An Investigation of Monitoring by Nose Blow Sampling

The potential for developing nose blow sampling into a robust screening method for exposure to radionuclides

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ABSTRACT

Nose blow sampling has long been used in special individual monitoring to identify people who may have received radionuclide intakes after a suspected incident. However, experience of such occupational monitoring has shown that the activities cleared by nose blows produced on-demand have little relationship to the magnitude of the intake. In contrast, a human volunteer study of nasal deposition and clearance has found that the activities of nose blow samples produced at will by the participants do show a relationship to the activity initially deposited in the extra-thoracic (ET) airways which depends on the time between intake and nose blow. A pilot study has therefore been conducted to investigate if a method of nose blow sampling can be developed that can give a quick and simple estimate of the order of magnitude of a suspected intake and to resolve the differences between the volunteer study findings and the results of occupational monitoring. As the key difference between nose blows produced at will and on-demand seems to be the presence or absence of mucus in the nasal passage, benign methods of stimulating mucus production have been investigated. Volunteer studies showed that by stimulating mucus production before nose blowing, the activities of the nose blows produced on-demand could be used to make an estimate of the initial ET deposition, if the time between intake and nose blow is known. The development of a robust and simple occupational monitoring methodology, taking into account the uncertainties arising from its use in an operational environment, is now being considered. Application as an emergency response rapid screening method is also being considered.

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EXECUTIVE SUMMARY

"On-demand" nose blow sampling becomes a significantly improved tool for monitoring intakes of radionuclides by inhalation if nasal mucus production is stimulated just before the nose is blown. Mild stimulation ensures that mucus is present in the nose when the sample is delivered, and the activity cleared is then much more representative of the initial intake, which can be assessed with an accuracy of about an order of magnitude. This is a significant improvement on the two to three orders of magnitude of uncertainty found in studies of non-stimulated "on-demand" nose blow sampling conducted in the workplace. Those findings are consistent with the results for non-stimulated nose blows found in this study. By introducing mucus stimulation, "on-demand" nose blow sampling can be improved from a technique capable of providing only a simple "yes/no" indication of radionuclide inhalation to one that provides a semi-quantitative measure of the magnitude of the intake. This information will enable much clearer identification of those people who need to take part in further bioassay monitoring for more accurate assessment of the intake and the resulting radiation dose. Work to develop a robust and simple occupational monitoring technique, taking into account the uncertainties arising from its use in an operational environment, is now planned. In addition work is proposed to develop stimulated on-demand nose blow monitoring into an emergency response rapid screening method.

CONTENTS

1 INTRODUCTION

Internal dosimetry assessment services have long used nose blow sampling as an initial test to identify staff who may have inhaled radioactive material as a result of an airborne release. On request, the staff involved can quickly provide nose blow samples. Samples to be monitored for gamma-ray or beta-particle emitting radionuclides require no chemical preparation, and gamma-ray spectrometry can generally identify those samples that contain radioactive material within hours of sampling. While samples collected to detect pure alpha-particle emitting radionuclides such as polonium-210 will require radiochemical analysis, so will all other types of bioassay sample. However, while nose blow samples are a useful indicator that activity has been inhaled, the experience of dosimetry services is that they are an unreliable means of estimating the magnitude of intakes. Earlier studies did find a positive correlation between activities cleared by nose blow and faecal samples for the first four days after an intake. However, the ratio of these two activities was found to vary by as much as a factor of 400 (Lister 1968, Hounam et al 1983, Spencer et al 2007).

This study has investigated the possibility that deliberate nose blow sampling can be developed into a quick and simple means of estimating the magnitude of intakes following single, accidental exposures. Used with a collection regime that minimises inadvertent contamination, it would aid the rapid identification of personnel who require further monitoring or investigations. This would both reduce stress to potentially exposed staff and improve the efficiency of the response to the suspected incident. Representative deliberate nose blow sampling would supplement other methods of intake assessment and in some specific circumstances (e.g. where doses can be shown to be well below reporting levels), may be a sufficient method of assessment in itself.

This study was conducted to investigate the potential for developing nose blow monitoring into a more useful method of identifying those who have inhaled significant amounts of radionuclides in the workplace. The study's findings might also be used to develop an emergency response rapid screening method.

All the volunteer studies referred to in this report were conducted at the HPA's Centre for Radiation, Chemical and Environmental Hazards (CRCE), in accordance with the ethical approval gained from the Central Oxford Research Ethics Committee (references: C95.289-Study of the deposition and clearance of inhaled particles in the nasal passage and C00.038- Study of the deposition and clearance of inhaled particles in the nasal passage: Part 2). All administrations of radionuclides to the volunteer subjects were made in accordance to the Administration of Radioactive Substances Advisory Committee (ARSAC) certification of the studies (certificate numbers: RPC 530-1114 (9080) issued 14 December 1995, extended 24 November 1997 and RPC 530-2417 (13912)).

2 REVIEW OF VOLUNTARY NOSE BLOW MEASUREMENTS

Nose blow clearance measurements from a study of the deposition and clearance of inhaled particles from the human nasal passage carried out at CRCE (Smith et al., 2002, Smith et al. 2011)) suggested that nose blow sampling could provide a method for assessing the magnitude of intakes. The study investigated the nasal clearance of monodisperse aerosols with particle sizes from 1.5 µm to 6 µm aerodynamic diameter (d_{ae}). Volunteer participants inhaled the insoluble radio-labelled aerosols while breathing through the nose according to their natural breathing pattern, either as they sat at rest, or performed light exercise as defined in the International Commission on Radiological Protection (ICRP) Human Respiratory Tract Model (HRTM) (ICRP, 1994). It should be noted that participants blew their noses at will, not on demand. Nasal clearance was measured for three to four days after intake. The participants blew their noses using standardised tissues, which they bagged and labelled with the date and time. Participants also recorded the time of any sneeze or nose blow for which they did not collect a sample.

TABLE 1: Summary of nose blow statistics for participants in the nasal deposition and clearance study

Subject ID in nasal deposition and clearance study[a]	Subject ID in deliberate nose blow pilot study	Total clearance by nose blow from each inhalation experiment that the participant took part in: % IETD[a]	Average number of nose blows per day
8		44%	4
6		7%, 48%, 58%	7
4	B	17%, 20%, 20%, 23%, 32%, 33%, 49%	9
3		22%, 25%	3
2		13%, 16%, 17%, 24%	3
5		5%, 10%, 30%	2
1	A	5%, 5%, 5%, 6%, 15%	2
9		5%	2
7	C	0.5%, 0.6%	1
Average		20%	3.6 ± 0.2 [b]

a. Subjects are listed in descending order of their clearance of nasal deposition by nose blowing, given as the average fraction of Initial Extra-Thoracic Deposition (IETD) from all inhalation experiments

b. The average number of nose blows per day plus or minus its standard deviation

In the nasal study, the nose-blow sample activities were measured using a UKAS-accredited gamma-ray spectrometry system. The activities were decay-corrected back to the time of inhalation, and were divided by the activity initially deposited in the extra-thoracic (ET) airways (the initial ET deposit or IETD) to give the nose blow clearance

fraction as a percentage of IETD for each sample. The total fraction of the IETD cleared by nose blows following each inhalation by each participant was determined by summing all the measured nose blow clearance fractions. Usually, collection of nose blow samples ceased approximately 50 hours after intake as this was when the sample activities tended to fall below the limit of detection or became insignificant. Therefore, total nose blow clearance fractions may be marginally higher than determined but only to an insignificant degree (Table 1).

Care had been taken that participants did not take part in the study while suffering from the effects of respiratory tract infections in order to minimise intra-subject variation from that cause. In fact it was found that an individual participant's nose blowing behaviour tended to be consistent between the different experiments they took part in. However, the study showed that nose blowing habits varied significantly between participants. The participants blew their nose between once and twelve times a day, and total clearance by nose blows accounted for as little as an average of 0.5% IETD for one participant and up to 40% IETD for another. On average, the participants blew their noses 3.6 times a day, clearing 20% of the IETD by that route.

The nose blow clearance fractions plotted as a function of time after intake seemed to indicate a similar trend for all participants, irrespective of their nose blowing habits (figure 1). No trend with particle size or exercise rate was found for the nose blow clearance fractions. One important source of scatter about the general trend of the data was identified as participants producing several nose blows in rapid succession. Generally, the activities of later samples in such a cluster are significantly lower than that of the first sample. Replacing the individual sample activities of such clusters with their summed activity enhanced the trend in the data. Therefore, the nose blow clearance fractions from each administration to each participant were summed to give the IETD clearance fractions for each successive three-hour interval after intake (figure 2). The three-hour integration period was chosen after an investigation into a range of interval lengths showed that this interval gave the best balance between minimising the degree of scatter about the clearance trend whilst retaining the maximum number of data points.

Mathematical functions were then fitted to the summed IETD clearance fractions to describe the trend of the data. To do this the "average" summed clearance fraction for each three hour interval and its uncertainty were defined as the geometric mean and the geometric standard error on the mean respectively of the summed clearance fractions for that three-hour interval (figure 3). The geometric mean and geometric standard error on the mean were used, rather than the normal mean and standard error on the mean, because the summed clearance fraction values within any specific three hour interval exhibit a distribution closer to that of a log-normal than a normal distribution.

The trend of the geometric mean nose blow clearance fractions with time after intake was investigated using the data-fitting program GIGAFIT (Birchall et. al., 1995). The midpoint of each three-hour interval was defined as the clearance time of the geometric mean summed clearance fraction for that interval.

It was found that, when considering nose blow samples taken up to forty-eight hours after intake, the trend was best described by the sum of two exponential functions (figure 3):

$$N_{V3,48}(t) = 0.146e^{-0.427t} + 0.062e^{-0.097t} \quad (1)$$

where $N_{V3,48}$ is the fitted estimate of the summed voluntary nose blow clearance fraction for a three hour interval with a midpoint at time t in hours after intake, fitted using nose blow data collected in the forty-eight hours after intake.

However for special occupational monitoring, nose blows collected soon after intake, e.g. within twenty-four hours, will be of most interest. Over this shorter period the trend in nose blow clearance fractions is well described by a single exponential (figure 4).

$$N_{V3,24}(t) = 0.121e^{-0.134t} \quad (2)$$

where $N_{V3,24}(t)$ is the estimate of the summed voluntary nose blow clearance fraction for a three hour interval with a midpoint at time t in hours after intake, fitted using nose blow sample data collected for up to twenty four hours after intake. The clearance rate of 0.134 h^{-1} indicates that, on average, nose blow activities (corrected for radioactive decay) will halve every 5.2 hours. If this trend is typical, then IETD can be estimated from an individual's voluntary nose blow activities as:

$$IETD_{V3,24}(Bq) = 8.27 \times A_{V3,24}(t) \times e^{0.134t} \quad (3)$$

where $A_{V3,24}(t)$ is the sum of voluntary nose blow activities taken over a three hour period with a midpoint of time t. With some knowledge of the physico-chemical properties of the inhaled aerosol and the conditions under which the inhalation occurred, it should therefore be possible to estimate the order of magnitude of the aerosol intake.

