ESVE Veterinary Endocrinology External Quality Assessment Scheme
ESVE REPORT

Release Month:	**May-23**
Release Number:	**018**
Species:	**Canine**

Overall Comments

General

This is the report of the seventeenth release of the ESVE EQA scheme. Welcome to new participants! The efforts made by participants to report their results were much appreciated. We had participation from 67 of 101 registered separate physical locations providing 523 analytical results. Changes in exportt/import procedures had an impact on our participation rate on this occasion particularly our EU lab members. It was also once again pleasing to see a few quality-conscious sites using in-clinic analysers participating in the scheme.

Although the numbers of participants within individual methodologies is still limited for some analytes, we can clearly see patterns of performance that should allow participants to get a feel for how their methods compare and in some cases that are raising questions that would be **best followed up by internal QC, reference range review and validation checks etc.**

We continue to be cautious with the public release of method names because of the limitations of so-far having only a small participant number but as was the case on previous releases we have highlighted a small number where it seems most relevant to do so.

INSULIN: The data on this occasion continues to support previous concern that Siemens Immulite methods do not pick up canine insulin to the same extent that other methods can.

Statistics

Although we have low numbers of participants for some analytes, for others we have sufficient to use robust measures of mean and SD. The scheme uses a 10% trimmed (censored) set of analyte results to calculate a robust trimmed mean and an appropriately adjusted standard deviation. The choice of 10% trimming means that analytes with n<20 participants (i.e., Oestradiol) will continue to be reviewed by traditional mean and standard deviation. Such an approach is common in EQA schemes and minimises the effect of very unusual results at the same time as retaining useful information about the distribution of the results submitted. The method used is that of Healy 1978 and 1979.

Healy (1979) Outliers in Clinical Chemistry Quality Control Schemes, Clinical Chemistry 25(5)675-677
http://clinchem.aaccjnls.org/content/25/5/675

Healy (1978) A mean difference standard deviation estimator in in symmetrically censored normal samples, Biometrika 65,643-646
https://doi.org/10.1093/biomet/65.3.643

Quality Goals

The report contains 2 approaches to the provision of "**quality goals**". For analytes that have had data published for biological variation (BV), it has been possible to determine "Allowable Total Error" (TEa) (see: http://vetbiologicalvariation.org/). TEa based Quality Specifications can be derived at "optimal", "desirable", and "minimum" levels For those analytes for which TEa can be calculated from BV, participants will see a classification under the heading **"TEa (BV)"** that tells them whether their result (bias from the consensus mean) is within the range for "optimal", "desirable" or "minimum" quality specifications or if the result falls outside the minimum specification ("Exceeds").
For those analytes for which BV has not been published, a different approach has been taken to derive candidate minimum quality specifications (cMQS). These are the maximum percentage bias from the consensus mean achieved by the closest 90% of analyses. Bias results for all participants, all releases and combined species were used in setting this cMQS. This specification will be reviewed and enhanced over time taking into account clinical relevance. They represent a "starting point" in quality specification for our scheme. Participants will see if their result is "Within" or "Exceeds" the cMQS under the heading **"cMQS-XX%"** where XX represents the combined Canine & Feline allowable bias for that analyte. No quality goals have been set for PTH and ACTH. See Appendix below for summary of quality goals.

This Release

This was a feline serum pool selected to enhance thyroxine concentrations.

Those of you familiar with other EQA schemes will recognise that the overall CV's we are seeing are high. By using robust measures for analytes with n>19, we are able to compare this scheme CV%'s to other schemes more directly. On this release, 4 analytes had CV% at or below 20% (Cortisol, Thyroxine, TSH, Creatinine) and 1 of these were below 10% (Creatinine). A wide CV% makes sense for our peptide representative (Insulin) but it is concerning when we see a high CV for non peptides.

For those of you that are clinicians or that work closely with clinicians, these reports serve as a reminder to exercise caution in making significant clinical management decisions based on relatively modest differences in results and when basing advice to third parties on laboratory results generated at locations or by equipment over which you have no control. Theoretically at least, we should feel relatively comfortable using literature reference ranges for steroids and non-species-specific analytes but these results indicate that we should be more cautious than we might expect to need to be. In this release a cortisol of 36 or 171 nmol/L could be obtained from the same sample depending on where the result originated.

