NIOSH's Reconsideration of the Application of the OPOS Methodology: Allowance for Time-Weighted Averaging

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In their review of NIOSH's proposed one person-one statistic (OPOS) approach to the analysis of coworker bioassay data, SC&A raised an objection to the general use of the mean value of a worker's bioassay result in the development of coworker models. In SC&A's opinion, the coworker dataset should contain all measured bioassay results during the modeled period without regard to how many samples a person contributed to that data set. SC&A did, however, acknowledge that in "clear cases of data dominance," the use of OPOS may be warranted, but this should be the exception rather than the norm.

After the recent SEC Issues Work Group discussions on this subject, NIOSH has reconsidered the use of the mean value of a worker's bioassay result. Although the OPOS method provides, in our opinion, a closer approximation of the urinary excretion patterns of workers than the previous method, it does suffer from several shortcomings that can be improved upon. As SC&A has suggested, OPOS fails to consider the temporal nature of the exposures and does not distinguish samples collected following an incident.

The original proposed OPOS method is the arithmetic average of the face values of all the exposures for one individual in one year (or other specified time period). After reconsidering this approach, NIOSH is proposing a version of the OPOS method that makes allowance for varying potential exposure patterns. The revised approach, designated as Time-weighted OPOS, is the weighted average of the same results that are used in the computation of the original OPOS method, with the only difference being that the days between the measurements are used as weights. NIOSH believes that this statistic provides a more accurate method to compute the yearly average exposure for an individual. In cases of incident samples, the values are weighted depending on the time of the incident during the modeled period. The weighting also accounts for the duration of the elevated sample if subsequent follow-up samples are collected. It should be noted that, for samples collected on a routine frequency, the time-weighted OPOS statistic is the same as the originally proposed OPOS that used the arithmetic mean.

While the computation of the Time-weighted OPOS is straightforward (a weighted average, instead of the simple average), three rules have been adopted to account for special circumstances. These are:

1) For an individual with more than one measurement in the same day, all the values (detects and non-detects) from the same day are averaged to arrive at an average daily excretion.

2) For an individual that had a sample in the previous year, it is assumed that the last sample from the previous year is representative of the excretion from the beginning of the current year until the first sample in the current year.

3) For an individual that had no sample in the previous year, it is assumed that the first sample from the current year is the exposure from the beginning of the current year until the first exposure observed in the current year.

Once all the average daily excretion and days between samples are computed for an individual during a year (or other specified time period), a weighted average is used to compute the Time-weighted OPOS statistic, where the days between samples are used as weights. Note here, that the sum of all the days between samples should be either 365 or 366 (for leap years), which means that we assume a continuous exposure during the year, even though some individuals might had started working sometime in the middle of the year.

The mathematical details of the computation of the Time-weighted OPOS are shown in Attachment A.

To test this new approach, NIOSH applied this methodology to the all the **[redacted]** bioassay data collected at **[redacted]**. Attachment B provides seven examples of the computation of the OPOS and Time-weighted OPOS values for workers that were monitored for exposure to **[redacted]** at the **[redacted]** site (the file that was used is **[redacted]**). These were chosen to demonstrate the calculation methodology that was used for the special circumstances described above.

A comparison of all the results of the original OPOS to the Time-weighted OPOS approach shows that, in about 83% of the cases, the two statistics are the same. In about 15% of the cases, the difference between the two statistics is less than 1 dpm/day in absolute value, and only 2% of the cases show differences between the two statistics of more than 1 dpm/day in absolute value, with some extreme cases where the two statistics are very far apart. For the total **[redacted]** data set, the average of all the Time-weighted OPOS values is about the same as the average of all the OPOS values in the data set, so it doesn't appear that one of the two methods is overall more claimant favorable than the other.

ATTACHMENT A
Mathematical Details of the Computation of Time-Weighted OPOS

The OPOS method was defined as the maximum possible mean (MPM) of the face values for all the censored and uncensored excretion results for one person in a year. The formula for the statistic computed using the OPOS method is the following:

$$\text{OPOS} = \frac{1}{n}\sum_{i=1}^{n} x_i$$

where:

$n =$ number of all excretion results for a person in a year,
$x_i =$ individual excretion result (can be either uncensored or censored).

Note that in the case in which there are censored excretion results, the face values of these excretion results are used in the formula above.

The Time-weighted OPOS method is defined as the maximum possible weighted mean of the face values for all the censored and uncensored excretion results for one person in a year, where the results are weighted by the numbers of days that the person was assumed to have excreted the measured value. The formula for the statistic computed using the Time-weighted OPOS method is the following:

$$\text{Time-weighted OPOS} = \sum_{j=0}^{m} y_j\, d_j \bigg/ \sum_{j=0}^{m} d_j$$

where:

$m =$ number of days when the person had excretion results in the year,
$y_j =$ average daily excretion results (can be either uncensored or censored),
$d_j =$ number of days that the person was exposed at result y_j.

The average daily excretion result y_j, is computed as the arithmetic mean of all the excretion results that a person had in one day:

$$y_j = \frac{\sum_{i=1}^{n_j} x_j}{n_j}, \text{ for } 1 \le j \le m$$

where:

$n_j =$ number of all excretion results for a person in a day.

The average daily excretion result y_0 that is used in the formula for the Time-weighted OPOS, represents the excretion result from the beginning of the current year until the first day when an excretion occurs during the current year, and is defined as follows:

$$y_0 = \begin{cases} y_p, & \text{if the individual had a sample in the previous year} \\ y_1, & \text{if the individual had no sample in the previous year} \end{cases}$$

where:

$y_p =$ the last average daily excretion result in the previous year.

Note that the denominator in the formula for the Time-weighted OPOS is $\sum_{j=0}^{m} d_j = 365$ (for non-leap years), or 366 (for leap years).

Similarly as in the OPOS method, the statistic computed using the Time-weighted OPOS will be used as an uncensored value, if the individual has at least one uncensored excretion result in the current year, or will be used a censored value, if all the excretion results in the current year are censored.

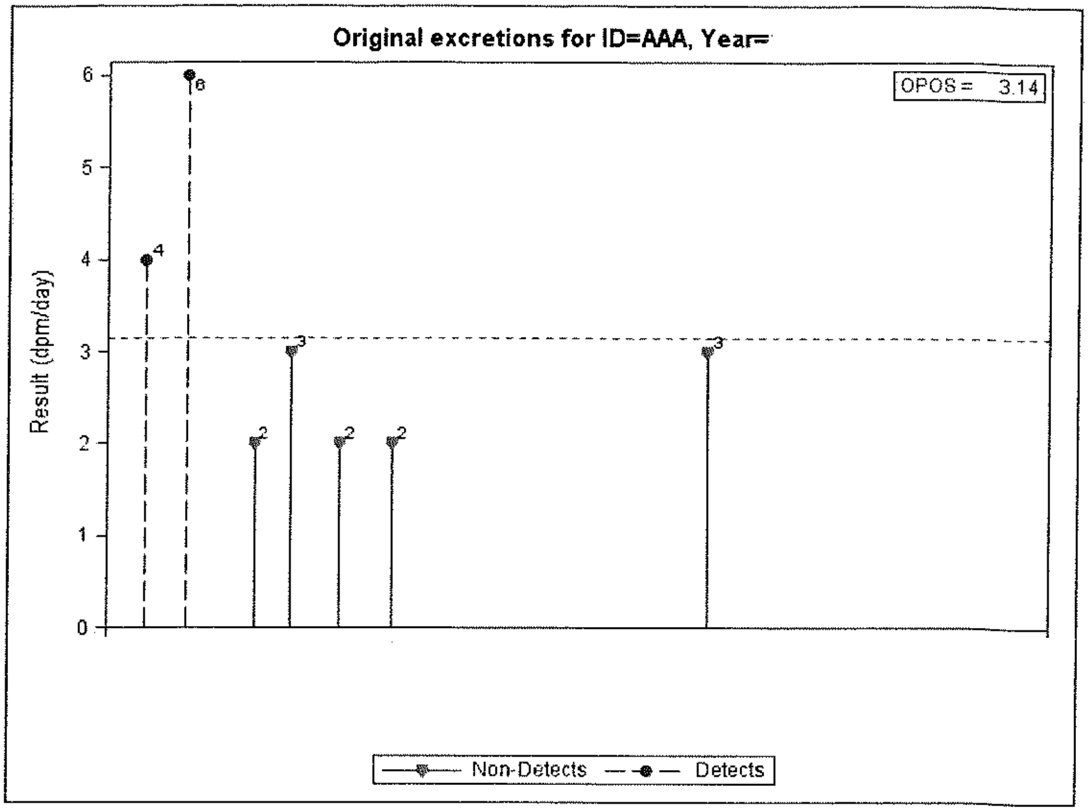
ATTACHMENT B
Example of Calculations of the Time-Weighted OPOS
([redacted] bioassay data)

Example 1

This example shows how the OPOS, and Time-weighted OPOS statistics are computed for a typical person in a year, when there are also samples for that person in the previous year.