3 PRELIMINARY INVESTIGATIONS INTO NOSE BLOW SAMPLING ON DEMAND

The use of nose blow sampling as a semi-quantitative monitoring method following a suspected inhalation incident would require samples to be provided soon after the exposure and then, ideally, at regular intervals during the following twenty-four hours. Therefore, a pilot study was set up to investigate if nose blow samples given on demand could give estimates of intakes similar in accuracy to those determined from voluntary nose blow samples.

Experiment 1 of the pilot study investigated whether nose blows produced on demand provide useful information on the magnitude of the intake. Two participants A and B, who had previously participated in the nasal deposition and clearance study, took part in Experiment 1. In the earlier study, A had exhibited below average nose blow clearance and B above average nose blow clearance (Table 1). For this experiment they inhaled an aerosol of monodisperse 6-µm d_{ae} ^{99m}Tc-labeled insoluble polystyrene particles whilst performing light exercise, using the inhalation protocol developed for the nasal clearance volunteer study (Smith et al. 2011). The administration conditions were

chosen so that the participants received an IETD of about 1 kBq, whilst minimising deposition in the lung. The IETD activity was determined by body measurements of the head and stomach made with an array of six 150mm diameter NaI(Tl) detectors in a steel room. These measurements were performed within half an hour of the aerosol being inhaled. The participants then produced nose blow samples on demand at set times after the intake for a period of approximately twenty-four hours (Table 2). They collected the nose blows on standard tissues, which they bagged and logged in the same way as in the nasal deposition and clearance study. They also collected, bagged and logged any additional spontaneous nose blows they produced. The nose blow sample activities were again measured using the UKAS-accredited gamma-ray spectrometry system, and the sample activities were decay-corrected to the time of intake. In total, participants A and B respectively cleared 0.09 and 0.17 IETD by on-demand nose blow sampling.

TABLE 2: Deliberate nose blow sampling regime with typical sampling times for an inhalation at 14:00 hours

Sample number	Sample collection time after administration	Actual time of sample[a]
1	1 hour	*15: 02*
2	2 hours	*15:58*
3	4 hours	*18:05*
4	6 hours	*20:00*
5	8 hours	*22:02*
6	10 hours	*N/A*[b]
Time to bed:	*23:15*	
7	On getting up (OGU)	*7:15*
8	OGU + 2 h	*9:17*
9	OGU + 4 h	*11:13*
10	OGU + 6 h	*13: 15*

a. Representative times typical of experiments 1,2 and 3

b. No nose blow as participant asleep

Sample activities, expressed as fractions of IETD, were then summed for each three-hour interval after intake and plotted against time after intake (figure 5). Time-dependent single exponential functions were fitted to the summed nose blow clearance fractions for each participant using GIGAFIT. It is thought that mucociliary clearance may stop or slow significantly during sleep (Bateman, 1978), and so it is useful to consider the nasal clearance fractions produced between administration and sleep. Aerosol administrations normally took place around mid-day and so samples were usually provided for about twelve hours before sleep. Exponential fits were therefore obtained both for the complete monitoring period and for the first twelve hours after intake (Table 3, Figure 6).

TABLE 3: Exponential functions fitted to nose blow clearance on demand

	Fitted exponential parameters					
	All data (~24 hours)			Data from first 12 hours after intake		
Participant	$N_{V3,24}(t=0)$ IETD	Clearance rate, λ h^{-1}	Clearance half-time, h	$N_{V3,12}(t=0)$ IETD	Clearance rate, λ h^{-1}	Clearance half-time, h
A	1.3%	0.075	9.2	0.6%	-0.047[a]	-14.9[a]
B	4.1%	0.087	7.9	10.1%	0.28	2.5

a. The negative clearance rate and half-time are artefacts caused by the activity of the nose blow provided by A at 10 hours after intake being greater than those of the previously produced nose blows.

The summed clearance fractions of the deliberate nose blows have a wide degree of scatter. The parameter values of exponential functions fitted to the two participants' full nose blow sample data sets (twenty four hour fit) and twelve hour data sets (twelve hour fit) are shown in Table 3 and figure 6. The participants' twenty four hour fits are similar, with a y-axis intercept of a few percent of IETD and a clearance half-time of 8 to 9 hours. However, this apparent similarity rests on Participant A's final nose blow sample, collected 25.5 hours after intake. If that data point is excluded, the fit to A's data changes from

$$0.013 \times e^{\left(\frac{ln(2)t}{-9.2}\right)} \quad \text{to} \quad 0.0037 \times e^{\left(\frac{ln(2)t}{+5.9}\right)}$$

implying that nose blow activities increase with time after intake. Similarly, the participants' twelve hour fits have dissimilar parameters. Thus, the trend of the nose blow clearance fractions measured from deliberate nose blow samples is weak and highly variable, depending on how long sampling continues after intake.

The findings of the nasal deposition and clearance study and these pilot trials were discussed informally with colleagues from industrial Approved Dosimetry Services (ADS). The nuclear industry has in excess of 50 years' experience of using nose blow sampling as both a routine and a special monitoring procedure for assessing occupational exposures. The consensus view of the ADS was that deliberate nose blow samples taken after such incidents did not give a reliable indication of intake. These observations came from practical experience of comparing nose blow sample activities with intakes assessed by other means. This observation agrees with a study by the Atomic Energy Research Establishments in the 1960s which found that the ratio of nose blow activity to faecal activity following an intake of an insoluble material varied by a factor of four hundred (Lister, 1968). A more recent study conducted at Dounreay gave very similar results (Spencer et al. 2007).

The difference in the results obtained from voluntary and deliberate nose blows shows that there must be a fundamental difference between these clearance methods. Participants stated that they experienced discomfort when attempting to provide repeated deliberate nose blow samples with little or no mucus present to act as a lubricant. As most voluntary nose blows are stimulated by a sensation of excess mucus in the nose, it was considered that this might be the main cause of the differences between the clearance efficiency of voluntary and deliberate nose blows. Methods of stimulating nasal mucus production were therefore investigated.

4 METHODS FOR STIMULATING MUCUS PRODUCTION

Non-toxic, non-hazardous, non-invasive methods of stimulating mucus production were investigated by measuring the mass of mucus that was cleared by a deliberate nose blow after various stimuli had been applied. The mucus masses cleared were compared with masses cleared by voluntary nose blows and by non-stimulated deliberate nose blows. Each participant provided a non-stimulated deliberate nose blow at the beginning of the mucus stimulation tests. This gave information on mucus masses cleared by non-stimulated nose blows and ensured that the second nose blow, taken at a set time after use of the test stimulant, gave an accurate measurement of mass of mucus produced as a result of using the stimulant. The mass of mucus cleared by a nose blow was determined by measuring the increase in weight of the tissue used. A standard type of tissue was used which was bagged, uniquely labelled and then weighed on a high precision balance before the experiments. The participant used the stimulant, produced the nose blow and replaced the used tissue in its bag. The bagged tissue was then re-weighed on the precision balance and the mass of the cleared mucus determined. To ensure that tissue masses were not affected by material picked up from the participants' hands, control measurements were made in which unused weighed tissues were removed from the bag, unfolded, handled, refolded, replaced in its bag and re-weighed. A mass gain of 0.006 grams was measured by this test, an order of magnitude less than the lowest mucus masses measured from any of the nose blow samples.

The tests (figure 7) showed that voluntary nose blows cleared the largest amounts of mucus, although the masses varied by more than an order of magnitude (0.07 grams to 1.2 grams). This arises because people are usually prompted to blow their nose by the weight of the mucus pressing on nasal hairs or causing sensation in the skin that lines the anterior of the nose. Mucus will typically have accumulated over many hours, or been produced in response to stronger stimuli than those used in this study. The non-stimulated on-demand nose blows provided at the beginning of the mucus stimulation tests produced mucus masses similar to the lower end of the mass range for voluntary nose blows (0.01 grams to 0.1 grams).

Nose blows given after inhaling a nebulised water aerosol for five minutes, using a CirrusTM nebuliser and aerosol mask from Intersurgical Complete Respiratory Systems, Wokingham, UK, yielded the lowest masses of mucus, (0.026 grams to 0.032 grams). This method was unsuccessful in either stimulating mucus production, or in depositing water in the nose that could aid clearance, because the nebuliser produced droplets in a size range that preferentially deposit in the lungs rather than in the nose. (This was demonstrated when eucalyptus oil was added to the distilled water in the nebuliser; while inhaling the aerosol the participants were only mildly aware of the odour of eucalyptus, but clearly felt its dilating action in the upper chest as it deposited in the lungs.) Nebulised water might be made more effective for stimulating nasal mucus production by changing the size characteristics of the nebulised particles. Two practical disadvantages of this method are that the nebuliser has to be powered by a compressed air supply, and that the subject must inhale the aerosol for several minutes.

Nose blows given after inhaling steam for five minutes yielded mucus masses between 0.037 grams and 0.18 grams, similar to the lower end of the voluntary nose blow mass range. The steam inhalation nose blows gave the largest degree of variation in cleared mass of all the stimulation methods investigated. For these trials the subjects inhaled the steam by breathing the air immediately above a bowl of hot water (80-90 C) with their head under a cowling. While acceptable for a small-scale trial, this would not be a practical or safe method to use in an occupational setting.

The other two methods of mucus stimulation that were investigated used a commercially available decongestant nasal spray (Vicks Sinex Decongestant Nasal Spray: Oxymetazoline, Proctor and Gamble, Weybridge, UK) and a decongestant herbal oil inhaler (Olbas® Inhaler, G. R. Lane Health Products Ltd., Gloucester, UK under licence from PO-HO-CO, Basle, Switzerland). These were each sprayed or inhaled into each nostril two or three times, two minutes before the nose blow sample was taken. Both methods have the advantage of being a quick and simple procedure requiring only the use of a small, portable container. Extended tests were therefore conducted with these two methods of nasal mucus stimulation, during which the participants provided several nose blows on demand over a period of a day. The nose blows taken after using the nasal spray yielded between 0.13 and 0.2 grams of mucus. The nose blows taken after using the herbal inhaler yielded between 0.06 and 0.08 grams of mucus. Both methods showed consistency in the mucus masses cleared during a series of deliberate nose blows, with the use of the nasal spray causing the clearance of larger amounts. However, the mass of decongestant spray dispensed from the bottle into the nose was variable, depending on how it was administered. The participants also found its action somewhat aggressive, causing irritation in the throat after repeated use. The herbal oil-based inhaler was therefore chosen as the stimulant that would be used in the first stimulated nose blow clearance experiment.

5 NOSE BLOW SAMPLING ON DEMAND WITH MUCUS STIMULATION

Experiments 2 and 3 investigated whether nose blow samples produced on demand after stimulating mucus production do give nose blow clearance fractions that can be used to determine the magnitude of the IETD.