Caution

It should be remembered that assays that are more commonly used may not turn out to be the ones that yield the most accurate results so at least for now, we may have to recognise that some of the methods with the most "outlying" results may not be the methods that are "wrong". Due to participant numbers, at present the target result for comparison is the All-method mean. It is accepted that this may be influenced by the distribution of methods. Where your method has several participants for a particular analyte, you should review your bias against that method mean.

Please note that the Method numbers bear no relationship to one another across analytes or releases. That is, for example, Immulite 1000, may be Method 1 for one analyte but Method 7 for another.

A simplistic way to check for the accuracy of your reconstitution of the freeze dried sample is to check if all your "SD Multiples" are consistently positive or consistently negative.

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Analytes

Cortisol As was the case for previous releases, the overall range of results generated for cortisol continues to surprise; especially taking into account that this is not a species specific hormone and the general consensus among endocrinologists in the interpretation of cortisol results in suppression and stimulation tests. However, variation between labs overall was the lowest the scheme has witnessed at 8.9%. This a further opportunity to see the impact of reagent change in the most popular methodology (Immulite 2000). The largest majority of users are using Veterinary Cortisol on the Immulite 2000, the popularity of a single method and perhaps better alignment with other technologies may have contributed to the reduction in variation between labs. In large human EQA schemes, CV for cortisol is 7-8%.

Fructosamine Although recent releases have given the impression that we were seeing reduced variation in results between labs (CV as low as 15.6%), on this occasion, CV was the highest it has been for 10years. The number of different methods being reported back from participants is higher than for many other analytes and this is likely to have contributed to the return of this variation. Also the longstanding Cobas-Roche reagent used for many early studies on veterinary fructosamine has had its application limited to Cobas -Roche equipment causing several labs to have to move away from this to less well established reagents.

Insulin As a peptide with some species differences, it is not too great a surprise to see variation in this analyte as different methods have different degrees of cross-reactivity between feline insulin and the method standards. This is an analyte where we should expect to see variation also in the reference ranges used by labs and clinicians should avoid textbook ranges for insulin and insulin: glucose ratios in reaching a diagnostic interpretation. **As has been the case in previous releases, the Immulite methods (Methods 1 and 6) yielded the lowest results.** The Immulite methods appear not to quantify low or normal insulin concentrations in dogs.

Progesterone This sample was of low progesterone concentration and there a reasonable agreement in results.

Thyroxine The adjusted all-method CV% achieved on this release was reasonable although it has been lower in the past. However, the range of results obtained continues to surprise.

Free T4 On a theoretical basis, the methods using dialysis should yield Free T4 results closest to the true value. We had three participants use dialysis methods in this release.

Oestradiol The difficulties measuring Oestradiol well have been recognised in this scheme previously.

Testosterone Testosterone was low in this sample. There was variation within as well as between methods.

TSH As is often the case, overall variation is low but heavily influenced by the dominance of a single manufacturer

Creatinine The CV for creatinine is good. No results breached the IRIS threshold for Stage 1 CKD (<125umol/L).

ACTH This sample was not modified to contain measurable quantities of labile ACTH. There was a range of results obtained. 16 labs generated results below their lower reporting limit.

PTH This sample was not modified to contain measurable quantities of labile PTH. There was close agreement between the 2 participants using different manufacturers' platforms.

17OHProg There a few participants thus far.

Aldosterone The majority of participants have used the same method, which has good within method variation.

TgAA All 3 participating labs reported results using the Oxford Laboratories method but different reporting styles Interpretations were not uniformly concordant.

Peter Graham, Program Coordinator, July 2022

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Appendix 1
Quality Goals: TEa and cMQS for dogs (expressed as percentage from consensus mean) used in release 018

DOG (all figures "%")	CVi	CVg	TEa (optimal)	TEa (desirable)	TEa (minimum)	cMQS (%bias)
Cortisol			0.0	0.0	0.0	34
Free T4	20.2	24.3	12.3	24.6	35.3	40
Fructosamine	11.1	4.2	6.1	12.1	17.6	*38*
Insulin			0.0	0.0	0.0	103
Oestradiol			0.0	0.0	0.0	116
Progesterone			0.0	0.0	0.0	62
Testosterone			0.0	0.0	0.0	97
Thyroxine			0.0	0.0	0.0	34
TSH	13.6	43.6	11.3	22.6	31.7	20
Creatinine	6.6	31	6.7	13.4	18.5	13

e.g., Cortisol cMQS 34% means that 90% of all cortisol results returned to the scheme since inception were within 34% of their respective all-method cortisol mean. Results that exceed this goal have a cortisol result that is more than 34% away from the consensus, i.e., has a bias that is worse than achieved by the scheme participants 90% of the time.