OPOS Samples for ID= AAA, Year=**[redacted]**

Obs	ID	Date	Sample Type	Result
1	AAA	[redacted]	Detect	4
2	AAA	[redacted]	Detect	6
3	AAA	[redacted]	Non-detect	2
4	AAA	[redacted]	Non-detect	3
5	AAA	[redacted]	Non-detect	2
6	AAA	[redacted]	Non-detect	2
7	AAA	[redacted]	Non-detect	3

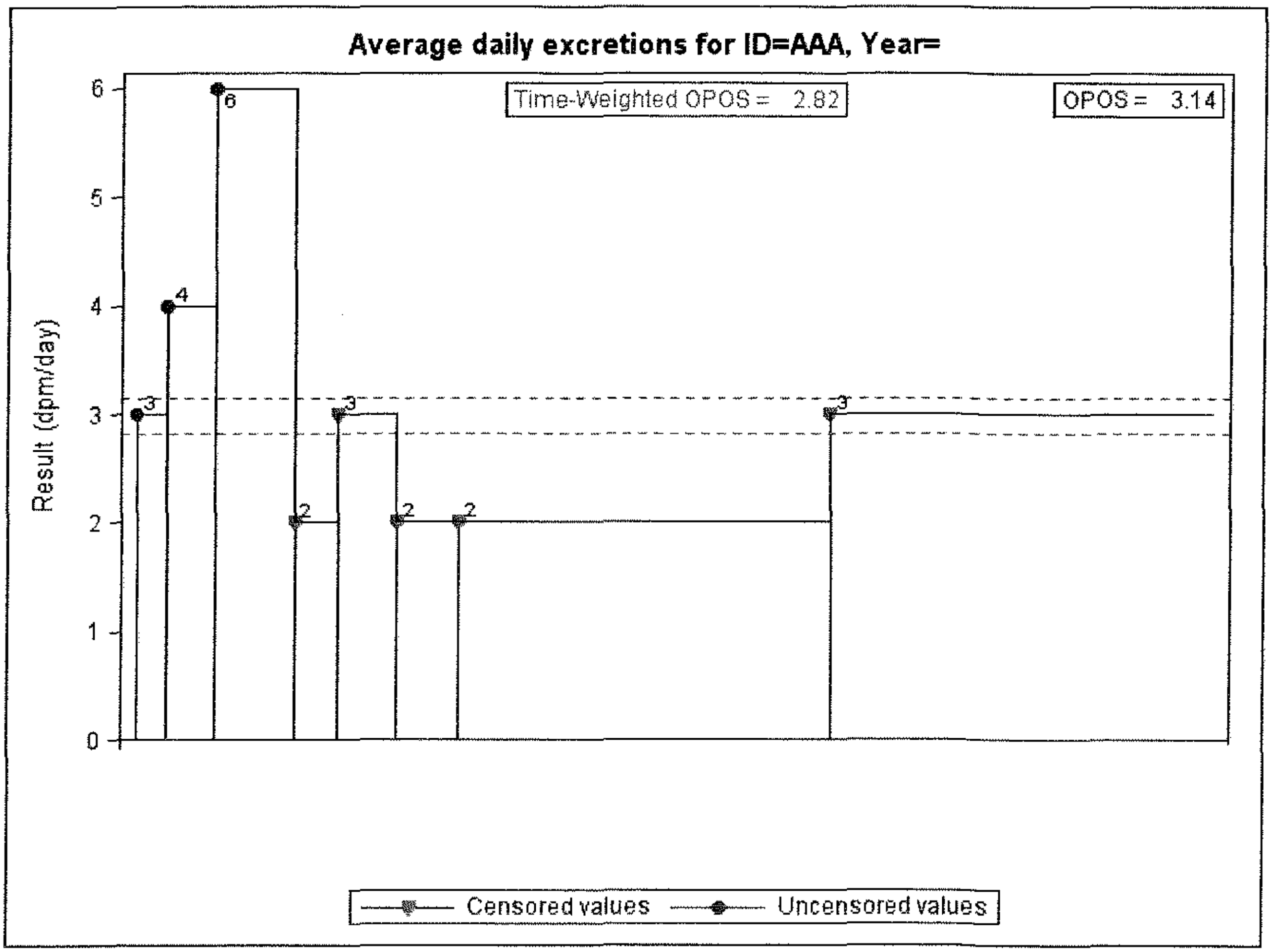


Last OPOS Sample for ID= AAA, Year=**[redacted]**

Obs	ID	Date	Sample Type	Result
15	AAA	**[redacted]**	Detect	3.0

Time-weighted OPOS Samples for ID= AAA, Year=**[redacted]**

Obs	ID	Date	Sample Type	Daily Excretion	Days Between Samples
1	AAA	**[redacted]**	Non-censored	3	**[redacted]**
2	AAA	**[redacted]**	Non-censored	4	**[redacted]**
3	AAA	**[redacted]**	Non-censored	6	**[redacted]**
4	AAA	**[redacted]**	Censored	2	**[redacted]**
5	AAA	**[redacted]**	Censored	3	**[redacted]**
6	AAA	**[redacted]**	Censored	2	**[redacted]**
7	AAA	**[redacted]**	Censored	2	**[redacted]**
8	AAA	**[redacted]**	Censored	3	**[redacted]**



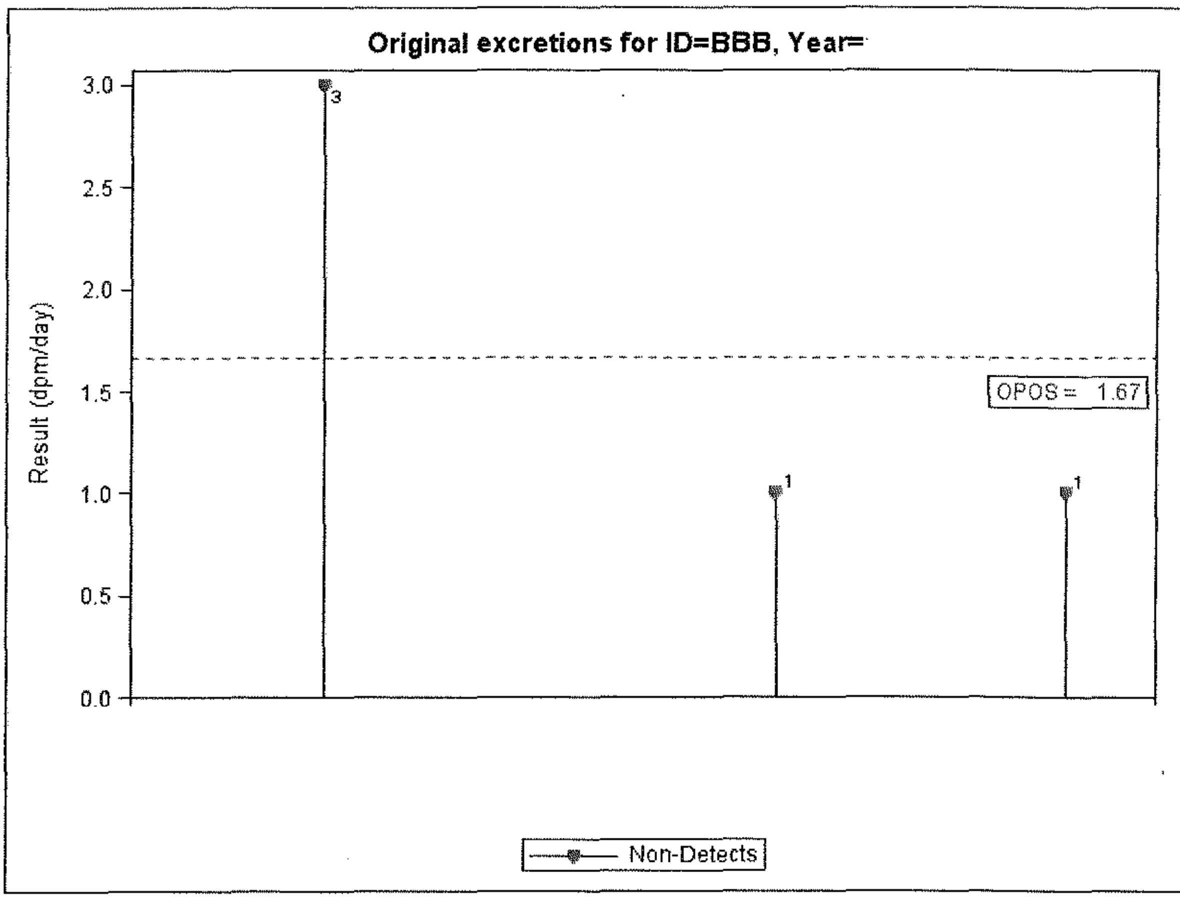
The last sample result from the previous year (a detect with a value of 3, from **[redacted]**) is assumed to be excreted from the beginning of the current year until the first sample in the current year (**[redacted]**). For this example, OPOS = 3.14, and Time-weighted OPOS = 2.82.