In Experiment 2, the herbal oil inhaler was used to stimulate mucus production. Participants A and B inhaled a monodisperse, 3-µm d_{ae}, ^{99m}Tc-labeled insoluble polystyrene aerosol under controlled conditions so that approximately 1 kBq of the labelled aerosol initially deposited in the nasal passage, using the same experimental regime as in Experiment 1. The change in aerosol particle size from Experiment 1 was due to technical considerations, but given the absence of particle size dependent behaviour seen in the voluntary nose blow data (Smith et al. 2011), this is not expected to have had any influence on clearance. As in Experiment 1, the IETD activity was determined by making body measurements soon after the aerosol was inhaled. The participants then produced nose blow samples on demand according to the same schedule as in Experiment 1 (Table 2), but on this occasion inhaled from the herbal oil

inhaler three or four times in each nostril two minutes before providing each nose blow. The same methods were used to obtain nose blow samples as in Experiment 1, with the small modification that the participants were provided with pre-weighed, bagged and uniquely labelled tissues that were re-weighed after use to measure the cleared mucus masses. Sample activities were determined as in Experiment 1 (section 3).

As a special monitoring method, mucus stimulation would have to result in the production of representative nose blow samples from all members of a work force, including those who naturally exhibit either high or low nasal clearance by nose blow. This was tested in Experiment 3 as a result of the participation of Participant C, who had exhibited exceptionally low natural nasal clearance by nose blow in the nasal deposition and clearance study. Participant C stimulated mucus production by sucking highly concentrated peppermint lozenges (Trebor extra strong mints, Trebor Bassett Ltd, Birmingham, UK.), as peppermint is one of the few substances that Participant C was aware could stimulate his nasal tissues, usually to sneeze. Participant A also took part in Experiment 3, as he had in Experiments 1 and 2. Other than the change in stimulant, Experiment 3 used exactly the same procedures as Experiment 2.

TABLE 4: Exponential functions fitted to stimulated nose blow clearance on demand

Experiment	Stimulant	Participant	Fitted exponential parameters					
			All data (~24 hours)			Data from first 12 hours after intake		
			$N_{S3,24}(0)$ IETD	λ, h-1	half-time, h	$N_{S3,12}(0)$ IETD	λ, h-1	half-time, h
2	1[a]	A	9.3%	0.233	3.0	19.3%	0.380	1.8
		B	18.8%	0.172	4.0	27.4%	0.287	2.4
3	2[b]	A	7.2%	0.101	6.8	29.7%	0.457	1.5
		C	18.9%	0.122	5.7	25.0%	0.495	1.4
Fit to geometric mean values of nose blow clearance fractions			7.0%	0.145	4.8	23.9%	0.392	1.8
Geometric mean of 15 to 24 h samples			119.3%	0.274	2.5	N/A	N/A	N/A

a. Olbas oil inhaler

b. Trebor extra strong mints

The stimulated nose blow data from the two experiments are shown in figure 8. Exponential functions were fitted to nose blow clearance fractions for each participant in each experiment for the complete monitoring period and for the first twelve hours of data (Table 4). Unlike the non-stimulated deliberate nose blows, the stimulated nose blow clearance fractions do show trends that are similar for both experiments and all three participants for both 12 hours and 24 hours of sampling (figure 8). The geometric mean values and geometric standard deviations for each three hour interval were calculated from the four data sets (figure 9) and an exponential function fitted to these values for the complete monitoring period (figure 8). The pattern of the geometric means

suggested that there might be a discontinuity in clearance between the day of intake, day 1, and the day after intake, day 2. Therefore, the data was also fitted using two independent single exponential functions one for nose blow clearance on day 1, the second for day 2 clearance (figure 9). This will be discussed in section 6.

The mucus masses measured from the nose blows taken in experiments 2 and 3 showed that using the stimulants caused the mucus masses cleared by an individual to be reasonably consistent (figure 10). The exception for participants A and B were the nose blows they produced on waking (morning nose blow) which cleared mucus masses greater than their other stimulated nose blows but similar to masses they had cleared in voluntary morning nose blows. Both Participants A and B report that they naturally tend to blow their nose on getting up. Participant C, consistent with his naturally low nasal clearance by nose blow, reports that he does not tend to give a morning nose blow, and the mass of his morning nose blow, 0.09 g, is similar to that of his other stimulated nose blows.

Participant B in Experiment 2 produced the only spontaneous nose blows of the study, which had masses slightly greater than his stimulated nose blows.

Participant C provided three non-stimulated nose blows on demand which cleared an average of 0.015g, significantly less than the average mass of 0.07g cleared by both participants A and C in their peppermint stimulated nose blows. Therefore, both stimulants have been shown to increase the mucus mass cleared by the participants when giving nose blows on demand.

TABLE 5: Comparison of IETD fractions cleared by stimulated and non-stimulated nose blows

Participant	Experiment	IETD cleared by first nose blow[a]	IETD cleared by second nose blow[b]	Total IETD collected from all nose blows	Total number of summed nose blow periods	Total sample collection period, h
A	1: non-stimulated	0.015	0.0028	0.09	6	27
	2: stimulated	0.180	0.0153	0.22	5	18
	3: stimulated	0.234	0.0155	0.29	6	18
B	1: non-stimulated	0.073	0.0304	0.17	7	24
	2: stimulated	0.228	0.0458	0.35	6	24
C	3: stimulated	0.077	0.0636	0.16	5	21

a. Collected on average 1.5 h after intake including any clearance by voluntary nose blowing between 0 and 3 hours after intake.

b. Collected on average4.5 h after intake including any clearance by voluntary nose blowing between 3 and 6 hours after intake.

Table 5 compares the IETD fractions cleared by the first, second and all nose blow samples for the non-stimulated and stimulated on-demand nose blow experiments. Participants A and B cleared at least twice the total fraction of IETD by stimulated nose blowing in experiments 2 and 3 compared with the amount cleared by non-stimulated nose blowing in experiment 1, collected over a similar or shorter time period by the same number or fewer samples. Stimulating mucus production increased the IETD

fractions of the first nose blow samples by an order of magnitude for Participant A in both experiment 2 and 3, and by a factor of three for Participant B. While the effect on the second nose blow sample was not as consistent, the activities cleared in the first two nose blow samples exceeded 0.78 of the total fractions cleared by all nose blows in all four tests of stimulated nose blowing, as opposed to 0.20 for Participant A and 0.61 for Participant B in experiment 1. This indicates that stimulating mucus production before nose blow collection increases both sample clearance fractions and consistency of results.

While Participant C only cleared a total of 0.08 IETD by stimulated nose blowing in experiment 3, it should be noted that this subject only cleared a total of 0.005 IETD by voluntary nose blowing in each of the two experiments in which the subject participated in the nasal clearance study (Smith et al. 2011).

The relationship between the IETD fraction and the mucus mass cleared by each stimulated on-demand nose blow was investigated. Other than the need for there to be sufficient mucus present to make the IETD fraction cleared representative of the activity present in the nose, no correlation was found between the two quantities. The IETD fraction cleared by a nose blow was far more dependent on nose blow order (1st nose blow after intake, 2nd nose blow after intake etc.) and/or time after intake. Therefore, when collecting nose blows for screening for intakes, subjects should be asked if they have already blown their nose since the time of the possible intake.

6 THE TIME DEPENDENCE OF STIMULATED DEMAND NOSE BLOW ACTIVITIES

The experimental results show that, when mucus production is stimulated, nose blows given on demand do result in the clearance of activities that follow a trend similar to that of voluntary nose blowing. As discussed in section 5, the time dependence of the summed stimulated nose blow clearance fractions, $N_{S3}(t)$, can either be described by a single exponential function (equation 4) representing the overall trend over the 24 hours following the intake (figure 8), or by separate exponential functions (equations 5 and 6) representing the discontinuous trend on days 1 and 2 of the study (figure 9):

$$\boldsymbol{N_{S3,24}(t) = 0.25 \times e^{-0.25t}} \quad (4)$$

$$\boldsymbol{N_{S3,d1}(t) = 0.34 \times e^{-0.38t}} \quad (5)$$

and

$$\boldsymbol{N_{S3,d2}(t) = 2.9 \times e^{-0.3t}} \quad (6)$$

The discontinuous nose blow trend is considered, despite being based on only four sets of data, because lung mucociliary clearance is known to slow, or possibly stop, in sleep (Bateman, 1978). Nasal ciliary clearance is thought to behave in a similar manner. Reduced nasal clearance in sleep is supported by the larger masses of mucus cleared by morning nose blows (figure 10), which may result from the clearance of mucus

accumulated during sleep. The stimulated nose blow regime of repeated nose blows does increase the nasal clearance rate in waking hours, reducing the clearance half-time for voluntary nose blows from 3 hours to 1.8 hours on day 1 (figures 4 and 9), and so would increase any discontinuity with a slower clearance rate during sleep.

This effect may cause the day 2 trend (equation 6) to vary with the time between intake and sleep on day 1 and with the duration of sleep. For this study, and the nasal deposition and clearance study, intakes took place at similar times of day (between 11a.m. and 3 p.m.) and so little information was gained on this potential effect.

7 A PROPOSED METHOD FOR ESTIMATING INTAKES AND DOSES FROM STIMULATED ON-DEMAND NOSE BLOW SAMPLES

The pilot study has shown that it should be possible to assess the magnitude of inhaled intakes from the activities of stimulated on-demand nose blow samples. The accuracy of such assessments will determine their potential usefulness as a special monitoring method for investigating suspected inhalation incidents. Therefore, the probable accuracy with which intakes can be assessed from nose blow activities was investigated in a desktop study that used the pilot study results and a provisional nose blow sampling and assessment regime for special monitoring. A note of caution is required about this assessment of accuracy. It makes use of data sets from only four experiments, which were also used to derive the formulae that are used to predict the initial nasal deposit, and so a comparison is being made between predicted and measured quantities that are not independent. This method represents a starting point which can be tested and refined as more stimulated demand nose blow data become available.

7.1 Proposed assessment methodology

The stimulated “on-demand” nose blow clearance trend for day 1 (equation 5) was used for this exercise. However, it should be noted that use of the 24 hours clearance trend (equation 4) would have been equally valid. As this assessment is based on results for the clearance by nose blow of insoluble particles, only intakes of insoluble particles will be considered. Further research is required to assess the possibility of estimating intakes from nose blow sampling of more soluble particles.

7.1.1 Step 1: Collection of stimulated “on-demand” nose blows

Potentially exposed staff will be asked to provide stimulated nose blows at set times after a suspected intake. In this example, where intake is assessed using a trend based three hour sampling periods, nose blow samples should be collected at three hour intervals, ideally at 90 minutes, 4½ hours and 7½ after intake. If the possibility of an intake is identified at a later time, e.g. at the end of the shift, the first nose blow should be collected as soon as possible and the subsequent samples at three hour intervals.

As the fraction of nasal deposition cleared by nose blowing decreases with a half-time of 2 to 3 hours (equations 5 and 4) the time of the intake should be identified as precisely as possible to minimise this source of uncertainty in estimating intake and dose. The mid-point of the possible period of intake may be used as the time of intake for this assessment. A decision may be made not to collect later nose blow samples if the initial nose blow samples and other indicators show no evidence of an intake.

Whenever possible, sample activities will be measured using gamma-ray spectrometry, identifying the gamma-ray emitting radionuclides present and their activities decay-corrected to the time of intake. Subjects should be provided with tissues, plastic bags and labels so that any voluntary nose blows they produce can also be collected, recorded, and measured. The decay-corrected activities of these samples should be added to that of the stimulated "on-demand" nose blow produced in the same three hour period.

