 Approaches for developing guidance levels

Two approaches for developing guidance levels have been considered: comparison with harms and benefits of Emergency Reference Levels (ERLs) of dose for sheltering, evacuation and stable iodine prophylaxis; and comparison with the cost–benefit balance that can be inferred from the management of other public health risks (see Appendix E).

6.2.1.1 Comparison with existing ERLs (NRPB, 1997)

The expected benefits of treatment with Prussian Blue, in terms of averted health risk and public reassurance, are judged to be similar to, or less than, those associated with the countermeasures of sheltering and stable iodine prophylaxis, and very much less than those associated with evacuation. This is because only one exposure pathway and one radioactive element are addressed, whereas sheltering and evacuation provide protection from internal and external exposure and from all radionuclides. Furthermore, whilst stable iodine prophylaxis only provides protection against one radioactive element and one exposure pathway, it has the potential to avert virtually all of the dose, whilst Prussian Blue can, at best, avert only two-thirds of the dose.

The associated harms from Prussian Blue treatment, in terms of disruption, side-effects, etc, are judged to be considerably greater than those associated with sheltering and stable iodine prophylaxis, and probably greater than those associated with evacuation, because of the need for treatment to continue over a number of months.

Overall, therefore, solely by comparison with existing ERLs, it can be argued that the guidance levels for Prussian Blue treatment should be at least comparable with those for evacuation, and possibly higher, ie at least 30 mSv (lower threshold) and 300 mSv (higher threshold) averted dose.

6.2.1.2 Comparison with the management of other public health risks

Actions (in the form of antibiotics and other drugs) to protect the public from biological health risks (eg meningitis) are generally introduced at fatality risks of between around 1 in 1,000 and 1 in 10,000. A simple cost–benefit analysis suggests that a lower guidance level of a few tens of millisievert total dose from internal contamination by radiocaesium would equate to the level of protection provided for biological health risks. However, there are uncertainties in this comparison due to the uncertainties in the data and the overall paucity of relevant data for estimating the level of risk at which public health protection actions are taken.

6.2.2 Guidance levels for administration of Prussian Blue

Taking the two approaches together, it is recommended that a lower guidance level of 30 mSv projected dose from internal exposure to radiocaesium be adopted to trigger investigation of whether or not to treat individuals with Prussian Blue. At this level of projected dose, the radiation health benefit to the patient would generally be small, but for some patients, the discomfort and disruption of the treatment might be far outweighed by the reassurance provided, and so should be considered. At a projected dose of 300 mSv the overall benefit to the patient would be expected to be significant. Only in exceptional circumstances (eg advanced age) would it be reasonable to consider not treating a patient with a projected dose at this level.

6.3 Other Comments

When planning emergency response under REPPIR 2001, it is possible to plan for measures that provide protection against a range of radionuclides and exposure pathways, eg sheltering, evacuation and food restrictions. Since these protective measures prevent (or reduce) intakes of radiocaesium, rather than relying upon removing the radiocaesium once it has entered the body, they are considered preferable protective actions to administration of Prussian Blue. Therefore, such plans should not normally include provision for Prussian Blue treatment.

6.4 Dosage of Prussian Blue

The recommended dosage for Prussian Blue Antidotum Thallii-Heyl® (UK) [equivalent to Radiogardase® (USA)], 500 mg insoluble Prussian Blue per capsule is:

a **adults and adolescents*:** 1 g (two capsules) orally three times daily (total of 3 g per day),

* In reviewing the evidence we have found ambiguity in the recommended dose in manufacturers' instructions, some US guidance and some US websites. This is assumed to arise from the way that the US guidance has interpreted the scientific evidence about daily amounts administered as divided doses. However, the scientific evidence supports the adult doses defined above. There is evidence that higher doses do not increase the effectiveness of the treatment and cause more side-effects (Lipsztein et al, 1991a,b). Even within the REAC/TS website there are different values given for Prussian Blue dose (REAC/TS, 2009a,b). Similarly, it is unclear why some of the international guidance extends infancy up to two years of age for the purposes of dose calculation.

b **children (1–12 year olds):** 0.5 g (one capsule) orally three times daily (total of 1.5 g per day), noting that this dose has little evidence base,

c **under 1 year olds:** there are variations in the developmental maturity of the biliary system and gastrointestinal tract of neonates and infants (0–1 year olds). The dose-related adverse effects of insoluble Prussian Blue on an immature gastrointestinal tract are not known. There may be more absorption of Prussian Blue into the body but the effects of this are unknown. Dosing in infants and neonates has not been established. In the absence of other guidance a dose per body mass extrapolated from the children's guidance above and under strict medical and radiological supervision would be indicated.

If patients cannot tolerate swallowing large numbers of capsules, the capsules may be opened and mixed with food or liquids. This may result in blue discolouration of the mouth and teeth.

In general, the dose of Prussian Blue should not be decreased as the body burden of caesium-137 falls; however, under medical supervision it may be considered to control side-effects with account taken of the effect on caesium elimination.

6.5 Special Considerations

6.5.1 Treatment of deterministic health effects

The diagnosis and treatment of deterministic health effects is not within the scope of this review. The HPA independent Advisory Group on Ionising Radiation has recently reviewed this topic and provided links to numerous other sources of advice (AGIR, 2009).

6.5.2 Pregnancy

Comprehensive animal reproductive studies have not been conducted with Prussian Blue. However, whilst caesium-137 is known to cross the placenta, Prussian Blue should not, since it is not absorbed from the mother's gut. The risk to a fetus from radiation-related adverse health effects of intakes of caesium-137 is therefore expected to be greater than any fetal toxic risk from Prussian Blue. Therefore pregnant women should be considered for treatment at doses near the lower guideline level (30 mSv).

6.5.3 Breast-feeding

Caesium is transmitted from mother to infant in breast milk. Prussian Blue does not enter the circulation and thus does not enter breast milk. The HPA has carried out a study for the Health and Safety Executive (Phipps et al, 2001) which shows that the committed effective dose to an infant resulting from an intake of radiocaesium by the mother would be no greater than about 30% of the dose to the mother. The risk of adverse health effects for the infant is not expected to exceed that for the mother, even though the risk per unit dose is somewhat higher for an infant than for an adult.

For a mother who has received an intake resulting in a committed effective dose less than the lower guidance level (30 mSv), the benefits of breast-feeding are presumed to outweigh the radiation risk and so the mother should be advised that there is no need to stop breast-feeding.

For a mother with a committed effective dose greater than the lower guidance level, Prussian Blue treatment is recommended. In this case, it is also recommended that doses and risk to the infant should be individually assessed to inform advice to the mother on whether to stop breast-feeding. If resources allow it, and depending on the nature of the incident and the numbers of people affected, such an assessment could also be carried out where the committed effective dose to the mother is less than the lower action level, but decisions should be made on a case-by-case basis.

6.6 Contraindications, Side-effects and Physiological Monitoring

Prussian Blue is well tolerated by the human body. Constipation and coloured stool are the only consistently reported side-effects. Constipation can be treated by co-administration of a laxative or increasing the amount of fibre in the diet. Because of its tendency to produce constipation it has been suggested that Prussian Blue should be used with caution in those with gastrointestinal motility disorders. With high doses given over a prolonged period, non-specific gastrointestinal distress is also a feature. In one source the incidence of constipation in patients treated with Prussian Blue was reported as 24% (Drugs.com, 2008).

Prussian Blue has the potential to bind to other elements (such as potassium and sodium) and cause an electrolyte or other nutritional imbalance. Serial monitoring of electrolytes has shown mild hypokalaemia in a few treated individuals (7%) (Drugs.com, 2008). This was rapidly reversed by potassium replacement. This may, however, indicate that patients with pre-existing electrolyte imbalance or cardiac arrhythmias are a sensitive subgroup and Prussian Blue should be used with caution in this group. Baseline levels of serum electrolytes should be measured and the subsequent monitoring frequency determined by clinical considerations. As a minimum, an on-treatment measurement of electrolytes should be made in the first week of treatment.

Since Prussian Blue is not systemically bioavailable and does not rely upon renal elimination or hepatic metabolism, its use is not specifically contraindicated in patients with impaired renal or liver function. It may be less effective in patients with impaired bile secretion due to liver or gall bladder disease because that is the route by which caesium in the body re-enters the gastrointestinal tract. Draft US FDA guidance (US FDA, 2003) suggested that patients with disorders associated with hypersecretory states, eg gastrinaemia and Zollinger-Ellison syndrome, may find that Prussian Blue is ineffective and they may be at risk of cyanide poisoning because Prussian Blue dissociates and may release cyanide in very acidic environments (eg pH 0–1). Updated evidence, US FDA guidance and manufacturers' information, has removed this precaution (US FDA, 2004, 2008; Yang et al, 2007).

Drug interactions are possible and the literature contains anecdotal reports of decreased bioavailability of oral tetracycline. Therefore blood levels or clinical responses should be carefully monitored. There is no evidence in the literature about the effect of Prussian Blue on effectiveness of the oral contraceptive pill. The package insert for the Radiogardase® preparation suggests that measurements of iron and ferritin

may also be appropriate during the first four days of a course of treatment but there is no reference to support the need for this (REAC/TS, 2009b).

6.7 Radiological Protection Issues for Patients Undergoing Treatment

Patients should be informed about the urinary and faecal excretion of caesium to enable them to minimise radiation exposure to others. As caesium may be excreted in sweat as well as urine and faeces, radiation risks to close contacts of people with large intakes may need to be considered by treating clinicians and specific advice given to protect household and other close contacts. Monitoring may be considered to protect those in close contact and to measure the efficacy of dose reduction measures taken.

Healthcare professionals should follow appropriate radiological protection advice to avoid unnecessary exposure and the spread of contamination. Radiological protection for healthcare employees should be managed under workplace health and safety arrangements. NHS medical physics and radiological protection services should be utilised.

For non-employees, specifically carers and comforters, incident managers should follow the guidance set out for these groups in other medical exposure situations. The ICRP in Publication 103 (ICRP, 2007), quoting its own Publication 94 (ICRP, 2004), provides recommendations for the release of patients after radiotherapy with unsealed sources. These recommendations state that young children and infants, as well as visitors not engaged in direct care or comforting, should be treated as members of the public for radiological protection purposes (ie be subject to the public dose limit of 1 mSv per year). For individuals directly involved in comforting and caring, other than young children and infants, a dose constraint of 5 mSv per episode (ie for the duration of a given release after therapy) is reasonable. The constraint needs to be used flexibly. For example, higher doses may well be appropriate for parents of very sick children.