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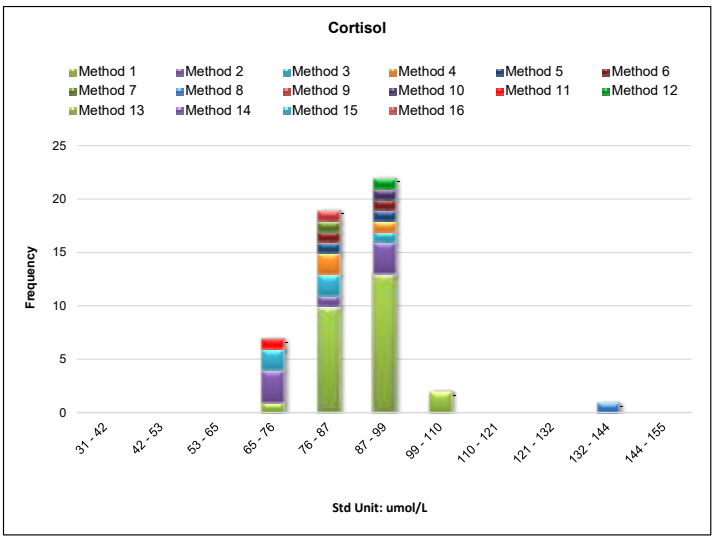
Analyte results

Cortisol

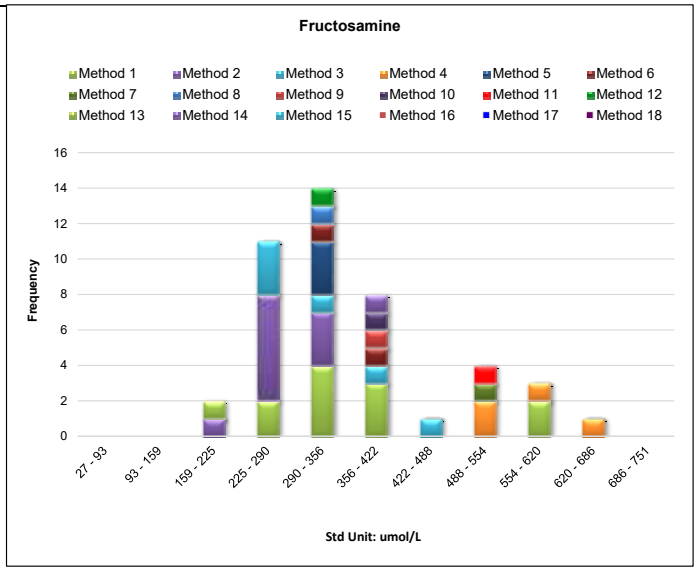
	n	Mean	StDev	%CV
Method 1	26	89	7.0	7.9
Method 2	7	84	8.6	10.3
Method 3	5	80	9.0	11.2
Method 4	3	86	6.6	7.7
Method 5	2	88	2.8	3.2
Method 6	2	85	8.5	10.0
Method 7	1	83		
Method 8	1	141		
Method 9	1	87		
Method 10	1	88		
Method 11	1	65		
Method 12	1	91		
Method 13	0			
Method 14	0			
Method 15	0			
Method 16	0			
		Trimmed	*Adjusted*	
All Methods	**51**	**86**	**7.7**	**9.0**



Note: Reported results ranged from 65 to 141nmol/L
Method 13 was an in-clinic analyser. Method 1 is Immulite 2000 Veteriary Cortisol. Method 2 and 3 were Immulite 2000 non-vet Cortisol adj and unadj respectively.

