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Guidelines for the Calibration of Routine Dosimetry Systems for use in Radiation Processing

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Guidelines for the Calibration of Routine Dosimetry Systems for use in Radiation Processing

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Abstract

A set of guidelines has been developed to assist in the calibration of routine dosimetry systems for use in industrial radiation processing plants. Topics covered include the calibration of equipment, the performance of calibration irradiations and the derivation of mathematical functions to represent the calibration. Guidance is also given on methods for the estimation of uncertainty.

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Foreword

This Report is a revision of NPL Report CIRM 29 “Guidelines for the Calibration of Dosimeters for use in Radiation Processing”, which was published in 1999 as part of a project funded by the European Commission.

The aim of the revision was to update the document in the light of changes in regulatory standards and technology and to amplify and clarify the guidance in several areas. The basic methods described are, however, the same as in the previous version. The main changes are:

- Reference to the current EN/ISO 11137 standards on radiation sterilization (ISO, 2006a; ISO, 2006b).
- Additional guidance on the interpretation of calibration verification exercises.
- Expansion of the section on measurement uncertainty, including an example of an uncertainty budget.
- The addition of an Annex on the calibration of dosimetry systems for use with low energy electrons.

These Guidelines are intended to be used in conjunction with other documents, such as the ASTM series of standards on Dosimetry for Radiation Processing, produced by Committee E10.01. In particular, they are compatible with the requirements in Standard ISO/ASTM 51261 (ISO/ASTM, 2002) with respect to the calibration of dosimetry systems.

Details on the use of specific dosimetry systems can be found in the ASTM standards mentioned above. The scientific basis and historical development of many of the dosimetry systems used in radiation processing can be found in the recently published ICRU Report 80 (ICRU, 2008).

Guidelines for the Calibration of Routine Dosimetry Systems for use in Radiation Processing

1. Scope

EN/ISO Standard 11137, 2006 Sterilization of health care products Radiation Part 1: "Requirements for development, validation and routine control of a sterilization process for medical devices" (ISO, 2006a) states:

> "Dosimetry used in the development, validation and routine control of the sterilization process shall have measurement traceability to national or International Standards and shall have a known level of uncertainty" (Sec 4.3.4).

The EN/ISO 11137 standard, particularly Part 3 (ISO, 2006b) does provide some guidance on how these requirements can be met, but does not include practical detail. The purpose of this document is to expand on the guidance given in EN/ISO 11137, and to provide details of suitable methods for the calibration of routine dosimetry systems and the estimation of dosimetry uncertainty.

The objective of dosimetry system calibration is to determine the relationship between the indication of a dosimetry system and the absorbed dose received by a dosimeter. This relationship will be dependent on many external conditions associated with the irradiation, such as dose rate, temperature during and after irradiation, time after irradiation, humidity, radiation type, etc. The calibration methods described in these Guidelines are designed to minimise the effects of these influence factors, and hence increase the overall accuracy of dose measurement. Estimation of the uncertainty associated with dose measurement is an essential component of dosimetry system calibration and practical approaches to quantifying the main components of uncertainty are outlined in the Guidelines.

The methods described in these Guidelines are intended for situations in which there is not significant dose variation in the part of the dosimeter being measured. For gamma and mega-voltage electron irradiation, this situation can generally be achieved by the careful selection of the type of dosimeter, but there are situations, for example in kilo-voltage electron beams, where this is not achievable. Annex A provides some information on calibration in these cases.

2. Basic principles

In order to ensure traceability to national standards, calibration laboratories formally accredited to EN/ISO 17025, "General requirement for the competence of testing and calibration laboratories" (ISO, 2005), or equivalent, should be used. Where reference dosimeters are referred to in this document, it is assumed that these will be supplied and measured by an accredited laboratory. If a laboratory not having formal accreditation is used, the laboratory's calibration certificate will not in itself be sufficient proof of traceability to national standards, and additional documentary evidence will be required.

3. Calibration of equipment

The ability to make accurate dose measurements depends on the calibration and stability of the entire dosimetry system. This means that all equipment associated with the measurement procedure, not just the dosimeters themselves, must be adequately controlled and its performance verified.

The measurement device is an integral part of the dosimetry system and the effect of any changes, or repairs, must be assessed. In general, the calibration of a dosimetry system should be regarded as being specific to a particular measurement device. A major repair to, or change of, the measurement device may require either a calibration check (e.g. a Calibration Verification exercise, see Section 5.2.1.1) or a complete recalibration.

According to the ISO 9000 series of standards, all measurement equipment must be calibrated and the calibration must be traceable to national standards. In practice, certain dosimetry measurement equipment cannot be formally calibrated as the readout is not in terms of a standardised quantity e.g. a scale reading from a wide bandwidth optical reader or the peak-to-peak height of a spectrum from an EPR spectrometer. In such cases it is necessary to demonstrate the stability of the equipment by the use of standard test pieces, such as optical filters or stable EPR spin standards. The same consideration could be applied to equipment such as spectrophotometers and thickness gauges, but in general, traceable calibration, combined with regular performance checks against specified acceptance criteria, is usually the easiest way to provide evidence of stability.

