Reduced Aliquot Size for a Plasma Organochlorine Assay for Use in Epidemiological Studies

Francine Laden,2 Mary S. Wolff, Nancy J. Niguidula, Donna Spiegelman, Susan E. Hankinson, and David J. Hunter

Department of Epidemiology [F. L., D. S., S. E. H., D. J. H.] and Department of Biostatistics [D. S.], Harvard School of Public Health, Boston, Massachusetts 02115; Division of Environmental and Occupational Medicine, Mount Sinai School of Medicine, New York, New York 10029 [M. S. W., N. J. N.]; and Channing Laboratory, Department of Medicine, Harvard Medical School and Brigham and Women’s Hospital, Boston, Massachusetts 02115 [F. L., S. E. H., D. J. H.]

Abstract
Because archived blood specimens are an important but limited resource for conducting epidemiological studies using biomarkers, it is important to develop analytical techniques that minimize the amount of sample needed. We modified an established 1.0-ml blood plasma organochlorine assay to use smaller volumes. We assessed its utility by comparing the accuracy and precision of measurements obtained with different-sized aliquots of spiked plasma from three pools of known concentration of 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE) and polychlorinated biphenyls (PCBs; low, medium, and high). There was a modest sacrifice in accuracy using 0.5 as opposed to 1.0 ml. However, the within-batch coefficients of variation, a measure of laboratory error, were consistently low when 0.5-ml aliquots were used. For both DDE and PCB concentrations, this error was less than 5% for the medium and high pools [5–20 parts per billion (ng/ml)] and less than 9% for the low pool (<1 part per billion). After determining that aliquots of 0.5 ml were sufficient, we performed a blinded quality control analysis of stored plasma. In this study, we found that the assay would rank subjects with reasonable precision. Our results suggest that use of 0.5-ml aliquots should not compromise the power of a nested case-control study to detect differences between subjects and would thus save plasma for future research. For populations with very low levels of organochlorines, however, the larger volumes should still be used.

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2 To whom requests for reprints should be addressed.

Introduction
Archived blood specimens are a valuable resource for conducting epidemiological studies; samples obtained prior to disease diagnosis are particularly useful for prospectively studying markers of possible causal exposures (1). Because the amount of stored sample is often small, sometimes less than 2 ml, and there are a multiplicity of biomarkers hypothesized to be associated with a multiplicity of diseases, there is an incentive to develop analytical techniques that minimize the amount of sample needed to measure each biomarker.

A recent focus in the epidemiology of breast cancer is on the potential adverse effect of exposure to environmental organochlorines. Studies examining the association of the disease with blood plasma levels of PCBs2 and DDE, the major metabolite of 2,2-bis(p-chlorophenyl)-1,1,1-trichloroethane (DDT), have been inconclusive (2, 3). Therefore, there is the need for further study, particularly in a prospective setting. In previous studies, methods have been optimized to measure plasma or serum levels of organochlorines with a satisfactory degree of accuracy and precision using aliquots of 1–4 ml. In this study, we modified the analytical technique to use smaller aliquot sizes. We present the comparison of the accuracy and precision for PCB and DDE measurement obtained with aliquots of 0.25, 0.5, 1.0, and 2.0 ml. In addition, we tested the reliability of the assay by analyzing blinded replicate (i.e., split) samples of 0.5-ml aliquots of stored plasma from the Nurses’ Health Study, a large ongoing cohort study of women’s health (4).

Materials and Methods
Three standard preparations of human plasma (low, medium, and high) were aliquoted into volumes of 0.25, 0.5, 1.0, and 2.0 ml. The pools were prepared in Dr. Wolff’s laboratory (Mt. Sinai Medical School) from dated blood bank plasma and solutions of DDE and Aroclor 1260 (PCBs) dissolved in DMSO. The low plasma pool was left unaltered, the medium pool was spiked to achieve concentrations of 10.45 ppb (ng/ml) DDE and 4.79 ppb PCBs, and the high pool was spiked to obtain 21.77 ppb DDE and 11.99 ppb PCBs. The concentrations of the two spiked pools were within the ranges obtained in previous case-control studies from United States women (2, 3); the unaltered pool had lower concentrations of both DDE and PCBs than measured in these populations. These three pools were used as reference materials in other investigations performed in this laboratory during 1994; therefore, data on the recovery obtained from replicate analysis of each pool were available. The overall mean recovery (referred to subsequently