Fructosamine

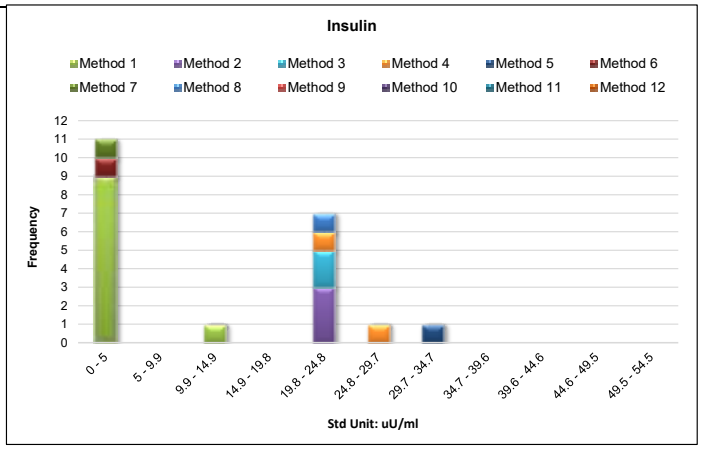
	n	Mean	StDev	%CV
Method 1	11	368	105.9	28.8
Method 2	10	265	29.4	11.1
Method 3	6	332	73.1	22.0
Method 4	4	577	59.4	10.3
Method 5	3	308	6.4	2.1
Method 6	2	383	55.1	14.4
Method 7	1	547		
Method 8	1	308		
Method 9	1	372		
Method 10	1	362		
Method 11	1	498		
Method 12	1	310		
Method 13	1	219		
Method 14	1	381		
Method 15	0			
Method 16	0			
Method 17	0			
Method 18	0			
		Trimmed	*Adjusted*	
All Methods	**44**	**350**	**110.3**	**31.5**



Note: Reported results ranged from 219 to 658umol/L
Method 5 was an in-clinic analyser method. Method 1 was Roche/Cobas.

Insulin

	n	Mean	StDev	%CV
Method 1	10	3.0	2.89	94.7
Method 2	3	20.7	0.69	3.3
Method 3	2	22.5	0.71	3.1
Method 4	2	24.9	0.87	3.5
Method 5	1	34.0		
Method 6	1	2.7		
Method 7	1	1.4		
Method 8	1	23.0		
Method 9	0			
Method 10	0			
Method 11	0			
Method 12	0			
		Trimmed	*Adjusted*	
All Methods	**21**	**11.2**	**11.87**	**106.0**



Note: Reported results ranged from 1 to 34uU/ml
Methods 1 & 6 were Siemens Immulite. Mehtod 7 was Abbot Alinity

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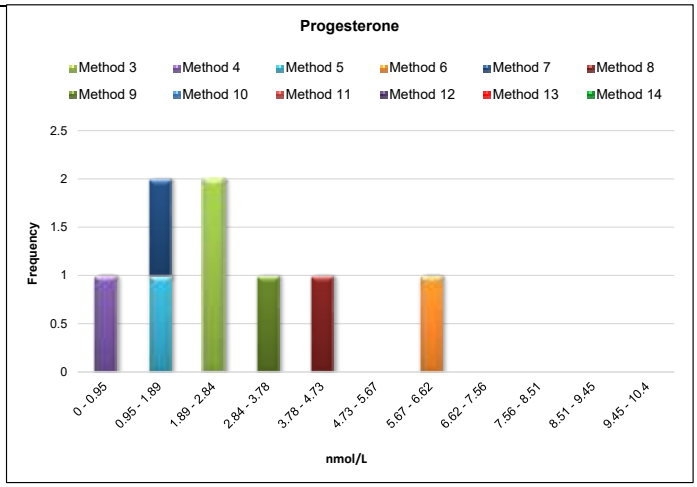
Progesterone

	n	Mean	StDev	%CV
Method 1	32	2.0	0.30	14.9
Method 2	4	2.4	0.31	12.5
Method 3	2	2.0	0.00	0.0
Method 4	1	0.3		
Method 5	1	1.6		
Method 6	1	6.6		
Method 7	1	1.6		
Method 8	1	4.0		
Method 9	1	3.3		
Method 10	0			
Method 11	0			
Method 12	0			
Method 13	0			
Method 14	0			
		Trimmed	*Adjusted*	
All Methods	**44**	**2.1**	**0.44**	**21.4**

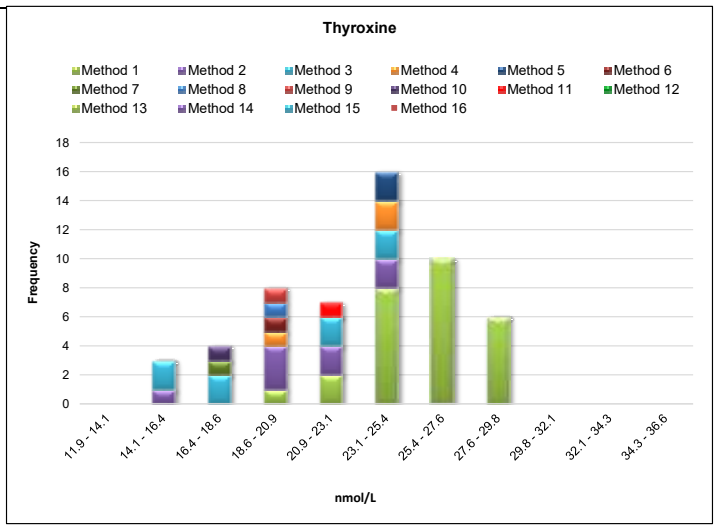


Note: Reported results ranged from 0.3 to 6.6nmol/L
The most popular methods were Siemens Immulite (Method 1; 2000; Method 2; 1000). Method 4 was an in-clinic analyser.

