Ann. Occup. Hyg., Vol. 55, No. 5, pp. 495–509, 2011

doi:10.1093/annhyg/mer014

Confidence Limits for Lognormal Percentiles and for Lognormal Mean Based on Samples with Multiple Detection Limits

KALIMUTHU KRISHNAMOORTHY* and ZHAO XU

Department of Mathematics, University of Louisiana at Lafayette, Lafayette, LA 70508-1010, USA

Received 2 December 2010; in final form 18 January 2011; published online 24 May 2011

The problem of assessing occupational exposure using the mean or an upper percentile of a lognormal distribution is addressed. Inferential methods for constructing an upper confidence limit for an upper percentile of a lognormal distribution and for finding confidence intervals for a lognormal mean based on samples with multiple detection limits are proposed. The proposed methods are based on the maximum likelihood estimates. They perform well with respect to coverage probabilities as well as power and are applicable to small sample sizes. The proposed approaches are also applicable for finding confidence limits for the percentiles of a gamma distribution. Computational details and a source for the computer programs are given. An advantage of the proposed approach is the ease of computation and implementation. Illustrative examples with real data sets and a simulated data set are given.

Keywords: exceedance probability; gamma distribution; left-censored samples; non-central *t*; ROS method; tolerance limits

INTRODUCTION

The consensus standard published by the American Industrial Hygiene Association includes two basic strategies for evaluating an exposure profile (see Mulhausen and Damiano, 1998 and Ignacio and Bullock, 2006): strategies based on the mean exposure and those based on an upper percentile of the exposure distribution. An upper confidence limit for an upper percentile is what is commonly referred to as an 'upper tolerance limit'. For instance, a 95% upper confidence limit for the 90th percentile of a population is referred to as the 0.90 content—0.95 coverage upper tolerance limit or simply (0.90, 0.95) upper tolerance limit. If the upper tolerance limit based on a sample of exposure measurements is less than a specified standard [e.g. occupational exposure limit (OEL)], then we conclude that majority of the exposures are within the standard, and hence, exposure monitoring might be reduced or terminated until a process change occurs. For the evaluation of an exposure profile, we can also consider an exceedance fraction θ (i.e. the proportion of exposure measurements that exceed an OEL) and test the hypotheses $H_0 : \theta \geq \varepsilon$ versus $H_a : \theta < \varepsilon$ for a specified value of ε (say, $\varepsilon = 0.05$). The exposure distribution can be declared to be acceptable if H_0 is rejected. These hypotheses can be tested by finding an appropriate upper tolerance limit. The strategy based on the mean exposure is to compare the upper confidence limit for the mean to a specified standard.

Solutions to the aforementioned problems are widely available if the samples are uncensored; see the articles by Rappaport and Selvin (1987), Selvin *et al.* (1987) Selvin and Rappaport (1989), Krishnamoorthy *et al.* (2006), and the references therein. However, occupational exposure data often include values below one or more analytical detection limits (DLs), which significantly complicates the data analysis. A commonly used strategy to handle samples with detection limits is to replace the DLs by their fractions, such

*Author to whom correspondence should be addressed.
Tel: +1-337-482-5283; fax: +1-337-482-5346;
e-mail: krishna@louisiana.edu

as DL/2, and then use the methods available for uncensored samples. However, recent industrial hygiene literature (for example, articles published in the recent issues of the *Journal of Occupational and Environmental Hygiene* and *The Annals of Occupational Hygiene*) shows that the substitution method continues to be routine, without giving adequate thoughts to the serious errors that can result from this strategy. It is easy to demonstrate that the conclusions regarding occupational exposures resulting from this routine practice can be seriously flawed. Simulation studies by several researchers, including Gleit (1985), Gilliom and Helsel (1986) Hass and Scheff (1990), Helsel (2006), and Krishnamoorthy *et al.* (2009), indicated that the substitution methods resulted in inaccurate results for various problems. In an Editorial by Ogden (2010) in the *Annals of Occupational Hygiene* (April 2010 issue), and in an article by Helsel (2010) in the same issue, the suggestion of even rejecting research articles and studies that use the substitution method is brought up.

In the presence of a detection limit, large sample procedures can be developed using likelihood approaches; see the report by Frome and Wambach (2005) and the articles by Hewett (2006) and Hewett and Ganser (2007) for a summary of the available procedures, especially in the context of lognormal exposure data. However, accurate small sample procedures are currently unavailable and are not discussed in their report. Also, it turns out that the usual asymptotic methods based on the maximum likelihood estimates (MLEs) can result in test procedures whose type I error rates can be significantly higher than or lower than a 5% nominal level, see Frome and Wambach (2005). In their recent article, Krishnamoorthy *et al.* (2009) have investigated an imputation approach to address the single detection limit scenario. They have noted that the imputation approach can be calibrated to achieve a high degree of accuracy for the purpose of computing confidence intervals, tolerance intervals, prediction intervals, etc. for the normal, lognormal, and gamma distributions. Recently, Krishnamoorthy *et al.* (2011) have proposed accurate methods based on modified signed likelihood approach and the generalized variable method for finding confidence intervals for a lognormal mean and for percentiles when the samples involve a single detection limit. It should be noted that all the methods proposed in the literature are approximate, and some of them work satisfactorily even for small samples. However, in the presence of multiple DLs, no procedure for computing confidence limits for a percentile or for the mean that is known to work for small samples is available. It should be noted that even in the case of single detection limit, the methods based on the asymptotic normality of the MLEs work poorly even for large samples as large as 100 (Krishnamoorthy *et al.*, 2011), and so they are not suitable to analyze small sample exposure data with multiple detection limits.

In this article, we consider the problems of estimating the percentile and the mean of a lognormal exposure distribution based on a sample with multiple detection limits. Assuming that the samples or log-transformed samples are from a normal distribution with mean μ and variance σ^2, we outline the method for finding the MLEs $\hat{\mu}$ and $\hat{\sigma}$ in the following section. On the basis of some distributional properties of the MLEs, we develop an upper confidence limit of the form $\hat{\mu} + f\hat{\sigma}$ for $100P$ percentile of the normal population. The factor f, referred to as the 'tolerance factor', should be determined so that $\hat{\mu} + f\hat{\sigma}$ is greater than the true percentile with the confidence level $1 - \alpha$. In the sequel, we provide a Monte Carlo method to find the factor f. To avoid simulation, we also provide simple formulas based on the non-central t percentiles to find approximate values of f when the samples include no more than four DLs. An approach of deducing upper confidence limit for an exceedance probability from an upper tolerance limit is also outlined. The proposed approaches for the percentile and exceedance probability can be easily extended to a gamma distribution via cube root transformation. The idea for estimating the percentile is extended to find confidence limits for a lognormal mean. The interval estimation procedures are evaluated with respect to coverage probabilities. Our studies indicate that the methods are very satisfactory even for small samples. Furthermore, simulation study regarding the powers of the test on exceedance probability indicates that the test has some desirable properties. Proposed methods are illustrated by two examples with real data and using a simulated sample from a lognormal distribution.

MLEs AND SAMPLING DISTRIBUTIONS

As the procedures for a lognormal distribution can be readily obtained from those for a normal distribution via logarithmic transformation, we shall explain the method for the normal case. Consider a simple random sample of n observations subject to k detection limits, say DL_1, DL_2, ... , DL_k, from a normal distribution with mean μ and variance σ^2. We denote this normal distribution

by $N(\mu, \sigma^2)$. We assume without loss of generality that $\mathrm{DL}_1 < \mathrm{DL}_2 < \ldots < \mathrm{DL}_k$. Further, we assume that n_i measurements were obtained by the ith laboratory procedure or device with detection limit (DL_i), which can be expressed in the same measurement unit as that of detected observations and $n = \sum_{i=1}^{k} n_i$. Suppose m_i non-detects are below DL_i and let $m = \sum_{i=1}^{k} m_i$. Here, m_i's are independent binomial random variable with number of trials n_i and 'success probability' $P_i = \Phi\left(\frac{\mathrm{DL}_i - \mu}{\sigma}\right)$, where $\Phi(x)$ is the standard normal cumulative distribution function. In the present context, P_i's are unknown proportions of non-detects. Let,

$$\bar{x}_d = \frac{1}{n - m}\sum_{i=1}^{n-m} x_i \text{ and } s_d^2 = \frac{1}{n - m}\sum_{i=1}^{n-m} (x_i - \bar{x}_d)^2, \tag{1}$$

where $x_1, \ldots, x_{n-m}$ are detected observations. The log-likelihood function, after omitting a constant term, can be written as

$$l(\mu, \sigma) = \sum_{i=1}^{k} m_i \ln\Phi\left(z_i^*\right) - (n - m) \times \ln \sigma - \frac{(n - m)\left(s_d^2 + (\bar{x}_d - \mu)^2\right)}{2\sigma^2}, \tag{2}$$

where $z_i^* = \frac{\mathrm{DL}_i - \mu}{\sigma}$, $i = 1, \ldots, k$. Now let $\hat{\mu}$ and $\hat{\sigma}$ denote the maximum likelihood estimates of μ and σ, respectively, obtained by maximizing the above log-likelihood function. These can be numerically obtained using the bivariate Newton–Raphson iterative method; for details, see the Appendix 1.