3 The abbreviations used are: PCB, polychlorinated biphenyl; DDE, 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene; ppb, parts(s) per billion; CVbb, between-batch coefficient of variation; CVsb, between-subject coefficient of variation percentage; CVsb, within-subject coefficient of variation percentage; r, Spearman correlation coefficient.
as the laboratory mean) for each pool for all 1.0-ml aliquots run in this laboratory, excluding the results from this experiment, was 0.75 ppb (SD, 0.38) DDE and 1.37 ppb (SD, 0.42) PCBs for the low pool \( (n = 18) \); 9.81 ppb (SD, 0.66) DDE, 4.72 ppb (SD, 0.39) PCBs for the medium pool \( (n = 18) \); and 19.59 ppb (SD, 0.97) DDE, 10.25 ppb (SD, 0.74) PCBs for the high pool \( (n = 19) \).

To assess optimal minimum aliquot size, we constructed four batches for each plasma pool. Each batch consisted of two to three replicates of each volume analyzed consecutively. A total of 107 samples were analyzed: 35, 36, and 36 for the low, medium, and high pools, respectively. In addition, a substudy was performed using only 0.5-ml aliquots. Two replicates of each plasma pool were run in each of three batches. This experiment was performed to demonstrate performance after further optimization (see “Laboratory Method.”)

We then performed a blinded quality control analysis with specimens from the Nurses’ Health Study to further assess the reproducibility of the assay optimized for 0.5 ml of plasma. Twenty-four replicate samples were aliquoted from the stored blood of samples of the Nurses’ Health Study, collected from participants from May 1989 through September 1990. The blood was drawn into sodium heparin Vacutainer tubes and sent to the Channing laboratory via overnight courier. Upon arrival at the laboratory, the blood samples were centrifuged, and blood components were aliquoted into eight cryotubes (two 5-ml and three 2-ml cryotubes of plasma, two 2-ml cryotubes of WBCs, and one 5-ml cryotube of RBCs), which were stored in liquid nitrogen freezers. For this study, plasma from 22 women (2 from each of the 11 states from which women were enrolled in the Nurses’ Health Study) and from two plasma pools (one consisting of plasma from premenopausal women and the other of plasma from postmenopausal women) were aliquoted into two separate samples of 0.55 ml each (the extra 0.05 ml was included to allow for loss during pipetting). The aliquots were stored in glass vials and coded to prevent identification of the pairs by the technician. The ordering of the samples for analysis was randomly assigned, although each member of a pair was analyzed in the same batch of 12. The samples were frozen and shipped to the analytical laboratory (Mt. Sinai) on dry ice.

**Laboratory Method.** The laboratory methods have been described in detail elsewhere (2, 5). Briefly, a polar extract of plasma lipids was further treated with a column chromatographic clean-up and enrichment step and then analyzed by gas chromatography with electron capture detection. All steps were scaled appropriately for smaller aliquot volumes. The amount of methanol was optimized (0.3 ml) to create a good interface between the aqueous layer and the ether-hexane extractant (1.25 ml). In the second phase of optimizing the method, additional measures were taken to control contamination and thereby reduce the background levels that are the chief determinant of the limit of detection. All glassware, including vials and inserts used for the gas chromatograph, was prewashed. In addition to the water and detergent wash that was routine for reusable glassware, a chromic acid soak was instituted after each use. This procedure had previously been included only periodically. Finally, we used a teflon-silicon sandwich septum instead of the teflon-lined rubber septum that had been used with the gas chromatography vials. Results are reported as ng/ml or ppb DDE and of the sum of the higher PCB congeners (those with retention times longer than that of DDE). The detection limits estimated previously for 1.0-ml aliquots were 1 ppb for DDE and 2 ppb for PCBs, based on 3 times the SD of the lowest quality control plasma pool (6).

**Statistical Analysis.** For each plasma pool, we calculated the arithmetic mean DDE and PCB concentrations obtained with each aliquot volume. To determine whether the results from this experiment were consistent with results regularly performed in this laboratory, we compared the mean concentrations of DDE and PCBs recovered from each plasma pool for each aliquot size (observed mean) to the laboratory mean (the average value for these pools in 1-ml aliquots from batches not included in this experiment but analyzed contemporaneously). We calculated the percent difference between the two values \( [(\text{observed mean} - \text{laboratory mean})/\text{laboratory mean}] \times 100 \). We also calculated the coefficient of variation for each aliquot volume was used. The laboratory mean was, as opposed to the spiked concentrations, because a laboratory mean accounts for error in measuring the amount of the spiked compound to be added to the plasma, endogenous levels of the contaminant in the original plasma, and uptake of DDE and PCBs by the plasma lipids.

