Doses in Radiation Accidents Investigated by Chromosomal Aberration Analysis XXIV: Review of Cases Investigated, 2003–2005

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ABSTRACT

During the three years 2003-2005, 23 persons suspected of being overexposed to ionising radiation were referred to the Health Protection Agency (formerly NRPB) for investigation by cytogenetic analysis. Of these, 18 were related to industrial uses of radiation, 1 was from a major nuclear organization and 4 were associated with radiation used in institutions of research, education or health. No evidence of radiation exposure, as indicated by dicentric or translocation aberrations in chromosomes from blood lymphocytes, was found in 15 persons. The most serious cases investigated involved a defective industrial x-radiography set and a poorly designed cell housing an electron beam accelerator. In all, six persons suffered localized erythema. Fortunately, the incident radiations were poorly penetrating so that their averaged whole body doses were low.

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1 INTRODUCTION

This report is the twenty-fourth in a series that summarises dosimetry investigations using chromosomal aberration analysis undertaken by the Health Protection Agency (formerly the National Radiological Protection Board). It covers the three years 2003-2005 and during this time 23 persons were referred for analysis. It brings the total number of persons examined since the laboratory was established in 1968 to 1019.

In common with previous reports in the series each of the cases is briefly described in an appendix comparing where possible biological and physical estimates of dose. The biological estimates are expressed in gray (Gy) and are equivalent whole body doses. They are derived mostly from the frequencies of dicentric aberrations in chromosomes from blood lymphocytes. The frequencies are referred to appropriate in vitro dose response calibration curves.

During the past three years the dicentric assay has become more formalised in that the International Organization for Standardization has issued a protocol (ISO, 2004) to which laboratories carrying out the assay should adhere. HPA cytogenetics staff contributed to the drafting of the Standard which, within UK, has been endorsed by the British Standards Institution. The dicentric assay as carried out in the HPA conforms to the Standard.

Occasionally, translocation frequencies obtained by the fluorescence in situ hybridization (FISH) method are used alongside or in preference to dicentrics. Translocations are used mostly when exposure was a long time prior to analysis and the dicentric yields would have declined.

Physical estimates are expressed in sieverts (Sv) and are obtained from personal dosemeters. Occasionally these are the traditional film badges but more frequently thermoluminescence (TL), optically stimulated luminescence (OSL) or electronic personal (EP) dosemeters are worn.

2 SUMMARY OF CASES INVESTIGATED

In common with previous reports in the series, brief details of each investigation are given in an appendix and the numbering system has continued on from the 2000-2002 report (Lloyd *et al*, 2003).

Table 1 shows a division into four categories of reasons for undertaking the investigations. Category A, comprising 16 persons during this reporting period, are situations where the first indication of a possible problem comes from an unexpectedly high reading on a personal physical dosemeter.

TABLE 1 Distribution of investigations between the four categories.

Category	Description	Previous reports	Present report	Totals
A	Possible non-uniform exposure in which the relationship between dose to the physical dosemeter and to the body is uncertain	611	16	627
B	Suspected overexposure of persons not wearing a dosemeter	240	7	247
C	Overexposure where satisfactory estimates of the whole-body dose can be made from physical measurements	7	0	7
D	Chronic internal or external exposure	138	0	138
Total		996	23	1019

Investigators then have to determine whether this truly reflects a dose received by the wearer. Seven persons were placed in Category B where an overdose is suspected but no dosemeter was worn. This could arise because a radiation worker omitted wearing his/her badge or because a non-radiation worker or a member of the public became involved in an incident. There were no cases during this 3-year period assigned to Categories C and D which would comprise respectively, serious overexposures that were so well defined that a detailed reconstruction of events was possible and protracted exposures such as from the intake of radionuclides.

Table 2 shows that most cases arose from industrial uses of radiation, especially gamma-radiography sources used for non-destructive testing of metal objects, and that for most persons the analysis led to the conclusion of a low or zero dose. In reality, the dicentric assay is unable to determine a truly zero dose. This is due to a combination of the background 'noise' in the assay, which in control surveys is ~1 dicentric per 1000 cells, but of course for any individual has to be an assumption, and the statistical uncertainty associated with the scoring of a manageable number of

TABLE 2 Origins of the cases and the number of 'zero' dose estimates.