It can be shown that the MLEs are location-scale equivariant (see Theorem E1 in Lawless, 2003). That is, if $(\hat{\mu}, \hat{\sigma})$ is the MLE of (μ, σ) based on the x_i's and DL_i's, then $(a\hat{\mu} + b, a\hat{\sigma})$ is the MLE of $(\mathrm{a}\mu + b, \mathrm{a}\sigma)$ based on the transformed data $\mathrm{ax}_i + b$ and $a\mathrm{DL}_i + b$, for some $a > 0$ and $-\infty < b < \infty$. This equivariant property implies that, conditionally given $m_1, \ldots, m_k$, the distributions of

$$\frac{(\hat{\mu} - \mu)/\sigma}{(\hat{\sigma}/\sigma)} = \frac{\hat{\mu} - \mu}{\hat{\sigma}} \text{ and } \frac{\hat{\sigma}}{\sigma}, \tag{3}$$

are free of the parameters μ and σ (see Theorem E2 in Lawless, 2003). Since m_i's are binomial (n_i, P_i) random variables, the unconditional distributions of the above quantities depend only on $(P_1, \ldots, P_k)$. In other words, the distributions of the quantities in (equation 3) depend on (μ, σ) via $P_1, \ldots, P_k$. As a consequence, if $P_1, \ldots, P_k$ are known, then the distributions of the quantities in (equation 3) can be evaluated by Monte Carlo simulation. As an example, if $P_1, \ldots, P_k$ are known, then

$$\frac{\hat{\mu} - \mu}{\hat{\sigma}} \text{ distributed as } \frac{\hat{\mu}^*}{\hat{\sigma}^*},$$

where $\hat{\mu}^*$ and $\hat{\sigma}^*$ are the MLEs based on a sample of size n from a standard normal distribution with proportions of non-detects $P_1, \ldots, P_k$. That is, $\hat{\mu}^*$ and $\hat{\sigma}^*$ are the values of μ and σ, respectively, that maximize the log-likelihood function in (equation 2) with $x_1, \ldots, x_{n-m}$ being a sample from $N(0,1)$ distribution with detection limits $\mathrm{DL}_i = \Phi^{-1}(P_i)$. Thus, if $P_1, \ldots, P_k$ are known, then the percentiles of $\hat{\mu}^*/\hat{\sigma}^*$ can be estimated using Monte Carlo simulation, and they can be used to test or compute a confidence interval for μ. For example, if c_1 and c_2 are determined so that $P(c_1 \le \hat{\mu}^*/\hat{\sigma}^* \le c_2) = 1 - \alpha$, then $(\hat{\mu} - c_2\hat{\sigma}, \hat{\mu} - c_1\hat{\sigma})$ is a $100(1 - \alpha)\%$ confidence interval for μ.

In the sequel, we shall use the above distributional property of the MLEs to find an approximate confidence limit for a normal or lognormal percentile and an approximate confidence interval for a lognormal mean.

UPPER CONFIDENCE LIMIT FOR A PERCENTILE

Monte Carlo method

We shall now describe an approximate method for finding an upper confidence limit for $100P$ percentile

$$\xi_P = \mu + z_P\sigma, \tag{4}$$

where z_P is the $100P$ percentile of the standard normal distribution. As in the complete sample case (see-Lawless, 2003, $Q_P = \frac{\xi_P - \hat{\mu}}{\hat{\sigma}}$, Section 5.3.1.1), consider the quantityand let $Q_{P;1-\alpha}$ denotes the $100(1 - \alpha)$ percentile of Q_P. If we can find $Q_{P;1-\alpha}$ approximately, then $\hat{\mu} + Q_{P;1-\alpha}\hat{\sigma}$ is an approximate upper confidence limit for ξ_P. To find an approximation to the percentiles of Q_P by Monte Carlo method, we write,

$$Q_P = \frac{\xi_P - \hat{\mu}}{\hat{\sigma}} = \frac{\mu - \hat{\mu}}{\hat{\sigma}} + z_P\frac{\sigma}{\hat{\sigma}} \sim \frac{z_P - \hat{\mu}^*}{\hat{\sigma}^*} = Q_P^*, \text{ say}, \tag{5}$$

where $\hat{\mu}^*$ and $\hat{\sigma}^*$ are the MLEs based on a sample of size n with proportions of non-detects $P_1, \ldots, P_k$ and detection limits $z_{P_i} = \Phi^{-1}(P_i)$, where $\Phi^{-1}(\cdot)$ is the inverse standard normal distribution function. Thus, Q_P is distributed as Q_P^* and so the percentiles of Q_P are equal to the corresponding percentiles of Q_P^*. We can summarize the distributional result as follows.

Result 1. Let $\hat{\mu}$ and $\hat{\sigma}$ be the MLEs based on a sample with DLs, $\mathrm{DL}_1, \ldots, \mathrm{DL}_k$ from a $N(\mu, \sigma^2)$

distribution. Assume that proportions of non-detects $P_1, \ldots, P_k$ are known. Then

$$\frac{\xi_P - \hat{\mu}}{\hat{\sigma}} \sim \frac{z_P - \hat{\mu}^*}{\hat{\sigma}^*}, \tag{6}$$

where $\hat{\mu}^*$ and $\hat{\sigma}^*$ are the quantities that maximize the log-likelihood function in (equation 2) with $x_1, \ldots, x_{n-m}$ being a sample (with detection limits $\mathrm{DL}_i^* = z_{P_i}$) from a $N(0,1)$ distribution.

In practice, P_i's are unknown, and they should be estimated. A natural estimate is $\hat{P}_i = \Phi\left(\frac{\mathrm{DL}_i - \hat{\mu}}{\hat{\sigma}}\right)$, $i = 1, \ldots, k$, where $\hat{\mu}$ and $\hat{\sigma}$ are the MLEs based on a given sample. Using these estimated proportions, we can estimate $Q_{P;1-\alpha}$ using Monte Carlo simulation as shown in Algorithm 1.

Algorithm 1

Let m_i denote the number of non-detects below the detection limit, DL_i in a set of n_i measurements that were made by the ith sampling device (or laboratory method) with detection limit, DL_i, $i = 1, \ldots, k$. Compute the MLEs, $\hat{\mu}_0$ and $\hat{\sigma}_0$, and $\hat{P}_i = \Phi\left(\frac{\mathrm{DL}_i - \hat{\mu}_0}{\hat{\sigma}_0}\right)$, $i = 1, \ldots, k$.

1. Set $\mathrm{DL}_i^* = z_{\hat{P}_i} = \Phi^{-1}\left(\hat{P}_i\right) = \frac{\mathrm{DL}_i - \hat{\mu}_0}{\hat{\sigma}_0}$, $i = 1, \ldots, k$, where $z_{\hat{P}_i}$ is the $100\hat{P}_i$ percentile of the standard normal distribution.

2. Generate k independent samples, each of size n_i, from $N(0,1)$ distribution.

3. For the ith sample, find $m_i =$ the number of observations below DL_i^*, $i = 1, \ldots, k$.

4. Pool the k samples generated above and compute the MLEs $\hat{\mu}^*$ and $\hat{\sigma}^*$ using the log-likelihood function (equation 2).

5. Set $Q_P^* = \frac{z_P - \hat{\mu}^*}{\hat{\sigma}^*}$, where z_p is the $100P$ percentile of $N(0,1)$ distribution.

6. Repeat Steps 2–5 for a large number of times, say, 10 000.

Let $Q_{P;1-\alpha}^*$ denotes the $100(1-\alpha)$ percentile of 10 000 Q_P^*'s generated above. Then an approximate $100(1-\alpha)$ % upper confidence limit for ξ_P is given by

$$\hat{\mu}_0 + Q_{P;1-\alpha}^* \hat{\sigma}_0. \tag{7}$$

An R program to compute $Q_{P;1-\alpha}^*$ along with a help file is posted at 'www.ucs.louisiana.edu/kxk4695'; to download *R* package, visit. www .r-project.org.

It should be noted that even though information on n_i's should be available, many published studies do not report the values of n_i's. In fact, we have not seen any published data that report the values of n_i's. However, we note that the log-likelihood function in (equation 2) depends on n_i's via $n = \sum_{i=1}^{k} n_i$, and so the result of Algorithm 1 is not affected by the choices of n_i's.

For most cases, one can select n_i's approximately equal, and for heavily censored data, n_i's can be selected on the basis of the number of non-detects m_i's. For a specific situation, see Example 1.

Coverage probabilities of upper confidence limits based on Algorithm 1. To judge the accuracy of the tolerance limit in (equation 7), we estimated its coverage probabilities using Monte Carlo simulation for various values of n, $\mu = 0$, $\sigma = 1$ and 3 and some assumed values of $P_1, \ldots, P_k$. For convenience, we chose $n_i = n/k$, $i = 1, \ldots, k$. The simulation study was carried out as follows. We first generated 2500 samples, each of size n with k DLs, from a $N(\mu, \sigma^2)$ distribution. For each generated sample, we compute the MLEs $\hat{\mu}_0$ and $\hat{\sigma}_0$ and used Algorithm 1 with 5000 runs to find the $100(1-\alpha)\%$ upper confidence limit for ξ_P. The percentage of 2500 upper confidence limits that exceed ξ_p is a Monte Carlo estimate of the coverage probability. The estimated coverage probabilities are reported in Table 1. For a satisfactory estimation method, these coverage probabilities should be close to the nominal level 0.95. As we can see in Table 1, these coverage probabilities are very close to the nominal level 0.95 for all the cases considered, even for proportions of censoring as large as 0.80. However, we also note that, for the cases $n = 6$ and $k = 1$ and $n = 10$ and $k = 2$, the coverage probabilities are slightly smaller than the nominal level 0.95, which indicates that the sample size should be moderate to large if the number of DLs ≥ 3. In general, we observed that our approximate method works satisfactorily for samples of size as small as 10 and the number of detected observations is at least 2. Note that computation of the MLEs requires at least two detected observations. In our simulation studies, we observed that our approximate method worked satisfactorily provided the number of detected observations is ≥ 2 and the sample size is ≥ 15.

