UK Health Security Agency

Radiation Chemical and Environmental Hazards Directorate

Version 1.1 (5/7/2023)

UK HSA Chromosome Dosimetry Service

The Cytogenetics Group at UK HSA provides a specialist biological dosimetry service to evaluate people known or suspected of being overexposed to ionising radiation. The service is based on analysing chromosome damage in blood cells to give an estimated dose (rather than a yes or no answer).

The standard chromosome test provided is the dicentric assay, which can indicate a recent radiation exposure that occurred within about 2 years. The lower limit of detection using this assay is about 100 mGy of X- or gamma-rays. The results of the test are given as the most likely estimate of averaged whole-body dose with 95% confidence limits. A more detailed description of the dicentric assay can be found in the document entitled UKHSA_CDS_DosimetryWithChromosomalAberrations.

Cells carrying dicentric chromosome damage are unstable and they are eliminated from the blood being replaced by undamaged cells. A chromosome test more suited to indicating an old radiation exposure is called Fluorescence *In Situ* Hybridisation (FISH). The test detects stable radiation induced chromosome translocations and can be used to assess total lifetime radiation dose. Spontaneous translocation levels increase with age, as chromosome damage accumulates, which determines the minimum detectable dose. As examples, for a 30-year old, an acute whole-body exposure of more than about 0.3 Gy can be detected using the FISH assay, but this rises to more than 0.5 Gy for someone aged 70.

Blood samples for the dicentric or the FISH assay can be sent to our laboratory as detailed in the pdf UK HSA CDS Sampling Instructions which is available on request. A 10 mL blood sample in lithium heparin anticoagulant is required per person. Blood samples should be sent at room temperature and packed to conform to United Nations Regulations 650. This packaging can be supplied by the Cytogenetics Group when a chromosome analysis is requested.

As chromosome analysis is a medical test, we are required for reasons of confidentiality to send our report to a medical doctor. An official request for the analysis would need to come from an appropriate doctor, who could also arrange for the blood to be taken by a trained person. Ideally this would be the company's occupational health doctor, but it could be the employee's own family physician. We can of course provide advice to anyone about the suitability of chromosome analysis on a case by case basis. Therefore, if an over exposure is suspected we need to be contacted either by phone or e-mail to discuss the case prior to a blood sample being taken. The information we need to know is outlined in the UK HSA CDS Questionnaire. If the exposure occurred in an occupational setting, the appropriate HSE representative should also be informed.

One drawback of the dicentric and FISH assays is the time each test takes. For the dicentric assay this can be a minimum of 3 – 5 working days from the receipt of a blood sample. The

FISH assay requires at least 10 – 14 working days. These times would increase if multiple blood samples were received. Another, more recent, technique for assessing exposure to ionising radiation is the gamma-H2AX assay. Gamma-H2AX is a marker for radiation induced DNA damage. The advantage of this technique is that a dose estimate can be given within 5 hours from the receipt of a blood sample. However, the rapid loss of gamma-H2AX means a blood sample needs to be taken within 1 to 2 days after a radiation exposure, with the minimum detectable dose increasing from a few mGy for a sample taken within 1 hour after the exposure to ~0.5 Gy for a lag time of 2 days between exposure and sampling. The applicability of this method would have to be decided on a case-by-case basis.

The Cytogenetics Group at UK HSA are currently validating the gamma-H2AX assay for biological dosimetry. Therefore, at present, if this assay was considered appropriate for use in a particular overexposure scenario, a dicentric assay would still be necessary to confirm the gamma-H2AX findings. The sending of a blood sample for gamma-H2AX analysis is similar to that used for the dicentric assay, but with several very important differences: 1) The blood must be kept cold using cooling packs or wet ice to prevent any loss of gamma-H2AX signal. 2) The sample should reach us as quickly as possible, within 24 hours of being taken. This could be achieved by using a commercial express courier service or samples being delivered by a member of the company's staff, for example. 3) If the first sample was taken only a few hours after exposure, a second sample should be taken at 24 hour in the case of a non-uniform exposure, to allow lymphocytes to mix completely. An additional sample would also be required approximately one week after exposure, to establish the individual base level for this marker and thus further reduce the uncertainty of the dose estimate.

The statistical analysis methods employed to calculate exposure dose and confidence limits are based on classical methods detailed in the IAEA manual for cytogenetic biodosimetry (http://www-pub.iaea.org/MTCD/publications/PDF/EPR-Biodosimetry%202011_web.pdf) and the ISO Standard 19238:2014. In brief, calibration curves are set up with blood samples irradiated *ex vivo* to known doses, between 0 and 5 Gy, using specific, well characterised radiation sources. Uncertainties and confidence limits are assessed on the basis of the Poisson counting error and the uncertainty in the calibration curves, as these are the most important sources of error. In addition, we now apply Bayesian assessment of uncertainties to give an estimate of probability – for instance the probability that the exposure dose received was below or above a certain limit or the probability that a dose was the same as a recorded badge dose. More information can be found in papers published in the open literature which can be provided on request.

The chromosomal dosimetry service is charged per analysis (with effect from April 2020 and subject to a yearly increase) is £750 (exclusive of VAT) for the standard dicentric assay, £1400 (exclusive of VAT) for the FISH translocation assay and £500 (exclusive of VAT) for the gamma-H2AX assay. In addition to the requesting doctor's details, a purchase order number and the name and address for sending an invoice will also be needed to by UK HSA.

The results will be provided in the form of a written report detailing the methods used, the estimated dose and associated uncertainty. The results of the assays, and the potential consequences, will vary greatly on a case-by-case basis. Thus, the medical professional responsible should use the reported results to council the potentially exposed individual on the appropriate level of risk. CDS staff are very happy to discuss the results with the responsible medical professional in further detail if required.