6.7.1 Specific guidance

6.7.1.1 Urine and faeces

As the primary routes of elimination from the body are urine and faeces, potential hazards with contamination exist. The dilution factor of matter arriving at the sewage treatment plant will mean that the sewage is unlikely to be hazardous. Patients taking Prussian Blue should be advised to use a toilet instead of a urinal, and a full flush or double flush should be carried out after each use. Patients should be advised to clean up spilled urine or faeces completely and wash hands thoroughly after using the toilet.

The HPA (when NRPB) issued guidance on Generalised Derived Constraints (GDCs) for discharges to sewers, which are convenient reference levels against which proposed discharges can be compared, based on an effective dose to members of the public of 0.3 mSv per year (NRPB, 2000). The GDC for discharge to sewers for caesium-137 is 10^8 Bq per year and the limiting pathway is the application of sewage sludge to land rather than the potential exposures in the sewage works.

6.7.1.2 Direct contact and sweat

Caesium-137 decays by beta and gamma emission so that direct irradiation through the body wall from an internally contaminated patient is possible. The dose to a sleeping adult partner is likely to be no more than 2% of the dose to a contaminated adult partner (assuming eight hours' sleep each day, and a gap of 30 cm between the sleepers). Measures to reduce exposure to sleeping partners and other very close contacts are unlikely to be needed but could be considered if calculated to be above the public dose limit of 1 mSv per year. Typically, a person will excrete radiocaesium into urine at the highest rate during the first few days after intake, but the amount excreted per day will be no more than about 2% of the amount taken up by the body. So, if a person initially has 1 MBq in the body, then they might excrete about 20 kBq per day over the first few days, decreasing after that. The typical urine volume per day is about 1.6 litre. Similar concentrations would occur in sweat. Normal volumes of sweat for people in the UK are about 0.5–1 litre per day. The maximum amount of sweat normally produced without adaptation to high temperatures is about 1 litre per hour. Unless high volumes are produced, or the level of radiocaesium contamination in the body is very high, the activity of radiocaesium in sweat would be expected to be negligible and would not necessitate any special precautions for discarded dirty clothing.

6.7.1.3 Foreign travel

Many airports and other ports now monitor passengers for radiation with instruments that can pick up low levels of radiocaesium. Therefore passengers with low levels of internal contamination may be stopped and subject to questioning. It may be prudent to warn patients about this and suggest they take documentary proof that they have been contaminated with radiocaesium, in order to speed passage through ports in the same way as cards are issued to those who have undergone brachytherapy radiation treatment.

6.8 Termination of Therapy

The decision to terminate therapy must be made by the patient based on advice from the prescribing clinician. Therapy should be continued until the whole-body concentration of radiocaesium is reduced substantially, based on the principle that any radiation exposure should be reduced to as low as is reasonably achievable. Other important factors include the rate of elimination with Prussian Blue treatment compared to natural elimination and the absolute value of additional dose saved from continuing therapy. If the dose averted by continued therapy is negligible, with negligible being an individual committed effective dose of 2 mSv (equivalent to background radiation levels and conferring a fatal cancer risk of about 1 in 10,000), then, with consideration, treatment can be stopped.

The following are also criteria for termination of therapy:

a no further reduction in the radiocaesium concentration in the body is observed in serial whole-body counting or excreta sampling beyond what would happen without treatment,

b concern about adverse reactions with continuing administration.

6.9 Other Indications for the Use of Prussian Blue

Clinical experience in the use of Prussian Blue for the treatment of thallium (or radiocaesium) poisoning in the UK is very limited. Only isolated cases have been reported in the world literature (Pai, 1987). Higher doses are generally used than for treatment of radiocaesium intakes (Kamerbeek et al, 1971). The recommended treatment for thallium poisoning is to give Prussian Blue orally at 250–300 mg per kilogram body weight per day until thallium can no longer be detected in the faeces. These dose levels are equivalent to about 20 g a day for a 70 kg adult, which is given in two divided doses of 10 g each. These dose levels are considered well tolerated (NPIS, 2010: TOXBASE Prussian Blue).

A review of the published literature by Hoffman (2003) identified reports of case studies of the treatment of thallium poisoning. These support the view that this treatment has few side-effects, although the signs and symptoms of thallium poisoning itself present some difficulties in this regard. However, treatment in the early stages of poisoning has been shown to prevent development of the major symptoms of thallotoxicosis, with no evidence of any adverse effects due to Prussian Blue other than constipation and blue colouration of faeces.

6.10 Pharmaceutical Formulation, Legal Status and Storage in the UK

Prussian Blue is not licensed as a medicine in the UK. Stocks are obtained from Germany. The formulation used in the UK is Prussian Blue Antidotum Thallii-Heyl® (UK) [equivalent to Radiogardase® Insoluble Prussian Blue (ferric hexacyanoferrate, Fe4[Fe(CN)6]3) (USA)]. Prussian Blue Antidotum Thallii-Heyl® capsules (500 mg Prussian Blue powder in a gelatin capsule) are packed in 30 capsule quantities. For the treatment of radiocaesium contamination, Prussian Blue would need to be prescribed by a physician on a named patient basis and subject to enhanced reporting of side-effects using the black triangle system. The legal status of Prussian Blue is not compatible with mass distribution using patient group directions or other means to prescribe without face-to-face consultation with a medical practitioner. It also implies continued medical supervision of patients being treated.

The Medicine and Healthcare products Regulatory Agency advises that Prussian Blue Antidotum Thallii-Heyl® capsules should be stored in the dark below 25°C, that the number of excursions between 25°C and 30°C be kept to a minimum and that the product should not be allowed to freeze (MHRA, personal communication). In its product literature the storage temperature requirements for Radiogardase® state that it should be stored at 25°C with excursions permitted to 15–30°C. It is understood that this is standard practice in the USA and does not imply that the product, which is chemically stable, will degrade if stored in cooler temperatures. The shelf-life of Prussian Blue is currently two years, in accordance with the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines. The storage experiments are continuing, and as a result the shelf-life of the product may be extended.

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Appendix A
International Guidance for Use of Prussian Blue for Treatment of Intakes of Radiocaesium

A1 Sources of guidance

There is limited experience of the use of Prussian Blue in humans internally contaminated with radiocaesium. However, there is literature about the effects of Prussian Blue in animal models and also some human experimental data (Lipsztein et al, 1991a,b). The largest body of human evidence was published following the radiological accident in Goiânia, Brazil, in 1987 (Melo et al, 1994; IAEA, 1998).

Guidance on the use of Prussian Blue for the treatment of internal radiocaesium contamination has been produced most recently by the US Armed Forces Radiobiology Research Institute (US AFRRI, 2005) and the US Food and Drug Administration (US FDA, 2008). This guidance is linked to published information about pharmacological aspects of Prussian Blue.

A2 Initiating therapy

Treatment with Prussian Blue is most effective when administered as soon as possible after ingestion or inhalation of radiocaesium. However, therapy is still effective when begun days after the intake. In Goiânia, therapy was started ten or more days after the intake. The only studies of the prophylactic use of Prussian Blue have been in rats (Dresow et al, 1993). However, US guidance states that Prussian Blue can be given prophylactically if the patients were unprotected during exposure, including first responders, but 'persons more than a few hundred yards downwind from the incident are unlikely to require treatment due to rapid dilution of the material in the atmosphere' (US AFRRI, 2005).

A3 Dosage of Prussian Blue

There is evidence that higher doses do not increase the effectiveness of the treatment and cause more side-effects (Lipsztein et al, 1991a,b). It should be noted that, in reviewing the evidence some ambiguity has been found in the recommended dose on manufacturers' instructions and some US guidance. This is assumed to arise from the way that the US literature expresses a total daily dose when administered in divided doses (3 g three times daily in some US literature may equate to 3 g daily in divided doses in the UK).

Doses (of insoluble Prussian Blue, Radiogardase®) defined in the US FDA guidance (US FDA, 2008) are:

a **adults and adolescents:** 3 g orally three times daily,

b **children (2–12 year olds):** 1 g orally three times daily.

REAC/TS expects that most cases of accidental intake will result in internal contamination that falls in the low to intermediate category (REAC/TS, 2009a,b). The US FDA suggests that treatment for these cases should be started at 1 g three times a day and titrated as necessary. To allow an evaluation of caesium-137 elimination curves it is expected that daily whole-body counting and collection of 24-hour urine and faecal bioassay samples will be performed. As the whole-body burden of caesium-137 decreases, consideration should be given to decreasing the Prussian Blue dose in parallel.

The dosing regime suggested by REAC/TS is directed primarily at the use of Prussian Blue in US Department of Energy (US DOE) facilities. These facilities are spread across the USA and are engaged in research, development, production and testing of nuclear materials. The level and availability of support in the event of an intake of radiocaesium, in terms of both equipment and expertise, is likely to be good. Accidents in US DOE facilities could involve either caesium-137 particulate inhalation or wound contamination. Whole-body counting or wound counting are suggested as the preferred method for initial determination of the magnitude of the incident. The dosage regime relies upon the availability of adequate whole-body/wound monitoring and the ability to process daily collection of 24-hour urine and faecal bioassay samples.

A3.1 International guidance for specific groups

Under 2 year olds: there are variations in the developmental maturity of the biliary system and gastrointestinal tract of neonates and infants (0–2 year olds). The dose-related adverse effects of insoluble Prussian Blue on an immature gastrointestinal tract are not known. Dosing in infants and neonates has not been established.

Pregnant women: comprehensive animal reproductive studies have not been conducted with Prussian Blue. However, whilst caesium-137 is known to cross the placenta, Prussian Blue should not since it is not absorbed from the mother's gut. The risk to a fetus from radiation-related adverse health effects of intakes of caesium-137 is therefore expected to be greater than any fetal toxic risk from Prussian Blue and pregnant women should be considered a high priority group for treatment.

Breast-feeding: caesium is transmitted from mother to infant in breast milk. Breast-feeding mothers internally contaminated with radiocaesium should therefore be advised of the benefits of stopping breast-feeding.

