ESVE Veterinary Endocrinology External Quality Assessment Scheme
ESVE REPORT

Release Month:	**May-14**
Release Number:	**004**

Overall Commentary

General

This is the report of the fourth release of the ESVE EQA scheme. The efforts made by the participants to report their results were much appreciated. Response time was improved and only one re-send of material was required on this occasion. We had participation from 30 separate physical locations providing 184 analytical results. The strength of a scheme such as this can only improve as more participants are recruited. If you are in contact with other laboratories that are generating veterinary endocrine analytical results that are not participants in the scheme, please encourage them to participate.

Given the numbers of participants within individual methodologies it would still be difficult to draw strong conclusions from much of the data at this stage. However, we are already seeing 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 the last release we have highlighted a small number where it seems most relevant to do so.

This Release

This was a feline serum pool selected for mid-range thyroxine concentration and modifed only to include a measurable quantity of oestradiol.

Those of you familiar with other EQA schemes will recognise that the overall CV's we are seeing are high. On this release, only Total T4 CV is below 20%. A wide CV% makes more sense for our peptide representative (insulin) but it is concerning that we are seeing high CV's for the analytes that don't have species differences including very commonly measured analytes such as cortisol and fructosamine.

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 particulary 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 128 or 223 nmol/L could be obtained from the same sample depending on where the result originated.

As was the case in the previous release and as has been the experience of the Michigan State University SCE EQUAS scheme, the range of results obtained for Oestradiol is tremendous (almost 10-fold range on this occasion). This is a notoriously difficult hormone to measure well which presents interpretative challenges.

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".

Please note that the Method numbers bear no relationship to one another across analytes. 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.

Cortisol

As was the case for previous releases, the range of results generated for cortisol was a real 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. Overall CV is more than 20%. In large human EQA schemes, CV for cortisol is 7-8%. One extreme result was excluded from statistical analysis (669 nmol/L).

Fructosamine

The range of fuctosamine results is wide and the overall CV high, however, more than 60% were in the range 301 - 353 umol/L suggesting that with some investigation and effort, this could be a parameter we could see improvement in. Although there are small numbers of participants per method, some methods (2, 5 and 9) appear to have good method CV's. These three methods are likey to be variations of the same/similar method (ABX, Roche, Cobas)

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 but also where appropriate insulin:glucose ratios) in reaching a diagnostic interpretation. There are some interesting findings in this release. Previously at low/nomal concentrations of insulin (Release 002), the Immulite method did not appear to detect feline insulin. On this occasion there appears to be a higher insulin concentration which the Immulite method is picking up (Immulite is Method 8) suggesting that it may only be a low/normal concentrations that this assay struggles.

Commentary (continued)

Progesterone We were lucky in being able to construct a sample with a concentration close to the common "luteal cut-off" of 3 nmol/L. Although a wide range of results from 0.03 to 6.95 nmol/L were obtained, 60% were in the much tighter range of 3.1 to 4.2 nmol/l which (like fructosamine) suggests that with investigation and effort, we could see this spread improve.

Thyroxine A mid-range T4 concentration was the target in mind when this release was being created. T4 is the best performing of our analytes in this release based on all-method CV albeit that it is nearly 20%. With a range of results between 13.6 and 42.8 nmol/l, I could certainly envisage significant differences in clinical patient management decisions for e.g, monitoring anti-thyroid therapy, deciding whether to continue to include hyperthyroidism as a differential etc. That said, 85% of results were in the tighter range of 22.2 to 31.0 and consequently I am hopeful that improvement can be made. At this concentration, there is a small difference between the Immulite canine methods (4, 5 and 6; mean 26.3 nmol/l) and the Immulite human methods (7 and 8; mean 22.2nmol/l).

Free T4 On a theoretical basis, the methods using dialysis or 2-step immunoseparation should yield the Free T4 results closest to the true value. Unfortunately, we have only one participant using such a method in this release.