To determine whether the accuracy of the measurements of DDE and PCBs obtained in this experiment differed significantly by volume, we performed an ANOVA using the PROC MIXED procedure in SAS (Version 6.07; Ref. 7) for each plasma pool. Estimation was made using the restricted maximum likelihood method (8). Batch was modeled as a random effect, the indicator variables for volume (0.25, 0.5, and 2.0 ml) were treated as fixed effects, and natural logarithm-transformed values of DDE and PCBs were the dependent variables for the calculation of variances in separate models. The natural logarithms of the concentrations were used in this analysis because the transformed values were more normally distributed than the untransformed values. We chose the 1.0-ml aliquot as the referent because it is the smallest aliquot size previously used in epidemiological studies of these compounds (2).

To quantify the precision of the analytical method when each aliquot volume was used, we calculated the CV\(_{wb}\) for both DDE and PCBs. Batch-to-batch variability was quantified by calculating the CV\(_{wb}\). High precision is reflected in small coefficients of variation. For log-transformed data that are normally distributed, the coefficient of variation is equivalent to the SD of the transformed data multiplied by 100 (9). We obtained the SDs for the CV\(_{wb}\) and CV\(_{wb}\), from 12 separate analyses of variance performed for each volume and each pool, controlling for batch as a random effect. Therefore, the CV\(_{wb}\) represents the amount of laboratory error remaining when variance between batches is accounted for.

We calculated the CV\(_{wb}\), the CV\(_{wb}\), and their ratio (CV\(_{wb}/CV_{wb}\)) for the Nurses’ Health Study replicate samples. Again, we estimated the SDs for CV\(_{wb}\) and CV\(_{wb}\) by ANOVA using the SAS PROC MIXED procedure on the natural log-transformed data. The magnitude of the between-subject variation relative to the laboratory error is estimated as the CV\(_{wb}/CV_{wb}\) ratio. In general, the larger the between-subject variation in a blood parameter, the greater the degree of within-subject error that is acceptable. Within-batch error only was evaluated (and was equal to within-subject error) because we assayed both members of a replicate pair in the same batch. Because cases and their matched controls are typically analyzed in the same batch, this was reasonable. We also calculated the arithmetic mean, variance, and CV\(_{wb}\) for each subject’s DDE and PCB concentration. To examine whether the magnitude of the variance and the CV\(_{wb}\) were associated with the concentration of the organochlorine on the original, untransformed scale, we calculated the r.
The CVWbS ranged from 2.10 to 8.56% for DDE and from 1.47 to 7.25% for PCBs obtained in the substudy are presented in Table 2. The 0.5-ml aliquots were run. The optimization decreased the amount of laboratory error present when measuring both DDE and PCB concentrations in all plasma pools. The CVWbS for the low pool were large: 10.18-39.60%. For DDE, the CVWbS for smaller volumes (less than 1.0 ml) ranged from 0 to 7.25%. The mean and the mean DDE and PCB concentrations for each plasma pool at each volume are presented in Table 1 (first experiment) and Table 2 (optimized experiment). For DDE in the first experiment, the mean recovery at 1.0 ml for each of the three plasma pools was similar to the laboratory mean, as can be seen by the small percent difference between the values (range, 0.6-3.9%). The 2.0-ml aliquots were also consistent, with the exception of that from the high pool, which differed from the laboratory mean by 11.7%. However, the smaller aliquots from this pool were very similar to the laboratory mean. The percent differences were 4.1 and 1.5% using 0.25- and 0.5-ml aliquots, respectively.

The PCB concentrations obtained from the 1.0- and 2.0-ml aliquots were less comparable to the laboratory averages than were the DDE concentrations. The differences ranged from 7.4 to 14.2%, with the exception of the 2.0-ml aliquot of the high pool. The latter differed from the laboratory mean by only 1.48%. The mean concentrations obtained from the smaller aliquots were also very different from the laboratory means. For example, using 0.5-ml aliquots, the percent differences between the laboratory mean and the observed were 107.9, 24.2, and 10.5% for the low, medium and high pools, respectively. Because the PCB concentrations are low, particularly for the low pool, a small absolute difference can account for a large percentage of the laboratory mean.