A4 Decision to continue therapy, termination of therapy

The clinical decision to continue interim therapy should be made on a case-by-case basis after evaluation of the available data. This requires a quantitative analysis of internal radiocaesium contamination, as soon as possible after the incident, by appropriate whole-body counting and/or by bioassay. In the event that large numbers of patients begin presumptive therapy, an interim assessment of these individuals may be necessary.

The ICRP has published guidance on radiation doses and intakes where therapy should be continued (ICRP, 2005). The intake is compared to the annual limit on intake (ALI). The ALI is defined by the ICRP as the intake by inhalation, ingestion or through the skin of a given radionuclide in a year by a reference man which would result in a committed dose equal to the relevant dose limit. The ALI is expressed in units of activity and values are given by the ICRP for occupational exposure related to the annual effective dose limit of 20 mSv. The level of internal contamination can be categorised in multiples of the ALI as low (1–5 ALI), intermediate (5–10 ALI), or severe (10 ALI or more).

The ICRP suggests that treatment is:

a not usually indicated for intakes below 1 ALI,

b usually recommended for intakes above 10 ALI.

The limits used in the REAC/TS schedule are based on an annual dose of 50 mSv per year (REAC/TS, 2009a,b), advice from the National Council on Radiation Protection and Measurements (NCRP, 1980) and the limit for classified workers in the USA. The equivalent figure for 1 ALI based on dose limits will be 40% of this value.

The US FDA guidance for Radiogardase® treatment suggests a minimum course of 30 days (US FDA, 2008). Serial measurements of internal radioactivity will be necessary to evaluate the efficacy of treatment and to determine when it may be terminated. US FDA guidance also notes that when internal radioactivity is substantially decreased, the dose of Prussian Blue may be decreased to 1–2 g, three times per day, to improve gastrointestinal tolerance.

A5 Side-effects, interactions precautions and patient monitoring

Most of the experience with the therapeutic use of Prussian Blue has been in cases of thallium poisoning (Hoffman, 2003). There are fewer published reports on the use of Prussian Blue in radiocaesium poisoning (Lipsztein et al, 1991a,b; Melo et al, 1994). The dose levels used have been less than those in the treatment of thallium poisoning, with 3 g a day (in three divided doses) for three weeks being reported to be well tolerated and effective at reducing the biological half-life of radiocaesium by 66%. Most of the data relate to the Goiânia incident when higher doses were used (up to 10 g per day, although 3 g per day was again considered the minimum effective dose). (The minimum effective dose was considered to be 3 g per day, administered in three divided doses, which was given for prolonged periods, up to six months.) This was well tolerated, as was 10 g per day, apart from the constipation necessitating co-administration of laxative.

Since Prussian Blue is a crystal lattice that exchanges potassium for caesium at the surface, it also has the potential to bind to other elements (such as potassium and sodium) and cause an electrolyte or other nutritional imbalance. In Goiânia, the medical team measured serum potassium levels in treated patients routinely twice a week and whenever there was a clinical indication (Brandão-Mello et al, 1991). Mild asymptomatic hypokalaemia was observed in 3 out of 46 individuals treated with

Prussian Blue (2.5–2.9 mEq l^{-1}, compared to the normal range of 3.1–4.8 mEq l^{-1}). The serum potassium levels were promptly re-established by oral and intravenous potassium replacement. Caution should be exercised, therefore, when treating patients with pre-existing cardiac arrhythmias or electrolyte imbalances. REAC/TS recommends that patients with potential for electrolyte abnormalities and/or cardiac problems should have periodic serum electrolyte tests at the discretion of the treating physician (REAC/TS, 2009a,b). It is suggested that blood samples be collected every 12 hours for the first 96 hours post-intake for serum chemistry, especially iron, ferritin and serum electrolytes as indicated.

Since Prussian Blue is not systemically bioavailable and does not rely upon renal elimination or hepatic metabolism, its use is not specifically contraindicated in patients with impaired renal or liver function. It may be less effective in patients with impaired bile secretion due to liver or gall bladder disease because that is the route by which caesium in the body re-enters the gastrointestinal tract.

Drug interactions are possible and the literature contains anecdotal reports of decreased bioavailability of oral tetracycline (US FDA, 2008). Therefore blood levels or clinical responses should be carefully monitored. There is no evidence in the literature about the effect of Prussian Blue on effectiveness of the oral contraceptive pill.

Draft US FDA guidance (US FDA, 2003) suggested that patients with disorders associated with hypersecretory states, eg gastrinaemia and Zollinger-Ellison syndrome, may find that Prussian Blue is ineffective and they may be at risk of cyanide poisoning because Prussian Blue dissociates in very acidic environments (eg pH 0–1) and may release cyanide. Updated evidence, US FDA guidance and manufacturers' information, has removed this precaution (US FDA, 2004, 2008; Yang et al, 2007).

Prussian Blue's affinity for caesium is greater than its affinity for nutritional elements, therefore food is not expected to appreciably interfere with Prussian Blue's ability to increase the elimination of caesium. Since food is known to increase bile production and enterohepatic circulation it may increase the amount of caesium in the gastrointestinal lumen available for binding. Food is also known to increase the pH of gastric and intestinal contents, thereby lowering the risk of dissociation.

The US FDA provides a Prussian Blue Patient Treatment Data Form (US FDA, 2008). This allows the radioactive body burden and bioassay results to be recorded at defined time intervals. It also gives a description of measurement methods to facilitate analysis of data and adverse events. The form is intended to develop long-term response data for the manufacturer but could be used as the basis of a patient treatment record.

A6 Radiological protection issues

Guidance in the USA is that patients should be informed about the urinary and faecal excretion of caesium to enable them to minimise radiation exposure to others. Precautions include using a toilet instead of a urinal, flushing several times after use, cleaning up spilled urine or faeces completely and washing hands thoroughly. Healthcare professionals should also follow appropriate radiological protection advice to avoid unnecessary exposure to themselves and the spread of contamination.

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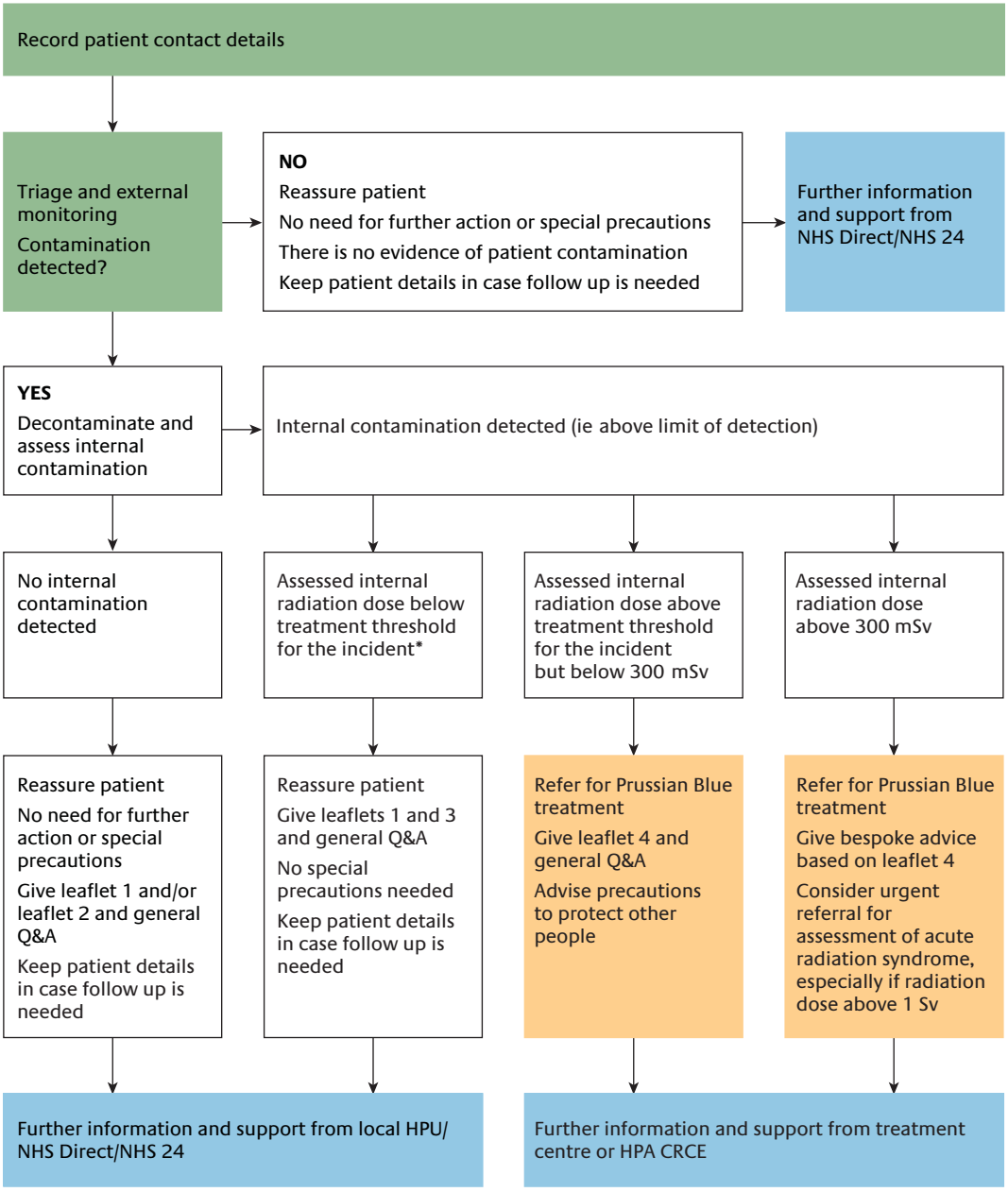
Appendix B
Treatment Algorithm and Draft Patient Information Leaflets

In this appendix draft patient information leaflets are provided. These are for use in situations where screening and monitoring for radiocaesium contamination is being carried out and members of the public are undergoing treatment with Prussian Blue.

It is intended that the monitoring and treatment algorithm and these draft leaflets are customised at the time to reflect the actual incident which has occurred. In an incident, consideration would be needed as to whether there should be specific information for special risk groups such as pregnant women, children or breast-feeding mothers.