Typical items - in addition to the dosimeters themselves - requiring calibration include:

a) Spectrophotometers / Dedicated optical readers
   Absorbance scale: Use calibrated filters
   Wavelength scale: Use rare earth filters or gas discharge lamps

   The frequency of spectrophotometer calibrations and checks will depend on the particular equipment and should be based on both the manufacturer's instructions and on the user's experience of the instrument. The checks must be independent of the internal standards used by the instrument for initialisation purposes.

b) Thickness gauge: Use calibrated gauge blocks

c) Humidity meters: Use saturated salt solutions, e.g.:

Salt	Temperature (^oC)	Relative humidity (%)
CH_3COOK	20	20
$CaCl_2.6H_2O$	24.5 20 18.5	31 32.3 35
$K_2CO_3.2H_2O$	24.5 18.5	43 44
$NaHSO_4.H_2O$	20	52

Source: "Handbook of Chemistry and Physics", CRC Press

d) Thermometers: Use calibrated thermometers

e) Thermolabels: Test in-house in an oven against a calibrated thermometer. Tests should be carried out on both irradiated and un-irradiated labels.

f) Ohm-meter (for use with calorimeters): Use calibrated reference resistor.

Equipment calibration and performance checks must be repeated at specified intervals depending on the known stability of the equipment. In the case of consumable items such as Thermolabels, checks need to be carried out on each batch. Independent evidence of the stability of all measurement standards or test pieces is required.

4. Calibration of dosimeters - General considerations

4.1 Dose range

The dosimetry system must be calibrated over a dose range larger than that of intended use. Measurement uncertainty becomes greater at the extremes of the dose range. The non-linear nature of most dosimeter calibration functions means that extrapolations outside the calibrated range are not acceptable.

Calibration curves must never be forced through zero unless there is independent evidence of the shape of the curve between the lowest calibration dose point used and the reading of an unirradiated dosimeter.

4.2 Number of dose points

For irradiations over less than one decade (factor of ten) of dose, at least 5 dose points distributed arithmetically (e.g. 10, 20, 30, 40, 50 kGy) should be used. For irradiations over more than one decade at least 5 dose points per decade should be used distributed geometrically (e.g. 1, 1.5, 2.3, 3.4, 5.1, 7.6, 11.4, 17, 26, 38, 58, 87 kGy).

At least four replicate dosimeters should be used at each dose point.

4.3 Batch calibration

Calibration must be carried out on each new batch of dosimeters.

Different lots purchased at different times from a batch identified by the manufacturer as the same should be cross-checked to ensure equivalent response. This could be achieved by irradiating dosimeters from both lots together, in such a way that they are known to have received the same dose. A statistical test, such as a t-test, should then be used to determine if there is any significant difference between the lots at a 95% confidence level. This should be repeated at several doses spread over the calibration dose range.

The calibration curve supplied by manufacturers of dosimeters should be considered as general information, and must not be used for dose calculation without further verification of its applicability.

4.4 Calibration frequency

The calibration of existing batches should be checked approximately annually. This check could take the form of a Calibration Verification exercise (see Section 5.2.1.1).

The validity of the calibration should also be checked if there has been a change in any influence quantity, such as temperature or dose rate, that may affect the dosimeter response.

Calorimeters for measurements at electron accelerators may need re-calibration at an interval determined by accumulated dose. This arises because of possible changes in the specific heat of the absorber. Polystyrene, for example, is reported (Miller, 1995) to exhibit changes in specific heat of approximately 1% for each megagray of accumulated dose.

4.5 Post irradiation stability

The response from many routine dosimeters is not stable and changes with time after irradiation. Tests should be carried out to determine the extent of post irradiation changes over the time scale between irradiation and measurement that is likely to be encountered during the use of the dosimeters. If significant changes are observed, it will be necessary to control the time between irradiation and measurement. This applies both for the preparation of the calibration curve and for routine dose

measurement. The extent of post irradiation changes may depend on both the dose level and the storage conditions of the dosimeters.

5. Calibration of dosimeters - Irradiation procedures

Dosimeter response may be influenced by a number of factors including radiation type and energy, temperature during and after irradiation, humidity, dose rate, and the measurement time relative to the time of irradiation. These are generally referred to as influence quantities. In order to limit errors due to these effects, it is necessary to calibrate using conditions as close as possible to those used during normal dose measurements. Two methods are possible:

i) irradiation in the plant, or
ii) irradiation in a calibration laboratory followed by a calibration verification in the plant.

The first method potentially leads to a lower measurement uncertainty, because better account is taken of influence quantities, and should be used if possible.

5.1 Irradiation in plant

This method involves irradiation of routine dosimeters alongside reference dosimeters in the irradiation plant where the dosimeters will be used. The routine and reference dosimeters are irradiated in close proximity to ensure that both receive the same dose. The reference dosimeters need to be supplied and measured by a laboratory that can demonstrate traceability.

Advantage: Inherently takes influence quantities into account.
Disadvantage: Difficult to obtain full dose range in certain plant designs.

5.1.1 Gamma - specific aspects

In irradiation plants giving doses in multiple dose fractions with each fraction obtained by a full cycle around the source, the calibration doses can be given as multiples of each cycle.