The results from the study of the optimized method (Table 2) more closely resemble the laboratory means of DDE and PCBs for the low and medium plasmas than do the results obtained with the original method. Using the optimized method, the percent difference was 4.6% for DDE and 73.6% for PCBs.

### Table 1: Evaluation of the precision and accuracy of the organochlorine assay using aliquots of different volumes and concentrations

<table>
<thead>
<tr>
<th>Plasma (laboratory mean)</th>
<th>Aliquot volume (ml)</th>
<th>n</th>
<th>Arithmetic mean (ppb)</th>
<th>SD</th>
<th>% difference between laboratory mean and observed mean</th>
<th>P from internal comparisons</th>
<th>CVWb (%)</th>
<th>CVWb (%)</th>
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<tr>
<td>DDE</td>
<td>Low (0.75 ppb)</td>
<td>0.25</td>
<td>9</td>
<td>0.98</td>
<td>0.11</td>
<td>29.4</td>
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<td>5.53</td>
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<td>Reference</td>
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<td>Medium (9.81 ppb)</td>
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<td>PCB</td>
<td>Low (1.37 ppb)</td>
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*p Mean recovery for all 1.0-ml aliquots of each pair run in this laboratory, not including this study. For low, n = 18; for medium, n = 18, and for high, n = 19.

At each volume, averaged across batch.

Significance of volume in individual models for each plasma pool. Volume was modeled as a fixed effect with three indicator variables comparing 0.25, 0.5, and 2.0 to 1.0 ml. Batch was included in the model as a random effect.

Calculated as the between-batch SD of the log-transformed data.

Calculated as the within-batch SD of the log-transformed data.

**Results**

**Precision.** The arithmetic mean concentrations of DDE and PCBs recovered for each plasma pool, averaged across batch, when 0.25-, 0.5-, 1.0-, and 2.0-ml aliquots were assayed, are presented in Table 1. Precision assessed as CVWb5 and CVWb5 is also presented. The CVWb5 for DDE measurements ranged from 0 to 6.60% for all pools. For PCB measurements, the CVWb5 ranged from 0 to 7.25% for the medium and high pools. The CVWb5 for the low pool were large: 10.18-39.60%. For DDE, the CVWb5 ranged from 2.61 to 11.53. With the exception of the high pool, the CVWb5 for smaller volumes (less than 1.0 ml) were greater than the CVWb5 for the larger volume aliquots. However, random variation due to laboratory (within-batch) error was low regardless of the size of the aliquot and the concentration of DDE in the plasma pool. For PCBs, the CVWb5 for the medium and high pools also indicated low laboratory error regardless of volume; the range was 1.73-9.94%. However, the PCB measurements of the low pool were highly variable at all volumes less than 2.0 ml.

The assay was further optimized, primarily to strictly contain contamination or background levels, and additional 0.5-ml aliquots were run. The optimization decreased the amount of laboratory error present when measuring both DDE and PCB concentrations in all plasma pools. The CVWb5 and CVWb5 obtained in the substudy are presented in Table 2. The CVWb5 ranged from 2.10 to 8.56% for DDE and from 1.47 to 8.77% for PCBs.

**Accuracy.** The percent differences between the laboratory mean and the mean DDE and PCB concentrations for each plasma pool at each volume are presented in Table 1 (first experiment) and Table 2 (optimized experiment). For DDE in the first experiment, the mean recovery at 1.0 ml for each of the three plasma pools was similar to the laboratory mean, as can be seen by the small percent difference between the values (range, 0.6-3.9%). The 2.0-ml aliquots were also consistent, with the exception of that from the high pool, which differed from the laboratory mean by 11.7%. However, the smaller aliquots from this pool were very similar to the laboratory mean. The percent differences were 4.1 and 1.5% using 0.25- and 0.5-ml aliquots, respectively.

The PCB concentrations obtained from the 1.0- and 2.0-ml aliquots were less comparable to the laboratory averages than were the DDE concentrations. The differences ranged from 7.4 to 14.2%, with the exception of the 2.0-ml aliquot of the high pool. The latter differed from the laboratory mean by only 1.48%. The mean concentrations obtained from the smaller aliquots were also very different from the laboratory means. For example, using 0.5-ml aliquots, the percent differences between the laboratory mean and the observed were 107.9, 24.2, and 10.5% for the low, medium and high pools, respectively. Because the PCB concentrations are low, particularly for the low pool, a small absolute difference can account for a large percentage of the laboratory mean.