B1 Monitoring and treatment algorithm



* The treatment threshold will be decided at the time of the incident and is likely to be in the range 30–300 mSv.

B2 Generic Q&As about Prussian Blue treatment

1 What is Prussian Blue?

Prussian Blue speeds up the removal of caesium and thallium from the body. It is also a pigment, used in industry and by artists.

2 What is caesium?

Caesium is a natural metal element. Caesium-137 is a radioactive form of caesium that is used in industry and also as a source of radiation in radiotherapy, so is the form of most concern. It has a radioactive half-life of 30 years and a half-life in the body of 50–150 days, due mainly to excretion but some is re-absorbed from the gastrointestinal tract. After being ingested or inhaled, caesium spreads throughout the body, leading to a whole-body radiation dose.

3 How could I have become internally contaminated with radioactive caesium?

A wide range of accidental or malicious events could potentially expose you to radioactive caesium. These include nuclear site accidents, unplanned releases from operating or shutdown nuclear reactors or other parts of nuclear licensed sites, lost sources of radioactive caesium, deliberate contamination of food and water, and deliberate dispersion.

4 What are the health risks from internal contamination with radioactive caesium?

Very high doses of radioactive caesium can cause illness within a few days or weeks of contamination (radiation sickness) but below a certain level there are no symptoms. Any radiation dose can lead to an increased risk of cancer in later life that is proportional to the dose of radioactive caesium received, but is often small when compared with the 'natural' lifetime fatal cancer incidence, which is about 25% in Europe.

The estimated increased lifetime fatal cancer risk is 5% per sievert of radiation dose. A millisievert (mSv) is a thousandth of a sievert and thus 10 mSv confers only a 0.05% (1 in 2,000) additional lifetime fatal cancer risk. A 10 mSv radiation dose increases the lifetime fatal cancer risk from 25% to 25.05%.

5 How does Prussian Blue work?

Prussian Blue works by using a mechanism known as ion exchange. Caesium that has been absorbed into the body is removed by the liver and passed into the intestine. From there most is re-absorbed back into the body and not expelled. Prussian Blue works by trapping caesium in the intestine, so that it can be passed out of the body with the faeces/stools. Each day's treatment expels a small proportion of the caesium still in the body.

6 Is Prussian Blue an antidote for other types of radiation or poisoning?

Prussian Blue has no value in the treatment of other radiation hazards. It is used in the treatment of thallium poisoning.

7 How will I know if I need treatment with Prussian Blue?

Specific radiation monitoring using hand-held, portal or whole-body monitors is usually used to assess the amount of caesium-137 in your body. In some cases urine or faeces may also be analysed. The Health Protection Agency has published guidance about who should be offered Prussian Blue treatment based on the levels in their body. However, the final decision is yours, in consultation with the doctor treating you.

8 How soon after exposure to radioactive caesium does somebody have to receive Prussian Blue?

Prussian Blue treatment should be started as soon as possible after exposure, ideally within seven days. However, it can still be effective if started up to a month after exposure.

9 Is the effectiveness of Prussian Blue affected by anything I may eat or drink?

You should eat normally. Food may increase the effectiveness of Prussian Blue by stimulating the production of bile from the liver carrying the caesium with it.

10 Is Prussian Blue safe for everyone?

Everyone can take Prussian Blue capsules. The HPA does not advise that people use non-pharmaceutical preparations or take it without medical supervision. Patients with heart disease or high blood pressure should tell their doctor as should those with any form of bowel disease. There is very little experience in treating pregnant women with Prussian Blue but there is no reason to believe it is unsafe. There is no evidence that Prussian Blue can pass in breast milk but radioactive caesium can, and women internally contaminated with radioactive caesium may be advised not to breast-feed.

11 Are there any side-effects from Prussian Blue?

The main side-effects from Prussian Blue are mild constipation which can be remedied by a change to a higher fibre diet or use of a simple laxative. Prussian Blue will have the effect of turning stools (faeces) blue, because it is not absorbed into the body and 99% is passed out unchanged. In certain patients the level of potassium in the blood may be lowered and your doctor may monitor this throughout your treatment. If you have side-effects from Prussian Blue, please inform your doctor.

12 What is the dose of Prussian Blue?

The dose of Prussian Blue for those above 12 years old is 1 gram (two capsules) three times per day. For children between 1 and 12 years the dose is 500 mg (one capsule, 0.5 g) three times per day. The dose for those under 1 year old is not established and will be as advised by the doctor responsible for the treatment.

13 For how long will I need to take Prussian Blue?

After you are prescribed the drug the level of radioactive caesium in your body will be monitored by 'whole-body monitoring' or analysis of urine or stool samples. You will be given Prussian Blue if a certain level of internal contamination is found. Your response to the therapy will be monitored to help decide how long you will need to take Prussian Blue. A course typically lasts between three and six months. When the levels of radioactive caesium have fallen to sufficiently low levels, treatment will be discontinued.

14 How will the level of radioactive caesium in my body be monitored?

Radioactive caesium in the body is measured by a technique called 'whole body monitoring'. You may be asked to attend at a location where this equipment is available. The test involves sitting/lying while a detector measures radiation coming from the radioactive caesium in your body. It usually lasts about 5–10 minutes. You may be asked to shower before and wear a gown during the procedure but no other preparation is needed. The whole-body monitoring equipment is not as enclosed as other types of medical scanners.

15 What happens if someone takes an overdose of Prussian Blue?

Prussian Blue has been taken in doses up to 20 g per day with no serious side-effects. At higher doses there is an increase in constipation. A massive overdose could cause bowel obstruction or low blood potassium levels. If an overdose is taken the doctor supervising your treatment should be informed.

16 Is different treatment needed if I am pregnant or breast-feeding?

If you are pregnant or breast-feeding it is important to tell the radiation monitoring staff and the doctor who prescribes Prussian Blue. Radiation monitoring itself does not pose any hazard to you or your baby.

Pregnant women can take Prussian Blue to protect both themselves and their babies. Radioactive caesium can cross the placenta and affect an unborn baby. Prussian Blue is not absorbed from the mother's gut and therefore cannot harm an unborn baby. Prussian Blue taken by the mother will also help to decrease radioactive caesium levels in her fetus.

Radioactive caesium can be transmitted from the mother to infant in breast milk. However, the radiation dose and risk of harm to the infant would not be expected to exceed that for the mother. Prussian Blue does not enter the circulation and there is no evidence that it enters breast milk and thus it is safe to take while breast-feeding.

If you have received a low level of internal contamination with radioactive caesium, below the threshold where Prussian Blue treatment is offered, the benefits of breast-feeding are presumed to outweigh the radiation risk and there is no need to stop breast-feeding.

For mothers who have been recommended to have Prussian Blue treatment, the radioactive caesium dose and risks to the infant should be individually assessed to inform advice about whether to stop breast-feeding.

17 Do I have to take any special precautions to protect other people while I am taking Prussian Blue?

While taking Prussian Blue, the amount of radioactive caesium in your body will fall over several weeks as it is excreted in your urine, stools and sweat. Anyone in close contact with you may receive a very small dose of radiation from the radioactivity within your body. The risks to other people are very small but you may be asked to take a few simple measures to ensure that those close to you are protected. These measures are described below.

Toilet

As radiation is excreted in urine and faeces, we do recommend that, while you are taking Prussian Blue, you use a toilet rather than a urinal, flush the toilet twice with plenty of water immediately after using it, wash hands thoroughly and clean up any spills immediately rinsing the cloth well.

Sleeping

If you regularly sleep with a partner you may be advised to sleep in a separate bed until the radiation levels fall. Your medical adviser can guide you if this is recommended.

Foreign travel

If you are planning to travel abroad whilst taking Prussian Blue please consult a medical adviser because many ports check for radiation sources and you could set off an alarm. If you are planning air or foreign travel, consult your medical adviser who can give guidance on whether this is advisable and provide you with a document explaining your condition.

Clothes

It is unlikely that special precautions are needed to deal with radioactivity in sweat on dirty clothes. Unless advised otherwise you should wear and wash clothes as normal.

B3 Draft Leaflets for Patients with Different Levels of Assessed Exposure

LEAFLET 1: External Contamination

For people who have been found to have external contamination with radioactive caesium and been decontaminated. It assumes no significant doses from the external contamination in the period before decontamination. It should be used in conjunction with other leaflets for people with internal contamination.

Incident xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx Date xxxxxxxxxxxxxxxxxxxx

Please quote this number when contacting any healthcare staff dealing with this incident.

1: xxxxxxxxxxxxxxx

Caesium Contamination

The results of the radiation check show that you have been contaminated on your clothes or skin by radioactive dust. You needed decontamination to remove radioactive particles from your clothes and skin.

You have also been monitored to see if you have taken any radioactive particles into your body and will be given separate advice about the results of these tests for internal contamination.

The radiation dose you received while still wearing your clothes before you were decontaminated is too small to have any health consequences.

You should be aware that several areas remain contaminated and these areas are restricted to emergency and remediation staff. You should comply with advice about access to these areas. If you enter a contaminated area you could become contaminated again, ingest or inhale radioactive particles and receive a significant dose of radiation.

Further details about this incident and advice will be broadcast on the local BBC Radio Station (name: frequency).

If you need more health advice regarding this incident or radioactive caesium please ring NHS Direct/NHS 24 on xxxx.xxx.xxxx quoting the above number.

LEAFLET 2: Internal Contamination: No Contamination Detected

For people who have been monitored for internal contamination, but in whom no contamination (or below the limit of detection) has been detected. It may be used in conjunction with the leaflet for people with external contamination.

Incident xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx Date xxxxxxxxxxxxxxxxxxxx

Please quote this number when contacting any healthcare staff dealing with this incident.

2: xxxxxxxxxxxxxx

Caesium Contamination

The results of the internal radiation monitoring show that you have not taken any radioactive particles into your body. There are no special precautions you need to take and the tests indicate that you are at little or no risk of any health effects following this incident.

You should be aware that several areas remain contaminated and these areas are restricted to emergency and remediation staff. You should comply with advice about access to these areas. If you enter a contaminated area you could become contaminated again, ingest or inhale radioactive particles and receive a significant dose of radiation.

Further details about this incident and advice will be broadcast on the local BBC Radio Station (name: frequency).