We also did coverage studies for the case of $k = 4$ DLs and some other values of $(P, 1-\alpha) = (0.95, 0.95)$ and $(0.90, 0.99)$. These coverage probabilities are not reported here because we observed that they were similar to the ones reported in Table 1 for the case of $(P, 1-\alpha) = (0.90, 0.95)$. Finally, we note that in the coverage study, we used Algorithm 1 with 5000 simulation runs rather than 10 000 as indicated in Algorithm 1. The simulation for estimating the

Table 1. Coverage probabilities of (0.90, 0.95) upper tolerance limits based on Algorithm 1

	σ									
	$n = 6$		$n = 10$		$n = 15$		$n = 20$		$n = 30$	
P_1	1	3	1	3	1	3	1	3	1	3
0.2	0.954	0.936	0.945	0.936	0.947	0.947	0.950	0.946	0.950	0.947
0.3	0.952	0.937	0.948	0.936	0.945	0.945	0.949	0.952	0.949	0.952
0.4	0.946	0.945	0.951	0.939	0.950	0.951	0.945	0.946	0.945	0.951
0.5	0.950	0.937	0.956	0.935	0.958	0.951	0.946	0.946	0.946	0.945
0.6	0.952	0.936	0.946	0.941	0.945	0.946	0.946	0.953	0.946	0.945
0.7	0.944	0.946	0.948	0.939	0.943	0.952	0.949	0.953	0.949	0.953
0.8	0.953	0.944	0.953	0.938	0.951	0.955	0.949	0.956	0.949	0.956

	σ									
	$n = 10$		$n = 16$		$n = 20$		$n = 24$		$n = 30$	
(P_1, P_2)	1	3	1	3	1	3	1	3	1	3
(0.1, 0.2)	0.949	0.932	0.953	0.947	0.951	0.946	0.950	0.946	0.949	0.947
(0.2, 0.3)	0.947	0.941	0.952	0.946	0.953	0.952	0.953	0.952	0.954	0.952
(0.2, 0.4)	0.944	0.934	0.950	0.955	0.951	0.947	0.951	0.951	0.952	0.951
(0.3, 0.5)	0.944	0.938	0.949	0.953	0.948	0.953	0.950	0.953	0.948	0.945
(0.5, 0.6)	0.941	0.933	0.946	0.952	0.949	0.951	0.948	0.951	0.952	0.945
(0.6, 0.8)	0.939	0.941	0.949	0.954	0.954	0.953	0.948	0.952	0.950	0.949

	σ									
	$n = 15$		$n = 21$		$n = 24$		$n = 30$		$n = 45$	
(P_1, P_2, P_3)	1	3	1	3	1	3	1	3	1	3
(0.1, 0.2, 0.3)	0.943	0.954	0.956	0.954	0.949	0.957	0.949	0.950	0.948	0.954
(0.2, 0.4, 0.5)	0.952	0.949	0.950	0.950	0.952	0.951	0.956	0.952	0.947	0.949
(0.3, 0.4, 0.5)	0.953	0.950	0.945	0.953	0.955	0.953	0.944	0.953	0.948	0.951
(0.4, 0.5, 0.6)	0.957	0.949	0.947	0.949	0.946	0.950	0.947	0.949	0.950	0.951
(0.3, 0.6, 0.7)	0.956	0.950	0.955	0.949	0.957	0.951	0.960	0.953	0.952	0.953
(0.5, 0.7, 0.8)	0.955	0.954	0.959	0.952	0.954	0.952	0.953	0.947	0.952	0.956
(0.6, 0.7, 0.8)	0.956	0.956	0.950	0.954	0.950	0.945	0.952	0.949	0.949	0.949

coverage probability of Monte Carlo estimates based on 10 000 runs is very time consuming because the simulation requires $2500 \times 10\,000 = 25\,000\,000$ runs for each coverage probability estimation. For this reason, we used 5000 runs. However, to compute an upper tolerance limit for a given data set, we recommend at least 10 000 runs, to get a more accurate and stable estimate than the one based on 5000 runs.

An approximate method for estimating percentiles based on non-central t

The proposed Monte Carlo method in the preceding section is conceptually simple and is easy to implement, provided the users have some computational skills. To avoid Monte Carlo simulation, we shall provide a simple approximation on the basis of non-central t percentiles.

Let $x_1, \ldots, x_n$ be an uncensored sample from a normal distribution. Define $\bar{x} = \frac{1}{n}\sum_{i=1}^{n} x_i$ and $s^2 = \frac{1}{n-1}\sum_{i=1}^{n}(x_i - \bar{x})^2$. Then a $100(1-\alpha)\%$ upper confidence limit for $\xi_P = \mu + z_P\sigma$ isgiven by

$$\bar{x} + \frac{1}{\sqrt{n}}\, t_{n-1;1-\alpha}\left(z_P\sqrt{n}\right)s, \tag{8}$$

where $t_{n-1;1-\alpha}\left(z_P\sqrt{n}\right)$ is the $100(1-\alpha)$ percentile of the non-central t distribution with degrees of freedom $n-1$ and the non-centrality parameter $z_P\sqrt{n}$. The above tolerance limit is based on the result that $\frac{\xi_P - \bar{x}}{s} \sim \frac{1}{\sqrt{n}} t_{n-1}\left(z_P\sqrt{n}\right)$, where the notation '$\sim$' means 'distributed as' and $t_m(\delta)$ denotes the non-central t distribution with the degrees of freedom m and the non-centrality parameter δ.

Following (equation 8), an approximate tolerance limit based on a sample with multiple

detection limits is proposed (see ProUCL Technical Guide by Singh and Singh, 2009) and is given by

$$\hat{\mu} + \frac{1}{\sqrt{n}} t_{n-1;1-\alpha}\left(z_P\sqrt{n}\right)\hat{\sigma}, \tag{9}$$

where $\hat{\mu}$ and $\hat{\sigma}$ are MLEs. Note that, to get the above tolerance limit, it is assumed that

$$Q_P = \frac{\xi_P - \hat{\mu}}{\hat{\sigma}} \sim \frac{1}{\sqrt{n}} t_{n-1}\left(z_P\sqrt{n}\right), \text{ approximately.} \tag{10}$$

In other words, the above approximation is based on the assumption that the sampling distribution of $\frac{\xi_P - \bar{x}}{s}$ based on uncensored samples and that of $\frac{\xi_P - \hat{\mu}}{\hat{\sigma}}$ based on censored samples are approximately the same at least for large sample sizes. Despite the facts that the MLEs are not in closed form and their distributions are unknown, the above distributional assumption dose not seem to be unreasonable, as will be seen in the sequel.

Accuracy of the non-central t method. A way to check the validity of the assumption (equation 10) is to compare the percentiles of Q_P with the corresponding percentiles of $\frac{1}{\sqrt{n}} t_{n-1}\left(z_P\sqrt{n}\right)$. For a given sample size n, and some assumed values of (μ, σ) and $P_1, \ldots, P_k$, the percentiles of Q_p can be obtained using Monte Carlo simulation. For the case of $k = 3$ and n = 21, we estimated the percentiles of $Q_{0.9}$ using Monte Carlo simulation and plotted them along with the percentiles of $\frac{1}{\sqrt{n}} t_{n-1}\left(z_{0.9}\sqrt{n}\right)$ in Fig. 1. It is clear from these plots that the upper percentiles of $Q_{0.9}$ are larger than the corresponding upper percentiles of $\frac{1}{\sqrt{n}} t_{n-1}\left(z_{0.9}\sqrt{n}\right)$ for all the cases considered. The differences increase with increasing proportions of non-detects. These findings imply that the upper tolerance limits based on the non-central t percentiles should be liberal (that is, the actual coverage probabilities are smaller than the intended nominal level). To understand the difference between the coverage probabilities and the nominal level, we further estimated the coverage probabilities of (0.90, 0.95) upper tolerance limits in (equation 9) for some values of proportions of non-detects. The coverage probabilities are given in Table 2 for some sample sizes ranging from 21 to 100. The table values clearly indicate that the coverage probabilities of the upper tolerance limits based on the non-central t distribution are always smaller than the nominal level 0.95 and they decrease with increasing proportions of non-detects. On the other hand, we also note that the coverage probabilities are at least 0.90 for all the cases considered, and so the tolerance limits based on the non-central t are not really so bad.