7.1.2 Step 2: Estimating initial nasal deposition

The initial activity deposited in the nose may be calculated using the inverse of the "day 1" trend for stimulated "on-demand" nose blow activities given by equation 5:

$$EIND = \sum_{n} \frac{1}{a(t)} \times \sum_{n} \frac{A(t) \times e^{0.38\,t} \times a(t)}{0.34} \pm \left(\mathrm{EIND} \times \sqrt{\frac{1}{\mathrm{n}} \times \sum_{\mathrm{n}} \left(\frac{\mathrm{a(t)}}{\mathrm{A(t)}} \right)^2} \right) \quad (7)$$

where "n" is the number of nose blow samples collected from the subject on the day of intake, t are the sample collection times after intake in hours, A(t) are the decay-corrected activities of the samples, a(t) are the measurement uncertainties of the decay corrected activities, and EIND is the estimate of initial nasal deposition. Using measurement uncertainties to weight equation 7 causes the calculated EIND value to be most influenced by the measurements that have the smallest relative uncertainties.

If multiple radionuclides are measured, EIND needs to be assessed for each. If other information is available on the relative abundances of radionuclides in the material that was inhaled, either from a prior assessment of the material or from measurements of surface contamination in the area where the suspected intake event occurred, it would be useful to compare those values with the radionuclides' relative EIND values. If radionuclides are measured on the nose blow samples but a radiologically significant radionuclide known to be present is not detected, or only measured with a large uncertainty, then it may be preferable to estimate its EIND or its intake (see next step) from its known ratio to the measurable radionuclides (e.g. assessing plutonium from its known ratio to americium). However, it should be noted that the nature of the event that gave rise to the intake may have changed the relative abundance of the radionuclides in the inhaled material.

7.1.3 Step 3: Determining intake from initial nasal deposition

Intake (I) (the activity in Bq of aerosol inhaled into the respiratory tract) for each measured radionuclide may be determined by dividing its EIND activity by D_n, the fraction of intake that deposits in the nasal passage:

$$I_j\ (Bq) = \frac{EIND_j}{D_n} \qquad (8)$$

where j is the j^{th} radionuclide of a total of i radionuclides detected and measured on the nose blow sample.

The value of D_n varies with the physiology of the subject's nasal passage, the particle size distribution of the aerosol and the subject's breathing parameters. The first of these is undoubtedly a significant source of inter- and intra-subject variation but, as its effect is difficult to assess (Smith et al. 2011), D_n cannot be adjusted for its influence. The principal aerosol parameters used in the HRTM that affect deposition are the median particle size, defined as either the Activity Median Thermodynamic Diameter (AMTD) or the Activity Median Aerodynamic Diameter (AMAD), and the geometric standard deviation (σ_g) of the particle size distribution. Particle density (ρ) and shape factor also influence deposition to a lesser degree. Breathing parameters can be reasonably approximated by categorising the subject's exercise level as one of the ICRP Human Respiratory Tract Model (HRTM) (ICRP, 1994) default exercise or work rates (Table 6: footnotes b-f). In most cases it will be appropriate to assume the subject is performing "light work". Only if it is specifically known what task the subject was doing at the time of intake should a default exercise rate be used, rather than a more general work rate. The nasal deposition fraction is also strongly affected by whether the subject is nose or mouth breathing. Figure 11 shows how the value of D_n varies as a function of AMTD and AMAD for both nose and mouth breathing for "light work", calculated using the ICRP HRTM as implemented by the IMBA software package (Birchall et al. 2007). The ICRP aerosol default parameter values of $\sigma_g = 1+1.5[1-(100\text{xAMTD}^{1.5})^{-1}]$ (ICRP 1994, equation 16), ρ = 3 and shape factor = 1.5 were assumed (Table 6: footnote a). The ratio of nasal deposition for mouth breathing compared to nose breathing ranges from 0.27 to 0.49 and has an average value of 0.38 ± 0.08 (1 standard deviation) for "light work" (Figure 12).

Many aerosols may be reasonable approximated by the ICRP default occupational AMAD of 5-μm and σ_g = 2.5 (Table 6: footnote a). Table 6 shows values of D_n for inhalation at the ICRP default exercise and work rates for both nose and mouth breathing. These values can be approximated to D_n (nose breathing) = 0.7 except when doing heavy exercise, D_n (mouth breathing) = 0.25 except when sitting at rest, and 0.4 for mouth breathing while sitting at rest and nose breathing while performing heavy exercise. Note that subjects are mouth breathing if they are talking at the time of the intake. While the ICRP default assumption is that subjects are nose breathing, mouth breathing is the more conservative assumption with respect to estimating intake and dose by nose blow sampling.

TABLE 6: Nasal deposition fractions, D_n, for inhalation of an ICRP default occupational aerosol[a] at default exercise and work rates

Work or exercise rate	Work rate, Watts	Nasal deposition as a fraction of intake, D_n	
		Nose breathing	Mouth breathing
Rest (Sitting)[b]	30	0.62	0.39
Light exercise[c]	80	0.76	0.26
Heavy exercise[d]	160	0.37	0.21
Light worker[e]	64	0.74	0.28
Heavy worker[f]	90	0.67	0.25

a. ICRP default parameters for an occupational aerosol: 5-µm AMAD, 2.5 geometric standard deviation, density 3 g ml^{-1}, shape factor = 1.5.

b. Rest corresponds to sedentary office work done while seated etc. Nose breathing = 100% through nose, Mouth breathing = 70% through nose

c. Light exercise corresponds to working in laboratories and workshops, active house cleaning, painting, woodworking etc. Nose breathing = 100% through nose, Mouth breathing = 40% through nose

d. Heavy exercise corresponds to vigorously active tasks encountered in fire fighting, construction work, farm work etc. and is usually not conducted for periods exceeding 2 hours. Nose breathing = 50% through nose, Mouth breathing =30% through nose

e. Light (or sedentary) work is defined in IMBA (Birchall et al. 2007) as spending 31.25% of an 8 hour shift sitting and 68.75% performing light exercise. Nose breathing = 100% through nose, Mouth breathing = 49% through nose

f. Heavy work is defined in IMBA as spending 87.5% of an 8 hour shift performing light exercise and 12.5% performing heavy exercise. Nose breathing = 94% through nose, Mouth breathing = 39% through nose

If the aerosol parameter values are known and use of the ICRP default 5-µm AMAD aerosol is inappropriate, D_n can be calculated using the ICRP HRTM using computer software packages such as IMBA (Birchall et al. 2007). If the subject can be assumed to be 100% nose breathing D_n is equal to total ET deposition as a fraction of intake (deposition in compartments ET_1 and ET_2). For mouth breathing, deposition in ET_2 from aerosol inhaled through the mouth needs to be excluded. Using the approximation that the relative fractions deposited in compartments ET_1 and ET_2 are the same for nose and mouth breathing D_n(mouth breathing) can be assessed as:

$$D_n(mouth\ breathing) = D_{ET1(mouth\ breathing)} \times \left[\left(1 + \frac{D_{ET2(nose\ breathing)}}{D_{ET1(nose\ breathing)}}\right)\right] \quad (9)$$

where D_{ET1}(mouth breathing), D_{ET1}(nose breathing) and D_{ET2}(nose breathing) are the deposition fractions of intake deposited in HRTM compartments ET_1 and ET_2 while mouth breathing and nose breathing respectively.

7.1.4 Step 4: Assessing dose from intake

The committed effective dose from the intake can be calculated by multiplying the intake activities, I_j (Bq) of the measured radionuclides by the committed effective dose coefficient for inhalation for each radionuclide, $e_{j,inhal}(50)$ (Sv Bq^{-1}) and summing the resulting values for all radionuclides:

$$E(50) = \sum_{j=0}^{j=i} e_{j,inhal}(50) \times I_j \quad (10)$$

where E(50) is the committed effective dose received from the intake of all i radionuclides, and i is the number of radionuclides associated with the intake. Note that the above equation evaluates the 50 year committed effective dose for a worker. If the assessment is being made for an intake by a member of the public, 70 year committed effective dose coefficients should be used to assess the 70 year committed effective dose ($e_{j,inhal}$ (70) and E(70) respectively). However, this will only result in a significant difference to the assessed dose if long-lived, long-retained radionuclides have been inhaled.

ICRP provides tabulations of committed effective dose coefficients for inhalation for a wide range of radionuclides for both workers and members of the public (e.g. ICRP Publication 72 (ICRP, 1995) and ICRP CD1 "Database of Dose Coefficients: Workers and Members of the Public" published in support of ICRP Publication 72). While the publications only include values for 1- and 5-µm aerosols, the CD provides values for 10 aerosol sizes ranging from 0.001-µm AMTD to 10-µm AMAD, which will be extended to 11 values, up to 20-µm AMAD, in the CD that will be published to support the appropriate part of the forthcoming ICRP publication "Occupational Intakes of Radionuclides". The CD also includes committed effective dose coefficients for six different ages (3 months to adult) for members of the public. These tabulated coefficients are calculated for the default intake conditions of nasal breathing, "light exercise" for workers, and an equivalent typical exercise rate for members of the public.

Committed effective dose coefficients may also be calculated using software packages that implement the ICRP HRTM if the aerosol properties and intake conditions are known and considered to be significantly different from default conditions. For consistency, these intake parameters should be consistent with those used to calculate the nasal deposition fraction; D_n. Dose coefficients for "Heavy working" are typically a few tens of percent higher than those for "Light working". However, for the insoluble materials being considered here, committed effective dose coefficients for mouth breathing are typically greater than those for nose breathing by a factor of 2 to 3.

7.2 Testing the potential methodology

The methodology described above was tested in a step by step manner. The nose blow sample activities were collected and assessed in the manner described in step 1 in section 7.1.1. To assess the accuracy of the methodology, decay corrected nose blow sample activities were expressed as fractions of the initial extra-thoracic deposition ($IETD_{BM}$) for that experiment determined from high accuracy in vivo gamma-ray spectroscopy measurements of the subject.

7.2.1 Step 2: Estimation of initial nasal deposition

The accuracy with which initial nasal deposition may be estimated from the nose blow sample measurements was tested as follows:

> EIND values were assessed for the four stimulated on-demand nose blow experiments from nose blow sample activities using equation 7. The accuracy of these values was assessed by dividing them by the high accuracy gamma-ray

spectroscopy in vivo measurements of the initial nasal deposition fractions ($IETD_{BM}$) for these studies, ratios of 1 indicating total agreement between the two assessments of initial nasal deposition. The values of EIND as a fraction of $IETD_{BM}$ given in column 2 of Table 7 show all four results are within 30% of the true value (Figure 13). EIND estimates were also made using the 24 hour trend (equation 4), $EIND_{24h}$, which gave values within a factor of two of the $IETD_{BM}$ values. The EIND and $EIND_{24h}$ estimates for the same experiments differed by between 0.3% and 70%. Similar EIND and $EIND_{24h}$ estimates for the same experiment do not indicate a more accurate estimate of IETD.

These results should be treated with caution as the EIND values are a subset of the data from which the nose blow clearance trend was determined, and the number of cases is small for determining a statistical distribution. However, the consistency of the results assessed using the day 1 and 24 h trends suggests that, statistically, 95% of EIND will be within a factor of 3 of the true IETD value. However, more data is needed to confirm this.