	Number of cases		Number of 'zero' dose estimates*
Case origin	2003-2005	All years	
Industrial radiography	18	659 (65%)	417
Major nuclear organisations	1	153 (15%)	91
Research, education and health institutions	4	207 (20%)	135
Total	23	1019	643 (63%)

* <100 mGy

cells. The procedure adopted in HPA is to score 500 metaphases and if no dicentric is observed to report the most likely dose as being zero but with an upper 95% confidence limit which for cobalt-60 would be 200 mGy and for 250 kVp x-rays 130 mGy. One dicentric in 500 cells, if no background is assumed, is equivalent to about 100 mGy of gamma radiation and, therefore, an observation of zero may better be reported as less than 100 mGy. If one or more dicentrics are seen in 500 cells the scoring is often extended to 1000 cells or occasionally more.

A long recognised value of biological dosimetry is the reassurance that it can provide to patients and their families when very few or no aberrations are found in the lymphocytes. Persons involved in radiation incidents, especially if there is no reliable physical dosimetry (eg Category B in table 1), often fear the worst. It is, therefore, important to be able to explain coherently the idea of uncertainty due to sampling statistics. Experience over many years has shown that recipients of biological dosimetry reports often have difficulty in comprehending the concept of confidence limits. This is especially so if the possible dose, as perhaps recorded on a monitoring badge, is close to the detection limit of the dicentric assay. This led to the development of the odds ratio which has proved very useful in presenting the results by using the more familiar language of horse race betting! Thus for example in case A505 a TLD recorded 66 mSv from low energy γ-rays, ~100 keV, and one dicentric was seen in 1000 cells. This is consistent with background but, nevertheless, carries an upper 95% confidence limit of 100 mGy. By taking just two possibilities; that either the dose was zero or that it was the recorded 66 mSv, the cytogenetics favoured zero with odds of almost 5:1. This was calculated as follows: the appropriate dicentric dose-response curve is $Y = 0.001 + 0.04D + 0.06D^2$, where Y denotes dicentrics per cell and D is dose in Gy. For doses of zero and 0.066 Gy, the dicentric yields per cell are 0.001 and 0.0039, respectively. As 1000 cells were scored, the expected numbers of dicentrics are 1 and 3.9. One dicentric was actually observed. The Poisson probability of observing 1 when 1 is expected is $1.0 exp(-1.0)/1! = 0.368$. The corresponding value for observing 1 when 3.9 is expected $3.9 exp(-3.9)/1! = 0.079$. Therefore, the odds ratio is $0.368/0.079 = 4.7$.

In case B135 a new approach was developed. Here there was no doubt that a man had been exposed in a brief incident with an iridium-192 source and that his exposure was more or less to the whole body. The best calculated estimate was 0.4 mGy and two dicentrics observed in 1000 cells seemed consistent with a small dose, albeit with wide confidence limits (95% UCL 200 mGy). In an effort to make this clearer the result was expressed graphically as a normalised probability distribution in dose (Figure 1, red curve). The method for deriving this distribution is to set up the probability distribution in yield which could have produced the observation 2 in 1000 cells, which is numerically the same as the likelihood function. Then for each value of yield a value of dose can be assigned leading to a distribution in dose. Arbitrarily, all situations where the yield is less than the control level have been assigned a dose of zero and thus the portion of the full bell-shaped curve that represents doses below zero has not been drawn.