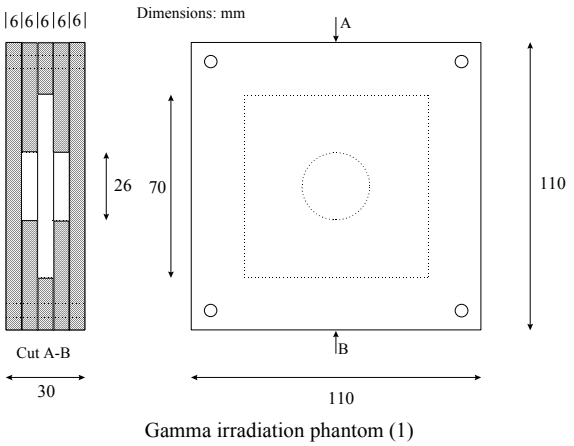
In other plants, which deliver the dose in one full cycle, it may be necessary to interrupt the process and to insert (or remove) dosimeters at points throughout the cycle in order to achieve a range of doses. In designing a procedure, consideration has to be given to the ease of access to boxes containing dosimeters at various points in the cycle. Dose should be delivered in one continuous period, as dose fractionation may lead to additional uncertainties. Care must be taken to ensure that the procedure does not unacceptably influence the dose to normal product being irradiated at the same time. The use of increased shielding to reduce delivered dose is not recommended as that may result in significant changes to the radiation spectrum, which could influence dosimeter response. Similarly, it is not recommended to

irradiate at a fixed position in the irradiation room, with normal product shielding the dosimeters.

5.1.1.1 Irradiation phantom

It is recommended that the dosimeters to be calibrated and the reference dosimeters are irradiated in a phantom, or standard absorber, in order to ensure that the dosimeters are irradiated to essentially the same dose. The phantom should be placed in a region of low dose gradient, for example, in the middle of a homogeneous product. The wall should be thick enough to ensure that the dosimeters are surrounded with material that is similar to the dosimeter material in order to limit effects from interfaces. Recommended material is polystyrene or similar radiation-resistant plastics with wall thicknesses of 5-8 mm. Increasing the wall thickness beyond this may create dose gradients within the phantom due to attenuation. Similarly, the mass of dosimeter material must not be so large that significant dose gradients are introduced - for double sided irradiations the thickness of material of density around 1 g cm^{-3} should not exceed ~15 mm. Single sided irradiation will introduce larger dose gradients, but provided the reference and routine dosimeters are arranged in a symmetrical "sandwich" along the direction of irradiation, no significant error will be introduced.

Examples of irradiation phantoms for in-plant gamma irradiation are given in figures 1 and 2. In fig. 1 the phantom allows routine dosimeters (e.g. up to 5 PMMA dosimeters) to be irradiated with a 6 mm thick alanine reference dosimeter on either side of them. Figure 2 contains a larger rectangular insert intended to hold a dosimeter box containing routine dosimeters and two cylindrical reference dosimeters arranged in a line.



Gamma irradiation phantom (1)

Figure 1

This geometry is suitable for either dichromate or ceric-cerous dosimeter ampoules, or alanine pellets in cylindrical holders. The orientation of the phantom with respect to the source is important and must be such that direct radiation from the source passes through the shortest axis of the phantom.

5.1.1.2 Temperature

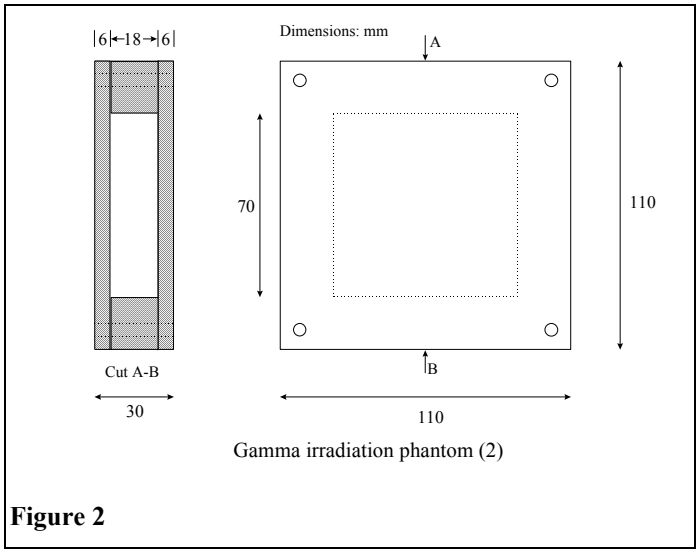


Figure 2

For in-plant irradiations, the effect of irradiation temperature on the reference dosimeters must be considered. The irradiation temperature in a gamma plant is a complex function of the passage of the product box through the plant (Sharpe *et al.*, 2000), but an effective temperature for the purpose of reference dosimeter correction may be calculated as 2/3 of the temperature difference between the minimum and maximum temperature that the dosimeter experiences. This is only an approximation and the effect of uncertainties in this estimate are considered in Sec 8.1.3

$$T(\text{effective}) = T(\text{min}) + 2/3(T(\text{max})-T(\text{min})).$$

The maximum irradiation temperature can conveniently be estimated by the use of temperature sensitive adhesive labels. Mechanical recording thermometers can also be used, but care must be taken to ensure that the device does not "over-read" due to local heating of the metal temperature sensor, whose specific heat may be lower than that of the product.