7.2.2 Step 3: Assessment of Intake

In equation 8 intake, I, is estimated by dividing EIND by D_n. The value of D_n, the estimate of the fraction of intake that deposits in the nasal passage, will depend on the choice of inhalation conditions (the aerodynamic properties of the inhaled aerosol and the subject's breathing parameters) used when calculating it. In this assessment it is possible to compare the estimates of nasal deposition, D_n, with each experiment's measured nasal deposition fractions, d_n. To evaluate how the choice of inhalation conditions might cause the estimates of intake to vary, intakes were assessed for the stimulated on-demand nose blow experiments using D_n values calculated using the HRTM for three different but reasonable sets of intake parameters.

The three sets of inhalation conditions chosen where:

- Intake specific parameters, the known aerosol and inhalation parameters of the four stimulated on-demand nose blow experiments (aerosol: 3-µm AMAD, 1.2 σ_g, ρ = 1.05, shape factor = 1, inhaled while performing "light exercise").

- ICRP default intake parameters for an occupational exposure (aerosol: 5-µm AMAD, 2.5 σ_g, ρ = 3, shape factor = 1.5, inhaled 100% through the nose while performing "light work").

- ICRP default intake parameters for an occupational exposure while mouth breathing (aerosol: 5-µm AMAD, 2.5 σ_g, ρ = 3, shape factor = 1.5, inhaled ~50% through the nose while performing "light work").

The calculated values of D_n, 0.823, 0.738 and 0.445 respectively for the above inhalation conditions, are given in Table 7, together with the measured nasal deposition fractions (d_n) for the four experiments. The intakes assessed from the EIND and D_n values using equation 8, expressed as percentages of the measured intakes, are also given in table 7 (columns 5-7, rows 3-6).

TABLE 7: Comparison of estimates of intake determined assuming different inhalation conditions

Volunteer and Nasal Stimulant	EIND, fraction of $IETD_{BM}$[a]	Measured deposition, fraction of intake[b]		Estimates of intakes as % measured intake, for the specified intake conditions[c]		
		Nasal, d_n	Lung, d_L	Study intake parameters[d]	ICRP default intake: nose breathing[e]	ICRP default intake: mouth breathing[f]
A, Olbus oil	0.83 ± 0.12	0.382	0.306	38.4%	42.8%	70.9%
B, Olbus Oil	1.29 ± 0.08	0.340	0.450	53.4%	59.5%	98.7%
A, Peppermint	1.07 ± 0.08	0.582	0.383	75.7%	84.5%	139.9%
C, Peppermint	0.71 ± 0.05	0.561	0.351	48.5%	54.2%	89.7%
Average	0.98 ± 0.10	0.466	0.373	54.0%	60.2%	99.8%
Deposition as fractions of intake, calculated using HRTM for specified intake conditions[g]						
Calculated nasal deposition fractions, D_n				0.823	0.738	0.445
Calculated lung deposition fractions, D_L				0.126	0.082	0.261

a. EIND, the initial nasal deposition estimates derived from nose blow measurements using equation 7 (section 7.2.1), expressed as a fraction of $IETD_{BM}$, the initial nasal deposition determined by body measurement.

b. Measured nose and lung deposition as fractions of intake (d_n and d_L), determined from body measurements and measurements of the activity deposited on the subject's face mask and the exhalation filter.

c. Estimated intake calculated by dividing EIND expressed as a fraction of the measured intake (column 2 multiplied by column 3) by the calculated nasal deposition fraction (D_n, row 8) determined for the intake conditions specified for the column (see footnotes d-f) using HRTM. Note: use of the above truncated values will cause rounding errors.

d. Intake estimated using nasal deposition fraction (D_n, row 8) calculated using HRTM and the intake parameters of the stimulated on-demand nose blow experiments (3-µm AMAD, σ_g = 1.2, ρ = 1.05, shape factor = 1, aerosol inhaled 100% through the nose while performing "light exercise").

e. Intake estimated using nasal deposition fraction (D_n, row 8) calculated using HRTM and the ICRP default intake parameters for workers, (5-µm AMAD, σ_g = 2.5, ρ = 3, shape factor = 1.5 aerosol inhaled 100% through the nose while performing "light work").

f. Intake estimated using nasal deposition fraction (D_n, row 8) calculated using HRTM and the ICRP default intake parameters for mouth breathing workers, (5-µm AMAD, σ_g = 2.5, ρ = 3, shape factor = 1.5 aerosol inhaled ~50% through the nose while performing "light work").

g. Nose and lung deposition as fractions of intake calculated using the ICRP HRTM for the intake conditions specified for each column (see footnotes d, e and f).

The accuracy of the assessment of intake depends on the accuracy of the EIND value and the nasal deposition fraction, D_n (equation 8). The values given in Table 7 show that the values of D_n calculated for the study intake conditions (0.823) and for the ICRP default nose breathing worker (0.738) are both significantly higher than the values derived by direct measurement for the four nose blow experiments (d_n, 0.34 - 0.58), with only the nasal deposition fraction calculated for the ICRP default mouth breathing worker being similar (0.445). Therefore, the intakes estimated using either the study intake conditions or ICRP default nose breathing worker values of D_n give values for intake that are respectively, on average, 50% and 60% that of the true value. The

intakes assessed using the value of D_n predicted for an ICRP default mouth breathing worker are similar to the true values. However, it should be noted that this agreement is partly by chance because of the aerosol size and intake conditions used in the nose blow study. The three sets of intake estimates for the four experiments range from 38% to 140% of the measured intake values.

The low values of the measured ET deposition fractions are consistent with the ET deposition fractions obtained in the nasal clearance study. Both are probably lower than HRTM predictions as a consequence of the subjects wearing tight fitting nasal masks while inhaling. This tends to dilate the nose, decreasing deposition. A similar effect may well occur at work when an individual wears a face mask, eye protection or glasses that presses on the bridge of the nose. As a consequence of nasal deposition being decreased, the measured lung depositions (0.3 - 0.45) are significantly higher than the values predicted using the HRTM, even for mouth breathing (0.08 – 0.26) (Table 7). This is of significance in the next step, the assessment of dose.

7.2.3 Step 4: Assessment and comparison of committed effective doses assessed for a unit intake of americium-241

For this part of the methodology it has been assumed that the nose blow samples were taken following a unit intake of Type S americium-241 as this is of more relevance to nose blow sampling in the work-place than the intakes of insoluble ^{99m}Tc and ^{111}In labelled particles used in the study. However, the other properties of study aerosol particles (geometric distribution, density etc.) were maintained to enable direct comparison of experimental and assessed values.

Experiment-specific committed effective dose coefficients for ^{241}Am were calculated using the IMBA software package (Birchall et al. 2007) for the four experiments using each experiment's measured nasal and lung deposition fractions. Dose coefficients calculated were also calculated for unit intakes of ^{241}Am for the three sets of inhalation conditions given in section 7.2.2 The values of the experiment-specific dose coefficients (column 2, rows 3-6) and the dose coefficients for three sets of inhalation conditions (columns 3-5, row 9) are given in Table 8. Note that the experiment-specific dose coefficients are between 1.4 to 5.6 times greater the value of the dose coefficients for three sets of inhalation conditions, primarily because the lung deposition measured in the experiments was significantly higher than that predicted by the HRTM.

Doses were calculated for each experiment for the three sets of inhalation conditions using the intakes estimated for those inhalation conditions that are given in columns 5-7 of Table 7. These doses are given in columns 3-5 of Table 8 and are expressed as a fraction of the true dose received from the intake in columns 6-8 of Table 8, the true dose being the experiment-specific committed effective dose coefficient for ^{241}Am given in column 2 of Table 8.

In Table 8 the doses that would be assessed for a unit intake of ^{241}Am using the nose blow methodology are compared with the experiment-specific doses assessed using the body measurements of nose and lung deposition fractions. The greater lung deposition fractions cause the experiment specific dose coefficients to be greater than the value predicted for the generic study intake conditions by a factor of three, and from the dose

coefficients predicted for the ICRP default nose and mouth breathing workers by factors of 4.6 and 1.7 respectively. These lower values of the dose coefficients combined with the low estimates of intake means that the dose estimates derived using the nose blow methodology range from 10% to 82% of the true dose. Of these the doses derived for the ICRP default mouth breathing worker are closest to the true value and the most conservative.

TABLE 8: Comparison of dose estimates for different assumed aerosol and inhalation parameter values

Volunteer and Nasal stimulus	Am-241 experiment specific committed effective dose coefficients[a]	Dose calculated for the column's specified intake conditions for the respective estimate of intake in Table 7[b] Sv Bq^{-1}			Doses estimated assuming different intake conditions expressed as percentages of true dose[c]		
	Sv Bq^{-1} true Intake	Study intake parameters[d]	ICRP default intake: nose breathing[e]	ICRP default intake: mouth breathing[f]	Study intake parameters[d]	ICRP default intake: nose breathing[e]	ICRP default intake: mouth breathing[f]
A, Olbus oil	3.26 x10^{-5}	5.14 x 10^{-6}	3.68 x 10^{-6}	1.70 x 10^{-5}	15.8%	11.28%	52.18%
B, Olbus Oil	4.79 x 10^{-5}	7.15 x 10^{-6}	5.12 x 10^{-6}	2.37 x 10^{-5}	14.9%	10.70%	49.46%
A, Peppermint	4.08 x 10^{-5}	1.01 x 10^{-5}	7.26 x 10^{-6}	3.36 x 10^{-5}	24.9%	17.82%	82.40%
C, Peppermint	3.73 x 10^{-5}	6.50 x 10^{-6}	4.66 x 10^{-6}	2.15 x 10^{-5}	17.4%	12.48%	57.70%
Average	3.96 x 10^{-5}	7.23 x 10^{-6}	5.18 x 10^{-6}	2.40 x 10^{-5}	18.3%	13.1%	60.4%
Committed effective dose coefficient for specified intake conditions[g], Sv Bq^{-1}		1.34 x 10^{-5}	8.60 x 10^{-6}	2.40 x 10^{-5}			

a. Am-241 committed effective dose coefficients calculated for each specific experiment for the experimental intake conditions (Footnote d) and the nose and lung deposition fractions determined from body measurements (Table 6, d_n and d_L).

b. The effective Am-241 dose per unit intake for the true intake, assessed as the committed effective dose coefficient for the intake conditions assumed for the column times the assessed intake expressed as a fraction of the true intake (Table 6).

c. The effective Am-241 dose per unit intake assessed for the intake conditions assumed for that column expressed as a fraction of the true dose per unit intake for that experiment.

d. Values calculated using HRTM and the intake parameters of the stimulated on-demand nose blow experiments (3-µm AMAD, σ_g = 1.2, ρ = 1.05, shape factor = 1 aerosol inhaled 100% through the nose while performing "light exercise").

e. Values calculated using HRTM and the ICRP default intake parameters for workers, (5-µm AMAD, σ_g = 2.5, ρ = 3, shape factor = 1.5 aerosol inhaled 100% through the nose while performing "light work").

f. Values calculated using HRTM and the ICRP default intake parameters for mouth breathing workers, (5-µm AMAD, σ_g = 2.5, ρ = 3, shape factor = 1.5 aerosol inhaled ~50% through the nose while performing "light work").

g. Am-241 committed effective dose coefficients calculated using the ICRP HRTM for the intake conditions specified for each column (see footnotes d, e and f).