Example 2

This example shows how the OPOS, and Time-weighted OPOS statistics are computed for a typical person in a year, when there are no exposures for that person in the previous year.

OPOS Samples for ID=BBB, Year=**[redacted]**

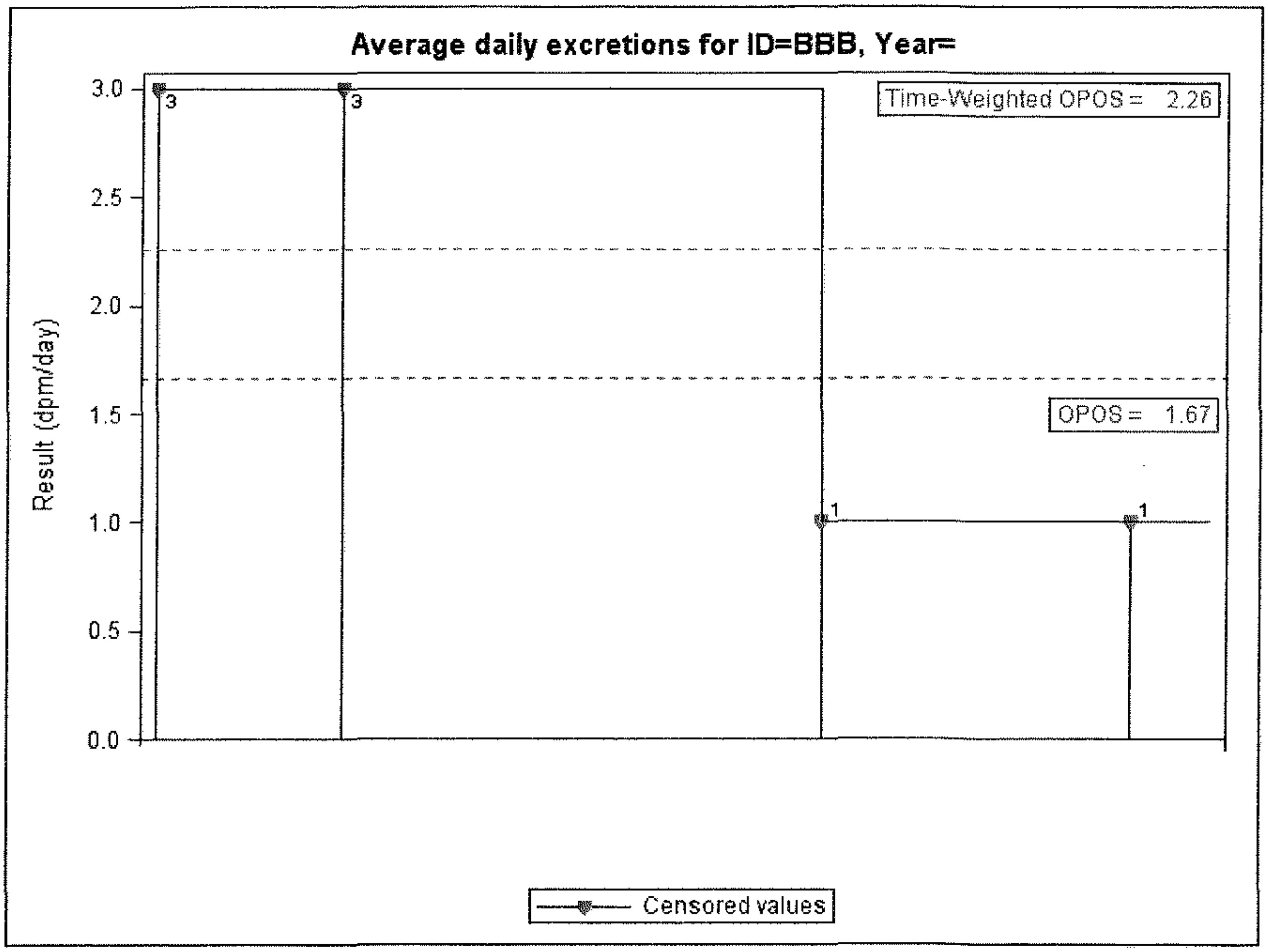
Obs	ID	Date	Sample Type	Result
1	BBB	**[redacted]**	Non-detect	3
2	BBB	**[redacted]**	Non-detect	1
3	BBB	**[redacted]**	Non-detect	1



There are no OPOS Samples for ID=BBB, Year=**[redacted]**

Time-weighted OPOS Samples for ID=BBB, Year=**[redacted]**

Obs	ID	Date	Sample Type	Daily Excretion	Days Between Samples
1	BBB	**[redacted]**	Censored	3	**[redacted]**
2	BBB	**[redacted]**	Censored	3	**[redacted]**
3	BBB	**[redacted]**	Censored	1	**[redacted]**
4	BBB	**[redacted]**	Censored	1	**[redacted]**



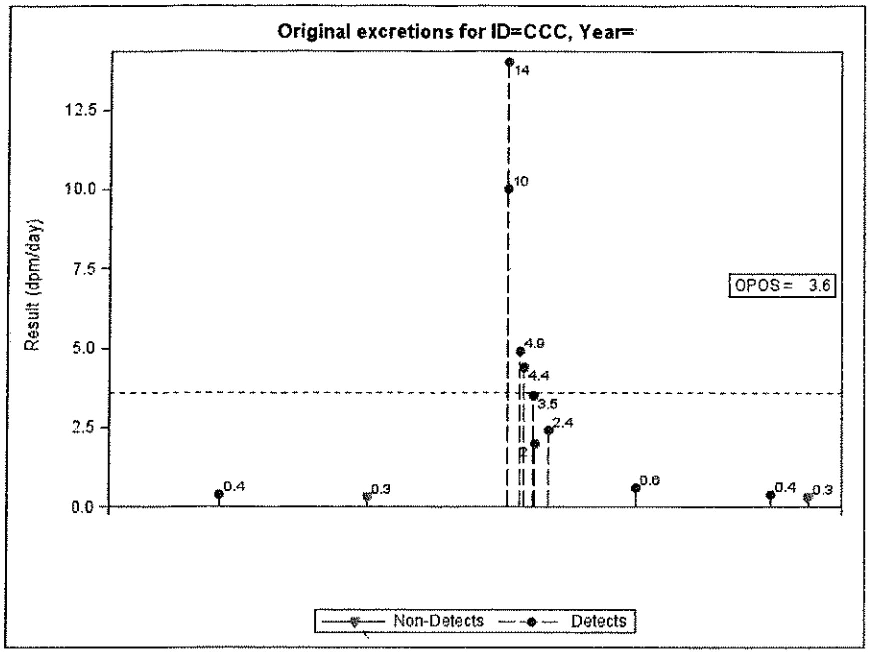
Since there are no exposures in the previous year (**[redacted]**), it is assumed that the first measurement in the current year (a non-detect with a value of 3, from **[redacted]**) is representative of excretion from the beginning of the current year. For this example, OPOS = 1.67, and Time-weighted OPOS = 2.26.