An approximation based on non-central t *percentiles.* As we noted earlier, the percentiles of $Q_{P;1-\alpha}$ are affected only by $(P_1, \ldots, P_k)$. This result along with the plots in Fig. 1 indicate that the percentiles of Q_P can be approximated by a function of non-central t percentiles and $P_1, \ldots, P_k$. For a given

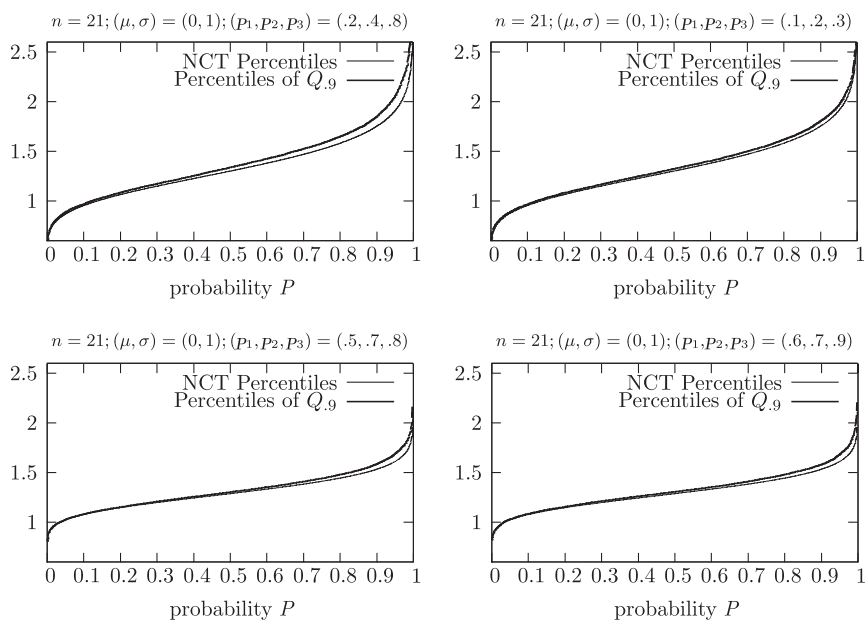

Fig. 1. Percentiles of $t_{n-1}\left(z_{0.9}\sqrt{n}\right)/\sqrt{n}$ and simulated percentiles of $Q_{0.9}$; the values on y-axis are $100P$ percentiles.

$(P, 1-\alpha)$, and sample size n, a way to find an approximation to $Q_{P;1-\alpha}$ is to fit a linear regression model by treating $Q_{P;1-\alpha}$ as response (dependent) variable and P_i's, the sample size n, and $\frac{1}{\sqrt{n}}t_{n-1;1-\alpha}\left(z_P\sqrt{n}\right)$ as explanatory (independent) variables. Specifically, we assume the linear regression model

$$Q_{P;1-\alpha} = \beta_0 + \beta_1 P_1 + \ldots + \beta_k P_k + \beta_{k+1}\frac{1}{\sqrt{n}}t_{n-1;1-\alpha}\left(z_P\sqrt{n}\right) + \beta_{k+2}n,$$

where β's are the unknown parameters. For a given $(P,\ 1-\alpha)$, $(P_1, \ldots, P_k)$ and n, Monte Carlo estimates of $Q_{P;1-\alpha}$ can be used as the training data to fit the model. For instance, for the case of $k = 3$ detection limits, we estimated $Q_{0.9;0.95}$ for various values of (P_1, P_2, P_3) and sample size n ranging from 15 to 100, with $n_i = n/3$, $i = 1, 2, 3$. These estimated values and the corresponding values of (P_1, P_2, P_3), n and $\frac{1}{\sqrt{n}}t_{n-1;1-\alpha}\left(z_P\sqrt{n}\right)$ were used to fit the model as

$$Q_{0.90;0.95} = -0.605 + 0.0222P_1 + 0.0390P_2 + 0.0700P_3 + 1.35\frac{1}{\sqrt{n}}t_{n-1;0.95}\left(z_{0.9}\sqrt{n}\right) + 0.0003n. \quad (11)$$

Note that the proportions of non-detects P_i's are unknown, and so they should be estimated. As noted

Table 2. Coverage probabilities of (0.90, 0.95) upper tolerance limits (equation 9) based on non-central t distribution

	σ									
	$n = 20$		$n = 30$		$n = 40$		$n = 50$		$n = 100$	
P_1	1	3	1	3	1	3	1	3	1	3
0.2	0.928	0.931	0.935	0.932	0.930	0.940	0.939	0.940	0.938	0.941
0.5	0.917	0.904	0.919	0.919	0.919	0.919	0.923	0.921	0.930	0.927
0.8	0.909	0.907	0.901	0.901	0.907	0.905	0.904	0.909	0.906	0.911
	σ									
	$n = 20$		$n = 30$		$n = 40$		$n = 50$		$n = 100$	
(P_1, P_2)	1	3	1	3	1	3	1	3	1	3
(0.1, 0.2)	0.933	0.934	0.935	0.938	0.937	0.939	0.936	0.937	0.942	0.942
(0.2, 0.4)	0.926	0.925	0.930	0.932	0.931	0.933	0.936	0.934	0.930	0.938
(0.5, 0.6)	0.905	0.908	0.916	0.909	0.919	0.921	0.920	0.920	0.925	0.929
(0.6, 0.7)	0.914	0.913	0.902	0.907	0.910	0.907	0.918	0.915	0.930	0.921
	σ									
	$n = 21$		$n = 27$		$n = 45$		$n = 60$		$n = 90$	
(P_1, P_2, P_3)	1	3	1	3	1	3	1	3	1	3
(0.1, 0.2, 0.3)	0.931	0.933	0.932	0.932	0.936	0.932	0.938	0.936	0.936	0.936
(0.2, 0.4, 0.5)	0.924	0.926	0.927	0.924	0.925	0.930	0.927	0.928	0.934	0.933
(0.5, 0.7, 0.8)	0.909	0.914	0.911	0.908	0.913	0.912	0.921	0.920	0.929	0.920

Table 3. Approximate percentiles $\tilde{Q}_{P;1-\alpha}$ based on $C_{p;1-\alpha;n} = \frac{1}{\sqrt{n}}t_{n-1;1-\alpha}\left(z_P\sqrt{n}\right)$

Number of *DL*s	
1	$\tilde{Q}_{0.90;0.95} = -0.669 + 0.164\hat{P}_1 + 1.38C_{0.90;0.95;n} + 0.0005n$
2	$\tilde{Q}_{0.90;0.95} = -0.573 + 0.0455\hat{P}_1 + 0.0759\hat{P}_2 + 1.34C_{0.90;0.95;n} + 0.0003n$
3	$\tilde{Q}_{0.90;0.95} = -0.605 + 0.0222\hat{P}_1 + 0.0390\hat{P}_2 + 0.0700\hat{P}_3 + 1.35C_{0.90;0.95;n} + 0.0003n$
4	$\tilde{Q}_{0.90;0.95} = -0.548 + 0.0336\hat{P}_1 + 0.0318\hat{P}_2 + 0.0135\hat{P}_3 + 0.0165\hat{p}_4 + 1.33C_{0.90;0.95;n} + 0.0003n$
1	$\tilde{Q}_{0.95;0.95} = -1.532 + 0.0435\hat{P}_1 + 1.67C_{0.95;0.95;n} + 0.0013n$
2	$\tilde{Q}_{0.95;0.95} = -1.126 + 0.2541\hat{P}_1 + 0.0827\hat{P}_2 + 1.51C_{0.95;0.95;n} + 0.0007n$
3	$\tilde{Q}_{0.95;0.95} = -1.001 + 0.1335\hat{P}_1 + 0.0766\hat{P}_2 + 0.0282\hat{P}_3 + 1.47C_{0.95;0.95;n} + 0.0006n$
4	$\tilde{Q}_{0.95;0.95} = -0.880 + 0.0831\hat{P}_1 + 0.0631\hat{P}_2 + 0.0311\hat{P}_3 + 0.0160\hat{P}_4 + 1.42C_{0.95;0.95;n} + 0.0005n$

Table 4. Coverage probabilities of (0.90, 0.95) upper tolerance limits based on the approximate factors $Q_{P;1-\alpha}$ given in Table 3

$k=2$; $\tilde{Q}_{0.90;0.95} = -0.573 + 0.0455\hat{P}_1 + 0.0759\hat{P}_2 + \frac{1.34}{\sqrt{n}} t_{n-1;0.95}\left(z_{0.9}\sqrt{n}\right) + 0.0003n$

	σ									
	$n = 16$		$n = 20$		$n = 24$		$n = 30$		$n = 40$	
(P_1, P_2)	1	3	1	3	1	3	1	3	1	3
(0.1, 0.2)	0.953	0.955	0.954	0.953	0.950	0.956	0.949	0.953	0.948	0.951
(0.2, 0.3)	0.952	0.953	0.953	0.954	0.953	0.953	0.954	0.953	0.947	0.948
(0.2, 0.4)	0.950	0.954	0.951	0.953	0.951	0.951	0.952	0.954	0.948	0.953
(0.3, 0.5)	0.949	0.953	0.948	0.952	0.950	0.953	0.948	0.955	0.950	0.951
(0.5, 0.6)	0.946	0.950	0.949	0.946	0.948	0.948	0.952	0.951	0.952	0.949
(0.6, 0.8)	0.946	0.951	0.946	0.952	0.946	0.952	0.950	0.947	0.952	0.953

$k=3$; $\tilde{Q}_{0.90;0.95} = -0.605 + 0.0222\hat{P}_1 + 0.0390\hat{P}_2 + 0.0700\hat{P}_3 + \frac{1.35}{\sqrt{n}} t_{n-1;0.95}\left(z_{0.9}\sqrt{n}\right) + 0.0003n$