7.2.4 Conclusions from assessment of methodology

This assessment of the methodology has shown that for the stimulated nose-blow assessments all the estimates of initial nasal deposition were within 50% of their true value, all assessed intakes where within a factor of 3 of their true values and all doses where within a factor of ten of the true value.

Given that the proposed use of the nose blow assessment method is to determine if further bioassay monitoring or other interventions are required, rather than provide a dose for dose records, these results suggest that in most cases it would be advisable to use the ICRP default mouth breathing worker as the default intake as this gives the most conservative assessment of dose.

8 CONCLUSIONS

This study has confirmed that nose blow samples produced on on-demand can be used as a means of estimating the magnitude of an intake by inhalation. When mucus production is stimulated before samples are given, the sample activities show a relationship to the activity deposited in the nose that depends on the time since intake. The trend of nose blow clearance fractions as a fraction of the activity deposited in the nose seems to be independent of particle size or breathing rate. However, particle size and breathing rate do need to be taken into account when determining intake from the estimated nasal deposit. It is preferable to make the conservative but realistic assumptions that subjects will be exercising heavily or talking (and therefore mouth breathing) at the time of intake. The technique has been shown to have the potential to be a quick and simple monitoring method of assessing the magnitude of intakes.

This was a pilot study in which it has only been possible to investigate a limited number of subjects, stimuli, and nose blow collection regimes. While the technique shows promise, further work is required before stimulated deliberate nose blow sampling could be implemented as an effective special monitoring method and as an emergency response rapid screening method for estimating the magnitude of suspected intakes. Methods appropriate for use in the occupational environment and in an emergency response situation need to be developed. The method and accuracy with which initial nasal deposit and intake are estimated need to be investigated further, taking into account such factors as nose/mouth breathing fractions and relative deposition in ET and the lungs for specific aerosols in the working environment.

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11 FIGURES

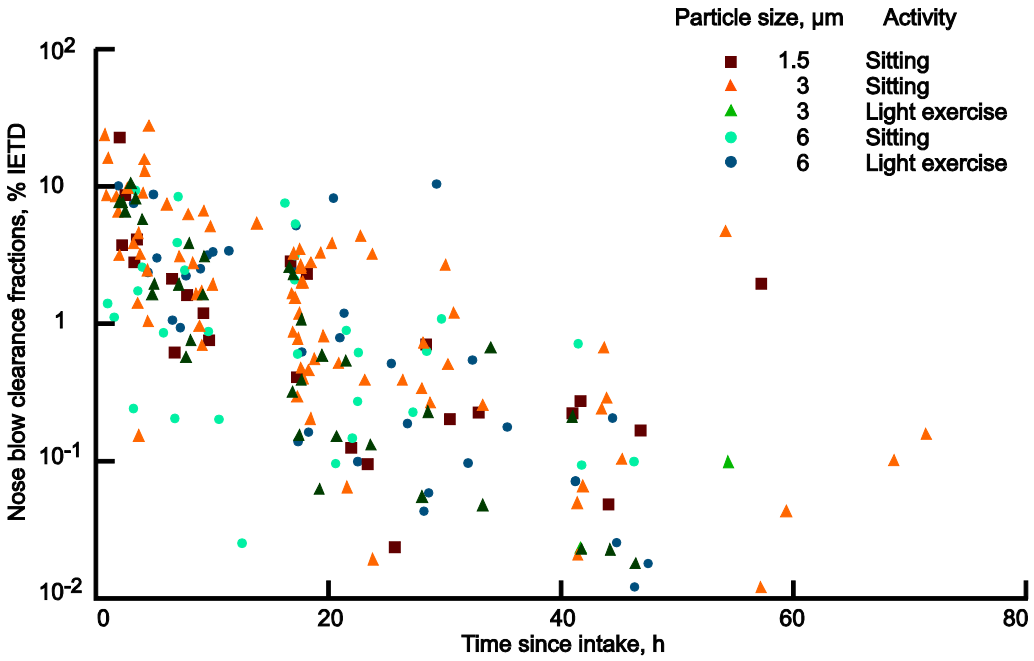

Figure 1: Clearance fractions measured from individual nose blow samples

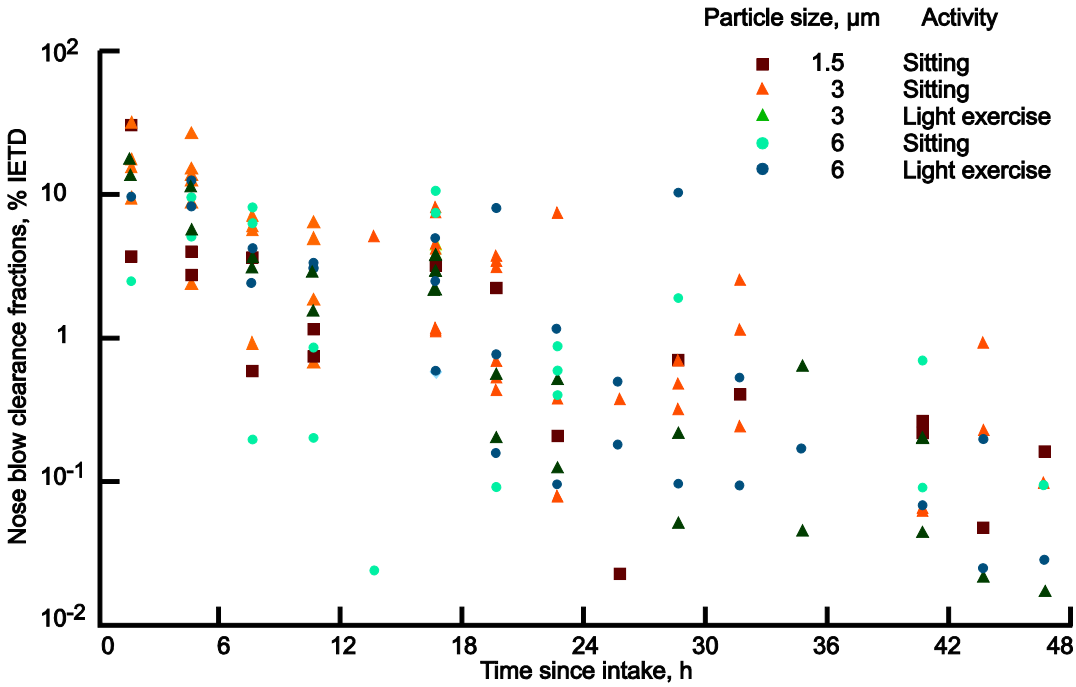

Figure 2: Nose blow clearance fractions summed into three-hour intervals

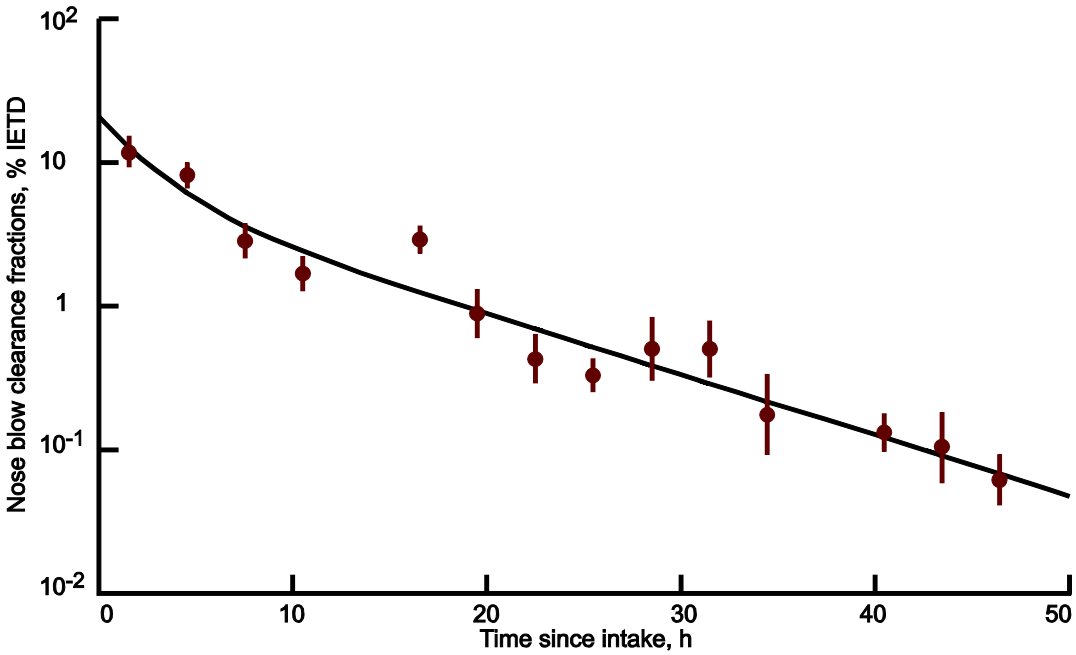

Figure 3: Geometric means and geometric errors of mean of nose blow samples in each three hour interval and fitted function (equation 1)

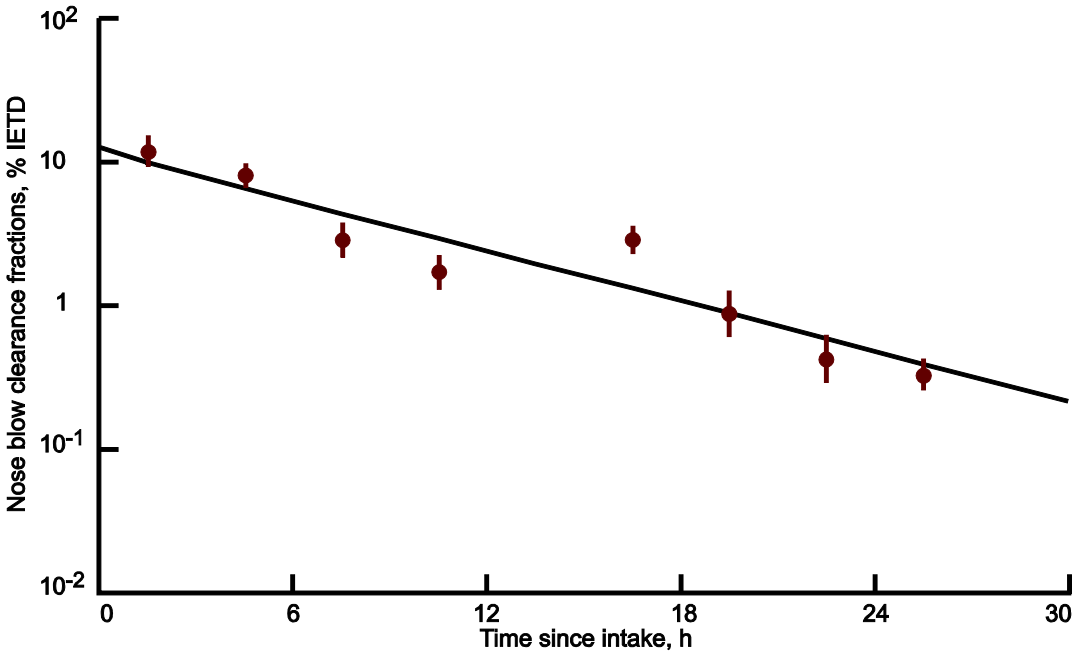

Figure 4: Single exponential function (Equation 2) fitted to three hour interval geometric means for spontaneous nose blow for 24 hours after intake