For statistical purposes, results lower than reportable limit have been converted to a value 0.5 x lowest reportable limit

Thyroxine

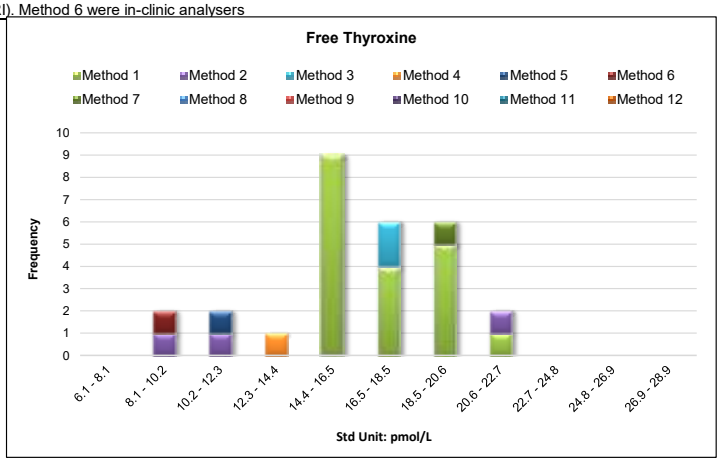
	n	Mean	StDev	%CV
Method 1	27	25.6	2.36	9.2
Method 2	8	21.0	2.93	14.0
Method 3	8	19.6	3.97	20.3
Method 4	3	22.9	2.17	9.5
Method 5	2	24.1	1.06	4.4
Method 6	1	20.6		
Method 7	1	17.6		
Method 8	1	20.5		
Method 9	1	18.7		
Method 10	1	17.0		
Method 11	1	21.6		
Method 12	0			
Method 13	0			
Method 14	0			
Method 15	0			
Method 16	0			
		Trimmed	*Adjusted*	
All Methods	**54**	**23.2**	**3.82**	**16.5**



Note: Reported results ranged from 14.5 to 29.5nmol/L
Methods 1, 4 and 11 were Immulite canine (KT4) methods. Methods 3 & 9 were Immulite TT4 (human) methods.
Method 2 was a homologous assay (Thermo Microgenics DRI). Method 6 were in-clinic analysers

Free T4

	n	Mean	StDev	%CV
Method 1	19	17.4	2.03	11.7
Method 2	3	14.4	5.79	40.2
Method 3	2	17.3	1.15	6.7
Method 4	1	13.6		
Method 5	1	10.9		
Method 6	1	8.3		
Method 7	1	19.6		
Method 8	0			
Method 9	0			
Method 10	0			
Method 11	0			
Method 12	0			
		Trimmed	*Adjusted*	
All Methods	**28**	**16.6**	**3.18**	**19.2**



A FT4 result by equilibrium dialysis was reported by 3 laboratories (Method 2; 10, 12 and 21 pmol/l)
Methods 1 and 7 were Immulite "veterinary" methods. Method 3 was Immulite human method.

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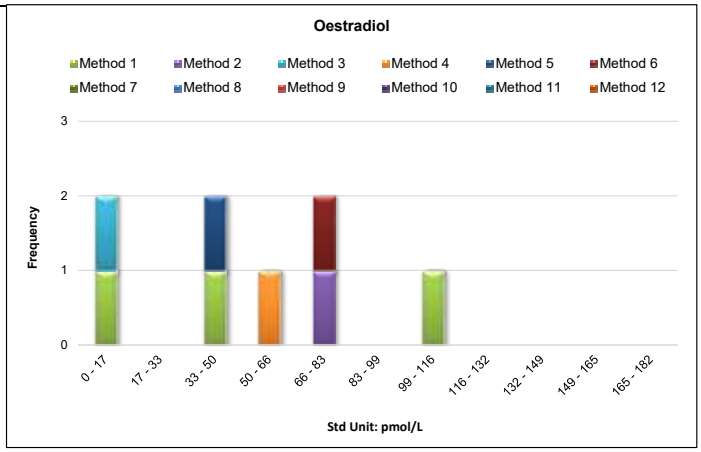
Oestradiol