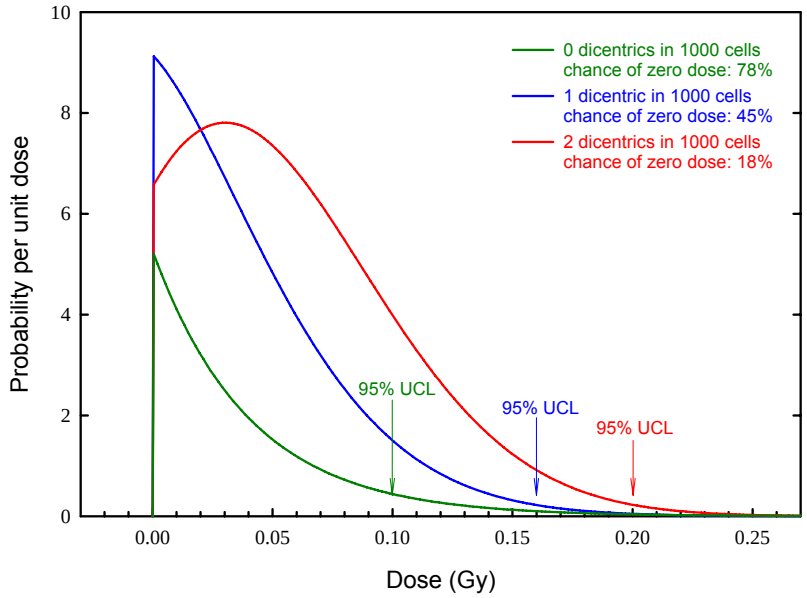

FIGURE 1 A probability distribution in dose derived from the observed number of dicentrics in 1000 cells, calculated for high energy γ-rays (e.g. cobalt-60).

The use of the curve is best illustrated by example. For the distribution in red, 2 dicentrics per 1000 cells, the area beneath the curve to the right of zero dose is 82% of the total area when one includes the zero dose component of 18%. Thus, there is only an 18 % chance that the dose was zero and an 82% chance the dose was above zero. The area to the right of 0.1 Gy is approximately 15% and thus there is a 67% (82 –15) chance that the dose lies between zero and 0.1 Gy. Two other curves are shown representing the distributions for observations of 0 and 1 dicentric in 1000 cells.

In summary, uncertainties in a biological dose estimate can be expressed in one of three ways, the choice of which depends on the circumstances of the case and how best to present the concept of uncertainty to the persons involved. These different approaches should not be confused. The first method is to use confidence limits, often at the 95% level. Confidence limits, based on the Poisson distribution, are calculated around the observed yield and are converted to dose using the calibration curve. The statistical inference is that the true dose will lie between these limits on at least 95% of occasions. In essence, it is a statement about reproducibility. The second approach can be applied when there is a choice between two estimates of dose resulting from two different scenarios. Probabilities of making the observation, assuming the two estimates of dose, are calculated and their ratio gives the odds in favour of one postulate or the other. The third new approach calculates a probability distribution in dose from the observation based on Bayesian methods. The prior distribution, in the absence of any information, is assumed to be uniform in yield. The posterior distribution in yield is then converted to a probability distribution in dose. This then allows one to calculate the probability that the dose lies within any given dose interval.

While each case is unique, a number of common threads have been noted over the 38 years that the laboratory has operated the biological dosimetry service. Several were again evident among the cases reported here. Often the first intimation of something amiss is when a radiation worker's routine dosemeter badge is returned for processing and it is found to have recorded an exposure. Sometimes the worker has a plausible explanation for how the badge might have been irradiated while not worn and a zero dose finding from cytogenetics lends support to the conclusion that no real exposure had occurred. Case A496 is such an example where the proffered explanation was that it was excessively exposed in an airport luggage security check. More frequently, however, no immediate explanation is available but if the recorded dose is high, sufficient to cause sickness, yet the wearer is obviously in good health, it is clear that the badge is not indicating a true dose. This alone is not sufficient to totally reject a real exposure because accidental irradiation is invariably inhomogeneous. Thus, there remains a chance that a real exposure to the wearer did still occur but that the badge exaggerated the whole body dose perhaps because it was in a primary beam while much of the body received only scattered radiation. Another situation that has to be explored is high but repeated or protracted irradiation so that the dose rate effect protects from the development of overt clinical responses. These possibilities become less likely if cytogenetics can find no supporting evidence for exposure. Cases A498 and A501 are examples of such situations where no explanations were ever found, the personal dosemeters had recorded > 1 Sv, the radiographers were adamant that they could not have been irradiated and the chromosome analyses also pointed to zero dose.