If you need more health advice regarding this incident or radioactive caesium please ring NHS Direct/NHS 24 on xxxx.xxx.xxxx quoting the above number.

LEAFLET 3: Internal Contamination: Estimated Dose above Limit of Detection but below Prussian Blue Treatment Threshold for the Incident

For people who have been monitored for internal contamination and their dose assessed as being between the limit of detection and the treatment threshold for the incident. It may be used in conjunction with the leaflet for people with external contamination.

Incident xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx Date xxxxxxxxxxxxxxxxxxxx

Please quote this number when contacting any healthcare staff dealing with this incident.

3: xxxxxxxxxxxxxxx

Caesium Contamination

The results of the internal radiation monitoring show that you have taken a small amount of radioactive caesium into your body. This radioactivity will be removed from your body over a period of a few months in your urine, stools and sweat.

The radiation dose you will receive from this internal contamination is too small to have any health consequences and is below the level at which treatment with Prussian Blue is indicated. You do not need to take any special precautions to protect yourself or other people.

You should be aware that several areas remain contaminated and these areas are restricted to emergency and remediation staff. You should comply with advice about access to these areas. If you enter a contaminated area you could become contaminated again, ingest or inhale radioactive particles and receive a significant dose of radiation.

Further details about this incident and advice will be broadcast on the local BBC Radio Station (name: frequency).

If you need more health advice regarding this incident or radioactive caesium please ring NHS Direct/NHS 24 on xxxx.xxx.xxxx quoting the above number.

LEAFLET 4: Internal Contamination: Estimated Dose above the Treatment Threshold for the Incident but below 300 mSv

For people who have been monitored for internal contamination and their dose assessed as being between the treatment threshold for the incident and 300 mSv. It may be used in conjunction with the leaflet for people with external contamination.

Incident xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx Date xxxxxxxxxxxxxxxxxxx

Please quote this number when contacting any healthcare staff dealing with this incident.

4: xxxxxxxxxxxxxxx

Caesium Contamination

The results of the internal radiation monitoring show that you have taken some radioactive caesium into your body. This radioactivity will be removed from your body over a period of a few months in your urine, stools and sweat.

Consider putting patient-specific information about estimated radiation dose here.

The radiation dose you will receive from this internal contamination is too small to make you ill now or in the next few years, but it may raise the risks of cancer in the long term. Because of this you have been recommended to take a three to six month course of Prussian Blue tablets which will increase the rate of removal of the radioactivity. While you are taking Prussian Blue arrangements will be made for you to be monitored to assess its effect and decide when you should stop taking it. There is a question and answer leaflet that explains in more detail the health risks from internal contamination and how Prussian Blue works.

Protecting other people

Despite your internal contamination, you are unlikely to need to take any special precautions to protect other people. But we do recommend that, while you are taking Prussian Blue, you use a toilet rather than a urinal, flush the toilet twice with plenty of water immediately after using it, wash hands thoroughly and clean up any spills immediately. There is low risk for people who have very close physical contact with you (eg a partner with whom you sleep). The exact period for which precautions will need to be taken will be determined later (depending on the monitoring of radiation in your body).

You should be aware that several areas remain contaminated and these areas are restricted to emergency and remediation staff. You should comply with advice about access to these areas. If you enter a contaminated area you could become contaminated again, ingest or inhale radioactive particles and receive a significant dose of radiation.

Further details about this incident and advice will be broadcast on the local BBC Radio Station (name: frequency).

If you need more health advice regarding this incident, radioactive caesium or Prussian Blue please contact the doctor who has prescribed your treatment or the Health Protection Agency on xxxx.xxx.xxxx quoting the above number.

Advice for Patients with Estimated Doses above 300 mSv

Advice should be based on leaflet 4 but it is expected than an individual risk assessment will be needed as well as information on arrangements for health monitoring and more advice for protecting others from direct contact, excreta and sweat, not sleeping with partners, hand washing, etc.

Appendix C
Decay Properties of Radiocaesium

Decay properties (energies, *E*, in keV) (from Delacroix et al, 2002)*

(a) Caesium-134 ($t_{½}$ = 2.07 years)

	Gamma or X		Beta		Electrons	
Main emissions	***E***	**%**	E_{max}	**%**	***E***	**%**
E_1	605	98	89	27	–	–
E_2	769	86	415	3	–	–
E_3	1365	3	658	70	–	–
% omitted		36.8		<1		–

(b) Caesium-137 / barium-137m ($t_{½}$ = 30.2 years)

	Gamma or X		Beta		Electrons	
Main emissions	***E***	**%**	E_{max}	**%**	***E***	**%**
E_1	32	6	512	95	624	8
E_2	36	1	1173	5	656	1
E_3	662	85	–	–	660	<1
% omitted		<1		0		<1

* Delacroix D, Guerre JP, Leblanc P and Hickman C (2002). Radionuclide and Radiation Protection Data Handbook 2002. *Radiat Prot Dosim,* **98**(1), 1–168

Appendix D
Hand-held Equipment Capable of Detecting Radiocaesium

Radionuclide data and guide to suitable detectors (McColl and Kruse, 2002)*

(a) Dose rate measurements

Nuclide	Energy compensated GM	End window GM	Ionisation chamber	Plastic scintillator
Caesium-134	S	U	R	S
Caesium-137 / barium-137m	S	U	R	S

(b) Contamination measurements

Nuclide	End window GM	Full energy beta scintillator	High energy beta scintillator	Xe-filled proportional	Refillable proportional	Alpha scintillator	NaI scintillator
Caesium-134	R	R	–	R	R	–	–
Caesium-137 / barium-137m	R	R	–	R	R	–	–

Key

R = Recommended

S = Recommended when the low energy X-rays or the beta emissions from the source are shielded either by packaging or because the material is in the form of an encapsulated source

U = Usable in the absence of recommended equipment

– = Not suitable

* McColl NP and Kruse P (2002). NAIR Technical Handbook 2002 Edition: Technical Handbook on the National Arrangements for Incidents Involving Radioactivity. Chilton, NRPB-W7. Available at www.hpa.org.uk

Appendix E
Approaches to Deriving a Risk-based Intervention Level for Radiocaesium Ingestion or Inhalation

E1 Introduction

The National Radiological Protection Board (now part of the Centre for Radiation, Chemical and Environmental Hazards (CRCE) of the Health Protection Agency – both organisations are termed 'HPA' throughout this document) has issued advice to the UK government on the principles to be applied in responding to radiological emergencies, and has specified intervention levels (Emergency Reference Levels (ERLs) of dose) for three emergency countermeasures, indicating the way in which these ERLs were determined (NRPB, 1997). The three emergency countermeasures considered were evacuation, sheltering and the administration of stable iodine. The administration of Prussian Blue was not considered.

The principles for protecting the public in the event of a radiological emergency advised by the HPA are as follows:

a countermeasures should be introduced if they are expected to achieve more good than harm – justification,

b the quantitative criteria used for the introduction and withdrawal of countermeasures should be such that protection of the public is optimised – optimisation,

c serious deterministic health effects should be avoided by introducing countermeasures to keep doses to individuals to levels below the thresholds for these effects.

These principles are consistent with more recent recommendations of the International Commission on Radiological Protection (ICRP, 2007). The consequences likely to result from application of each countermeasure were identified as:

a averted individual dose and averted collective dose (for exposures below those that could cause deterministic injuries, these are appropriate surrogates for individual and collective radiation risk),

b public reassurance (provided by knowledge that the countermeasure was implemented),

c public anxiety (caused by knowledge that the countermeasure was considered necessary),

d direct and indirect costs,

e physical risks,

f radiation risks to those implementing the countermeasure.

Qualitative and quantitative methods were used to weigh the beneficial outcomes against the harmful ones. The point of balance was expressed in terms of the averted individual dose to a child. Averted doses where the expected harms and benefits of implementing each countermeasure were judged to just

balance (ie the point at which the implementation became justified) were the values specified for the ERLs. In order to take account of favourable and unfavourable circumstances, pairs of ERLs were specified. The ERLs were intended to provide a common planning baseline for individual emergency plans. The HPA advised that the plans themselves should not specify ERLs as the basis for 'triggering' countermeasures, since averted dose is not a directly measurable quantity, but rather, having identified a robust response, should specify directly observable or measurable triggers for it.

The remainder of this appendix explores and extends the application of this approach to the derivation of guidance levels for the administration of Prussian Blue. In particular, an aspect not considered in the earlier advice is developed, that of consistency of health protection with other, non-radiological, incident responses.

E2 Deriving guidance levels by two approaches

There are two main approaches to developing guidance levels for Prussian Blue. The first approach is similar to that adopted for the ERLs, ie a balancing of the expected resulting benefits and harms. The second approach compares implementation of this treatment with the levels of risk for which intervention would normally be considered in other health protection contexts.

E2.1 Comparison with stable iodine ERLs

Superficially, the administration of Prussian Blue appears to be a similar countermeasure to that of stable iodine prophylaxis. However, there are some important differences between the two.

Firstly, stable iodine is planned primarily to be given in a single administration as a prophylactic measure. Its action is to prevent uptake of radioactive iodine by the thyroid from the bloodstream, and so is only effective when taken shortly before or within hours after an intake. By contrast, to be effective Prussian Blue requires repeat administration, several times a days over a prolonged period (months) as a treatment under direct medical supervision.

Secondly, the administration of over one million dosages of stable iodine, following the accident at the Chernobyl nuclear power reactor in 1986, provides evidence that a single administration of stable iodine in the recommended quantities will not give rise to significant side-effects. Whilst there are no strong data to suggest that Prussian Blue may have deleterious effects if administered to large population groups, there is insufficient evidence to give confidence that Prussian Blue could be administered without medical supervision. Its legal status would also preclude such usage.

Finally, whereas a timely administration of stable iodine has the potential to avert nearly all of the dose from radioiodine, the most effective application of Prussian Blue is only likely to avert around two-thirds of the dose from radiocaesium.

Because of these differences, it is therefore not possible simply to adopt the ERLs for stable iodine prophylaxis for application to Prussian Blue.

E3 ERL approach: balancing the benefits and harms

Table E1 lists the expected benefits and harms resulting from implementing Prussian Blue as a countermeasure.