	σ									
	$n = 15$		$n = 21$		$n = 24$		$n = 30$		$n = 45$	
(P_1, P_2, P_3)	1	3	1	3	1	3	1	3	1	3
(0.1, 0.2, 0.3)	0.953	0.954	0.954	0.954	0.950	0.957	0.949	0.950	0.948	0.953
(0.2, 0.4, 0.5)	0.952	0.949	0.953	0.950	0.953	0.951	0.954	0.952	0.947	0.949
(0.3, 0.4, 0.5)	0.950	0.950	0.951	0.953	0.951	0.953	0.952	0.953	0.948	0.946
(0.4, 0.5, 0.6)	0.949	0.949	0.948	0.949	0.950	0.950	0.948	0.949	0.950	0.947
(0.3, 0.6, 0.7)	0.946	0.950	0.949	0.949	0.948	0.951	0.952	0.953	0.952	0.952
(0.5, 0.7, 0.8)	0.946	0.954	0.946	0.952	0.946	0.952	0.950	0.947	0.952	0.950
(0.6, 0.7, 0.8)	0.950	0.956	0.950	0.956	0.950	0.945	0.952	0.949	0.949	0.949

earlier, we can estimate P_i by $\hat{P}_i = \Phi\left(\frac{\mathrm{DL}_i - \hat{\mu}}{\hat{\sigma}}\right)$, $i = 1, \ldots, k$, where $\hat{\mu}$ and $\hat{\sigma}$ are the MLEs based on a given sample. Replacing the P_i's in (equation 11) by $\hat{P}_i$, we can get an approximation to $Q_{0.9;0.95}$. We obtained approximation to $Q_{P;1-\alpha}$ when $P = 0.90$ and 0.95, $1 - \alpha = 0.95$, and the number of detection limits $k = 1, 2, 3, 4$. These approximate formulas are given in Table 3.

As an example, consider a sample of 30 measurements with two detection limits, DL_1 and DL_2. Let $\hat{\mu}$ and $\hat{\sigma}$ be MLEs based on the sample. Thus, we have $n = 30$, $\hat{P}_i = \Phi\left(\frac{\mathrm{DL}_i - \hat{\mu}}{\hat{\sigma}}\right)$, $i = 1, 2$, and $\frac{1}{\sqrt{30}} t_{29;0.95}\left(z_{0.9}\sqrt{30}\right) = 1.777$. An approximation to $\tilde{Q}_{0.9;0.95}$ (see Table 3) can be found as

$$\tilde{Q}_{0.9;0.95} = -0.573 + 0.0455\hat{P}_1 + 0.0759\hat{P}_2 + 1.34 \times 1.777 + 0.0003 \times 30.$$

An approximate (0.90, 0.95) upper tolerance limit, or equivalently, a 95% upper tolerance limit for the 90th percentile, is given by $\hat{\mu} + \tilde{Q}_{0.9;0.95}\hat{\sigma}$.

Coverage studies of the upper tolerance limits based on $\tilde{Q}_{P;1-\alpha}$. To judge the accuracy of the approximate percentiles given in Table 3 we further evaluated the coverage probabilities of the upper tolerance limits of the form $\hat{\mu} + \tilde{Q}_{P;.1-\alpha}\hat{\sigma}$, where $\tilde{Q}_{P;1-\alpha}$ is determined by the formulas in Table 3. The coverage probabilities were evaluated using Monte Carlo simulation for the cases of $k = 2$ and 3 and they are given in Table 4. It is clear from the table values that the estimated coverage probabilities are very close to the nominal level 0.95 for all the cases considered. These coverage results indicate that the approximate factors given in Table 3 are very satisfactory for constructing (0.90, 0.95) or (0.95, 0.95) upper tolerance limits for a normal or lognormal distribution.

A METHOD FOR ASSESSING EXCEEDANCE PROBABILITY

An upper confidence limit for an exceedance probability can also be used to assess the exposure level in a workplace. For instance, if x_0 denotes the OEL, then the exceedance probability is defined by $P(X > x_0)$, where X is the exposure level for a random worker. If an upper tolerance limit is in closed form, then the approach described in Krishnamoorthy and Mathew (2009a, p. 5) can be used to find an upper confidence limit for the exceedance probability. In general, trial-error method can be used to find a $100(1-\alpha)\%$ upper confidence limit for an exceedance probability as follows. A $(P, 1-\alpha)$ upper tolerance limit is being less than x_0 implies that at

least $100p\%$ of exposure measurements are less than x_0 with confidence $1-\alpha$, or equivalently, at most $100(1-P)\%$ of exposure measurements exceed x_0 with confidence $1-\alpha$. Thus, if a $(P, 1-\alpha)$ upper tolerance limit is less than x_0, then we can conclude that the exceedance probability is no more than $1-P$ with confidence $1-\alpha$. As a result, if P_0 is chosen so that the $(P_0, 1-\alpha)$ upper tolerance limit is equal to the OEL, then $1-P_0$ is a $100(1-\alpha)\%$ upper confidence limit for the exceedance probability. The value of P_0 can be found by a trial-error method as shown in Example 1.

POWERS OF THE TEST FOR A PERCENTILE OR EXCEEDANCE PROBABILITY

A test for a normal percentile or for a lognormal percentile can be easily carried out by comparing an appropriate confidence limit with the specified value. Suppose it is desired to test

$$H_0 : \xi_P \geq x_0 \text{ versus } H_\alpha : \xi_P < x_0,$$

where $\xi_P = \mu + z_P\sigma$, and x_0 is a specified value. In the context of present study, x_0 is OEL (or logarithm of OEL). The above null hypothesis is rejected if a $(P, 1-\alpha)$ upper tolerance limit is less than x_0. Rejection of H_0 implies that $100P\%$ of the exposure distribution is less than the OEL, or equivalently, exceedance probability is no more than $1-P$. The coverage study of the upper confidence limits in the earlier section indicates that the maximum Type I error rate of the test is approximately α. However, we need to assess the power of the test (i.e. probability of rejecting the null hypothesis when it is actually false).

We computed Monte Carlo estimates of the powers of the test for various values of sample sizes

Table 5. Powers of the test for $H_0 : \xi_{0.9} \geq x_0$ versus $H_\alpha : \xi_{0.9} < x_0$, Level α=0.05, $x_0 = 2.782$ and $\xi_{0.9} = x_0 - d$

	$n = 15$					$n = 24$					$n = 36$				
	d					d					d				
(P_1, P_2, P_3)	0	0.2	0.6	0.8	1	0	0.2	0.6	0.8	1	0	0.2	0.6	0.8	1
(0.2, 0.4, 0.5)	0.049	0.12	0.39	0.54	0.71	0.049	0.15	0.56	0.78	0.91	0.049	0.20	0.74	0.91	0.98
(0.3, 0.4, 0.5)	0.053	0.12	0.38	0.54	0.71	0.050	0.15	0.56	0.76	0.91	0.050	0.20	0.74	0.90	0.98
(0.3, 0.5, 0.6)	0.053	0.12	0.38	0.53	0.70	0.047	0.15	0.55	0.76	0.90	0.051	0.19	0.73	0.89	0.98
(0.5, 0.7, 0.8)	0.054	0.12	0.37	0.53	0.69	0.046	0.14	0.53	0.75	0.90	0.053	0.18	0.73	0.88	0.98

Table 6. Coverage probabilities of (0.90, 0.95) upper tolerance limits for a lognormal mean based on the generalized variable approach

	σ									
	$n = 15$		$n = 20$		$n = 25$		$n = 30$		$n = 40$	
(P_1, P_2)	1	3	1	3	1	3	1	3	1	3
(0.1, 0.2)	0.945	0.946	0.947	0.954	0.946	0.946	0.949	0.945	0.945	0.948
(0.2, 0.4)	0.954	0.948	0.945	0.950	0.948	0.946	0.946	0.949	0.948	0.952
(0.3, 0.4)	0.948	0.945	0.950	0.953	0.948	0.945	0.951	0.951	0.950	0.953
(0.4, 0.5)	0.949	0.952	0.953	0.949	0.946	0.942	0.953	0.952	0.951	0.947
(0.3, 0.6)	0.946	0.947	0.945	0.949	0.949	0.952	0.954	0.957	0.947	0.951
(0.5, 0.7)	0.953	0.946	0.948	0.947	0.952	0.951	0.957	0.946	0.946	0.948
(0.6, 0.7)	0.944	0.946	0.947	0.953	0.954	0.947	0.952	0.947	0.948	0.949

	σ									
	$n = 15$		$n = 21$		$n = 24$		$n = 30$		$n = 39$	
(P_1, P_2, P_3)	1	3	1	3	1	3	1	3	1	3
(0.1, 0.2, 0.3)	0.949	0.954	0.945	0.951	0.946	0.953	0.949	0.954	0.945	0.948
(0.2, 0.4, 0.5)	0.951	0.949	0.945	0.946	0.948	0.954	0.946	0.949	0.949	0.950
(0.3, 0.4, 0.5)	0.948	0.950	0.953	0.947	0.948	0.953	0.952	0.949	0.944	0.945
(0.4, 0.5, 0.6)	0.947	0.949	0.943	0.949	0.946	0.945	0.953	0.946	0.953	0.947
(0.3, 0.6, 0.7)	0.945	0.950	0.945	0.951	0.949	0.946	0.947	0.952	0.953	0.945
(0.5, 0.7, 0.8)	0.953	0.954	0.948	0.950	0.952	0.947	0.949	0.948	0.946	0.949
(0.6, 0.7, 0.8)	0.955	0.956	0.954	0.955	0.954	0.949	0.952	0.954	0.948	0.953

n with three DLs and presented them in Table 5. We observe from the table values that for fixed values of sample size and (P_1, P_2, P_3), the power is increasing with increasing $d = x_0 - \xi_{0.9}$, the difference between the true value and the specified value. When d and (P_1, P_2, P_3) are fixed, the power is increasing with increasing sample size. Thus, the test satisfies some basic requirements of a good test. Finally, we notice that, for fixed value of n and (P_1, P_2, P_3), the power is not much affected by censoring intensity.