If, as more often occurs, the recorded dose is below the threshold for acute clinical effects the situation is less clear-cut. Cases A497, A504 and A505 were instances where no explanations were forthcoming from the badge wearers or colleagues and investgators could find no faults in equipment or procedures. The absence of chromosome damage helped to strengthen the workers' presumption that the badge had been lost or accidentally left in a radiation area. Case A505 was less certain because the recorded dose was low within the upper confidence limit even when no chromosomal damage was found. Here the odds ratio approach, as described earlier, was helpful. Unresolved cases may lead, by default, to a suspicion of deliberate exposure of a person's badge and in case A503 there were other indications that this is what happened to a nurse's badges on two separate occasions.

In some instances (cases A499, A502, A506 and A507) it was clear that badge doses were reflecting real exposures to the wearers. Indeed in A502 and A507, which involved 2 and 4 people, respectively, their exposures were sufficient to cause erythema. However both events involved inhomogeneous exposures and to radiations that had depth/dose profiles such that most of their exposure was limited to superficial tissues. By contrast, cytogenetic dosimetry based on blood lymphocytes provides a value of averaged whole body dose. Where inhomogeneity does occur it is sometimes possible to detect it if the distribution of aberrations among the cells is overdispersed with respect to the Poisson distribution that characterises a uniform exposure.

Case A507 is a good example of the difficulties in evaluating inhomogeneous exposures. It involved a radiography team of 4 men using a faulty portable x-ray apparatus to examine the integrity of aircraft components. There were two separate events, two months apart and at each event three of the team members worked. Each man wore a TLD and two self-reading quartz fibre electrometer (QFE) dosemeters attached to the upper chest. In the first incident, the TLDs recorded exposures but this information only became known belatedly after they were returned for processing. Their QFEs had registered no doses. Thus, it was only on the second occasion, when new TLDs had been just been issued and both they and the QFEs recorded overdoses, that the alarm was raised. Extensive reconstructions of the radiography procedures, coupled with depth/dose calculations suggested that their averaged whole body doses were low; ~ 100 mGy. However, each man had received brief and very high skin surface doses from collimated x-rays of up to 160 kV to limited areas of the body resulting in erythema. The chromosomal analyses were consistent with the calculated averaged whole body doses but in one man one heavily damaged cell was found. It is not possible to use this single cell in any quantitative way but qualitatively it does accord with a localised high dose.

Situations arise where genuine exposures are known to have been received by persons who were not issued with a personal dosemeter (Category B in table 1). Cases B131, B134 and B135 are examples where the doses were calculated to be low, this was confirmed by cytogenetics, the irradiated persons suffered no ill effects and could be reassured. When known exposures, albeit low, coincide by chance with illness then people may link their symptoms with radiation. If medical advice is that radiation was not the cause, but the doctors can offer no definitive alternative diagnosis then anxiety persists. Cases B130, B132 and B133 were such situations and because there was delay between exposure and chromosomal analysis the FISH translocations assay was employed. This overcomes the persistence problems associated with the dicentric assay but with the disadvantage that the higher and more variable control frequency of stable translocations reduces the assay's ability to discriminate low doses. In these three cases, however, this was not a problem because the reported symptoms, if really due to radiation, would have required doses of many grays. In none of the cases were high doses confirmed but this did not shift deeply held beliefs that radiation was to blame.

During the past 3 years a major EU supported initiative, co-ordinated by NRPB (HPA), to optimise the FISH method of retrospective biodosimetry was completed (Edwards *et al*, 2005; Whitehouse *et al*, 2005). One very important outcome was a firmer understanding of the background frequency of translocations and its dependence on age. Having controlled for age, other possible confounders, e.g. smoking appear, perhaps surprisingly, to be so small that they can be ignored. Figure 2 shows the very marked age effect and is the best data set currently available for assuming an individual's background frequency for retrospective dosimetry. These data are expressed as translocations per genome equivalent cell i.e., as if all the chromosomes had been FISH painted. In practice a restricted number of chromosomes are painted; at HPA normally 3 pairs nos, 2, 3 and 5. Generally, 3000 cells are scored which converts to around 1000 genome equivalents.