Example 3

This example shows how the OPOS, and Time-weighted OPOS statistics are computed for a person in a year, when there is more than one detectable measurement in the same day.

OPOS Samples for ID=CCC, Year=**[redacted]**

Obs	ID	Date	Sample Type	Result
1	CCC	[redacted]	Detect	0.4
2	CCC	[redacted]	Non-detect	0.3
3	CCC	[redacted]	Detect	10.0
4	CCC	[redacted]	Detect	14.0
5	CCC	[redacted]	Detect	4.9
6	CCC	[redacted]	Detect	4.4
7	CCC	[redacted]	Detect	3.5
8	CCC	[redacted]	Detect	2.0
9	CCC	[redacted]	Detect	2.4
10	CCC	[redacted]	Detect	0.6
11	CCC	[redacted]	Detect	0.4
12	CCC	[redacted]	Non-detect	0.3



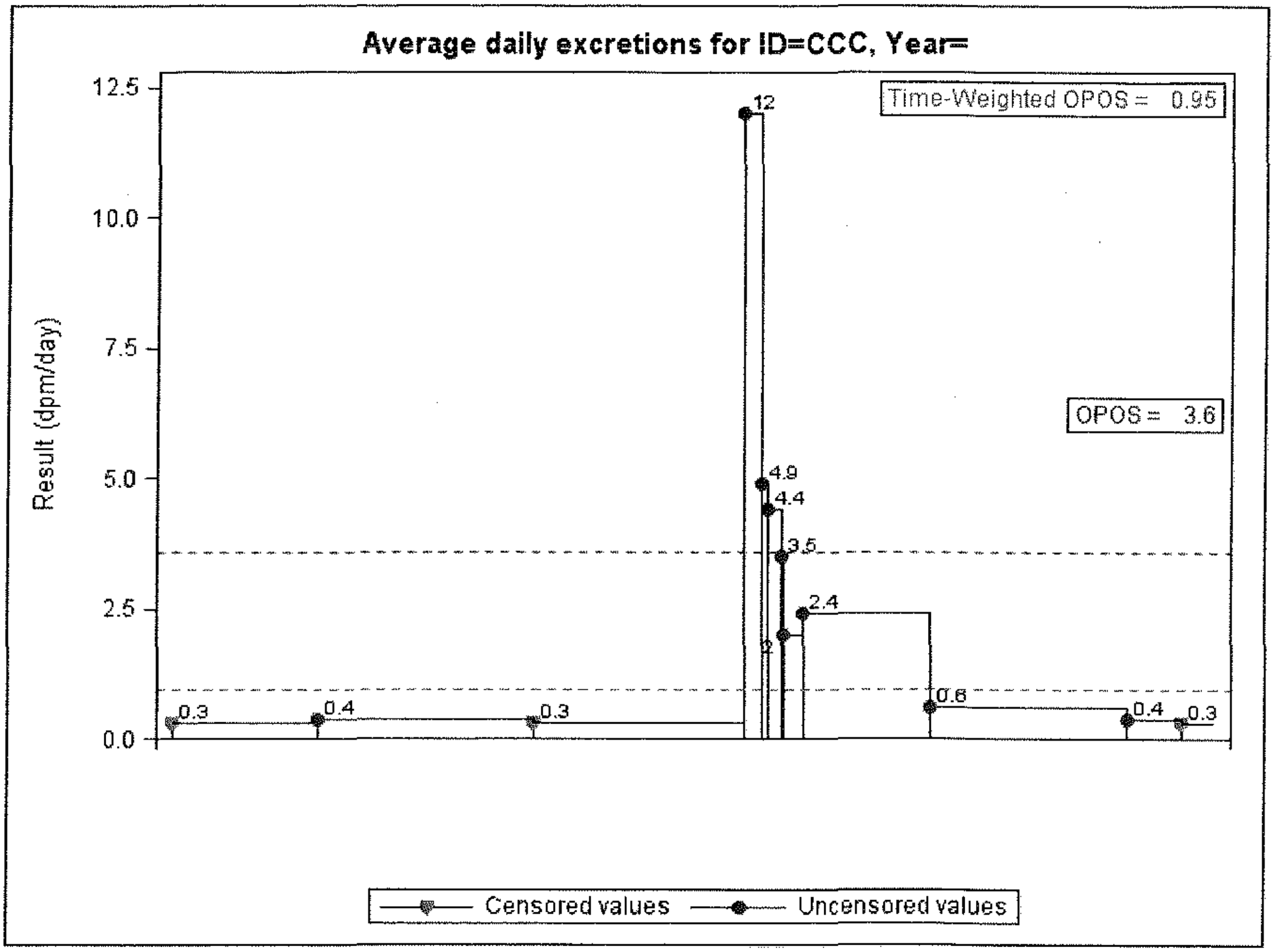
Last OPOS Sample for ID=CCC, Year=**[redacted]**

Obs	ID	Date	Sample Type	Result
2	CCC	[redacted]	Non-detect	0.3

Time-weighted OPOS Samples for ID=CCC, Year=**[redacted]**

Obs	ID	Date	Sample Type	Daily Excretion	Days Between Samples
1	CCC	**[redacted]**	Censored	0.3	**[redacted]**
2	CCC	**[redacted]**	Non-censored	0.4	**[redacted]**
3	CCC	**[redacted]**	Censored	0.3	**[redacted]**
4	CCC	**[redacted]**	Non-censored	12.0	**[redacted]**
5	CCC	**[redacted]**	Non-censored	4.9	**[redacted]**
6	CCC	**[redacted]**	Non-censored	4.4	**[redacted]**
7	CCC	**[redacted]**	Non-censored	3.5	**[redacted]**
8	CCC	**[redacted]**	Non-censored	2.0	**[redacted]**
9	CCC	**[redacted]**	Non-censored	2.4	**[redacted]**
10	CCC	**[redacted]**	Non-censored	0.6	**[redacted]**
11	CCC	**[redacted]**	Non-censored	0.4	**[redacted]**

Obs	ID	Date	Sample Type	Daily Excretion	Days Between Samples
12	CCC	**[redacted]**	Censored	0.3	**[redacted]**