TABLE E1 Benefits and harms from implementing Prussian Blue as a countermeasure*

Benefits	Harms
Averted dose (risk)	Disruption
Individual	Individual
Collective	Collective
Reassurance provided by countermeasure	Anxiety caused by countermeasure
	Monetary costs
	Direct
	Indirect
	Side-effects (health)

* The derivation of the ERLs for sheltering, evacuation and administration of stable iodine also considered the risk to workers implementing the countermeasure. However, in the case of Prussian Blue administration, this risk is considered to be negligible, as the countermeasure is administered as a treatment, not a prophylaxis, and can be done well away from a contaminated area.

E3.1 Evaluation of expected harms

Treatment using Prussian Blue involves taking tablets several times a day for up to six months, together with regular medical reviews and determination of the effectiveness of the treatment. For the individual this is highly disruptive, with the impact on society also being disruptive, depending on the number of people being treated.

The cost of drugs to treat one individual is around £2000 (assuming six months' treatment). However, since the lead time for producing more stocks of Prussian Blue is of the order of months, in order for an individual to be treated several months' supply of Prussian Blue must be stockpiled. This stockpile must be renewed every two years, regardless of whether the treatment has been required. Therefore there is an ongoing cost associated with planning for this treatment that is directly proportional to the number of people planned for, and which will be incurred whether or not an exposure situation occurs. The annual restock cost of a stockpile for one three-month course, assuming one-third goes out of date each year, is approximately £300 including VAT. There are also indirect costs of treatment, which are linked to the collective disruption mentioned above. In particular, there will be a loss of economic activity whilst individuals are undergoing medical review.

The literature provides indications of the side-effects of Prussian Blue and these health problems are likely to be promptly detected and treated, as the individuals will be under medical surveillance. Whilst the risk

cannot be quantified, it seems reasonable to assume that the greater the number of people who are treated, the more likely it is that serious and possibly unexpected side-effects are reported.

'Countermeasure anxiety' as discussed in the context of the ERLs is defined as the public anxiety created simply from the knowledge that risks are sufficient to require implementation of the countermeasure. This anxiety is considered to be minimal for Prussian Blue treatment, as it will be administered on an individual basis, rather than as a widespread countermeasure. However, the process of selection for treatment might well generate anxiety, as resources for undertaking whole-body monitoring in the UK are limited. In a very large incident, early screening of all potentially contaminated individuals may not be practicable. Therefore a triage system would need to be put in place to prioritise people for screening. Perceived slowness of screening programmes may raise anxiety in those awaiting screening. Anxiety might also arise if serious side-effects from the treatment occur and are publicised. This would make it more likely that some of those being treated would cease to comply, thereby reducing the effectiveness of the treatment.

E3.2 Comparison of 'harms' with those evaluated for other countermeasures

Overall, the likely scale of these harms is at the upper end of those evaluated for other emergency countermeasures, particularly for sheltering and stable iodine prophylaxis. For sheltering, the short-term disruption caused was judged significant, but this would be limited to at most a couple of days. The anxiety raised by implementation of sheltering and stable iodine prophylaxis is likely to be short lived but it is uncertain if it will be higher than that associated with long-term treatment with Prussian Blue and ongoing radiation monitoring. There are also higher monetary costs and disruption associated with Prussian Blue. The comparison with evacuation is less straightforward. For evacuation, the indirect monetary costs and both the individual and collective disruption are relatively high, but they are only likely to continue for days or weeks. Whilst the direct monetary costs are also high, they are only realised in the event of an emergency; the planning costs are relatively small. Overall, the net harm from treating patients with Prussian Blue is judged to be of the same order as that incurred with evacuation, and in both cases, this harm increases approximately directly in proportion to the number of people involved.

E3.3 Evaluation of expected benefits

The administration of Prussian Blue over a prolonged period has the potential to avert up to two-thirds of the committed dose from inhaled or ingested intakes of radiocaesium. It does not provide protection against external exposure to radiocaesium or exposure from other radionuclides. Therefore, at most, the level of protection is similar to that afforded by sheltering for a release containing only radiocaesium. It is not as effective as precautionary evacuation or sheltering in the event of a release containing radionuclides other than radiocaesium. Whilst stable iodine prophylaxis only provides protection against intakes of radioiodine, if administered promptly following intake it has the potential to provide almost 100% protection. In comparison with other countermeasures, therefore, Prussian Blue is generally less effective or, at best, no more effective for protection against airborne releases. Food restrictions can be implemented to prevent or reduce the ingestion of radiocaesium in situations where

contamination in food supplies is known or suspected. In such situations, food restrictions are a more cost-effective approach to reducing exposures. However, for situations where significant amounts of radiocaesium have been inhaled or ingested (eg because there was no prior knowledge that the food or air was contaminated), treatment by Prussian Blue is likely to be the only countermeasure that can be effectively employed.

Overall, for emergency response planning for accidental releases from sites managing a range of radioactive materials, Prussian Blue is unlikely to be considered as a prime countermeasure. If releases are postulated that contain radiocaesium, then sheltering and/or evacuation, coupled with food restrictions are likely to be the preferred planned options, as these provide protection from a range of radionuclides and exposure pathways. Only in the event that it was judged these protective options might not be effective for practical reasons, might consideration be given to planning for treatment with Prussian Blue. Planning for Prussian Blue is therefore more likely to be used in response to an incident involving deliberate contamination of a food, water or air source.

In terms of the reassurance provided by Prussian Blue treatment, it is expected that this would be high for the individuals being treated and their families, unless serious side-effects occur in the patient or others receiving the treatment. However, the reassurance provided by treatment is unlikely to be more widely felt. If the screening results for a wider population demonstrate minimal risk to people, publication of this information could provide reassurance – an indirect benefit from the testing needed to define patients who would benefit from Prussian Blue treatment.

E3.4 Guidance levels for Prussian Blue based on balancing harms and benefits, and consideration of other ERLs

The preceding discussion has shown that the expected net harm from implementing Prussian Blue treatment is generally higher than that from implementing sheltering or stable iodine prophylaxis, and of the same order as that from implementing evacuation. The benefits are generally judged to be lower than those provided by sheltering or evacuation, except in the specific situation of an unexpected intake of radiocaesium.

Any guidance levels set for Prussian Blue should reflect the relative balance of harms and benefits. In emergency planning for sites or shipments containing radioactive materials, this balance would be expected to be similar to that for the existing ERLs for evacuation, ie between 30 and 300 mSv averted effective dose. However, set against this is the difficulty of estimating the likelihood of such an occurrence and the numbers of people who have been contaminated, and weighing this against the costs of stockpiling Prussian Blue. There may also be presentational issues in advising different guidance levels for Prussian Blue administration, depending on whether the release was an accident for which emergency plans had been specifically developed, or whether it was a deliberate contamination event. The alternative of providing only one set of guidance levels at a lower level than those for evacuation, might result in the non-optimal outcome of unbalancing robust emergency plans based on evacuation and sheltering, in favour of focusing on the provision of Prussian Blue treatment that provides no protection against external exposure or radionuclides other than radiocaesium.

E4 Comparison of risks with other health protection contexts

This approach will consider a number of factors that may influence the decision on the selection of guidance levels for Prussian Blue administration.

E4.1 Level of acceptable risk

Involuntary risks should, in principle, be lower than elective risks. In health protection and emergency planning, risks are not usually easy to estimate precisely and therefore tend to be classed into broader categories. Recognising this, Calman (1996) proposed that risks should be expressed by order of magnitude on a logarithmic scale (ie 1/10, 1/100, 1/1000, 1/1,000,000). Descriptors of the order of risk were devised that can be applied consistently.

A summary of well-known events with the order of magnitude of the risk is given in Table E2. It should be noted that many of the risks in the table are risks per year, whilst risks calculated following a single radiation exposure are lifetime risks. It is also clear that significant protective measures are already in place to ensure that some of the risks are as low as they are (eg railway accident deaths).

There are very few data on the level of risk of adverse events or death that would demand an intervention, either a preventive strategy or a direct countermeasure (primary or secondary prevention).

TABLE E2 Categorisation of risk by risk order with examples (after Calman, 1996) (risks quoted are incidence per year where appropriate)

Term used	Risk range	Examples	Risk estimate
High risk	More than 1 in 100	Transmission to a susceptible household of measles or chickenpox	1/1 to 1/2
		Transmission of HIV from mother to child (Europe)	1/6
Moderate risk	1 in 100 to 1 in 1,000	Attributable death from smoking 10 cigarettes per day	1/200
		Death from all natural causes aged 40 years	1/850
Low risk	1 in 1,000 to 1 in 10,000	Death from all kinds of violence	1/3,300
		Death from influenza	1/5,000
		Death from accident on the road	1/8,000
Very low risk	1 in 10,000 to 1 in 100,000	Death from leukaemia	1/12,000
		Death from playing soccer	1/25,000
		Death from accident at work	1/43,000
Minimal risk	1 in 100,000 to 1 in 1,000,000	Death from accident on the railway	1/500,000
Negligible risk	Less than 1 in 1,000,000	Death from lightning strike	1/10,000,000

Empirically it would be suspected that for primary prevention there would be a lower threshold of risk before measures were implemented, as primary prevention measures tend to be more suitable for dealing with large numbers of people and are less disruptive than secondary prevention measures.

A consensus amongst health protection professionals suggested that a risk of between 1/1,000 and 1/10,000 justifies a 'safe' intervention if that intervention eliminates or very substantially reduces the risk of harmful effects from the agent against which it was directed (J Astbury, personal communication).

E4.2 Risks associated with the exposure

Ingested or inhaled caesium spreads uniformly throughout the body and does not accumulate in any organ. Therefore any dose from caesium-137 can be considered a whole-body dose. Caesium-137 emits beta particles to become metastable barium-137 (which has a half-life of only 2.55 minutes) and this becomes stable barium-137 by emitting a 661 keV gamma ray.

The risks from radiation are well quantified compared to other environmental hazards. In Publication 103 the ICRP gives fatal cancer risks of 4–5% per Sv for a population of all ages (depending on whether risk models based on cancer incidence or mortality data are used), and concludes that 'the approximated overall fatal risk coefficient of 5% per Sv on which current international radiation safety standards are based continues to be appropriate for the purposes of radiological protection' (ICRP, 2007).