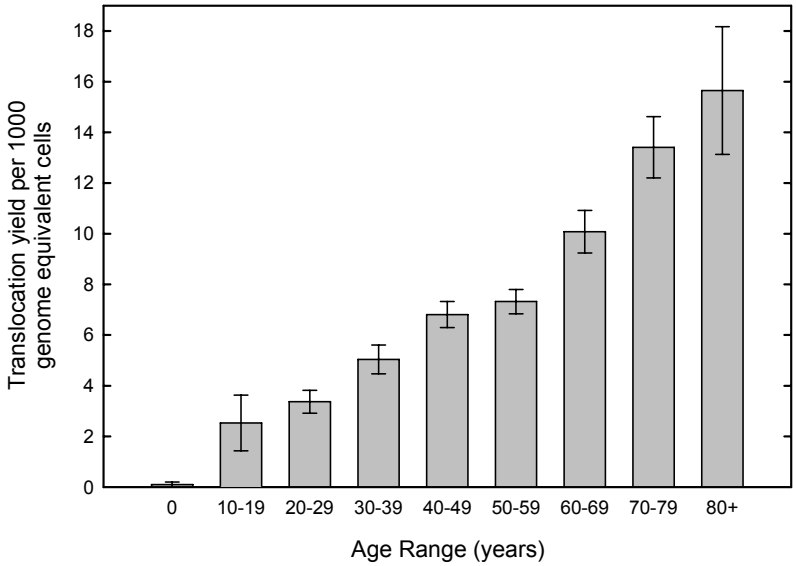

FIGURE 2 Dependence of the background level of FISH translocations on age (meta-analysis data from Whitehouse *et al*, 2005).

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APPENDIX SUMMARY OF INDIVIDUAL CASES INVESTIGATED IN 2003 – 2005

A. Possible non-uniform exposure in which the relationship between dose to a personal dosemeter and to the body is uncertain

A496

Cells scored	500
Dicentrics	1
Centric rings	0
Other aberrations	1
Biological dose (Gy)	0.1
TLD body (Sv)	0.39
TLD skin (Sv)	0.85

The only workplace source of ionising radiation was an electron beam welding facility. As this is carried out in a vacuum, it was not possible for any part of the operator's body to enter the radiation field. If the badge had been placed in the beam it would have been destroyed. The most likely explanation was that the badge had been inside a bag that became stuck inside an airport luggage screening x-ray cabinet.

A497

Cells scored	500
Dicentrics	0
Centric rings	0
Other aberrations	1
Biological dose (Gy)	0
TLD body (Sv)	0.34

A hospital technician who operated linear accelerators returned an inexplicably overexposed monthly TLD. Investigators could find no cause for the badge reading. The chromosome analysis showed that he had not received such a dose.

A498

Cells scored	500
Dicentrics	0
Centric rings	0
Biological dose (Gy)	0
TLD body (Sv)	6.0

An engineer employed in maintaining medical imaging systems recorded a very large dose on his TLD with no plausible explanation. He was, nevertheless, in good health and after the chromosomal analysis it was concluded that the badge had been irradiated while not worn.

A499

Cells scored	500
Dicentrics	0
Centric rings	0
Other aberrations	0
Biological dose (Gy)	0
Film badge dose (Sv)	0.013

A man picked up an industrial gamma source that was emitting a beam of radiation because it was contained in a collimator. The main concern was for the dose to his hand, although, he experienced no skin reactions. His chest worn badge recorded a small exposure but because of the uncertain geometry of the incident it was not clear whether this reflected his real whole body dose.

A500	
Cells scored	500
Dicentrics	1
Centric rings	0
Other aberrations	1
Biological dose (Gy)	0.1
OSL dose (Sv)	1.23
EPD dose (mSv)	0.09

A man worked with a gamma radiography source for only 3 days during the month that his OSL badge was issued. He undertook examinations of welds and castings and during the three days he also wore an EPD that registered only 90 µSv. He had a companion whose EPD recorded 120 µSv.