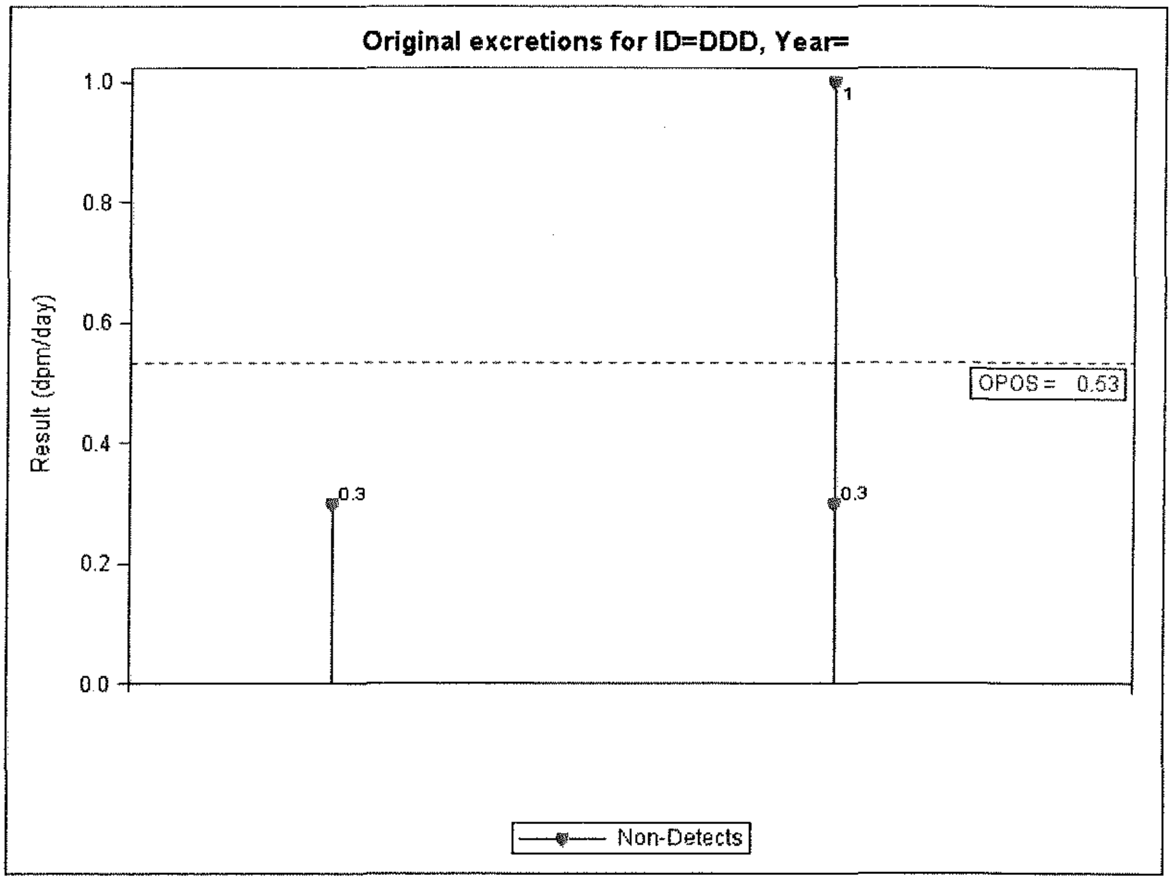
In this example, since there are two samples in the same day (two detects with values of 10 and 14, on **[redacted]**), the average of the two (12) is used as the excretion for that day in the computation of the Time-weighted OPOS statistic. For this example, OPOS = 3.6, and Time-weighted OPOS = 0.95.

Example 4

This example shows how the OPOS, and Time-weighted OPOS statistics are computed for a person in a year, when there is more one non-detect in the same day.

OPOS Samples for ID=DDD, Year=**[redacted]**

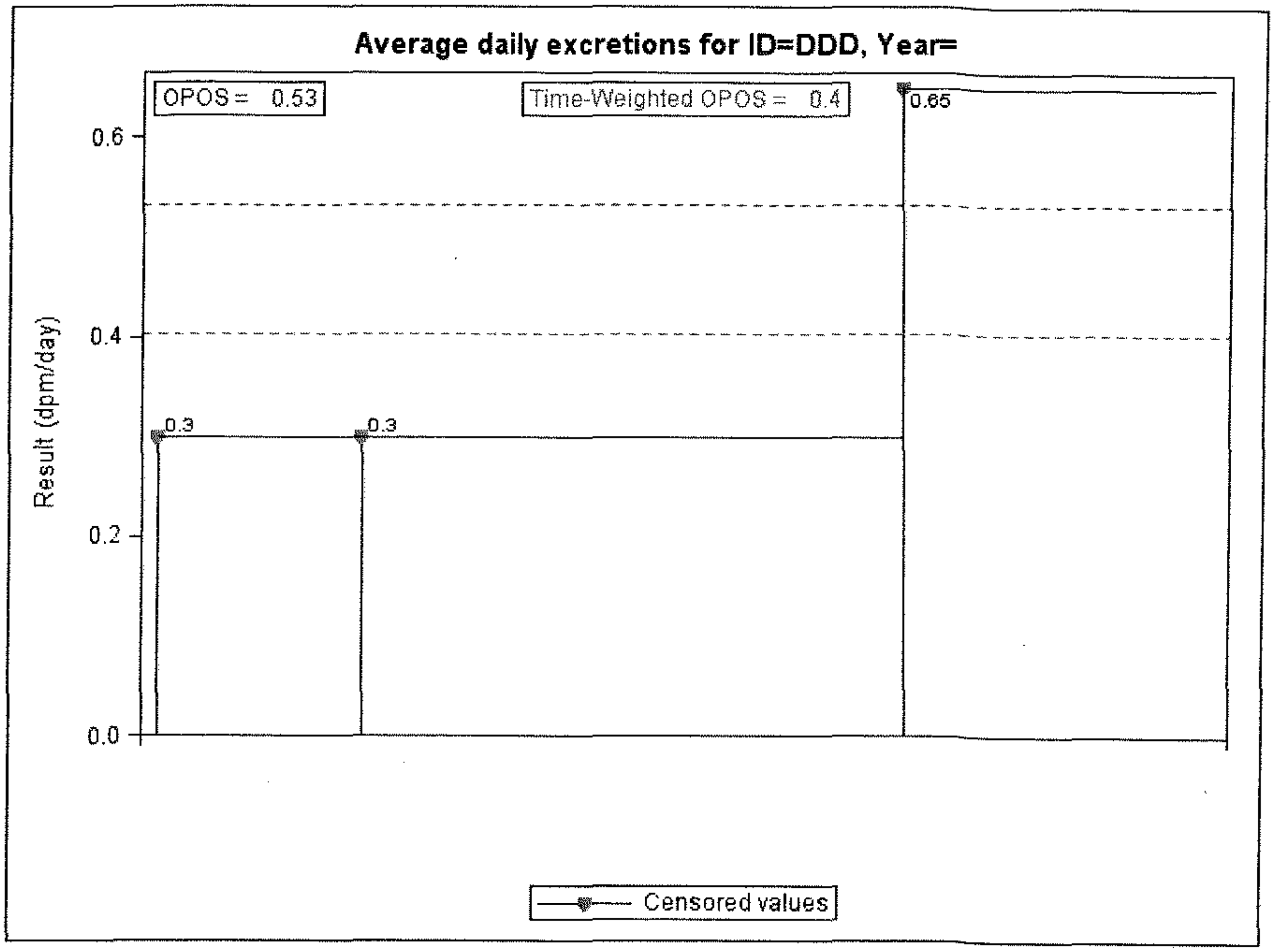
Obs	ID	Date	Exposure Type	Exposure
1	DDD	**[redacted]**	Non-detect	0.3
2	DDD	**[redacted]**	Non-detect	0.3
3	DDD	**[redacted]**	Non-detect	1.0



There are no OPOS Samples for ID=DDD, Year=**[redacted]**

Time-weighted OPOS Samples for ID=DDD, Year=**[redacted]**

Obs	ID	Date	Sample Type	Daily Excretion	Days Between Samples
1	DDD	**[redacted]**	Censored	0.30	**[redacted]**
2	DDD	**[redacted]**	Censored	0.30	**[redacted]**
3	DDD	**[redacted]**	Censored	0.65	**[redacted]**