The results from the study of the optimized method (Table 2) more closely resemble the laboratory means of DDE and PCBs for the low and medium plasmas than do the results obtained with the original method. Using the optimized method, the percent difference was 4.6% for DDE and 73.6% for PCBs.
for PCBs in the low pool and 6.8% for DDE and 21.4% for PCBs in the medium pool. The percent difference for PCBs in the high pool was comparable to that obtained before (12.9 versus 10.5%). The percent difference for DDE in the high pool was not as low as before, but it was still acceptable (8.2%; Table 2).

In the first experiment, we also compared the concentrations recovered for the 0.25-, 0.5-, and 2.0-ml aliquots with the 1.0-ml aliquots run at the same time in an ANOVA model (Table 1). For DDE, the mean concentration obtained at 2.0 ml for the low pool was not significantly different from the mean concentration obtained at 1.0 ml, and for the high pool the means at 0.25 and 0.5 were not significantly different from those at 1.0 (P > 0.05). However, at the lower concentrations the means obtained using aliquots of 0.25 and 0.5 ml were significantly different from the 1.0-ml aliquot means. Mean PCB concentration obtained at 2.0 ml aliquots in the low pool, 2.0 ml in the medium pool, and 0.5 ml in the high pool also were not significantly different from the respective 1.0-ml aliquot means. The other mean PCB concentrations were significantly different from the 1.0-ml means.

Blinded Quality Control Analysis. The overall CV_{bs} and CV_{ws} for DDE and PCBs were obtained from the analysis of 24 replicate pairs of plasma samples from the Nurses’ Health Study. For DDE, the CV_{bs} was 81.74 and the CV_{ws} was 10.61. For PCBs, the CV_{bs} was 47.74 and the CV_{ws} was 9.72. The ratios of CV_{bs} to CV_{ws} were 7.69 and 4.91 for DDE and PCBs, respectively. Scatter plots of measured DDE and PCB concentrations for the second replicate versus the first replicate are presented in Fig. 1. The rs are 0.96 (P < 0.001) and 0.95 (P < 0.001) for DDE and PCBs, respectively.

The arithmetic mean, variance, and CV_{ws} of each subject’s DDE and PCB concentration, obtained using the optimized method, were also calculated. The mean concentrations ranged from 1.0 to 20.65 ppb DDE and from 2.30 to 11.90 ppb PCBs. The range of the CV_{ws} was 0.00−32.07 (mean, 6.38; SD, 8.66) for DDE and 0.41−24.06 (mean, 7.53; SD, 6.28) for PCBs. For both residues, all but two of the CV_{ws} were below 15%. Mean DDE was positively correlated with the variance (r = 0.56; P = 0.004). However, mean DDE was not significantly correlated with CV_{ws} (r = 0.002; P = 0.99). Mean PCBs was not significantly correlated with the variance (r = −0.23; P = 0.27), but it was significantly correlated with CV_{ws} (r = −0.63; P = 0.001); variances were higher at lower PCB concentrations.

Discussion

The utility of a new analytical method for determination of DDE and PCBs in human plasma should be evaluated by comparing both the accuracy and precision obtained from this method with those available from the established method. In epidemiological studies, it is desirable to maximize both accuracy and precision. Random laboratory error (lack of precision), quantified by the coefficient of variation due to within-subject error, results in misclassification of the exposure measure. If misclassification occurs, the differences between case-control pairs, if a difference exists, will be reduced and there will be attenuation of the relative risk between exposure and outcome (10). Accuracy is important in epidemiological studies, particularly for comparing results between populations and in choosing threshold limits for regulation of exposures. Error in accuracy also leads to misclassification; however, if the error is constant throughout the range of values represented in the study and is not differential between cases and controls, then systematic error should not affect the relative risk. If the error in accuracy depends on the true underlying concentration, as was the case here, then the relative risks will be biased if the measurement error is not corrected. These issues and the statistical approach to evaluating them have broad applicability to the analysis of other biomarkers in epidemiological research.