CONFIDENCE INTERVALS FOR A LOGNORMAL MEAN

As the mean of a lognormal distribution with parameters μ and σ^2 is given by $\exp(\mu + 0.5\sigma^2)$, it is enough to find a confidence interval for $\eta = \mu + 0.5\sigma^2$, where μ and σ^2 are, respectively, the mean and variance of a normal distribution. A confidence interval for η can be obtained along the lines of the method for the percentiles given in earlier section and using the generalized variable approach. For more details on the generalized variable approach in the present context, see the articles by Krishnamoorthy *et al.* (2006, 2011) and Krishnamoorthy and Mathew (2009b). Specifically, an approximate 'generalized pivotal quantity (GPQ)' for η, which can be constructed following the lines of Krishnamoorthy *et al.* (2010), as follows. Let $\hat{\mu}_0$ and $\hat{\sigma}_0$ be observed values of the MLEs based on a sample of n observations with k detection limits. An approximate GPQ for η, denoted by G_η, is given by

$$G_\eta = \hat{\mu}_0 + \frac{\mu - \hat{\mu}}{\hat{\sigma}}\hat{\sigma}_0 + 0.5\frac{\hat{\sigma}_0^2}{\hat{\sigma}^2}\sigma^2 \sim \hat{\mu}_0 - \frac{\hat{\mu}^*}{\hat{\sigma}^*}\hat{\sigma}_0 + 0.5\frac{\hat{\sigma}_0^2}{\hat{\sigma}^{*2}}, \quad (12)$$

where $\hat{\mu}^*$ and $\hat{\sigma}^*$ are the MLEs based on a sample of size n from a $N(0,1)$ distribution with detection limits $z_{\hat{P}_1}, \ldots, z_{\hat{P}_k}$ and $\hat{P}_i = \Phi\left(\frac{\mathrm{DL}_i - \hat{\mu}_0}{\hat{\sigma}_0}\right)$, $i = 1, \ldots, k$.

A confidence interval or one-sided confidence limit for η based on the GPQ G_η can be evaluated using Algorithm 2.

Algorithm 2

For a given data set with k detection limits, compute the MLEs $\hat{\mu}_0$ and $\hat{\sigma}_0$.

1. Set $\mathrm{DL}_i^* = \frac{\mathrm{DL}_i - \hat{\mu}_0}{\hat{\sigma}_0}$, $i = 1, \ldots, k$.
2. Generate k independent samples, each of size n_i, from $N(0,1)$ distribution. Note that $\sum_{i=1}^{k} n_i$ should be n.
3. For the ith sample, find $m_i =$ the number of observations below DL_i^*, $i = 1, \ldots, k$.
4. Pool the k samples generated above and compute the MLEs $\hat{\mu}^*$ and $\hat{\sigma}^*$ using (equation 2).
5. Set $G_\eta = \hat{\mu}_0 - \frac{\hat{\mu}^*}{\hat{\sigma}^*}\hat{\sigma}_0 + 0.5\frac{\hat{\sigma}_0^2}{\hat{\sigma}^{*2}}$.
6. Repeat Steps 2–5 for a large number of times, say, 10 000.

The $100(1-\alpha)$ percentile of 10 000 G_η's (denoted by $G_{\eta;1-\alpha}$) is the $(P, 1-\alpha)$ upper confidence limit for η. The interval $\left(G_{\eta,\alpha/2}, G_{\eta,1-\alpha/2}\right)$ is a $1-\alpha$ confidence interval for η. An R program to compute confidence limit for a lognormal mean using the above algorithm is posted at 'www.ucs.louisiana.edu/∼kxk4695';

We estimated the coverage probabilities of 95% upper confidence limits for a lognormal mean based on Algorithm 2 along the lines for the percentile in the earlier section and reported them in Table 6. Estimated coverage probabilities clearly indicate that the proposed Monte Carlo method in Algorithm 2 is quite satisfactory. In general, we noted that the method described in Algorithm 2 works satisfactorily provided sample sizes are around $\geq$15, and the number detected observations is at least two.

GAMMA DISTRIBUTION

The gamma distribution has found limited applications in industrial hygiene (see Singh *et al.* (2002)), and our proposed methods for normal percentiles can be adapted to the case of the gamma distribution. Specifically, our procedure can be extended to a gamma distribution using the Wilson-Hilferty (1931) normal approximation: if Y follows a gamma distribution, then the distribution of $Y^{1/3}$ is well approximated by a normal distribution. To construct a confidence limit for a gamma percentile, we simply apply the normal based method to cube root transformed samples and then transform the result back (by taking third power) to get a confidence limit for the gamma percentile. Krishnamoorthy *et al.* (2008) used this cube root transformation to find tolerance limits and prediction intervals for a gamma distribution when the samples are uncensored, and Krishnamoorthy *et al.* (2009) used it for the samples with a single detection limit. Simulation studies in their articles indicated that the resulting procedures are not only simple but also very satisfactory and are comparable to those based on other complex methods.

If a sample from a gamma distribution includes multiple detection limits, then after taking cube root of the detected observations and *DL*s, we simply

apply normal based approaches in the preceding sections to obtain an upper tolerance limit. For an illustration, see Example 3.

OTHER APPROACHES

Regarding other possible approaches to the problems considered in this article, we investigated (not reported in this article) the regression of order statistics (ROS) method, which seems to be popular among industrial hygienists; see the technical guide to Pro UCL and Chapter 6 of Helsel's (2005) book. In this method, a regression line is fit to the normal scores of the order statistics for the detected observations and then extrapolate non-detects from the fitted straight line. Thus, this method produces a complete data set, and methods for uncensored samples can be easily applied to compute tolerance limits or to find confidence intervals for a mean. However, the results based on the ROS method are not satisfactory for the problems considered in this article. Specifically, we found via simulation studies that the distributions of certain pivotal quantities depend not only on proportion of non-detects but also on the parameters μ and σ. As a result, the coverage probabilities of confidence limits are satisfactory for some parameter values and unsatisfactory for other values. For instance, the coverage probability of a (0.90, 0.95) upper tolerance limit could go as low as 0.85 even for samples of moderate sizes. For this reason, we have not pursued this approach further.

ILLUSTRATIVE EXAMPLES

We shall now illustrate the methods of estimation using three examples. The first example involves real data, with two detection limits, taken from the book by Helsel (2005). For this data set, the values of n_i's are not known, and we obtain confidence limits using Algorithm 1 for a few different choices of n_i and compare them. In the second example, we shall use a simulated data set where the values of n_i's are known. The third example is to illustrate the method of obtaining tolerance limit for a gamma distribution. The uncensored sample for this example is taken from Gibbons (1994). We give the results based on the uncensored sample, as well as the results based on artificially censored sample (with a single detection limit), and compare the results to judge the loss of precision due to censoring.

Example 1. We shall use the Atrazine concentration data as given in Table 9.7 of Helsel (2005, p. 159) to illustrate the procedures described in the preceding sections. The original data were altered by adding a second detection limit at 0.05 (see Helsel, 2005, p. 229). The probability plot in Figure 5.5 of Helsel (2005) indicates that lognormality assumption is tenable.

For this data set, $n = 24$, $m_1 = 9$ and $m_2 = 2$. The MLEs based on the log-transformed data are $\hat{\mu} = -4.206$ and $\hat{\sigma} = 1.462$. To compute a (0.90, 0.95) upper tolerance limit based on the non-central t method, we found $\frac{1}{\sqrt{24}} t_{23;0.95}\left(z_{0.9}\sqrt{24}\right) = 1.853$ using the 'StatCalc' PC calculator by Krishnamoorthy (2006). The (0.90, 0.95) upper tolerance limit based on this tolerance factor is $\exp(-4.206 + 1.853 \times 1.462) = 0.224$. To compute the tolerance limit using the formulas in Table 3, recall that the proportions of non-detects should be estimated by $\hat{P}_i = \Phi\left(\frac{\ln(\mathrm{DL}_i) - \hat{\mu}}{\hat{\sigma}}\right)$. For this example, $\hat{P}_1 = 0.392$ and $\hat{P}_2 = 0.796$. Using these numbers in the appropriate formula in Table 3, we calculate

$$\begin{aligned}\tilde{Q}_{0.90;0.95} \simeq & -0.573 + 0.0455 \times 0.392 \\ & + 0.0759 \times 0.796 + 1.34 \\ & \times 1.853 + 0.0003 \times 24 = 1.995.\end{aligned}$$

This factor yields the tolerance limit $\exp(-4.206 + 1.995 \times 1.462) = 0.275$.