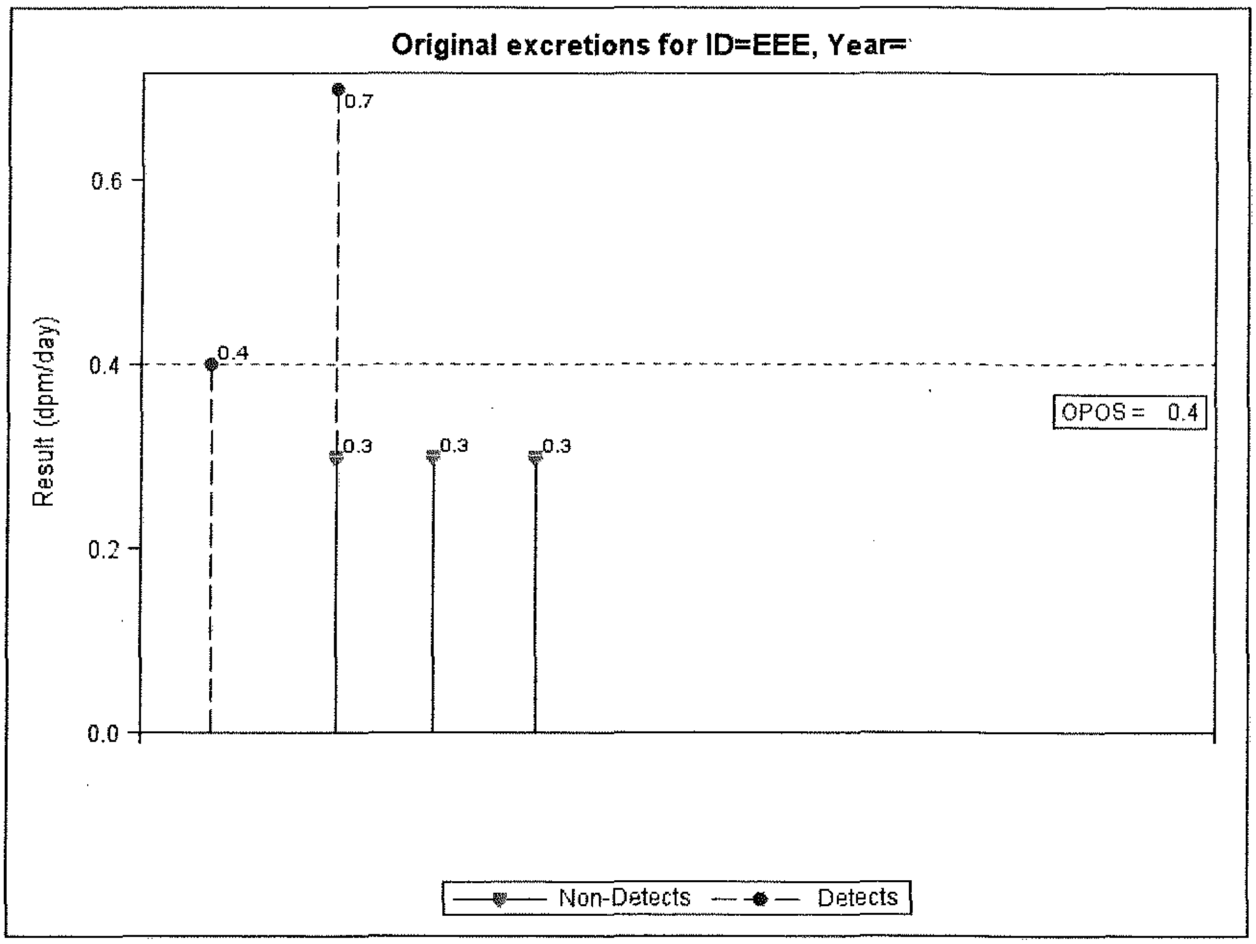
In this example, since there are two samples in the same day (two non-detects with values of 0.3 and 1.0, on**[redacted]**), the average of the two samples (0.65) is used as the excretion value for that day in the computation of the Time-weighted OPOS statistic. For this example, OPOS = 0.53, and Time-weighted OPOS = 0.4.

Example 5

This example shows how the OPOS, and Time-weighted OPOS statistics are computed for a person in a year, when there are both detects and non-detects in the same day.

OPOS Samples for ID=EEE, Year=**[redacted]**

Obs	ID	Date	Sample Type	Result
1	EEE	**[redacted]**	Detect	0.4
2	EEE	**[redacted]**	Non-detect	0.3
3	EEE	**[redacted]**	Detect	0.7
4	EEE	**[redacted]**	Non-detect	0.3
5	EEE	**[redacted]**	Non-detect	0.3