A501	
Cells scored	500
Dicentrics	0
Centric rings	0
Other aberrations	0
Biological dose (Gy)	0
EPD dose (Sv)	1.20

An exposure recorded on an EPD was inexplicable. It was received during one day, mostly within a 10 min logging interval. The radiographer was adamant that he had not worked with any sources on that day.

A502	(i)	(ii)
Cells scored	1000	1000
Dicentrics	5	16
Centric rings	0	0
Other aberrations	8	14
Biological doses (Gy)	0.07	0.23
TLD dose (Sv)	0.39	-
OSL dose (Sv)	1.44	-

Two men worked with a 4.5 MeV electron beam accelerator located within a shielded cell. Only one of them wore dosemeters. Their exposure was to 20keV bremstrahlung photons whilst they stood in the maze passage of the cell. At one point they looked around a corner into the cell and both later developed facial erythema. The depth dose characteristics of the photons (HVL ~14 mm) meant that the dose estimated from dicentrics which represents penetrating radiation underestimates surface dose by a factor in the region of 20.

A503	(a)	(b)
Cells scored	500	500
Dicentrics	0	0
Centric rings	0	0
Other aberrations	0	0
Biological dose (Gy)	0	0
TLD dose (Sv)	0.14	0.66

A badge worn by a hospital nurse in a x-ray diagnosis department recorded an inexplicable overdose. No chromosome damage was found but the statistical uncertainty meant that a small dose could not be formally ruled out. Expressed as an odds ratio the cytogenetics favoured zero dose compared with 0.14 Sv by 30 : 1. Investigators finally concluded that the badge had been deliberately exposed in order to cause trouble. Nine months later it happened again. A second chromosome analysis (b) again showed no evidence of overexposure.

A504	
Cells scored	1000
Dicentrics	1
Centric rings	0
Other aberrations	0
Biological dose (Gy)	0
Film badge dose (Sv)	0.55

Despite extensive investigation there was no explanation for the overexposed badge worn by a man who worked with industrial x-ray sets. The dosimetry service company expressed doubts that the exposure was genuine and the chromosomal analysis also supported this view.

A505

Cells scored	1000
Dicentrics	1
Centric rings	0
Other aberrations	1
Biological dose (Gy)	0
TLD dose (Sv)	0.066

There was no obvious explanation for the dose recorded on the badge worn by a technician at a radiation research institute. For various reasons it could not be discounted as a false reading; exposure to gamma rays of ~100 keV was possible. The finding of 1 dicentric, whilst consistent with background, meant that a dose consistent with that recorded still could not be ruled out. However using the odds ratio approach on the two possibilities of zero dose or 0.066 Sv the odds favoured zero by 4.7:1.

A 506

Cells scored	1000
Dicentrics	2
Centric rings	0
Other aberrations	0
Biological dose (Gy)	0.1
OSL dose (mSv)	0.04

An industrial radiographer was exposed for 1-3 min. to a 2.4 TBq (~66 Ci) iridium-192 source. Despite the low dose recorded on his badge it was clear that his exposure was heterogeneous. A worst case calculation of averaged whole body dose was 0.2-0.25 Gy and a much higher value was calculated for one hand. The result of the chromosome analysis suggested that the badge had underestimated his true dose but it was not so serious as had been calculated.

A507	(I)	(ii)	(iii)	(iv)
Cells scored	500	500	500	500
Dicentrics	0	1	7	0
Centric rings	0	0	1	0
Other aberrations	3	0	5	0
Biological dose (Gy)	0	0.1	see note	0
TLD doses (mSv)				
a body	238	2.8	11.4	-
a skin	227	2.8	11.4	-
b body	-	1.0	33.5	1.0
b skin	-	9.4	35.1	1.0
QFE doses (mSv)				
a body	0	0	0	-
a skin	0	0	0	-
b body	-	OS	0.8	1.8
b skin	-	OS	OS	1.1

OS = off scale (max reading 2 mSv)

A switch failure caused an x-ray set to be energized up to 160kV despite the kV indicator showing zero. A radiography team of 4 men was exposed on 2 occasions (*a* and *b*) while examining aircraft components. Extensive re-enactments combined with depth dose calculations suggested that their averaged absorbed doses were low but that all four had received localized skin surface exposures up to 10 Gy. They all suffered small areas of erythema. The aberrations recorded for man (iii) were all in the same cell. The case is further described in the main text.