Although, in general, a larger volume of serum will provide more stable estimates, we determined that aliquots of 0.5 ml are adequate to measure DDE and PCBs in human plasma with sufficient precision and acceptable accuracy. The accuracy of the DDE measurement using 0.5 ml aliquots and the optimized assay was acceptable as compared to the “gold standard,” represented by the laboratory mean concentration. The accuracy of the PCB measurement was not as good, particularly at lower concentrations. However, the best estimate of the concentration of PCBs in the low plasma pool (1.38 ppb) was 40% lower than the lowest value observed in our study of 22 Nurses’ Health Study participants, and it fell in the low end of the distribution observed in the studies of both Wolff et al. (2) and Krieger et al. (3). In subsequent applications in the Nurses’ Health Study, the lowest measured value of PCBs was 2.30 ppb, 70% greater than the estimated value for the low pool. The loss of accuracy was reduced in the range of values more typically observed in United States women. Despite the fact that for all but the highest plasma pool the concentrations of DDE and PCBs recovered from 0.5 ml aliquots were significantly different from the concentrations obtained in this exper-
The large CVw, observed for the low pool (38.73%) was not feasible for this assay using current techniques is 0.5 fluent. Therefore, we decided that the smallest aliquot size this small volume, and any contamination could be more intrusions recovered were less comparable to the 1.0 ml recover-aliquot was lower than that for the 0.5-mi aliquot, the concen-and high pools and approximately 9% for the low pool.

PCBs using the optimized assay were below 5% for the medium pool is near the limit of detection. The CVw,5 for both DDE and unexpected given that the concentration of PCBs in this plasma still less than or close to 5% when the original assay was used. The results from the reproducibility study using plasma from Nurses' Health Study participants confirmed that an epidemiological study using an aliquot size of approximately 0.5 ml will have the power to distinguish between subjects. The CVw,5 were low for DDE and for PCBs and in all cases lower than the CVw, suggesting that the assay would rank subjects with reasonable precision. Relative laboratory error of the DDE measurements, represented by the CVw,5, was not dependent on concentration (r = 0.002). However, the CVw,5 for PCBs were negatively correlated (r = -0.63) with the mean concentration, implying that the test was not as precise and underestimated the true level at lower concentrations. Therefore, for populations in which the PCB levels are expected to be very low, the smaller aliquot size would not be appropriate.

Although in some cases the CVw, obtained for the 0.25-ml aliquot was lower than that for the 0.5-ml aliquot, the concentrations recovered were less comparable to the 1.0 ml recover-ies. Furthermore, there are technical difficulties in working with this small volume, and any contamination could be more influential. Therefore, we decided that the smallest aliquot size feasible for this assay using current techniques is 0.5 ml.

The data from our study indicate that the loss of accuracy and precision associated with using smaller aliquots of blood plasma (specifically 0.5 compared to 1.0 ml) is acceptable, particularly in the range of concentrations typical of United States women. The laboratory error, or within-sample variation, was similar at the two volumes, and the differences in mean recovery should not influence case-control comparisons within a single study. Furthermore, in analysis of blinded splits using the 0.5-ml aliquots, the random laboratory error was considerably smaller than the variation between individual samples, suggesting that the assay would rank subjects acceptably from high to low concentration. Use of smaller volumes of stored serum or plasma should not compromise the power of the study to detect differences between DDE and PCB concentrations of cases and controls in prospective studies of populations with

This study had several limitations. First, the numbers of aliquots assayed at each volume were limited (volume = 0.25, n = 27; volume = 0.5, n = 45; volume = 1.0, n = 26; volume = 2.0, n = 27); this is a time-consuming and expensive assay. Furthermore, the samples were run under more controlled conditions than would be present in a routine study, and the technician could not be blinded to aliquot volume. The batches were run very close together in time (over two months), and the aliquot sizes were precise. The second part of the study was also performed under somewhat controlled conditions in that the laboratory personnel knew that a quality control test was being conducted. However, although the technician knew that replicates were being analyzed, she was blinded to the identity of replicate pairs, and all samples were handled as they would be in a real case-control study. It is thus reassuring that the CVw,5 were less than 5% for both DDE and PCBs in the range of values typically found in human plasma.

The scatter plots of results from blinded quality control analysis of Nurses' Health Study replicate samples (n = 24).
Reduced Aliquot Size for Organochlorine Assay

338 distributions of the organochlorines typical of United States studies, and more of each sample will be saved for future research. For populations with very low levels of organochlorines, however, the larger volumes should still be used. It is important to note that although using the smaller aliquots should maintain the internal validity of the epidemiological study, their use needs to be taken into account, along with other interlaboratory variations, when comparing results from different studies.

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References

Reduced aliquot size for a plasma organochlorine assay for use in epidemiological studies.


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