In situations where significant uncertainties may be introduced by the lack of information about irradiation temperature, it is possible to eliminate the effect of irradiation temperature by using both dichromate and alanine reference dosimeters irradiated in close proximity. The effect of irradiation temperature on these two dosimeters is almost equal in magnitude, but opposite in direction, allowing correction for the effect of irradiation temperature.

5.1.2 Electron - specific aspects

Electron accelerators can normally be set to deliver doses for calibration over the full dose range of the dosimeter, although very small doses may present problems if an unusually high conveyor speed has to be used. In extreme situations, high conveyor speeds can lead to uneven irradiation due to insufficient overlap of a pulsed and scanned electron beam. Calibration doses should, whenever possible, be delivered using the same accelerator, and the same operating conditions, that would be experienced during normal use. If calibration doses are given using an accelerator or operating conditions different from those of normal use, then additional checks should be carried out to ensure that the change in conditions has not significantly influenced dosimeter response. This can most conveniently be carried out by a calibration verification exercise. An example where this might be necessary is the calibration of

dosimeters using a single irradiation, when during routine use the dose would be fractionated, such as by a double sided irradiation of product.

5.1.2.1 Irradiation phantom

An irradiation phantom must be used to ensure that the dosimeters to be calibrated and the reference dosimeters receive the same dose. This phantom is irradiated separately, not in reference or dummy product. The same general consideration as for the gamma phantom apply, with the difference that due to the inherent dose gradients with electron accelerator irradiation, a specific location on the depth dose curve should be chosen, e.g. at the peak of the depth dose curve or on the ascending slope of the curve. The uniformity of dose across the irradiated area needs to be considered when deciding dosimeter layout within a phantom.

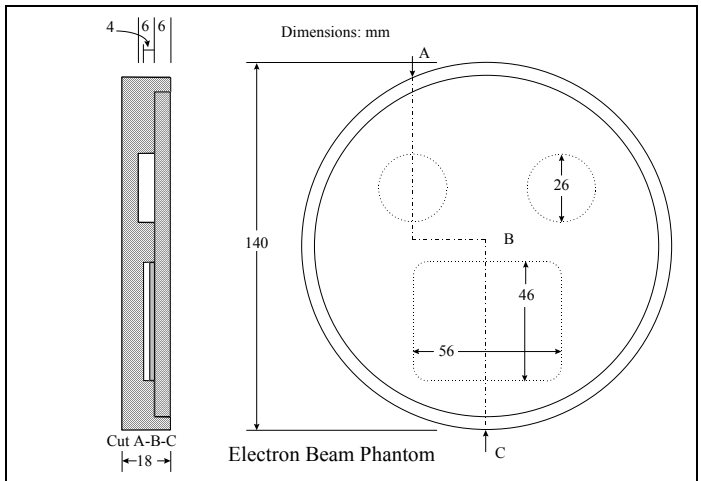


Figure 3

An example of an irradiation phantom for 10 MeV electron irradiation is shown in fig 3. This phantom will hold alanine reference dosimeters (in the form of 3 mm pellets enclosed in disc holders 25 mm diameter, 6 mm thickness) and film routine dosimeters. If used without the 6 mm thick top plate, this design is also suitable for use at energies down to 4 MeV.

The phantom shown in fig. 3 also allows comparison with calorimeters, which are available commercially with the same geometry. When used with such calorimeters, it is important that the phantom and calorimeter absorber are positioned on an approximately linear portion of the depth dose curve. This ensures that the mean dose to the calorimeter and the dose to the dosimeters in the phantom are close and will minimise errors arising from small variations in position. Calorimeters calibrated in this way can subsequently be used as local reference standards to calibrate other dosimeters in phantoms of this type.

5.1.2.2 Temperature.

Because of the short irradiation time, the irradiation temperature will rise almost adiabatically during irradiation, and the effective irradiation temperature can therefore be considered to be equal to the mean temperature

$$T(\text{effective}) = (T(\text{min}) + T(\text{max}))/2$$

5.2 Irradiation at a calibration laboratory

This method involves irradiation of the dosimeters to be calibrated in the reference radiation field of a calibration laboratory, followed by a "calibration verification" in the irradiation plant. Calibration verification involves checking the derived calibration curve in actual plant conditions by the use of reference dosimeters. Without this step, systematic errors arising from environmental effects could go undetected and it is difficult to prepare a realistic estimate of the calibration uncertainty.

Advantage: Easy to obtain full dose range.
Disadvantage: Environmental effects may not be dealt with in an adequate way.

5.2.1 Gamma - specific aspects

It is generally not possible to match actual plant conditions in a calibration irradiator, but an attempt should be made to irradiate dosimeters under conditions of dose rate and temperature as close as possible to those that will be experienced in actual use. Dose rate can usually be matched only in very broad terms, but would not be expected to present significant problems, except possibly in the case of very low dose rates (full cycle times of more than one day). An effective temperature for the plant can be estimated as described in Section 5.1.1.2.

Transport of irradiated dosimeters from the calibration laboratory to the industrial plant can potentially introduce significant errors if the conditions between irradiation and measurement are not the same for calibration and use. This concerns effects of, for example, time, temperature and humidity. One way of checking for effects during transport is to irradiate a number of control dosimeters at the plant requesting the calibration. Some of these dosimeters can then be shipped to and from the calibration laboratory with the dosimeters being calibrated. Any differences between the measurements with un-travelled and travelled dosimeters when returned to the originating plant can then be used as an indication of effects during transport.