B. Suspected overexposure of persons not wearing a dosemeter

B 130

Cells scored	3000
Dicentrics	1
FISH translocations (# 2, 3, 5)	7
Age (years)	32
Assumed translocation background	4.2
Biological dose (Gy)	0.25

A mechanic walked close by an aircraft where x-radiography was underway. He immediately experienced abdominal pains and dizziness. It was confirmed that the set had been activated at that moment but his likely dose was very small. 13y later he was diagnosed as azoospermic and failing other explanations the radiography incident was blamed. FISH revealed a translocation frequency just above the expected background but the opinion was given that cytogenetics could not support the possibility of an old exposure sufficiently large to have caused acute illness.

B131

	(i)	(ii)
Cells scored	500	500
Dicentrics	0	0
Centric rings	0	0
Other aberrations	0	1
Biological dose (Gy)	0	0

A 37 GBq (1 Ci) caesium-137 source used for oil well logging was accidentally left unshielded in a work place for two days. Two men had access to the area but were unable to remember clearly their movements or timings. Chromosomal analysis was requested for reassurance.

B132

Cells scored	3000
Dicentrics	0
FISH translocations (# 2, 3, 5)	4
Age (years)	38
Assumed translocation background	5.1
Biological dose (Gy)	0

A man picked up an object in his employer's car park. It was surface contaminated with thallium –201. The employer was later prosecuted for this and other safety lapses. One week later the man became very ill with a range of symptoms, some of which, could be consistent with acute radiation sickness from a whole body dose of around 10 Gy. However this was quite impossible from the contamination present. This plus the timing and persistence of his sickness that also included features not known to be associated with radiation led several medical consultants to advise him that radiation was not the cause of his condition. 2.5 y later, unconvinced and still ill, he requested a chromosomal examination that showed an unremarkable level of aberrations.

B133

Cells scored	3000
Dicentrics	0
FISH translocations (# 2, 3, 5)	5
Age (years)	32
Assumed translocation background	4.2
Biological dose (Gy)	0

A patient received a series of diagnostic chest x-rays and the same day felt nauseous. This progressed to refractory oesophagitis, pharyngitis and chest wall pain. Despite reassurances that the diagnostic procedures had been correct, and the absence of concurrent skin reactions, he developed a fixation that he had been heavily overexposed. Three months later he requested a chromosomal analysis which proved unremarkable but nevertheless his conviction remained. It was learned that he later approached another cytogenetics laboratory which also reported no evidence of radiation overexposure.

B134		
Cells scored	500	A 2 GBq (~50 mCi) caesium-137 source fell out of a level gauge attached to a crushed stone hopper. A quarry worker held it for ~3 min. while taking it to his work hut where it remained for 2 days. About 70% of his working day was spent inside the hut. The surface dose rate on the source led to a calculated hand dose of ~ 200 mSv and a whole body dose of a few mSv. Chromosomal analysis proved reassuring.
Dicentrics	0	
Centric rings	0	
Biological dose (Gy)	0	
B135		
Cells scored	1000	A quality control inspector was briefly exposed to an iridium-192 source when he accidentally walked into an area where pipe welds were being radiographed. A whole body dose of ~0.4 mSv was calculated and a small exposure was indicated by the dicentric analysis. However the statistical uncertainty associated with this was very wide and this led the laboratory to develop a new way to present the uncertainty when reporting results. This is described further in the main text.
Dicentrics	2	
Centric rings	0	
Other aberrations	0	
Biological dose (Gy)	0.1	