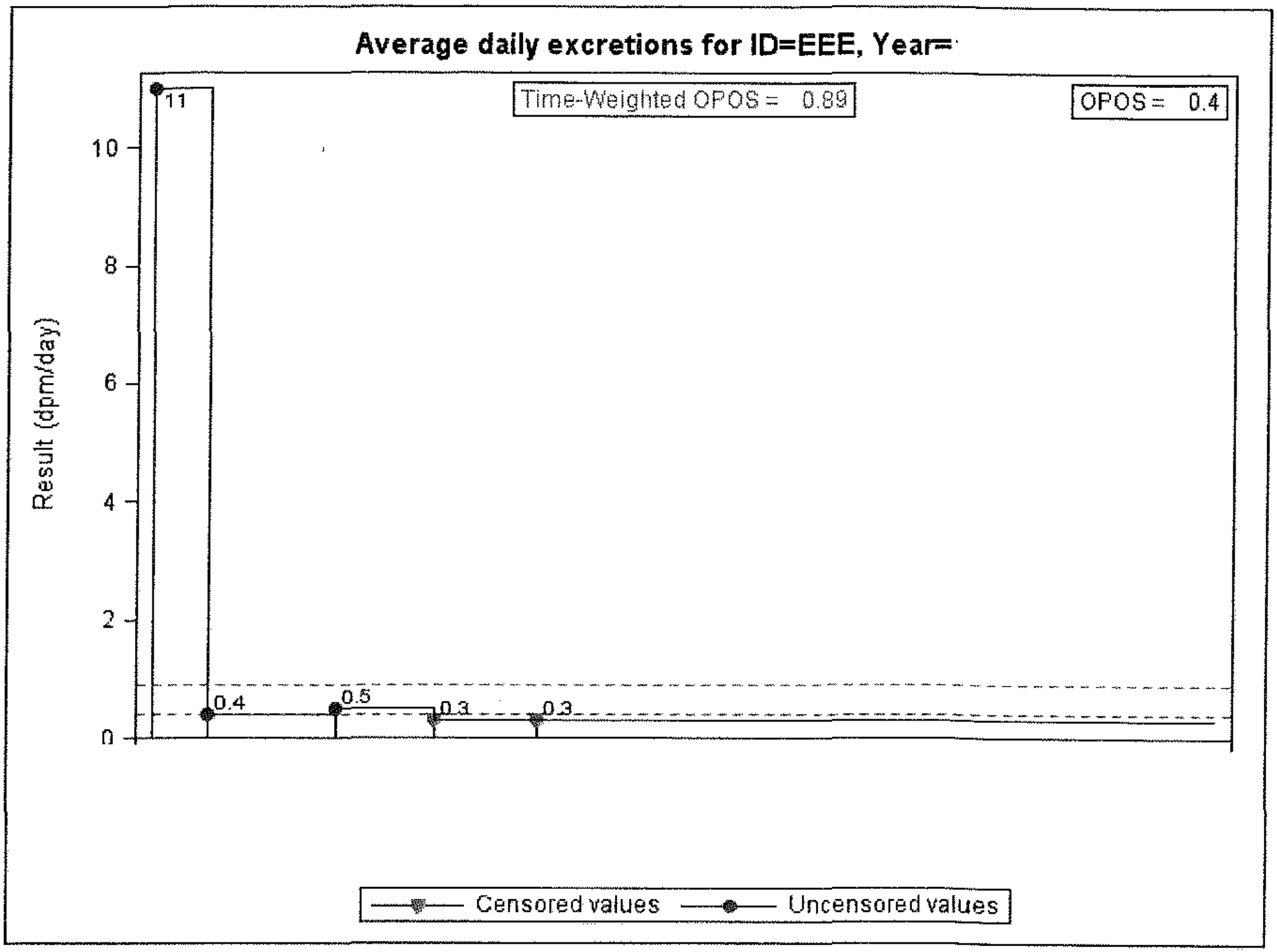


Last OPOS Sample for ID=EEE, Year=**[redacted]**

Obs	ID	Date	Sample Type	Result
1	EEE	**[redacted]**	Detect	11

Time-weighted OPOS Samples for ID=EEE, Year=**[redacted]**

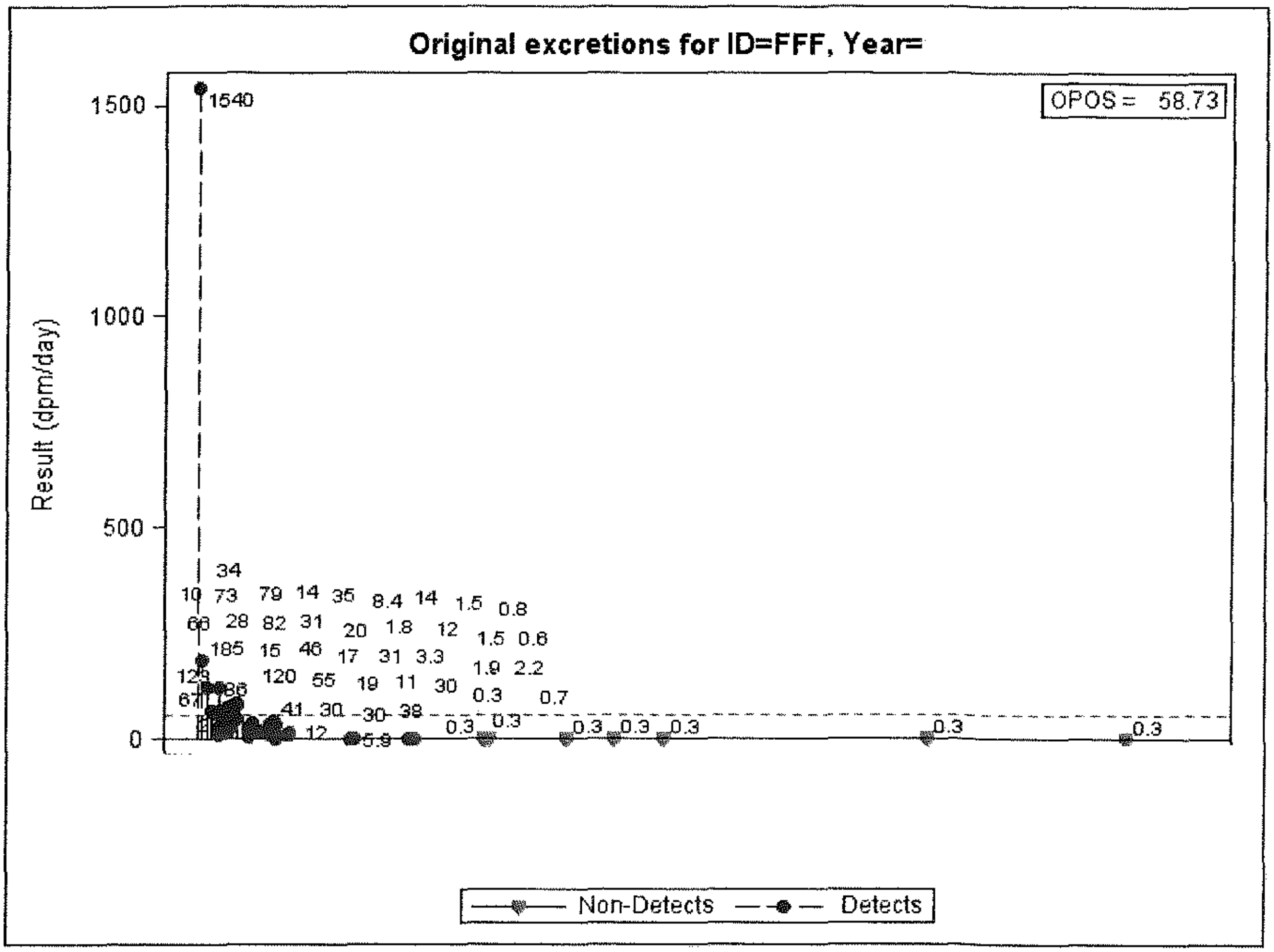
Obs	ID	Date	Sample Type	Daily Excretion	Days Between Samples
1	EEE	**[redacted]**	Non-censored	11.0	**[redacted]**
2	EEE	**[redacted]**	Non-censored	0.4	**[redacted]**
3	EEE	**[redacted]**	Non-censored	0.5	**[redacted]**
4	EEE	**[redacted]**	Censored	0.3	**[redacted]**
5	EEE	**[redacted]**	Censored	0.3	**[redacted]**



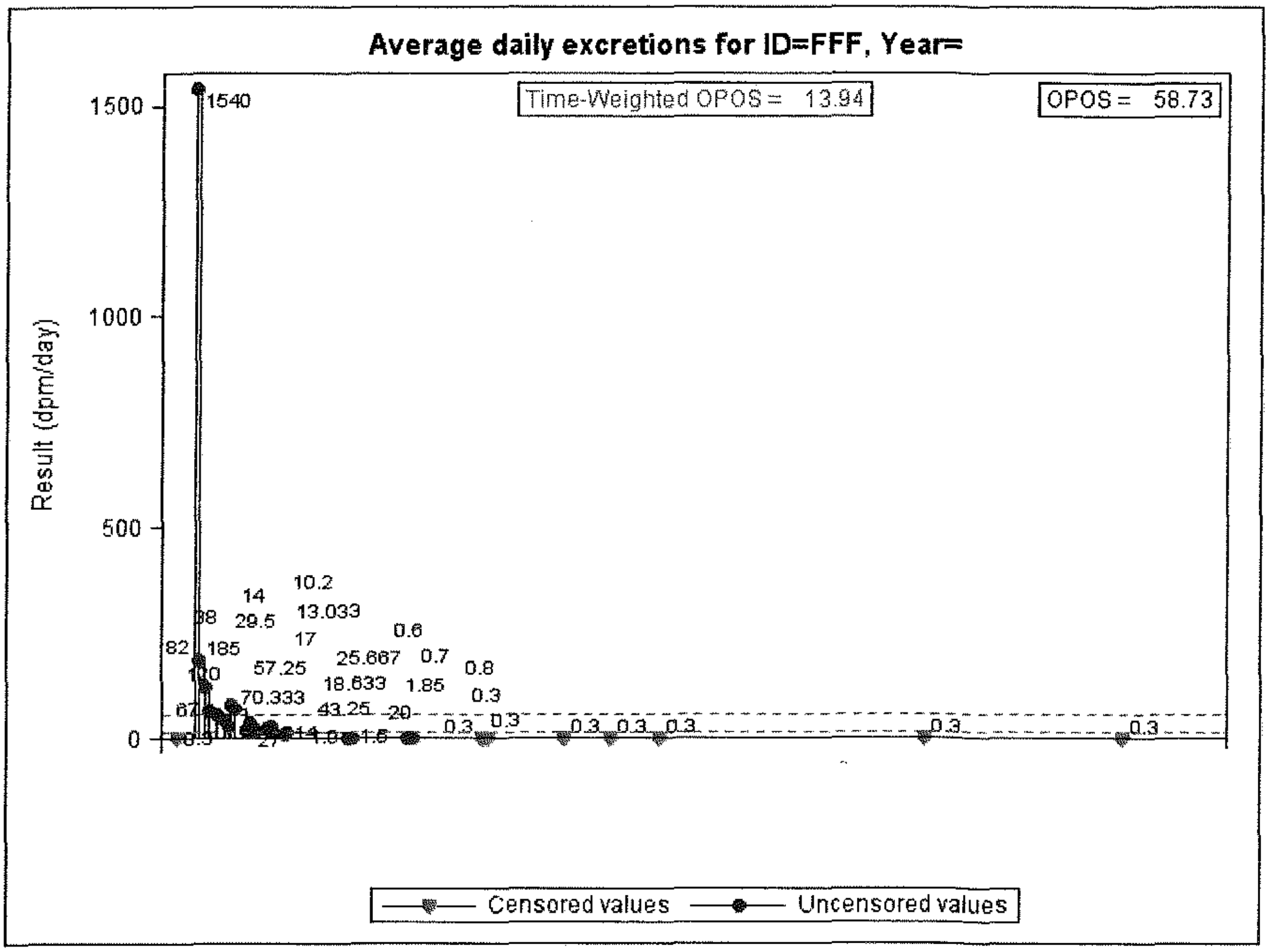
In this example, since there are two samples in the same day (a detect value of 0.7, and a non-detect value of 0.3, on **[redacted]**), the average of the two samples (0.5) is used as the excretion for that day in the computation of the Time-weighted OPOS statistic. For this example, OPOS = 0.4, and Time-weighted OPOS = 0.89.

Example 6

This example shows a scenario when the OPOS statistic produces a much higher value than the Time-weighted OPOS statistic.