5.2.1.1 Calibration verification

Having prepared a calibration curve using dosimeters irradiated at a calibration laboratory, it is necessary to perform a calibration verification exercise in order to detect any systematic errors that may have arisen due to differences between the conditions of calibration and use. Dosimeters from the batch being calibrated should be irradiated alongside reference dosimeters in the industrial

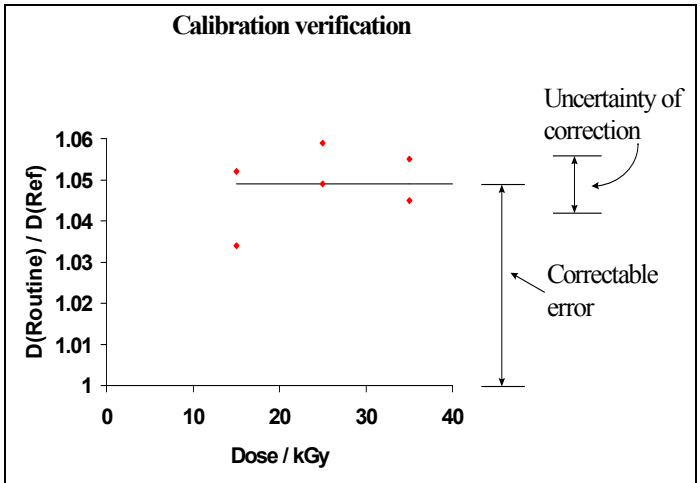


Figure 4

plant. Both types of dosimeter must be in close proximity in order to ensure they receive the same dose. The points discussed in Section 5.1.1 concerning the irradiation phantom and estimation of temperature apply. At least three dose points should be chosen at as wide a range of doses as possible within the calibration range. Each reference dosimeter should be accompanied by several of the dosimeters being calibrated, although care must be taken to avoid attenuation in a large bulk of dosimeter material (see Section 5.1.1.1).

The difference between the dose measurements of the reference dosimeters and those from the dosimeters being calibrated should be determined and the results examined for any systematic trends. Each case needs to be treated individually, but the following general considerations should be taken into account:

- Differences greater than 5% may indicate the presence of an error somewhere in the procedure and this should be investigated before applying any corrections.

- If the results indicate a significant offset between measurements from the two types of dosimeter, that is essentially constant over the dose range of use, then a correction factor may be applied to the calibration curve to bring the dose measurements from the dosimeters being calibrated into line with those from the reference dosimeters. An example of such results is given in Fig 4, where a correction of 5% is indicated.

- Corrections that are not constant over the entire dose range should not be applied without some other supporting evidence that justify the form of the correction.

- An alternative approach is to set an acceptance limit and not make any corrections if ratios smaller than this value are obtained. This is a straightforward approach, but, depending on the limit chosen, may unnecessarily increase the calibration uncertainty (see Section 8.1.3). Ratios outside the acceptance limit results in the calibration being rejected, and an alternative method such as in-plant calibration should be chosen, or the calibration should be repeated with conditions that agree better with the conditions of use.

5.2.2 Electron - specific aspects

Irradiation at a calibration laboratory would not usually be employed for dosimeters to be used in electron beams If special circumstances dictate that irradiation at a calibration laboratory is necessary for electron beam dosimeters, then the same general procedure as outlined above for gamma should be used, except that the specific sections on electron beam phantoms and temperature measurement apply (Sec 5.1.2).

6. Preparation of calibration curve

It is necessary to convert the measured calibration data into some form of smooth function that will enable dose to be obtained from a measured dosimeter signal. This could be as simple as a hand drawn graph, but in practice a mathematical fitting

procedure of some form is generally used to obtain the relationship between dosimeter signal and absorbed dose. The most common methods are based on least squares techniques, in which the best fit is determined to be that which results in the smallest difference (residual) between the measured and calculated values.

Strictly, the least squares fitting procedure will result in different answers depending on whether a fit is made in terms of *signal=f(dose)* or *dose=f(signal)*. A function of the form *signal=f(dose)* is statistically correct, but can result in expressions which are difficult to solve for dose, the quantity required. (Note: Many spreadsheets have functions which will solve equations of the form *signal=f(dose)* for dose given a signal value, e.g. in EXCEL the "solver" function may be used). In practice, for radiation processing dosimeters, functions of the form *dose=f(signal)* will not result in appreciable error provided the dose range is not greater than a factor of ten. If the dose range is significantly greater than a factor of ten, then the fitting procedure becomes more complex with functions of the form *dose=f(signal)* and care should be taken to ensure that unnecessary errors are not being introduced.

A complication in the least squares fitting procedure can arise if the calibration curve is being prepared over a wide dose range (more than a factor of ten) and the magnitude of the residual is proportional to dose. In such cases in order to produce an acceptable fit, it may be necessary to either use a weighted least squares fitting procedure, or to break the calibration into two, or more, sections, each of which can adequately be fitted using non-weighted least squares methods.

In general, there is not a specific mathematical relationship between signal and dose, and it is necessary to select an empirical function that fits the observed data. In many cases a polynomial function (e.g. $signal=a+b \bullet dose+c \bullet dose^2+.....$) will adequately describe the relationship, but other functions, such as exponentials can be used. Because of their general applicability, polynomial functions will be described in this document, although the general principles can be applied to other functions.