To apply the Monte Carlo approach, we need to determine the value of n_i, the number of measurements that was obtained when the detection limit was DL_i. Since the numbers of non-detects $m_1 = 9$ and $m_2 = 2$, n_1 must be at least 9 and n_2 must be at least 2.

Table 7. Atrazine concentrations (μ g/l) in a series of Nebraska wells before June

0.38	<0.05	<0.01	0.03	0.03	0.05	0.02	<0.01	<0.01	<0.01	0.11	0.09
<0.01	<0.01	<0.01	<0.01	0.02	<0.05	0.02	0.02	0.05	0.03	0.05	<0.01

Table 8. Simulated data from a lognormal distribution with μ=0.5 and σ=1.5; $\mathrm{DL}_i = exp(\mu + z_{P_i}\sigma)$, $(n_1, n_2, n_3) = (10, 6, 9)$, and $(P_1, P_2, P_3) = (0.2, 0.4, 0.7)$

<0.47	<0.47	0.78	1.10	<1.13	<1.13	<1.13	1.36
1.54	1.67	2.30	2.71	<3.62	<3.62	<3.62	<3.62
<3.62	<3.62	<3.62	<3.62	5.78	7.30	15.26	17.43 28.38

Table 9. Alkalinity concentrations in ground water

X:	28[a]	32[a]	39[a]	40[a]	40[a]	42[a]	42[a]	42[a]	49[a]
	51	51	52	54	54	55	58	59	59
	60	63	66	70	79	82	89	96	118

[a]These values are assumed to be non-detects below DL=50.

Table 10. $100(1-\alpha)\%$ upper confidence limits for $100P$ percentile

	Uncensored		Censored			
$(P, 1-\alpha)$	Factor	Upper limit	[a]Factor	[a]Upper limit	[b]Approximation factor in Table 3	[b]Approximation upper limit
(0.90, 0.95)	1.8114	97.71	1.904	100.7	1.905	100.7
(0.95, 0.95)	2.2601	110.5	2.418	115.9	2.440	116.6
(0.99, 0.95)	3.1165	137.9	3.340	146.9	—	—

[a]Based on Algorithm 1.
[b]Based on the approximations in Table 3.

We assume that $n_1 = 18$ and $n_2 = 6$. Using these values in Algorithm 2 with 10 000 simulation runs, we computed the factor $Q^*_{0.9;0.95}$ as 1.986, which yields the upper tolerance limit as $\exp(-4.206 + 1.986 \times 1.462) = 0.272$. For $n_1 = 12$ and $n_2 = 12$, we estimated (0.90, 0.95) upper tolerance limit as 0.276, and for $n_1 = 20$ and $n_2 = 4$, it was 0.274. Thus, as noted earlier, the choices of n_i's do not affect the tolerance limits, and the observed small differences among these estimated limits are due to simulation errors. We also note that these tolerance limits are close to the one based on the approximate formula given in the preceding paragraph, and they are all appreciably different from the tolerance limit based on the non-central t, which is 0.224. These results are in agreement with the conclusion of our simulation studies which indicated that upper tolerance limits based on the non-central t are liberal, and as a result, they tend to be smaller than those based on other accurate methods.

Suppose it is desired to find a 95% upper confidence limit for the probability that Altrazine concentration exceeds 0.20 μ g/l in a well. To find this upper confidence limit, we evaluated $(P, 0.95)$ upper tolerance limits for various values of P until we find the one for which the upper tolerance limit is close 0.20. Our search method yielded (0.87, 0.95) upper tolerance limit as $0.1985 \simeq 0.20$, and so, a 95% upper confidence limit for $P(X > 0.20)$ is $1-0.87 = 0.13$. This means that the probability that Altrazine concentration in a Nebraska well exceeds 0.20 is no >0.13 with confidence 0.95.

We also computed 95% confidence interval for the mean Altrazine concentration using Algorithm 2 with $n_1 = 18$ and $n_2 = 6$ as $(\exp(-3.79), \exp(-1.40)) = (0.023, 0.247)$. The 95% upper confidence limit is computed as $\exp(-1.798) = 0.166$.

Example 2. To illustrate the procedures to a situation where the numbers of measurements obtained by different methods are recorded, we generated independent samples of sizes $n_1 = 10$, $n_2 = 6$, and $n_3 = 9$ from a lognormal distribution with assumed parameters $\mu = 0.5$ and $\sigma = 1.5$ with detection limits, $\mathrm{DL}_i = \exp(\mu + z_{p_i}\sigma)$, where $P_1 = 0.2$, $P_2 = 0.4$, and $P_3 = 0.7$. These independent samples were pooled to create a sample of size $n = 25$ with three detection limits. This simulated sample along with the assumed values of parameters and the proportions of non-detects are given in Table 8.

The MLEs based on log-transformed data are $\hat{\mu} = 0.229$ and $\hat{\sigma} = 1.537$. To compute a (0.90, 0.95) upper tolerance limit, the required tolerance factor is $\frac{1}{\sqrt{25}} t_{24;0.95}\left(z_{0.9}\sqrt{25}\right) = 1.838$. The upper tolerance limit based on the non-central t is $\exp(0.229 + 1.838 \times 1.537) = 21.20$. To compute the tolerance limit using the approximation in Table 3, we computed $\hat{P}_1 = \Phi\left(\frac{DL_1 - \hat{\mu}}{\hat{\sigma}}\right) = 0.260$. Similarly, we computed $\hat{P}_2 = 0.472$ and $\hat{P}_3 = 0.754$. Thus, the approximate tolerance factor

$$\begin{aligned}\tilde{Q}_{0.90;0.95} = & -0.605 + 0.0222 \times 0.261 \\ & + 0.0390 \times 0.472 + 0.0700 \\ & \times 0.754 + 1.35 \times 1.838 + 0.0003 \\ & \times 25 = 1.961.\end{aligned}$$

The tolerance limit based on this factor is $\exp(0.229 + 1.961 \times 1.537) = 25.61$. To apply the Monte Carlo method, we estimated the 95th percentile of $Q^*_{0.9}$ using Algorithm 1 with 10 000 simulation runs as 1.956. The tolerance limit based on this factor is $\exp(0.229 + 1.956 \times 1.537) = 25.42$. We again see that the tolerance limit based on the approximate formula in Table 3 and the one based on Monte Carlo method are practically the same, and they are larger than the one based on the non-central t.

We also computed 95% confidence interval for the mean using Algorithm 2 with $n_1 = 10$, $n_2 = 6$, and $n_3 = 9$ as $(\exp(0.733), \exp(3.28)) = (2.08, 26.58)$. The 95% upper confidence limit is computed as $\exp(2.86) = 17.52$.

Example 3. In this example, we shall use the uncensored data reported in Gibbons (1994, p. 261). This data set was also used by Krishnamoorthy *et al.* (2008) to compute tolerance limits for a gamma

distribution. The measurements represent alkalinity concentrations in ground water obtained from a 'greenfield' site (the site of a waste disposal landfill prior to disposal of waste) and they are reproduced here in Table 9. The probability plot in Bhaumik and Gibbons (2006) indicates that gamma distribution is a good fit for the data.

Let $y_i = x_i^{1/3}$, $i = 1, \ldots, 27$. Based on all 27 observations, the mean $\bar{y} = 3.8274$ and the standard deviation $s_y = 0.4298$. The $(P, 1-\alpha)$ upper tolerance limit for alkalinity concentrations is given by $\left[\bar{y} + \frac{1}{\sqrt{27}} t_{26;1-\alpha}\left(z_P\sqrt{27}\right)s_y\right]^3$. One-sided upper tolerance limits for some values of $(P, 1-\alpha)$ are given in Table 10.

For illustration purpose and to assess the loss of information due to censoring, let us assume that the data with [a] are non-detects that are below the single DL of 50. Note that the number of non-detects is $m = 9$. The MLEs based on the cube root of this censored sample is $\hat{\mu} = 3.824$ and $\hat{\sigma} = 0.435$. The (0.90, 0.95) factor using Algorithm 1 is computed as 1.910, and the (0.90, 0.95) upper tolerance limit is $[3.824 + 1.910 \times 0.435]^3 = 100.9$. Other tolerance limits are computed similarly, and they are reported in Table 10. To compute tolerance limits using the approximate factors given in Table 3, we first note that $\hat{P}_1 = \Phi\left(\frac{50^{1/3} - 3.824}{0.435}\right) = 0.374$. The (0.90, 0.95) factor using the formula in Table 3 is $-0.669 + 0.164 \times 0.374 + 1.38 \times 1.811 + 0.0005 \times 27 = 1.905$, and the upper tolerance limit is $[3.824 + 1.905 \times 0.435]^3 = 100.7$. This limit and others are given in Table 10.

We once again observe from Table 10 that the results based on the approximations in Table 3 and the Monte Carlo method in Algorithm 1 are very similar. Furthermore, the differences between the tolerance limits from the censored sample and the corresponding ones from the uncensored sample indicate the loss of information due to censoring which, given that one-third part censored, are not appreciable.

