PPD®

SIGNIFICANT DIGIT Rules

Introductory Quiz

- Number of seats in a stadium = 6000

- I Just looked around the stadium and noticed around ¾ of seats are filled.

Question:-

How many seats are filled ?

or

How many tickets are sold out ?

Answer = 4500. ?

You don't really mean count is *exactly* 4500

It may be 4501 or 4450, even 4300, But you are sure that the number wasn’t 3500 or 5500

Here the 0’s in 4500 are just place holders

You’re certain about the 4, and the 5 is estimated but approximately correct.

Answer = 4500

Summary Output – Example 1

Protocol [redacted]

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Table 14.1.3
Descriptive Statistics for Laboratory Results

Characteristic	Statistics	TRT A (N=1121)	TRT B (N=1101)
Creatinine (µmol/l)	N	1038	947
	Mean	86.618	84.955
	S.D	28.2908	45.3160
	Minimum	35.00	33.59
	Median	82.000	80.000
	Maximum	252.55	654.16
Fasting Glucose (mmol/l)	N	1087	1005
	Mean	7.533	10.067
	S.D	2.2785	3.9623
	Minimum	2.90	3.90
	Median	7.100	8.700
	Maximum	25.20	29.85

Summary Output – Example 2

Clinical Study: [redacted]

Table 14.2-2.1. Summary of Plasma Pharmacokinetic Parameters for Each Treatment (Pharmacokinetic Analysis Set)

Compound: [redacted], Matrix: Plasma

Analyte	Cohort/ Treatment [a]	Summary Statistic	AUCinf (ng*h/mL)	AUClast (ng*h/mL)	Cmax (ng/mL)	Tmax (h)	T1/2 (h)
[redacted]	C1/A1(N=28)	n	28	28	28	28	28
		Arithmetic Mean	27300	26400	3870	ND	ND
		SD	8460	8390	1350	ND	ND
		CV% Mean	31.0	31.8	34.9	ND	ND
		Minimum	11300	11000	1290	2.00	6.70
		Median	27200	26400	3910	3.00	11.39
		Maximum	41700	40700	6280	4.00	35.78
		Geo-Mean	25900	24900	3600	ND	ND
		CV% Geo-Mean	36.4	37.2	43.6	ND	ND
	C1/B1(N=28)	n	27	28			
		Arithmetic Mean	28800	27800			
		SD	9440	9250			
		CV% Mean	32.8	33.3			
		Minimum	13600	13200			
		Median	27300	26700			
		Maximum	53300	52000			
		Geo-Mean	27300	26400			
		CV% Geo-Mean	34.3	34.2			

STATISTIC	A
N	20
MEAN	4.16
S.D.	0.828
GEO. MEAN	4.09
%CV	19.9
MEDIAN	4.10
MIN	2.78
MAX	6.34

Note(s): Geo = geometric; CV% = coefficient of variation; ND = not determined; SD = standard deviation.

Why ?