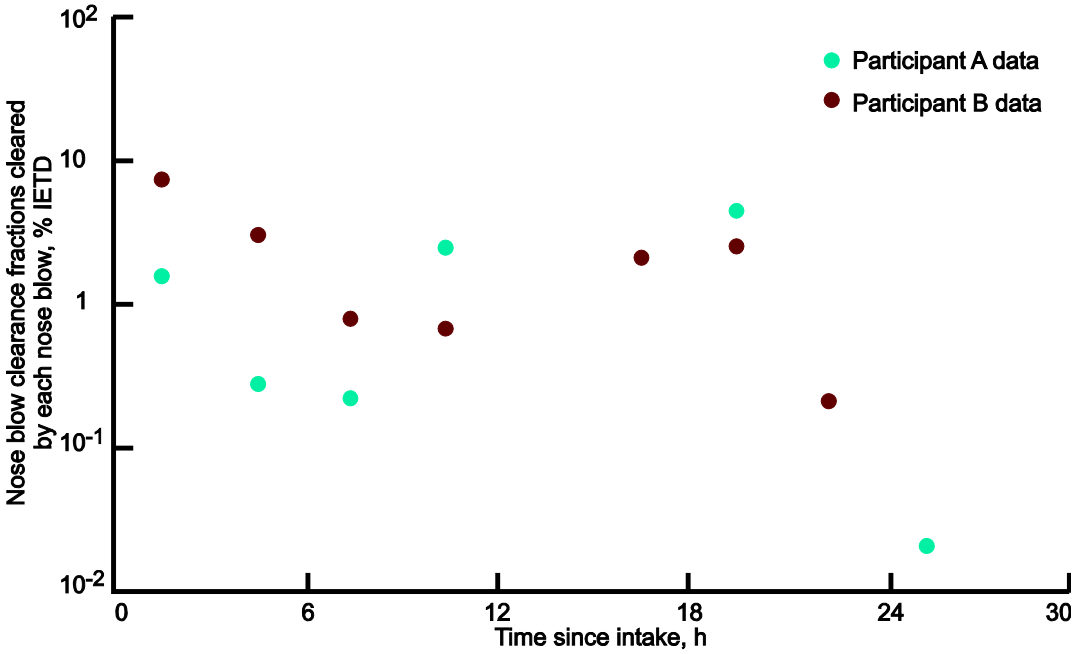

Figure 5: Non-stimulated deliberate nose blow summed into three hour intervals

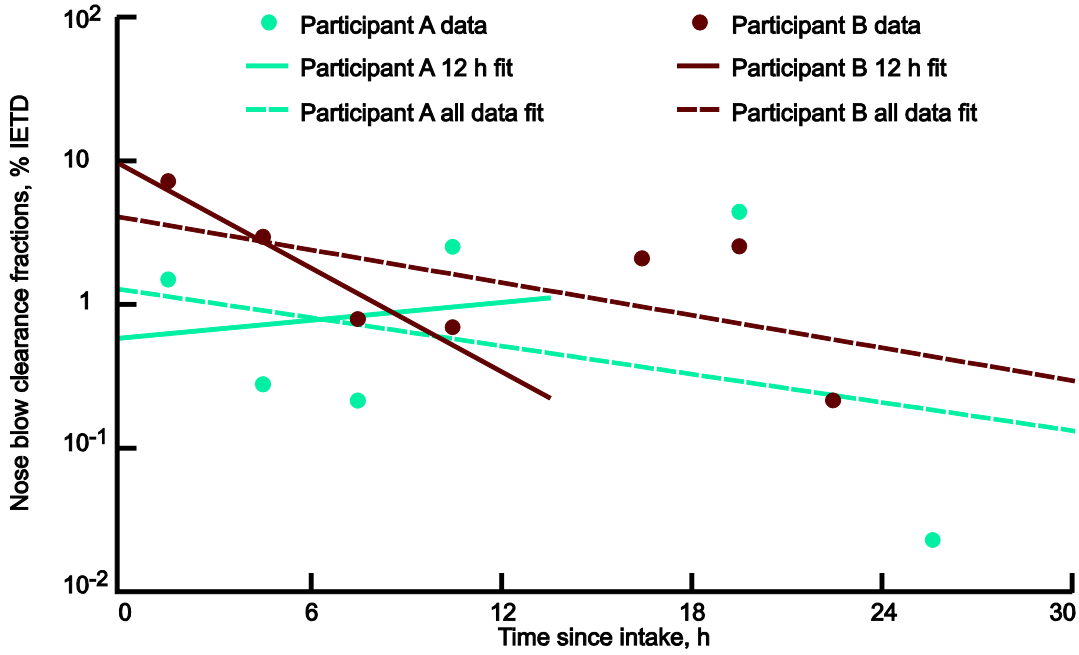

Figure 6: Exponential functions fitted to non-stimulated deliberate nose blows from Participants A and B (Table 4)

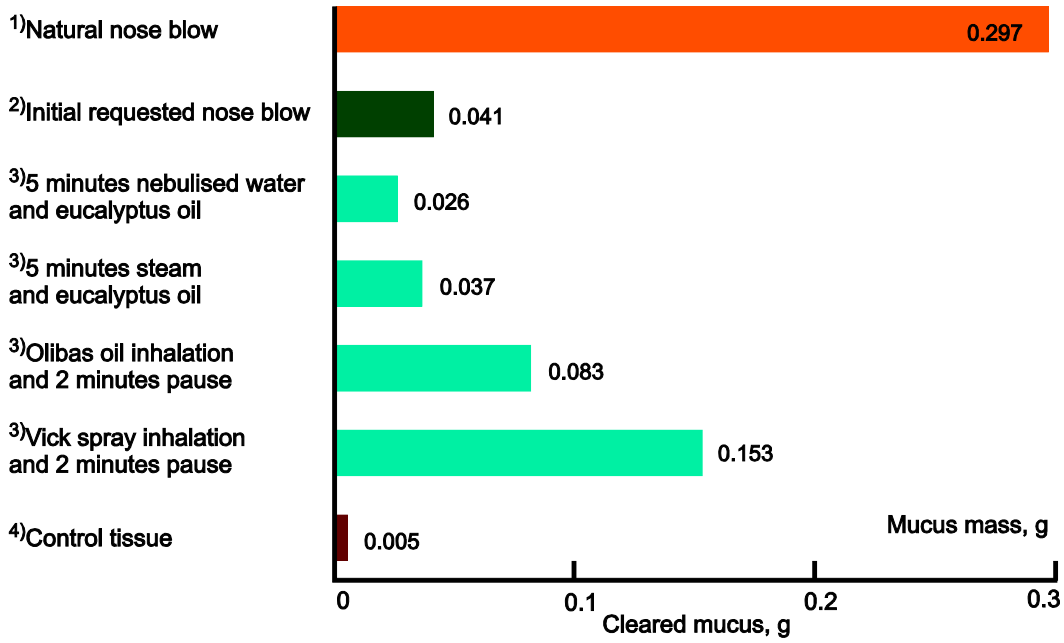

Figure 7: Typical mucus masses cleared by nose blows after different methods of mucus stimulation

1: Mucus mass cleared when subjects bow their noses at will; mucus having accumulated over several hours or been produced in response to a strong stimulus.

2: Mucus cleared at start of stimulant test to ensure only mucus produced in response to stimulus is collected by post-stimulus nose blow: equivalent to non-stimulated on-demand nose blow.

3: Mucus cleared from nose by nose blow at set short interval after use of potential stimulant.

4: Change in mass of tissue that has been removed from bag, opened, handled, and returned to bag.

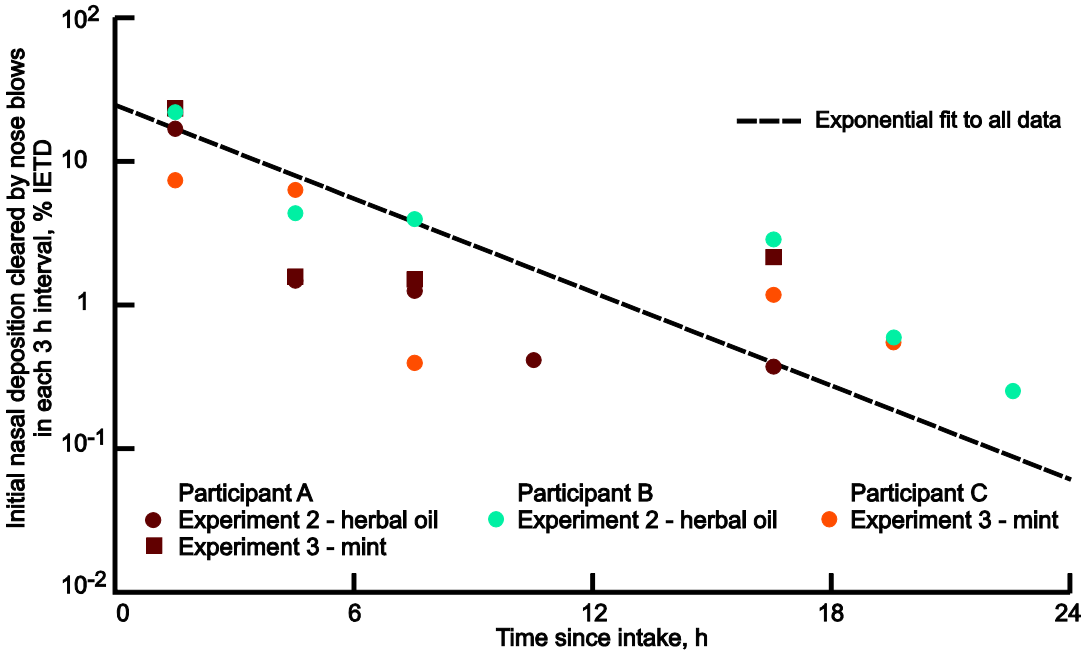

Figure 8: Stimulated deliberate nose blow clearance fractions and their overall trend (Equation 4)