E4.3 Level of risk reduction by implementing the countermeasure

The level of risk reduction achieved by administration of Prussian Blue can be calculated from its observed effect on the biological half-life of radiocaesium, ie the time taken for the body to eliminate 50% of the initial uptake by excretion. This is discussed in Section 2 of the main text which concludes that delaying commencement of treatment with Prussian Blue for seven days after intake would not significantly decrease its efficacy, but that treatment should commence within about 28 days. From a consideration of dose saving, treatment should continue until at least three months post-exposure. No significant benefit is obtained by extending treatment duration beyond about six months. Reduction in doses to 40–55% of the doses expected in the absence of Prussian Blue treatment would then appear to be achievable. If treatment extends only over one month, only about half of this dose saving is achieved.

This is consistent with other public health interventions that are given on the basis of avoiding undesirable health outcomes based on calculated risk levels; examples include statins for heart disease and anti-hypertensives for high blood pressure where the risk reduction is significant but only around 33–50%. The radiation ERLs are cited in terms of averted dose and not total dose due to the incident. The proportion of the total potential dose that can be averted varies with each countermeasure but would in general be largest for prophylactic measures (eg pre-treatment with stable iodine before exposure to radioiodine).

Emergency planning does not usually take levels of risk reduction into account and there is little information on the topic.

In the following analysis a pragmatic approach has been adopted. It is proposed that for population interventions a minimum protective factor of 1.33 (the dose in untreated patients divided by the dose in treated patients, corresponding to a 25% dose reduction) should be adopted for risks that fall within a 1/1,000 to 1/10,000 long-term risk of death. Less effective treatments may be indicated for immediately life-threatening radiation doses. It is unlikely that the public would accept treatments that were perceived as ineffective because they do not make significant inroads into long-term residual risks.

Applying the 5% per Sv risk coefficient and a dose reduction of 25% of the total projected committed dose, the intervention level in terms of dose saved would be between 2 and 20 mSv, depending on whether an intervention risk level was 1/10,000 or 1/1,000.

E4.4 Risks associated with the countermeasure

The only reported side-effects of Prussian Blue are constipation and hypokalaemia which could result in cardiac arrhythmias (US CDER, 2004; US CDC, 2005; Drugs.com, 2008). In one source the incidence of constipation in patients treated with Prussian Blue was reported as 24% and the incidence of hypokalaemia was 7% (Drugs.com, 2008).

When the risks from not having the intervention are significant and proximate in time people are generally willing to accept relatively high risks from interventions. However, for most scenarios of Prussian Blue use, where deterministic effects are not expected, the risks of the radiation dose are low and will occur in the future. In this case, people will tend to be more averse to the risks associated with interventions. In the case of Prussian Blue, the risk of serious side-effects from the treatment have not been quantified. However, the risks of taking Prussian Blue are considered to be low for previously healthy people. Greater risks may exist for patients with metabolic, cardiac or some gastric conditions or those allergic to food dyes. These patients will require consideration of personal circumstances before treatment with Prussian Blue.

In general, patients are willing to accept lower risks of side-effects from treatments than the risks posed by the conditions for which they are being treated. Therefore it is relevant to consider the ratio of the risk of side-effects from the intervention to the risk reduction achieved by the countermeasure. This has not been studied systematically but empirically a ratio of between 1 : 100 and 1 : 1,000 could be assumed. If, in the absence of data on the incidence of life-threatening side-effects from Prussian Blue, a normative value for this is assumed to be between 1/100,000 and 1/1,000,000, then to achieve the ratio of the numbers of patients who benefit from the treatment and the numbers who are harmed by the treatment of 100 : 1 to 1,000 : 1, the intervention would have to benefit 1/1,000 to 1/10,000 of the people treated.

E4.5 Scale of the incident

The practicalities of selecting people for Prussian Blue treatment in large-scale incidents are discussed in Section 5 of the main text.

Whilst the overall scale of the incident and numbers to be treated should not be the major consideration it is material with respect to resources available. In large-scale events, consideration should be given to

using available stocks for maximum community, rather than personal, benefit. This would give priority to patients with higher radiation doses, especially those at risk of deterministic injury, and is in line with existing radiological protection practice.

E4.6 Compliance with treatment

The dosage regime for Prussian Blue is 1 g three times a day for up to six months. As the potential harm from a stochastic dose of caesium-137 is many years in the future, compliance may be an issue. The situation is analogous to anti-hypertensives where the patient is asymptomatic and is taking the medication to prevent future harm.

Although there is an extensive literature on the factors that affect compliance with medical treatment, this is rarely the primary objective of the studies and methodological designs are not ideally adapted to look at this aspect. In the case of anti-hypertensives, about 50% of patients will stop taking the medication within the first year, with a median time to cessation of 90 days (Klein, 1988; Benson et al, 2000; Bloom, 1998; Gold and Silverman, 2005). Compliance is better in older patients and women (Gislason et al, 2006). There is a weak relationship mentioned in several papers with respect to social class, with those of higher socioeconomic status being more compliant.

The number of doses per day has a significant effect on compliance. A study carried out in 1988 looking at compliance with non-steroidal anti-inflammatory drugs found an inverse relationship between compliance and the number of doses per day. Compliance varied from 72% for once daily to 60% for administration four times per day (Bloom, 1988).

One of the most important factors identified in most studies was the presence of side-effects, which is the most commonly cited reason for non-compliance. There is some evidence in that newer drugs with lesser side-effects have better compliance.

Several of the studies mention the importance of the prescriber explaining clearly the risks and benefits of taking the therapy – the patient has to be convinced that the benefits outweigh the inconvenience.

In practical terms many factors affecting compliance are not amenable to change. There is no evidence on the use of Prussian Blue administered once daily, but its method of action suggests that it needs to be constantly present in the intestines so divided doses are important. Given the experience with anti-hypertensives, full patient compliance is unlikely. Strategies need developing to maximise compliance, especially for those least likely to comply – young males of lower socioeconomic status.

Using the evidence available, for a six-month course of treatment a default rate of about 50% by the end would be expected, with a corresponding decrease in treatment effectiveness.

E4.7 Health economic appraisal

There are several ways of approaching the area of economic appraisal, ranging from considering Prussian Blue as a medical treatment to using methodologies devised for health and safety interventions. There are likely to be substantial differences in the results from different approaches. Health and Safety Executive

guidance is recommended for use in Control of Major Accident Hazards (COMAH) plans, so this may be more appropriate to be used in emergency situations (HSE, 2008).

Results of economic analyses, especially with benefits realised well into the future, are heavily reliant upon the discount rate. Traditionally health interventions have been discounted at a rate of 5% per year. The Department of Health advised that for health benefits, the discounting should be zero (Parsonage and Neuburger, 1992; Drummond et al, 2005). The HSE (2008) recommends a discount rate on benefits of 1.5% maximum and 3.5% on costs.

For this analysis drug costs are viewed as at the point of administration rather than the time of purchase.

Benefits are realised after the time that a fatal cancer might have been expected to arise. Long-term follow-up studies of radiation-exposed groups such as the Japanese atomic-bomb survivors indicate that the raised risk of cancers other than leukaemia persists for many decades after exposure, whereas much of the increased leukaemia risk is expressed in the first 25 years after exposure (Preston et al, 2003). Calculation of the mean latency period depends on various factors, such as the age profile of the population and the length of time for which they are followed. Consequently, in a health economic appraisal, both the discounting rate and the latent period should be subject to a sensitivity analysis.

Cost benefit

It has not been in the scope of this work to produce a full economic analysis of the costs and benefits of Prussian Blue treatment for decorporation of radiocaesium. However, the following analysis does evaluate some of the basic costs and benefits that would need to be weighed up if such an evaluation were to take place.

Costs The costs could be substantial if 1000 patients were treated to avoid one death. The drug costs of treating one patient for five days in the UK with Prussian Blue currently are £51.38 (excluding VAT as at December 2008). This means a drug cost of about £2000 per patient, including VAT for a six-month treatment course (£2,000,000 per 1,000 patients treated to avoid one death).

Benefits The approach used by the HSE (2008) to look at the cost-effectiveness of accident prevention involves putting a value on human life of £1,336,800. This cost is multiplied by two to £2,673,600 in the case of a fatal cancer, the predominate health effect due to radiation exposure. Associated with the loss of life from cancer there is also an incidence of 0.2 non-fatal cancers associated with the exposure (IAEA, 2004) and the HSE estimate of costs for this should be included in the analysis. The HSE estimates the cost of permanently incapacitating illness to be £193,100, which is probably the most appropriate category for a non-fatal cancer. The total benefit for each life saved is therefore £2,712,220 (£2,673,600 + 0.2 x £193,100) before discounting and adjusting to present-day prices. This equates to £2,061,652 (£1,915,834.4 before Retail Price Index adjustment) using a discounting rate of 1.5%, discounting period of 23 years and upgrading by the Retail Price Index.

The costs and benefits in monetary terms are presented in Table E3 and benefits and costs are nearly equal when the risk intervention level is set at 1 in 1,000, which corresponds to an intervention level of about 25 mSv.

TABLE E3 Cost and benefits by various levels of risk and corresponding intervention levels

Risk intervention level	Drug costs and benefits to save 1 life and prevent 0.2 non-fatal cancers (present-day values) (£)	Benefits – life saved and non-fatal cancer prevented (discounted to present-day values) (£)	Intervention level (mSv) assuming 67% dose averted by countermeasure
1/100	198,744	2,061,652	250
1/1,000	***1,987,440***	***2,061,652***	***25***
1/5,000	9,937,200	2,061,652	5
1/10,000	19,874,400	2,061,652	2.5
1/1,000,000	198,744,000	2,061,652	0.25

The HSE methodology includes all costs to society not just health costs, whereas the National Institute for Health and Clinical Excellence (NICE) evaluates medical treatments in the UK on the basis of Quality Adjusted Life Years (QALYs) saved. NICE sets a limit for £30,000 per QALY (NICE, 2004). It is difficult to estimate the number of additional years of life by preventing a fatal cancer across the whole population, but 20 years plus an additional 2 years for the proportion of a non-fatal cancer is a reasonable estimate, which would put a value on a life saved and associated health benefits at £660,000 undiscounted (£466,205 discounted).