CONCLUSIONS

Multiple detection limits present difficulties in data analysis, even for commonly used distributions such as the normal and the lognormal. Procedures for computing confidence intervals and hypothesis testing are investigated in this article. Our proposed methods are approximate, but our extensive simulation studies showed that the procedures are very satisfactory in terms of coverage probabilities (or Type I error rates in a hypothesis test) and powers. They are conceptually simple and they can be safely used in applications. The computational algorithms given in this article are quite easy to implement in any programming language. As noted earlier, we have posted programming codes in R language with a help file because R package is freely available and is very popular among statisticians and statistical practitioners in other disciplines. Fortran subroutines, which are used for all calculations in this article, are also available from the first author upon request. We also note that the Monte Carlo and the generalized variable procedures that we have developed for the lognormal distribution are applicable to any location-scale family since approximate pivotal quantities based on the MLEs can be developed in a similar fashion. We are currently working on procedures for some location-scale families and plan to publish the work elsewhere.

FUNDING

National Institute of Occupational Safety and Health (NIOSH) (2R01OH003628-07A1).

APPENDIX 1

Although many software packages compute the MLEs based on samples with detection limits, we are providing here necessary computational details because to apply the proposed methods in Algorithms 1 and 2, the MLEs should be evaluated large number of times. As we are not sure of the efficiency of methods used in software packages and convergence of the iterative scheme, we provide here the following computational details. The MLEs $\hat{\mu}$ and $\hat{\sigma}$ are the solutions of the equations

$$f_1(\mu, \sigma) = \frac{\partial l(\mu, \sigma)}{\partial \mu} = (n - m)\frac{\bar{x}_d - \mu}{\sigma} - \sum_{i=1}^{k} m_i \frac{\phi(z_i^*)}{\Phi(z_i^*)} = 0.$$

$$f_2(\mu, \sigma) = \frac{\partial l(\mu, \sigma)}{\partial \sigma} = -(n - m) + \frac{1}{\sigma^2}(n - m)\left(s_d^2 + (\bar{x}_d - \mu)^2\right) - \sum_{i=1}^{k} m_i z_i^* \frac{\phi(z_i^*)}{\Phi(z_i^*)} = 0.$$

The necessary partial derivatives to implement the Newton–Raphson method are

$$f_{1\mu}(\mu,\sigma)=\frac{\partial^2 l(\mu,\sigma)}{\partial\mu^2}=-\frac{(n-m)}{\sigma}-\frac{1}{\sigma}\sum_{i=1}^{k}m_i F(z_i^*).$$

$$f_{1\sigma}(\mu,\sigma)=\frac{\partial^2 l(\mu,\sigma)}{\partial\mu\partial\sigma}=-\frac{(n-m)(\bar{x}_d-\mu)}{\sigma^2}-\frac{1}{\sigma}\sum_{i=1}^{k}m_i z_i^* F(z_i^*).$$

$$f_{2\sigma}(\mu,\sigma)=\frac{\partial^2 l(\mu,\sigma)}{\partial\sigma^2}=-\frac{2(n-m)(s_d^2+(\bar{x}_d-\mu)^2)}{\sigma^3}+\frac{1}{\sigma}\sum_{i=1}^{k}m_i z_i^*\frac{\phi(z_i^*)}{\Phi(z_i^*)}-\frac{1}{\sigma}\sum_{i=1}^{k}m_i z_i^{*2}F(z_i^*).$$

where $z_i^*=(\mathrm{DL}_i-\mu)/\sigma$ and $F(x)=\phi(x)[x\Phi(x)+\phi(x)]/\Phi^2(x)$. Here, $\phi(x)$ denotes the standard normal probability density function and $\Phi(x)$ denotes the standard normal cumulative distribution. In these notations, the Newton–Raphson iterative relation is given by

$$\begin{pmatrix}\mu\\ \sigma\end{pmatrix}\leftarrow\begin{pmatrix}\mu_0\\ \sigma_0\end{pmatrix}-\begin{pmatrix}f_{1\mu}(\mu_0,\sigma_0) & f_{1\sigma}(\mu_0,\sigma_0)\\ f_{1\sigma}(\mu_0,\sigma_0) & f_{2\sigma}(\mu_0,\sigma_0)\end{pmatrix}^{-1}\begin{pmatrix}f_1(\mu_0,\sigma_0)\\ f_2(\mu_0,\sigma_0)\end{pmatrix},\tag{13}$$

where μ_0 and σ_0 are the initial guess values for the roots. The mean $\bar{x}_d$ and the standard deviation s_d based on the detected observations can be used as initial values for μ_0 and σ_0, respectively. During the iterative process, the term $\phi(x)/\Phi(x)$, involved in F(x) above, may cause overflow error. To avoid this overflow error, we restrict the argument x within the interval $[-7, 7]$. Note that the argument of the function $\phi(x)/\Phi(x)$ is $z_i^*=(\mathrm{DL}_i-\mu)/\sigma$, and $|z_i^*|<7$ holds if and only if the detection limits DL_i's are within seven standard deviations from the mean. The latter condition should hold because for any laboratory method or instrument, the detection limit should be within seven standard deviations from the mean of an exposure distribution.

Acknowledgements—The authors are grateful to two reviewers for providing useful comments and suggestions.

REFERENCES

Bhaumik DK, Gibbons RD. (2006) One-sided approximate prediction intervals or at least p of m observations from a gamma population at each of r locations. Technometrics; 48: 112–9.

Frome EL, Wambach PF. (2005) Statistical methods and software for the analysis of occupational exposure data with non-detectable values. Report prepared by the Oak Ridge National Laboratory for the U.S. Department of Energy. Available at www.hss.doe.gov/healthsafety/WSHP/be/docs/statmethods.pdf.

Gibbons RD. (1994) Statistical methods for groundwater monitoring, New York, NY: Wiley.

Gilliom RH, Helsel DR. (1986) Estimation of distributional parameters for censored trace level water quality data. Water Resour Res; 22: 135–46.

Gleit A. (1985) Estimation for small normal data sets with detection limits. Environ Sci Technol; 19: 1201–6.

Hass CH, Scheff PA. (1990) Estimation of averages in truncated samples. Environ Sci Technol; 24: 912–9.

Helsel DR. (2005) Nondetects and data analysis. New York, NY: Wiley.

Helsel DR. (2006) Fabricating data: how substituting values for nondetects can ruin results, and what can be done about it. Chemosphere; 65: 2434–9.

Helsel DR. (2010) Much ado about next to nothing: incorporating nondetects in science. Ann Occup Hyg; 54: 257–62.

Hewett P. (2006) Analysis of censored data. In: Ignacio JS and Bullock WH, editors. A strategy for assessing and managing occupational exposures. Fairfax, VA: American Industrial Hygiene Association Press; pp. 415–22.

Hewett P, Ganser GH. (2007) A comparison of several methods for analyzing censored data. Ann Occup Hyg; 51: 611–32.

Ignacio JS, Bullock WH. editors. (2006) A strategy for assessing and managing occupational exposures. 3rd edn. Fairfax, VA: AIHA Press.

Krishnamoorthy K. (2006) Handbook of statistical distributions with applications. Boca Raton, FL: Chapman & Hall/CRC. [The PC calculator accompanying this book is free, and is posted at 'www.ucs.louisisana.edu/∼kxk4695'].

Krishnamoorthy K, Mallick A, Mathew T. (2009) Model based imputation approach for data analysis in the presence of non-detectable values: Normal and Related Distributions. Ann Occup Hyg; 59: 249–68.

Krishnamoorthy K, Mallick A, Mathew T. (2011) Inference for the lognormal mean and quantiles based on samples with left and right type I censoring. Technometrics; 53: 72–83.

Krishnamoorthy K, Mathew T. (2009a) Statistical tolerance regions: theory, applications and computation. New York, NY: John Wiley.

Krishnamoorthy K, Mathew T. (2009b) Inference on the symmetric-range accuracy. Ann Occup Hyg; 53: 167–71.

Krishnamoorthy K, Mathew T, Mukherjee S. (2008) Normal based methods for a gamma distributions: prediction and tolerance interval and stress-strength reliability. Technometrics; 50: 69–78.

Krishnamoorthy K, Mathew T, Ramachandran G. (2006) Generalized p-values and confidence intervals: a novel approach for analyzing lognormally distributed exposure data. J Occup Environ Hyg; 3: 642–50.

Lawless JF. (2003) Statistical models and methods for lifetime data. New York, NY: Wiley.

Mulhausen JR, Damiano J. editors. (1998) A strategy for assessing and managing occupational exposures. 2nd edn. Fairfax, VA: AIHA Press.

Ogden TL. (2010) Handling results below the level of detection. Ann Occup Hyg; 54: 255–6.

Rappaport SM, Selvin S. (1987) A method for evaluating the mean exposure from a lognormal distribution, Am Ind Hyg Assoc J; 48: 374–9.

Selvin S, Rappaport SM. (1989) Note on the estimation of the mean value from a lognormal distribution. Am Ind Hyg Assoc J; 50: 627–30.

Selvin S, Rappaport SM, Spear R *et al*. (1987) A note on the assessment of exposure using one-sided tolerance limits. Am Ind Hyg Assoc J; 48: 89–93.

Singh A, Singh AK. (2009) ProUCL version 4.00.04 technical guide. Washington, DC: U.S. Environmental Protection Agency. EPA/600/R-07/041.

Singh A, Singh AK, Iaci RJ. (2002) Estimation of the exposure point concentration term using a gamma distribution. (EPA/ 600/R-02/084). Washington, DC: U.S. Environmental Protection Agency, (www.qe3c.com/dqo/training/289cmb02.pdf).

Wilson EB, Hilferty MM. (1931) The distribution of chi-squares, Proceedings of the National Academy of Sciences; 17, 684–88.