In selecting a function the main consideration is to use the lowest order of polynomial that will adequately represent the data. One of the best methods of determining the required order is by examination of the residuals for increasing orders of the polynomial, as described below:

a) A statistical software package should be used to determine the coefficients of the selected polynomial. Start with a first order polynomial unless the data is obviously non-linear. Individual dosimeter measurement points from the batch being calibrated should be used i.e. not the average of the measurements from replicate dosimeters irradiated to the same dose. This enables an estimation of the dosimeter-to-dosimeter precision and allows outlying results to be identified.

b) Using the coefficients derived in a), the dose for each of the dosimeters from the batch being calibrated is calculated, based on its measured signal.

c) The “percentage residuals” are calculated as follows:

$$(D_{calculated} - D_{delivered}) / D_{delivered} * 100$$

d) The “percentage residuals” are plotted against dose and the data examined for any systematic trends i.e. patterns of residuals gradually moving from positive to negative and vice versa, (see Figs 5 & 6). If such patterns are apparent then the exercise should be repeated using the next highest order of polynomial. The polynomial order of choice is the lowest order that does not exhibit systematic trends.

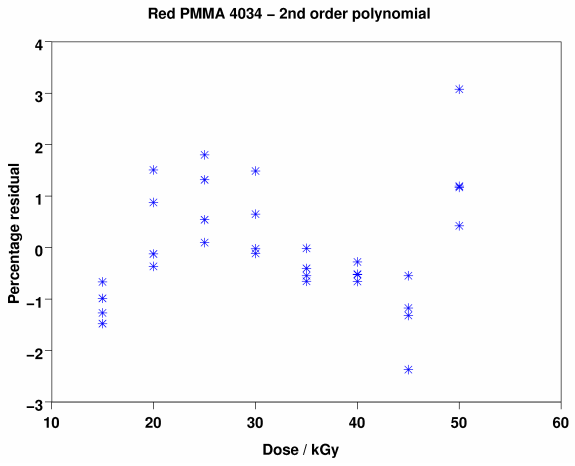


Figure 5

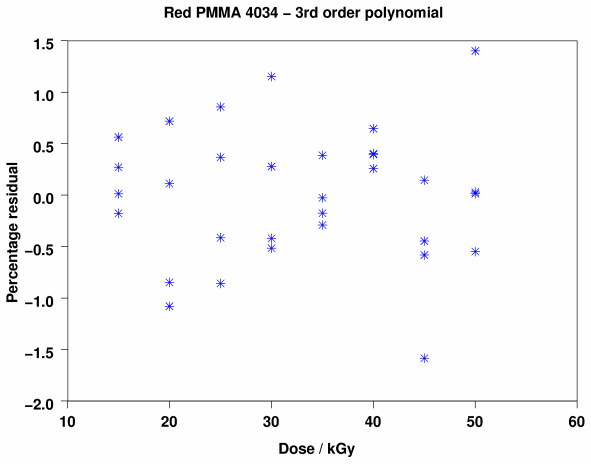


Figure 6

Alternative methods to determine the optimum order of polynomial are generally based around the “correlation coefficient” or “F-statistic”. These factors have the advantage of often being generated automatically by statistical packages, but in general are less sensitive than the examination of residuals method outlined above.

As an example, the "correlation coefficients" and "F-statistics" derived for the polynomial fits shown in Figs 5 & 6 are given below:

Order of fit	2	3
Correlation coefficient (R^2)	0.99931	0.99972
F-statistic	20850	33333

7. Software considerations

All software used to manipulate dosimetry data must be validated to ensure its correct operation, and the results of the validation must be documented. Formal requirements for the development and testing of software have been produced by a number of bodies, the most relevant for the radiation processing industry are probably those of the US Food and Drug Administration (FDA, 1997; FDA 2003).

Spreadsheets are particularly prone to error and the in-built "auditing" procedures available in some packages should be fully utilised. It is essential that results are checked either manually or by the use of another independent package (Note: the method of examination of residuals, described above, implicitly provides a degree of self checking of the system). Protection of the software and data against unauthorised changes is also a vital consideration, particularly when the system is to be used by relatively unskilled personnel.

8. Estimation of uncertainties

In order to establish the uncertainty associated with a dose measurement, it is necessary to first identify and then quantify all possible sources of uncertainty. This is most easily done by considering, in turn, each step involved in the calibration and use of a dosimetry system, and assessing what uncertainties are likely to be associated with each of these steps. The uncertainty associated with a dose measurement can then be calculated by combining the individual components together. The philosophy used is to ascribe to each component of uncertainty an effective standard deviation, known as a standard uncertainty, and it is these standard uncertainties that are then combined to produce the overall uncertainty (ISO, 1995). A tabulation of the individual components of uncertainty, along with their values and methods of estimation is often referred to as an "uncertainty budget".

When dealing with statistical effects, such as the random scatter between replicate dosimeters, the concept is clear and it is straightforward to calculate the relevant standard uncertainty. Such components of uncertainty are known as "Type A" components.