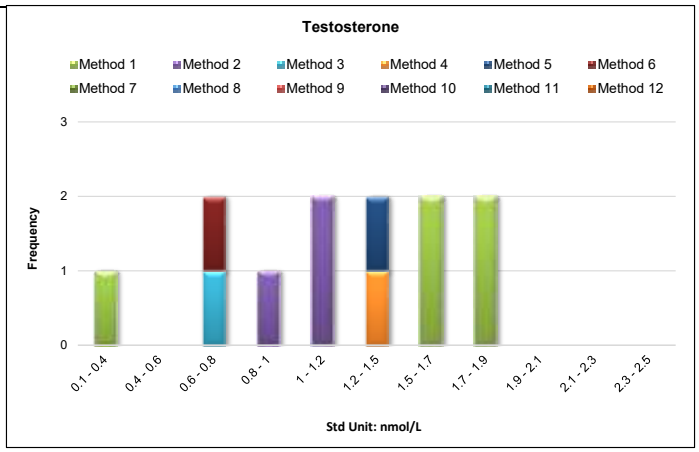
	n	Mean	StDev	%CV
Method 1	3	49	56.1	114.1
Method 2	1	78		
Method 3	1	3		
Method 4	1	58		
Method 5	1	46		
Method 6	1	78		
Method 7	0			
Method 8	0			
Method 9	0			
Method 10	0			
Method 11	0			
Method 12	0			
All Methods	**8**	**51**	**38.1**	**74.7**



Note: Reported results ranged from 0.4 to 111pmol/l

Testosterone

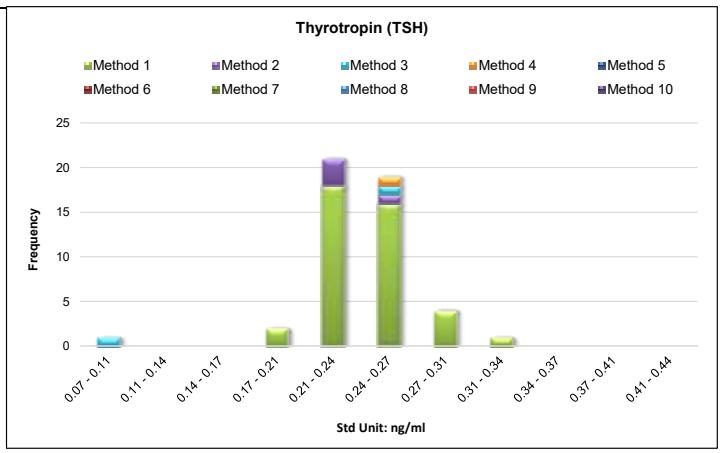
	n	Mean	StDev	%CV
Method 1	5	1.4	0.60	42.6
Method 2	3	1.1	0.08	7.1
Method 3	1	0.8		
Method 4	1	1.4		
Method 5	1	1.4		
Method 6	1	0.7		
Method 7	1	1.7		
Method 8	0			
Method 9	0			
Method 10	0			
Method 11	0			
Method 12	0			
All Methods	**13**	**1.2**	**0.45**	**37.5**



Note: Reported results ranged from 0.3 to 1.8nmol/l

TSH

	n	Mean	StDev	%CV
Method 1	41	0.244	0.02	10.1
Method 2	4	0.230	0.02	7.1
Method 3	2	0.175	0.11	60.6
Method 4	1	0.270		
Method 5	0			
Method 6	0			
Method 7	0			
Method 8	0			
Method 9	0			
Method 10	0			
Method 11	0			
Method 12	0			
		Trimmed	*Adjusted*	
All Methods	**48**	**0.240**	**0.022**	**9.2**



Note: Reported results ranged from 0.1ng/ml to 0.32ng/ml.
Methods 1 and 2 are Siemens Immulite. Method 4 was an in-clinic analyser.