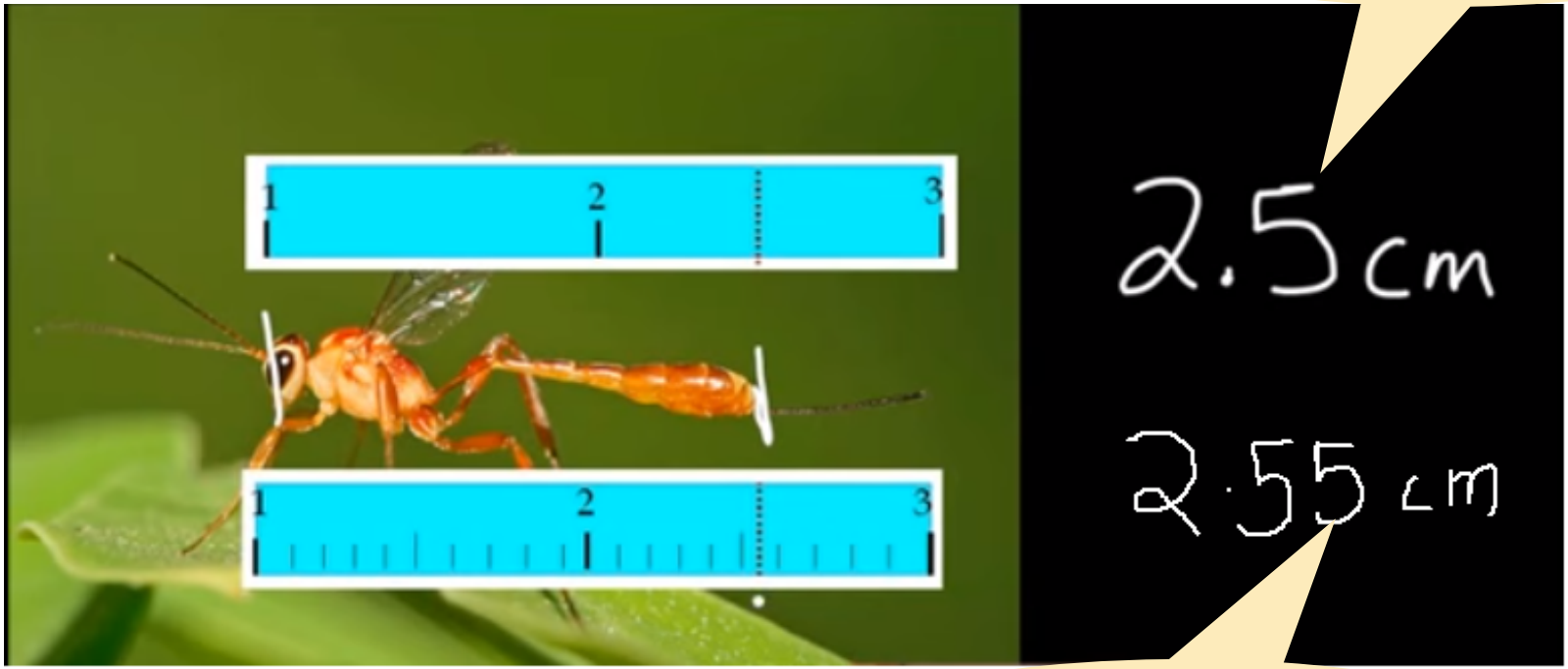
- No measurement can be exactly 100% perfect, every measurement involved some degree of uncertainty

Precision & Accuracy

Actual Weight of an Object = 110 lbs.

Measuring Instruments

Uncertainty in measurements



Example - PK data

Period	Parameter name	PK result (numeric)	Parameter unit	Character Result/Finding in Std Format	Numeric Result/Finding in Standard Units
1	AUCINF_obs	265.99517127	h*ng/mL	266	266
2	AUCINF_obs	268.44283638	h*ng/mL	268	268
3	AUCINF_obs	302.53210075	h*ng/mL	303	303
1	AUCINF_obs	25236.2245	h*ng/mL	25200	25200
2	AUCINF_obs	30130.302317	h*ng/mL	30100	30100
3	AUCINF_obs	26519.855129	h*ng/mL	26500	26500
1	AUCINF_obs	308.05905412	h*ng/mL	308	308
2	AUCINF_obs	266.31755137	h*ng/mL	266	266
3	AUCINF_obs	262.94682305	h*ng/mL	263	263
1	AUCINF_obs	33132.051635	h*ng/mL	33100	33100
2	AUCINF_obs	31824.956345	h*ng/mL	31800	31800
3	AUCINF_obs	35977.109636	h*ng/mL	36000	36000
1	AUCINF_obs	303.90158176	h*ng/mL	304	304
2	AUCINF_obs	309.34075712	h*ng/mL	309	309
3	AUCINF_obs	293.82674362	h*ng/mL	294	294

Decimal rule Vs Significant digit

- Types of rounding in which the approximation is done based on the digits of the number

Example:- 0.00112346

Result: 0.00 (rounded to 2 decimal places)
0.0011 (rounded to 2 sig. digits)

Significant figure means

- The minimum number of digits required to report a value, which contributes to the precision of a measurements or calculated data without loss of accuracy, starting from the first nonzero digit is the number of significant digits.