Other components of uncertainty, for example the effect of irradiation temperature on dosimeter response, are not easily calculated from a set of statistical data, and a more subjective approach has to be taken. A common situation is that prior knowledge indicates that an effect is very unlikely to be greater than ±a%, but no other information is available as to its exact value. An alternative way of stating this is to say that there is a 100% probability of the effect being between ±a%, and a 0% probability of it taking any other value. If, in addition, the value is equally likely to be anywhere between ±a%, then this is known as a "rectangular probability distribution" and an effective standard deviation can be calculated for it. The mathematics behind the calculation of an effective standard deviation for a rectangular distribution are beyond the scope of this document, but its value can be taken as a / √3. Components of uncertainty derived by non-statistical methods, such as this, are known as "Type B" components.

The combined uncertainty associated with a particular measurement is obtained by summing in quadrature the individual component standard uncertainties i.e. by taking the square root of the sum of the squares of the individual components:

$$u_c = (u_1^2 + u_2^2 + u_3^2 + ...)^{½}$$

In reporting the uncertainty associated with a particular measurement, the value given should imply a high level of confidence that the correct result will lie within the reported range. Historically, uncertainties have been reported based on either a 95% or a 99% probability that the correct value is within the range. The accurate calculation of such values is, however, complex, and current practice is to report standard uncertainties multiplied by a *coverage factor (k)* of either 2 or 3. For most situations, a coverage factor of 2 is very close to a 95% confidence interval, and a coverage factor of 3 is very close to a 99% confidence interval.

8.1 Uncertainties in the Preparation of a Calibration Function

8.1.1 *Uncertainty in calibration doses* - The certificate provided by the calibration laboratory will contain statements about the uncertainty of dose delivery or dose measurement. Unless specifically stated otherwise in the certificate, the overall uncertainty should be taken as the value to be used in subsequent calculations. Uncertainties quoted at 95% or 99% confidence should be interpreted as being equivalent to 2 or 3 standard uncertainties, respectively. The calibration laboratory may provide a breakdown of the individual components of uncertainty into Types A and B, but it is more likely that a single, combined, figure will be given. In the latter case, the uncertainty in calibration doses should be listed as Type B in the uncertainty budget of the user of the dosimetry system.

Variability in the positioning of dosimeters within a phantom may also contribute significantly to the uncertainty in delivered dose. This is a particularly important consideration for electron beam irradiations. The magnitude of the uncertainty can be estimated from a knowledge of the possible variation in positioning of dosimeters, and the dose distribution in the phantom (see also Sec 8.1.3).

8.1.2 *Uncertainty due to fit of calibration function* - The calibration function will have associated with it an uncertainty arising both from the fact that the form of the expression may not truly represent the data, and also from the fact that it was derived from a finite number of data points, each of which have an associated uncertainty. Accurate determinations of the uncertainty due to curve fitting are complex for all but straight lines, and uncertainty data are not generally produced by curve fitting software packages. In general terms, the uncertainty will be smallest in the centre of the calibration dose range and increase steadily towards the extremes. Uncertainty often increases markedly at low doses, where the "signal-to-noise" ratio increases, and also at high doses if the calibration function begins to "saturate".

If a good mathematical fit has been selected, the uncertainty due to the fit of the calibration function should be a relatively minor component of the overall uncertainty and it is justifiable to use a simple approximate method to obtain a value for inclusion in the uncertainty budget. One method is to use a percentage dose residual plot of the type described above (Sec 6). In this case the replicate residuals at each dose point should be averaged in order to reduce the influence of dosimeter-to-dosimeter scatter. Assuming the residuals do not show any significant tendency to increase, or decrease, in magnitude with dose, the root-mean-square residual can be calculated and used as a reasonable approximation of the standard uncertainty of the fit. This approximation is, however, likely to be an overestimate at the centre of the dose range, and an underestimate at the extremes.

8.1.3 *Uncertainty due to influence quantities* - In the case of an "in-plant" calibration against reference dosimeters it is necessary to consider two significant sources of uncertainty: a) the effect of uncertainties in irradiation temperature on the dose measurement of the reference dosimeters, and b) the possible difference in dose delivered to the reference and calibration dosimeters due to dose variation within the calibration phantom. Both of these are best treated as Type B estimates i.e. prior knowledge of the temperature variation in the plant or the dose distribution in the phantom will enable maximum limits of the likely effects to be estimated. These can then be converted into standard uncertainties using the formula "a / $\sqrt{3}$", discussed above.

An additional component of uncertainty due to environmental effects must be considered, when calibrations are carried out using irradiations at a calibration laboratory followed by calibration verification using reference dosimeters. This additional uncertainty arises from the incomplete correction for the effects seen in the calibration verification, and can be estimated from the difference between the measurements of the reference dosimeters and those from the dosimeters being calibrated - in this case, the dosimeter measurements are those obtained **after** replicates have been averaged and correction made for any systematic offsets (see Sec 5.2.1.1 and fig. 4). Two approaches are suggested for estimating an approximate value for this standard uncertainty: a) calculate the root-mean-square value of the individual differences observed between the two types of dosimeter, or b) use the formula "a / $\sqrt{3}$", where "a" is the maximum difference observed between the two types of dosimeter.

If the decision has been taken to accept the results of a calibration verification when the differences between measurements of reference dosimeters and those being calibrated are within predefined limits, then a component of uncertainty has to be included based on the limit chosen. This should be estimated as a Type B uncertainty using the "a / √3" formula, where "a" is the acceptance limit.