E5 Discussion

Taking all the approaches together, it is recommended that a lower guidance level of 30 mSv projected dose from internal exposure to radiocaesium be adopted to trigger investigation of whether or not to treat individuals with Prussian Blue. At this level of projected dose, the radiation health benefit to the patient would generally be small, but for some patients, the discomfort and disruption of the treatment might be far outweighed by the reassurance provided, and so it should be considered. At a projected dose of 300 mSv the overall benefit to the patient would be expected to be significant: only for patients in exceptional circumstances (eg advanced age) would it be reasonable to withhold treatment for projected doses at this level.

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Glossary

Absolute risk	The proportion of a population expected to get a disease over a specified time period. See also risk, relative risk.
Absorbed dose	The quantity of energy imparted by ionising radiation to unit mass of matter such as tissue. Absorbed dose is measured in gray, symbol Gy. 1 Gy = 1 joule per kilogram. It does not take into account the radiobiological effectiveness of the radiation under consideration (see also effective dose).
Activity (radioactivity)	The rate of decay of radioactive material expressed as the number of atoms breaking down per second, measured in becquerel (Bq).
Acute exposure	An exposure to radiation that occurred in a matter of minutes rather than continuing exposure over a longer period of time. See also chronic exposure.
Acute radiation syndrome (ARS)	A serious illness caused by receiving a dose greater than 1 Gy of penetrating radiation to the body in a short time (usually minutes). The earliest symptoms are nausea, fatigue, vomiting and diarrhoea.
Antidotum Thallii-Heyl®	See Prussian Blue.
Background radiation	Ionising radiation from natural sources, such as terrestrial radiation due to radionuclides in the soil or cosmic radiation originating in outer space.
Becquerel (Bq)	See activity.
Bioassay	An assessment of radioactive materials that may be present inside a person's body through analysis of the person's blood, urine, faeces or sweat.
Biological half-life	The time required for one-half of the amount of a substance, such as a radionuclide, to be expelled from the body by natural metabolic processes, not counting radioactive decay, once it has been taken in.
Caesium	A metallic element that has a number of radioactive isotopes. Some isotopes are used in medicine as radiotherapy sources. Radioactive isotopes of caesium (radiocaesium) are also found in nuclear reactors.
Chronic exposure	Exposure to a substance over a long period of time, possibly resulting in adverse health effects. See also acute exposure.

COMAH	Control of Major Accident Hazards Regulations 1999. They implement European Directive 96/82/EC known as the Seveso II Directive, as amended by Directive 2003/105/EC. COMAH applies mainly to the chemical industry, but also to some storage activities, explosives and nuclear sites, and other industries where threshold quantities of dangerous substances identified in the regulations are kept or used.
Committed dose	A dose that accounts for continuing exposures expected to be received over a long period of time (such as 30, 50 or 70 years) from radioactive materials that were deposited inside the body.
Contamination (radioactive)	The deposition of unwanted radioactive material on the surfaces of structures, areas, objects or people.
Cumulative dose	The total dose resulting from continuous exposures of all or part of the body to ionising radiation.
Decontamination	The removal or reduction by cleaning of radioactive contamination from structures, areas, objects or people.
Decorporation	Decorporation is the removal of toxic material from the body. In the case of Prussian Blue treatment it means using an inert substance (Prussian Blue) that binds the toxic material (in this case radiocaesium) and allows it to be excreted from the body faster than by normal metabolism.
Deterministic effect	Health effects that can be related directly to the radiation dose received. The effect is more severe with a higher dose. It typically has a threshold, below which the effect will not occur. These are also called tissue reactions. For example, the acute radiation syndrome is caused by a deterministic effect. See also stochastic effect, tissue reaction.
Discount rate	Costs and perhaps benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present.
Dose coefficient	The factor used to convert radionuclide intake to dose. Usually expressed as dose per unit intake (eg sievert per becquerel).
Dosimetry	Assessment (by measurement or calculation) of radiation dose.
Effective dose	Different ionising radiations have individual characteristics in terms of energy transfer and biological effectiveness. The effective dose is the quantity obtained by multiplying the equivalent dose to various tissues and organs by a weighting factor appropriate to each and summing the products. Effective dose is measured in sieverts, symbol Sv, frequently abbreviated to dose. Effective doses are often expressed as thousandths of a sievert, or millisievert (mSv).

ED_{50}, effective dose 50%	The dose of toxin (in this case radiocaesium) required for 50% of the sample to develop the symptoms under consideration. It is therefore the median dose at which symptoms occur. The ED_{50} can also be applied to therapeutics in which case it means the dose of a drug that is pharmacologically effective for 50% of the population exposed to the drug or a 50% response in a biological system that is exposed to the drug.
Emergency Reference Levels (ERLs) of dose	Quantitative criteria for the introduction of countermeasures to protect the public. The HPA has a formal duty to recommend such measures that are couched in terms of the dose to an individual that could be averted if the countermeasure is taken. The ERLs are specific to each countermeasure because the harm associated with each countermeasure is different.
Exposure pathway	A route by which a radionuclide or other toxic material can enter the body. The main exposure routes are inhalation, ingestion, absorption through the skin, and entry through a cut or wound in the skin.
External exposure	Exposure to radiation outside the body. See also internal exposure.
Gray (Gy)	See absorbed dose.
Half-life	The time taken for the activity of a radionuclide to lose half its value by decay. Symbol $t\,½$.
Hot Zone	Area nearest to an incident where access is normally restricted to the emergency services.
Internal exposure	Exposure to radioactive material taken into the body, commonly by ingestion, inhalation or through a wound. See also internal exposure.
Ionising radiation	Radiation that produces ionisation in matter. Examples are alpha particles, gamma rays, X-rays and neutrons. When these radiations pass through the tissues of the body, they have sufficient energy to damage DNA.
Isotope	A nuclide of an element having the same number of protons but a different number of neutrons.
LD_{50}, lethal dose 50%	In toxicology, the median lethal dose, LD_{50} (abbreviation for 'Lethal Dose, 50%'), of a toxic substance or radiation is the dose required to kill half the members of a tested population. LD_{50} figures are frequently used as a general indicator of a substance's acute toxicity.
Nuclide	A species of atom characterised by the number of protons and neutrons and, in some cases, by the energy state of the nucleus.
Portal monitor	A portal monitor is a gamma-ray detector system designed to make rapid measurements of external or internal contamination on or in people. Measurements are not radionuclide-specific, and have limited accuracy. Detectors are positioned in a 'gateway' arrangement so that walk-through measurements can be made.

Prophylactic treatment	Treatment aimed at preventing a disease or illness. This would include administration of Prussian Blue to emergency services staff and other responders before they entered highly contaminated areas after a dispersal of radiocaesium in the environment.
Prussian Blue	A blue dye, ferric hexacyanoferrate, which is used in the printing industry (the blue in 'blueprints'). It is used in medicine as a decorporation agent because, when ingested, it is not absorbed into the body but binds strongly to elements such as caesium, thallium and potassium. The pharmaceutical formulations are Antidotum Thallii-Heyl® (UK) and Radiogardase® (USA).
Quality adjusted life-year (QALY)	An index of survival that is adjusted to account for the patient's quality of life during this time. QALYs have the advantage of incorporating changes in both quantity (longevity/mortality) and quality (morbidity, psychological, functional, social and other factors) of life. Used to measure benefits in cost–utility analysis.
The Radiation (Emergency Preparedness and Public Information) Regulations (REPPIR) 2001	REPPIR 2001 implement in Great Britain the articles on intervention in cases of radiation (radiological) emergency in Council Directive 96/29/Euratom, also known as the Basic Safety Standards Directive and Council Directive 89/618/Euratom (known as the Public Information Directive). They subsume the Public Information for Radiation Emergencies Regulations 1992 (PIRER). REPPIR 2001 establish a framework of emergency preparedness measures to ensure that members of the public are properly informed and prepared, in advance, about what to do in the unlikely event of a radiation emergency occurring and provided with information if a radiation emergency actually occurs. REPPIR 2001 place legal duties on operators of premises where work with ionising radiation is carried out, eg licensed nuclear sites, hospitals, universities, ports, airports, transport carriers, local authorities and employers of people who intervene in a radiation emergency, such as the emergency services.
Radiation sickness	See acute radiation syndrome (ARS).
Radioactive contamination	See contamination.
Radioactive half-life	See half-life.
Radioactivity	The property of radionuclides of spontaneously emitting ionising radiation.
Radiocaesium	See caesium.
Radiogardase®	See Prussian Blue.
Radioisotope (radioactive isotope)	Isotopes of an element that have an unstable nucleus which undergoes spontaneous radioactive decay.
Radionuclide	An unstable and therefore radioactive form of a nuclide.
Relative risk	The ratio between the risk of disease in an irradiated population to the risk in an unexposed population. A relative risk of 1.1 indicates a 10% increase in cancer from radiation, compared with the 'normal' incidence. See also risk, absolute risk.

Risk	The probability of injury, harm or damage. Risk is often expressed as a percentage that ranges from 0% (no injury or harm will occur) to 100% (harm or injury will definitely occur). Because many risk factors are not exactly measurable, risk estimates are uncertain. See also absolute risk, relative risk.
Sievert	See effective dose.
Stochastic effect	An effect that occurs on a random basis independent of the size of dose. The effect typically has no threshold and is based on probabilities, with the chances of seeing the effect increasing with dose. If it occurs, the severity of a stochastic effect is independent of the dose received. Cancer is a stochastic effect. See also deterministic effect, tissue reaction.
Threshold dose	The intake giving a threshold dose is based on the dose that will give rise to an effect in 1% of the exposed population.
Tissue reaction	This term is used in recent ICRP documents to describe the deterministic health effects of radiation. See deterministic effect; see also stochastic effect.
Transportable body monitor	A transportable body monitor is a gamma-ray detector system for making radionuclide-specific measurements of contamination in people with a reasonable level of accuracy. It has to be transported to the desired location in a vehicle or trailer, and usually requires a small team to operate it. A portable system is one that is light enough to be carried by hand, and usually requires only one person to operate it.
Triage	Triage consists of the use of simple procedures for rapidly sorting affected people into groups so as to expedite treatment and maximise the effective use of medical and monitoring resources.
Whole-body count	The measure and analysis of the radiation being emitted from a person's entire body, detected by a counter external to the body.

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