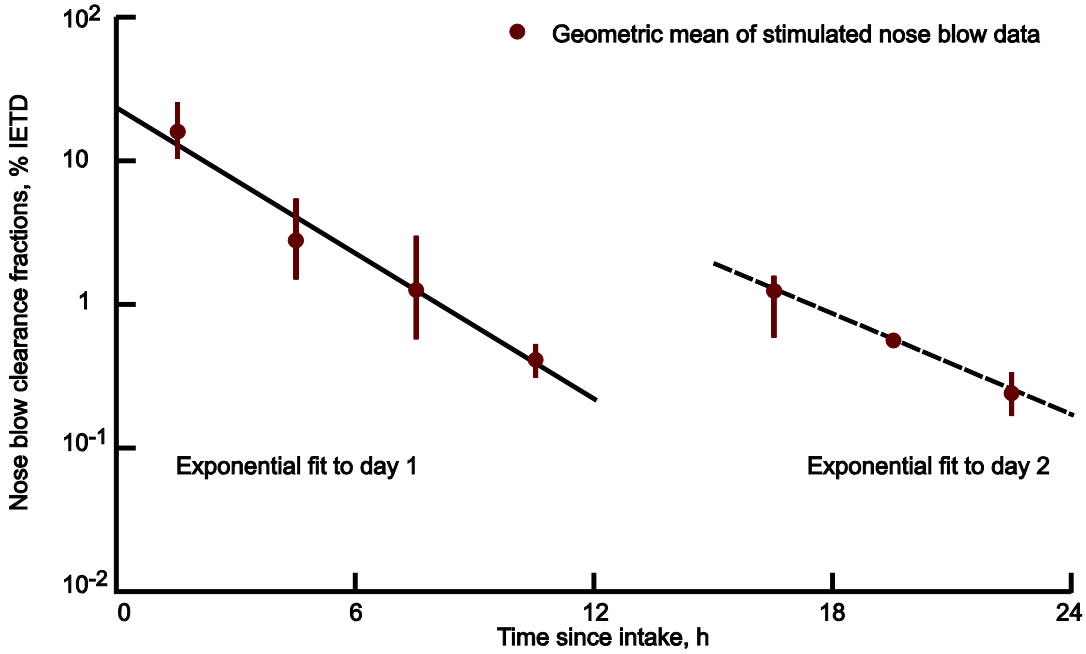

Figure 9: Geometric mean and geometric standard deviations of stimulated nose blow samples with exponential functions fitted to days 1 and 2 (Equations 5 and 6)

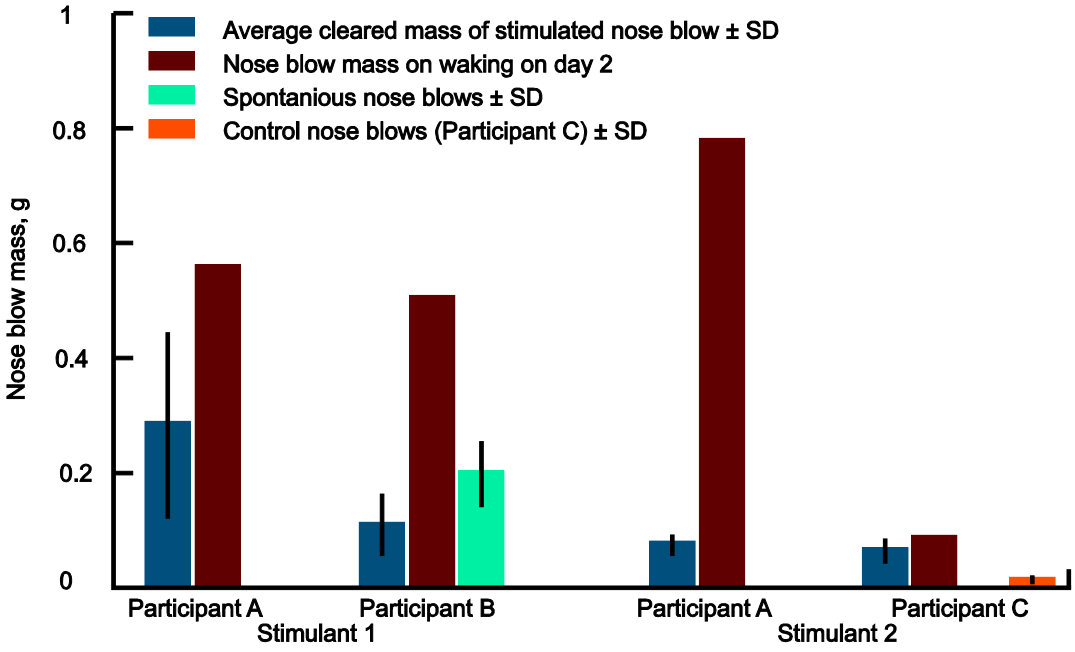

Figure 10: Mucus masses cleared in stimulated nose blow experiments and associated measurements

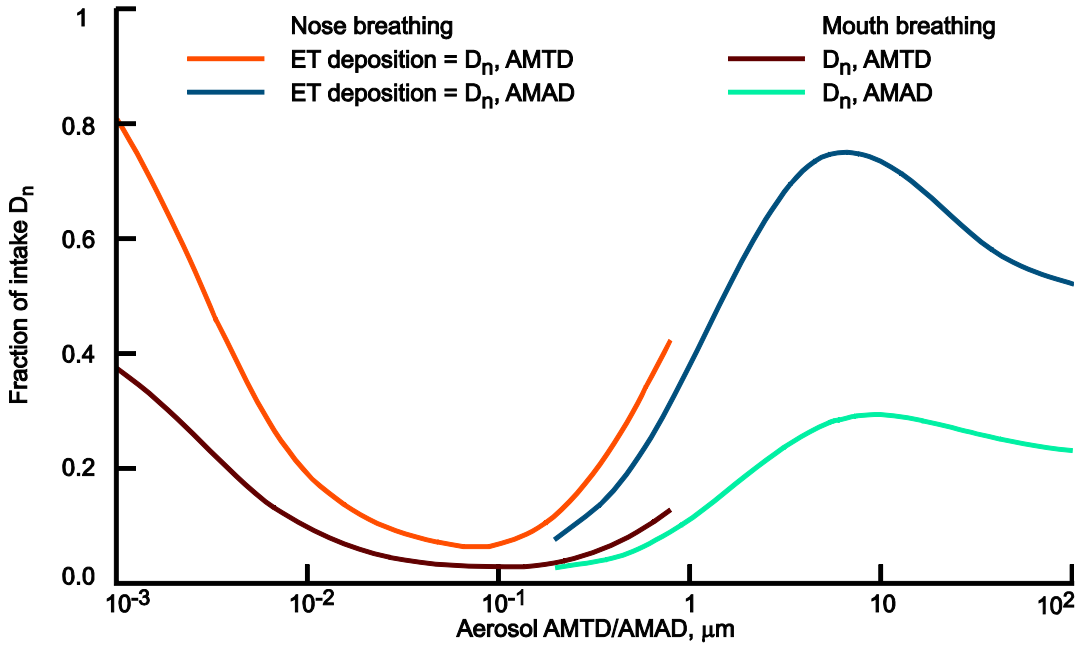

Figure 11: Nasal deposition fraction, Dn,as a function of aerosol size for nose and mouth breathing

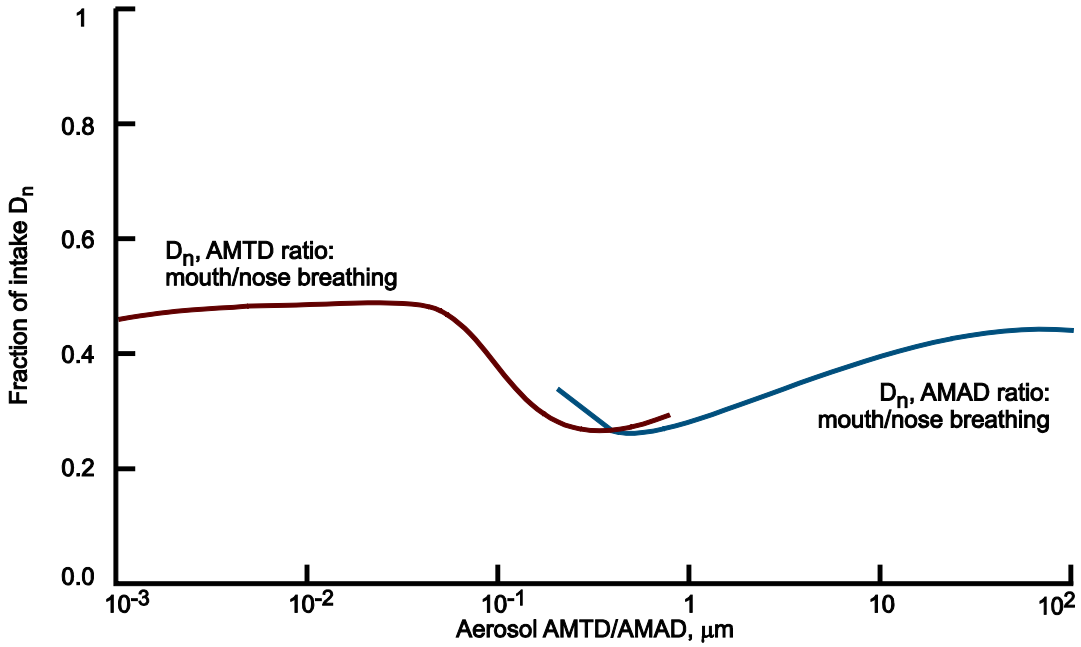

Figure 12: Ratio of nasal deposition fraction values for mouth breathing compared to nose breathing

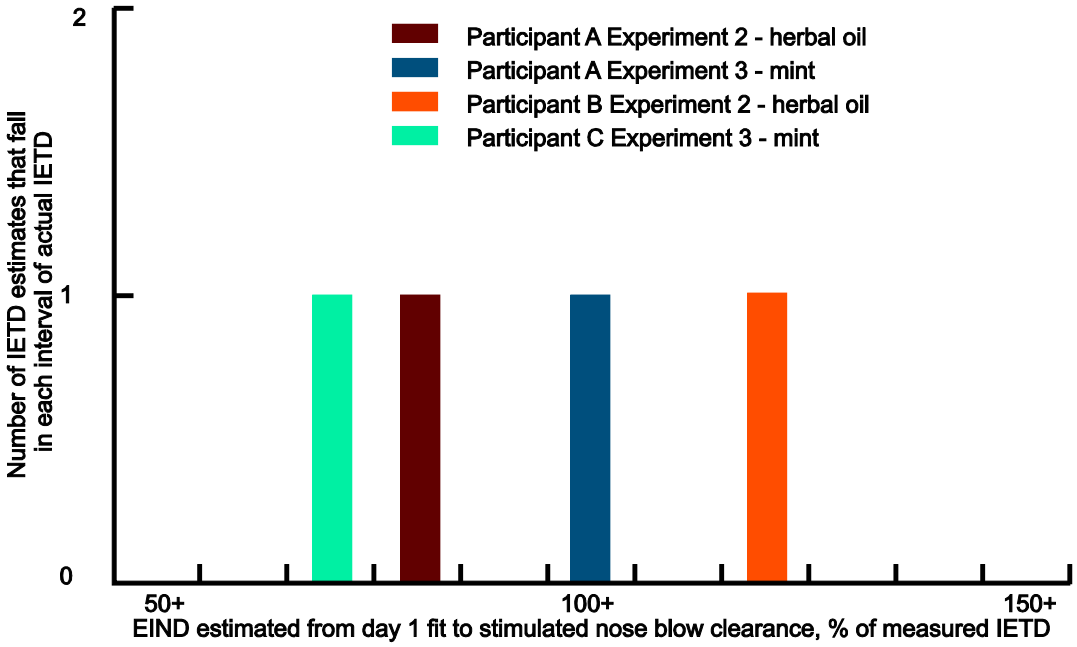

Figure 13: Stimulated nose blow "day 1 trend" EINT values as % of IETD measured by body monitoring