8.2 Uncertainties in use of dosimeters

8.2.1 *Uncertainty due to dosimeter-to-dosimeter scatter* - This can be obtained from the percentage dose residual plot described above (fig. 6.). Individual calibration dosimeter points should be used i.e. do not average the readings from replicate dosimeters irradiated to the same dose. The standard uncertainty is calculated using the following formula:

$$u = \sqrt{\frac{\sum (Residuals)^2}{n_d - n_c}}$$

where n_d is the number of dosimeters and n_c is the number of coefficients in the selected mathematical fitting function.

An alternative approach is to determine the standard deviation of the replicates at each dose level separately and then combine these using the formula:

$$u = \sqrt{\frac{\sum \left((n_i - 1) * \sigma_i^2 \right)}{\sum (n_i - 1)}}$$

where n_i and σ_i are the number of dosimeters and the standard deviation of the dose measurements at a given dose level, respectively. The standard deviations are generally expressed as percentages of the mean dose at each dose level.

8.2.2 *Uncertainty due to variation in plant environmental conditions* - Changes in the environmental conditions in the plant (e.g. temperature, dose rate or humidity) can potentially influence the response of routine dosimeters and lead to additional uncertainties. It is necessary to estimate the maximum effect of such changes on the routine dosimeters and then calculate an effective standard uncertainty using the formula "a / √3". If seasonal variations in temperature and humidity lead to significant effects, it may be necessary to recalibrate dosimeters at intervals during the year. Calibration verification exercises conducted, for example, during summer and winter, or immediately following a source reload in a gamma plant, can be used to detect effects resulting from changes in plant environment.

8.2.3 *Uncertainty due to instability of dosimeter measurement* - The signal from many routine dosimeters is not stable and changes with time after irradiation. The magnitude of such instability needs to be determined and limits estimated for the maximum effect that variability in time of measurement will have on the dose measurement. The standard uncertainty can then be calculated using the "a / √3" formula.

8.2.4 *Uncertainty due to instability of instrumentation* - Variations in the performance of the measurement instrumentation e.g. spectrophotometers, thickness gauges, etc., will have a direct effect on dosimetry uncertainty. Periodic recalibration of the instrumentation, and/or checks using standard reference items, enable the stability to be determined, and this can be expressed in terms of its effect on dose measurements. If frequent stability data are available it may be possible to derive a Type A uncertainty estimate from the measured distribution of results, but it is more likely that a Type B estimate will have to be made using limits of stability data.

8.3 **Example uncertainty budget**

An example of an uncertainty budget listing some of the components of uncertainty in the previous section is given below. It is based on a calibration carried out by irradiation in plant (Sec 5.1), but should be taken only as guide to the form of an uncertainty budget. It represents the uncertainty associated with the calibration of a dosimetry system, but does not include all components of uncertainty associated with the subsequent use of the system (see Sec 8.2).

Component of uncertainty	Value	Probability distribution	Divisor	Relative standard uncertainty	
				Type A	Type B
Calibration doses from laboratory certificate	2.6% (k=2)	Gaussian	2		1.3%
Fit of calibration function	0.5%	Gaussian	1	0.5%	
Correction of reference dosimeters for irradiation temperature	1.0%	Rectangular	√3		0.6%
Difference in dose to reference and calibration dosimeters	1.0%	Rectangular	√3		0.6%
Dosimeter-to-dosimeter scatter (reproducibility)	0.6%	Gaussian	1	0.6%	
Combined uncertainty				1.8%	
Expanded uncertainty (k=2)				3.6%	

9 References

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Annex A

Low Energy Electrons

These Guidelines are intended for situations in which there is not a significant dose variation within the part of the dosimeter being measured. This is normally the case for gamma and x-ray irradiation and for electron irradiation at energy above approximately 4 MeV, but at lower energies, dose gradients can become significant for thicker dosimeters. This situation might be acceptable if the dosimeter can be irradiated so that an average dose over the thickness of the dosimeter can conveniently be calculated. This is the case if the dosimeter is irradiated at the ascending part of the depth dose curve, but it is difficult if the dosimeter is thicker than approximately 1/3 of the electron range. Three millimetre alanine pellets, for example, can be used down to approximately 2.5 MeV. At lower energies thinner dosimeters must be used, and 130 micrometre alanine films can be used down to approximately 300 keV.

It must be recognized that irradiation of many dosimeters with low energy electrons (less than 300 keV) will lead to dose gradients through the thickness of the dosimeter. When the dosimeter is measured, this will lead to an apparent dose that is related to the dose distribution. For a given set of irradiation conditions, the apparent dose will depend on the thickness of the dosimeter, i.e. different thickness dosimeters will measure different apparent doses.

One solution to overcome this problem is that all dose measurements are specified as dose to water in the first micrometre of the absorbing material. This is given the symbol D_{μ} and is independent of dosimeter thickness (Helt-Hansen *et al*., 2009)

The relationship between D_{μ} and the apparent dose strongly depends on dosimeter response function, dosimeter thickness, dose, radiation energy, accelerator window material and thickness, distance window to dosimeter, and temperature of air between window and dosimeter. The relationship must be calculated for each set of irradiation conditions.