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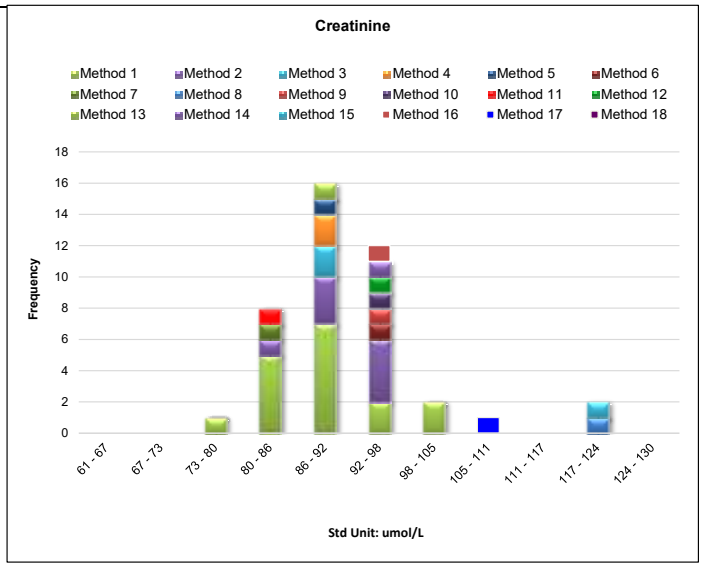
Creatinine

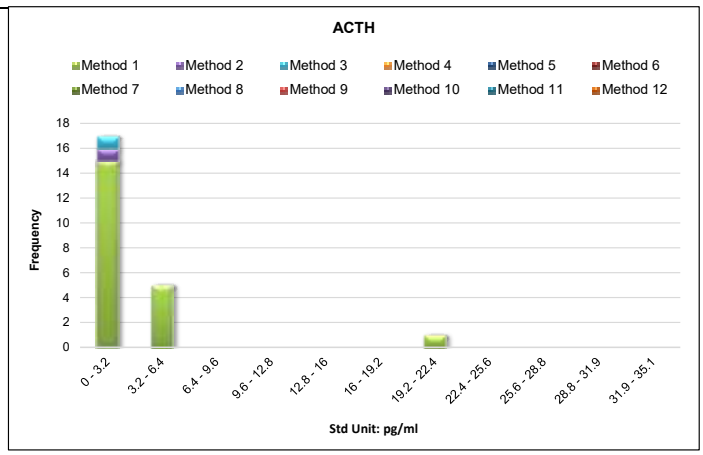
	n	Mean	StDev	%CV
Method 1	17	89.5	6.36	7.1
Method 2	8	90.7	4.66	5.1
Method 3	2	87.2	1.70	1.9
Method 4	2	90.0	1.41	1.6
Method 5	1	90.2		
Method 6	1	93.0		
Method 7	1	82.0		
Method 8	1	119.0		
Method 9	1	96.0		
Method 10	1	95.0		
Method 11	1	84.0		
Method 12	1	96.0		
Method 13	1	90.6		
Method 14	1	96.0		
Method 15	1	121.0		
Method 16	1	95.5		
Method 17	1	110.7		
Method 18	0			
		Trimmed	*Adjusted*	
All Methods	**42**	**91**	**6.9**	**7.6**



Note: Reported results ranged from 79 to 121umol/l

ACTH

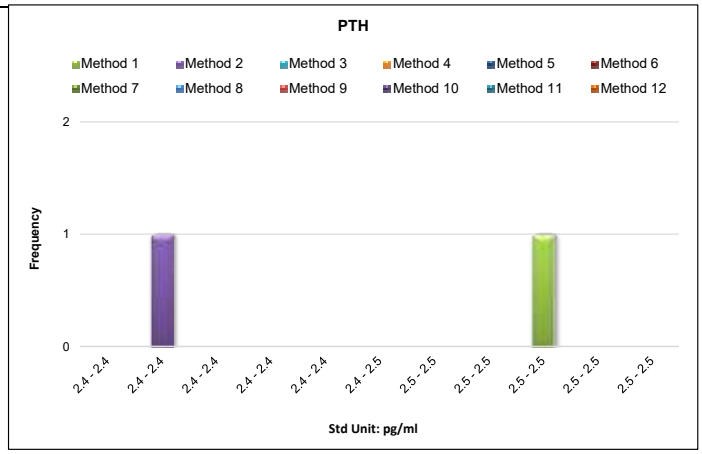
	n	Mean	StDev	%CV
Method 1	21	4.0	4.15	102.5
Method 2	1	0.0		
Method 3	1	2.5		
Method 4	0			
Method 5	0			
Method 6	0			
Method 7	0			
Method 8	0			
Method 9	0			
Method 10	0			
Method 11	0			
Method 12	0			
		Trimmed	*Adjusted*	
All Methods	**23**	**3.10**	**1.200**	**38.7**



Note: Results ranged from 2 to 21 pg/ml
The most popular method (Method 1) was Immulite 2000.