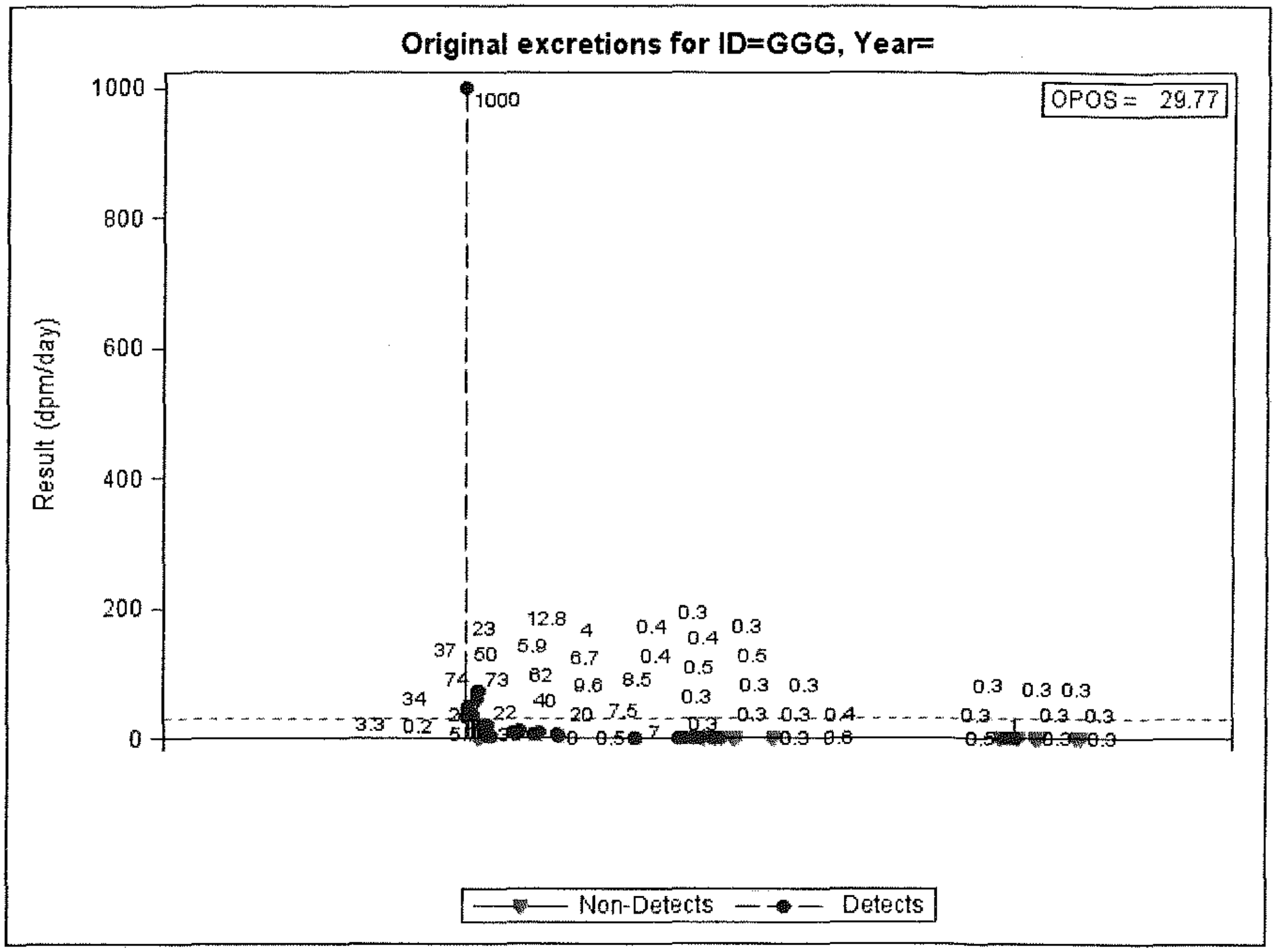
This individual had 52 samples during the year (not listed here), of which 44 were detects.



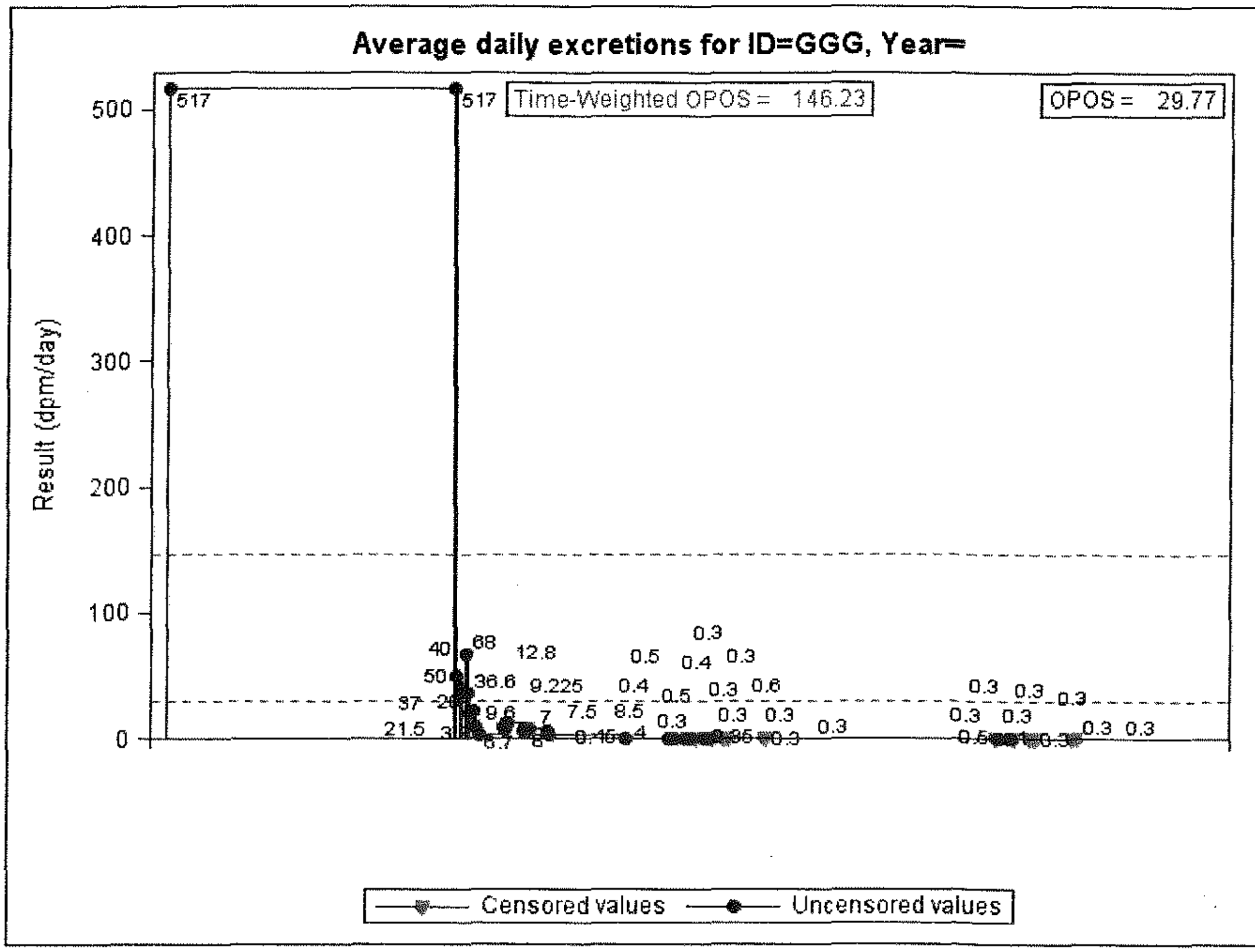
There are 34 daily samples for the individual, that were used in the computation of the Time-weighted OPOS statistic (the first exposure of the current year is assigned on the first day of the year, based on the last exposure from the previous year). For this example, which is typical for an individual that had an incident during the year, OPOS = 58.73, and Time-weighted OPOS = 13.94, so the OPOS statistic is much higher than the Time-weighted OPOS statistic, due to the fact that the high exposures lasted for only a few days, so the samples received very small weights in the computation of the Time-weighted OPOS statistic.

Example 7

This example shows a scenario when the Time-weighted OPOS statistic is much higher than the OPOS statistic.



This individual had 52 samples during the year (not listed here), of which 38 were detects.



There are 44 daily samples for the individual, that were used in the computation of the Time-weighted OPOS statistic (the first sample of the current year is assigned on the first day of the year, based on the first observed sample in the current year, since there is no measurement for this individual in the previous year). For this example OPOS = 29.77, and Time-weighted OPOS = 146.23, so the Time-weighted OPOS statistic is much higher than the OPOS statistic, due to the fact that the high exposure of 517 was assumed to occur from **[redacted]** until **[redacted]**, in the absence of any other exposure before the incident.