A. 10.001 (5 significant Digits)
B. 0.102010 (6 significant Digits)
C. 0.042 (2 significant Digits)

3 Rules to determine sig.fig

1. Non-zero digits are always significant (22.3 or 345)

2. Zeroes placed between other digits are always significant (4006 , 40.06)

3. A final zero or trailing zeros in the decimal portion ONLY are significant. (5.0 , 5.00, 4.60, 0.0011)

Examples

42g = 0.042kg

- A mass of 42 g has two significant digits.
- The mass of 0.042kg should still have two significant digits

Examples

Value	No. of sig.fig	Rounded Value
56	1	60
56	2	56
56.6	1	60
56.6	2	57
56.6	3	56.6
0.01	1	0.01
0.01	2	0.010

Special Examples

Value	No. of sig.fig	Rounded Value
10	1	10
10	2	10.
10	4	10.00
4500	4	4500.

- In the number 4500, it is not clear the zeroes are significant or not.
- The number of significant digits in 4500 is at least two, but could be three or four

Scientific notation method

To avoid uncertainty, use scientific notation to place significant zeroes behind a decimal point:

4.500×10^3 has four significant digits

4.50×10^3 has three significant digits

4.5×10^3 has two significant digits

SAS Code

```
proc format ;
        picture SIGDIGI2_ (round)
            0 = '9'
            0.0000001-0.000999999 = '9.00099'
            0.001-0.00999999 = '9.0099'
            0.01-0.0999999 = '9.099'
            0.1-0.999999 = '9.99'
            1-9 ='9.9'
            10-99 ='99'
            100-999 = '990' (MULT =.1)
            1000 - 9999 = '0900' (MULT =.01)
            10000 - 99999 = '09000' (MULT =.001)
            100000 - 999999 = '090000' (MULT =.0001)
            1000000 - 9999999 = '0900000' (MULT =.00001)
            10000000 - 99999999 = '09000000' (MULT =.000001)
        ;
        picture SIGDIGI3_ (round)
            0 = '9'
            0.0000001-0.000999999 = '9.000999'
            0.001-0.00999999 = '9.00999'
            0.01-0.0999999 = '9.0999'
            0.1-0.999999 = '9.999'
            1-9 ='9.99'
            10-99 ='99.9'
            100-999 = '999'
            1000 - 9999 = '0990' (MULT =.1)
            10000 - 99999 = '09900' (MULT =.01)
            100000 - 999999 = '099000' (MULT =.001)
            1000000 - 9999999 = '0990000' (MULT =.0001)
            10000000 - 99999999 = '09900000' (MULT =.00001)
        ;
        picture SIGDIGI4_ (round)
            0 = '9'
            0.0000001-0.000999999 = '9.0009999'
            0.001-0.00999999 = '9.009999'
            0.01-0.0999999 = '9.09999'
            0.1-0.999999 = '9.9999'
            1-9 ='9.999'
            10-99 ='99.99'
            100-999 = '999.9'
            1000 - 9999 = '9999'
            10000 - 99999 = '99990' (MULT =.1)
            100000 - 999999 = '999900' (MULT =.01)
            1000000 - 9999999 = '9999000' (MULT =.001)
            10000000 - 99999999 = '99990000' (MULT =.0001)
        ;
run ;
```

```
x_sig2 = compress(put(x, sigdigi2_.));
x_sig3 = compress(put(x, sigdigi3_.));
x_sig4 = compress(put(x, sigdigi4_.));
```

Conclusion

- Significant digits help to the reviewer to understand the results in better way when very low numerical quantity and very big numerical quantity presented in same time in terms of different PK parameters

- Many digits of a quantity doesn’t have impact in PK and in that situation 3 significant digits facilitate a better comparison when you have more PK profiles for different treatment groups

Thank you