PTH

	n	Mean	StDev	%CV
Method 1	1	2.5		
Method 2	1	2.4		
Method 3	0			
Method 4	0			
Method 5	0			
Method 6	0			
Method 7	0			
Method 8	0			
Method 9	0			
Method 10	0			
Method 11	0			
Method 12	0			
All Methods	**2**	**2**	**0.1**	**3.3**



Note: Reported results ranged from 2.4 to 2.5pg/ml

For statistical purposes, results lower than reportable limit have been converted to a value 0.5 x lowest reportable limit

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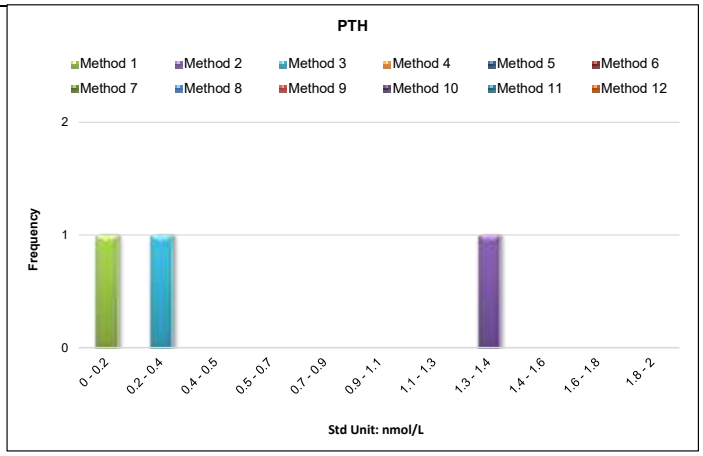
17OHProgesterone

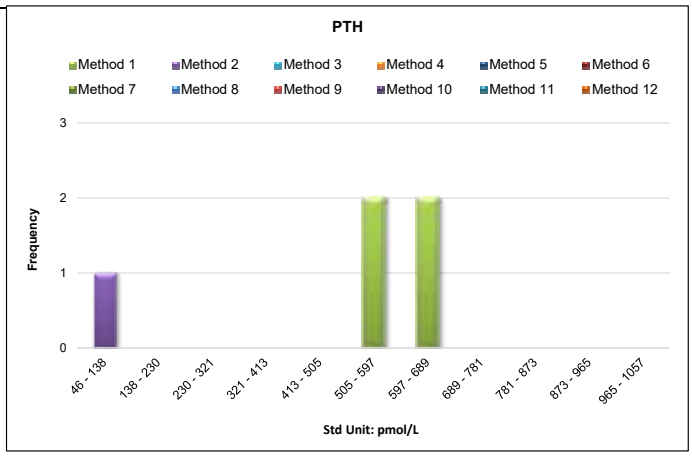
	n	Mean	StDev	%CV
Method 1	1	0.1		
Method 2	1	1.3		
Method 3	1	0.3		
Method 4	0			
Method 5	0			
Method 6	0			
Method 7	0			
Method 8	0			
Method 9	0			
Method 10	0			
Method 11	0			
Method 12	0			
All Methods	**3**	**0.50**	**0.630**	**126.0**



Note: Reported results ranged from 0.1 to 1.3nmol/l

Aldosterone

	n	Mean	StDev	%CV
Method 1	4	612.9	77.4	12.63
Method 2	1	75.0		
Method 3	0			
Method 4	0			
Method 5	0			
Method 6	0			
Method 7	0			
Method 8	0			
Method 9	0			
Method 10	0			
Method 11	0			
Method 12	0			
All Methods	**5**	**505**	**249.7**	**49.4**



Note: Reported results ranged from 75 to 688pmol/L
Method 1 was Diasorin Liaison

For statistical purposes, results lower than reportable limit have been converted to a value 0.5 x lowest reportable limit.
Results above the upper reporting limit have been reported as the upper reportable limit.

TgAA

The sample was feline making this test irrelevant to the sample. Two reporting labs generated appropriately "negative" results.

Method	Reported as	Result	Interpretation	Reference limits
Oxford Labs Canine TGAA	% of negative	228	Borderline positive	200%
Oxford Labs Canine Thyroglobulins Auto-Antibody VT1(	Percentage and Negative/Positive	13	Negative	Positive - 35%, Inconclusive 20-35%, Negative <20%
Oxford Laboratories	Text (e.g. Positive, negative etc)		Borderline	