Oestradiol The variation in results obtained for Oestradiol is a well known phenomenon to anyone participating in the MSU/SCE EQUAS scheme. One result was excluded from analysis for being too extreme (552 pmol/l). Methodologic and calibration differences along with poor low-end sensitivity have been considered to play their part. Some laboratories are using extraction procedures to improve their analyses. Unfortunately, it was not possible to assess the impact of clinical diagnosis of such disparate results as only a very few participants (n=2) provided their interpretative guidance values. There should be considerable caution in interpreting oestradiol results against literature ranges particularly where oestradiol is being used in isolation to support diagnoses of adrenal dysfunction.

Testosterone We were pleased with the take up of participation in testosterone measurement from 4 participants last time to 12 on this occasion. All participants generated a result greater than 0.5nmol/L a cut-off that has been used for determining the likely presence of functional testicular tissue although there was a four-fold range in results obtained.

TSH The concentration of TSH in this sample was relatively low but all participants generated a result above their LOQ/LOD. The Immulite 1000 (Method 3) generated slightly lower values than the Immulite 2000 (Method 4) and also shows a higher method CV than the Immulite 2000. The isotopic variant of the Siemens method (Canine TSH IRMA) was used by one participant (Method 5) and it generated a higher result than the chemiluminescent version. The IRMA version is scheduled to be discontinued so we will not be able to explore potential differences between these methods in future releases.

Peter Graham, Program Coordinator, July 2014

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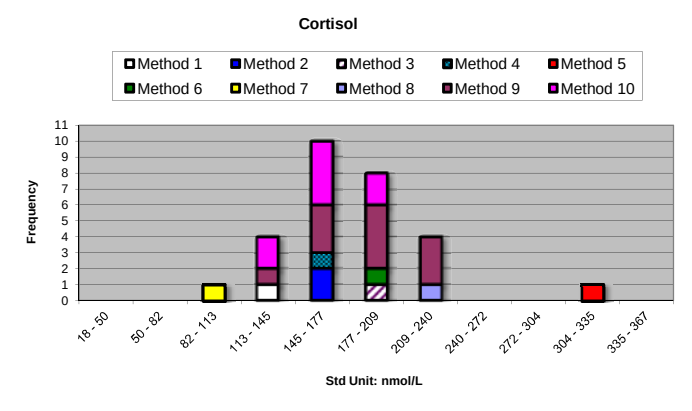
Cortisol

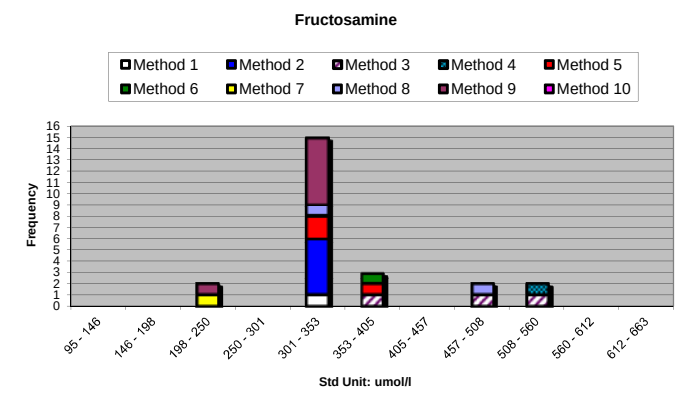
	n	Mean	StDev	%CV
Method 1	1	140.7		
Method 2	2	157.4	3.76	2.4
Method 3	1	198.5		
Method 4	1	147.0		
Method 5	1	313.0		
Method 6	1	191.4		
Method 7	1	101.5		
Method 8	1	211.0		
Method 9	11	184.7	26.79	14.5
Method 10	8	162.5	21.02	12.9
All Methods	**28**	**177.0**	**39.30**	**22.2**



Note: Reported results ranged from 102 to 669 nmol/l. One extreme result was excluded from statistical analysis (Method 6; 669 nmol/L)
Overall CV was 17% when the 2 most extreme high values were excluded

Fructosamine

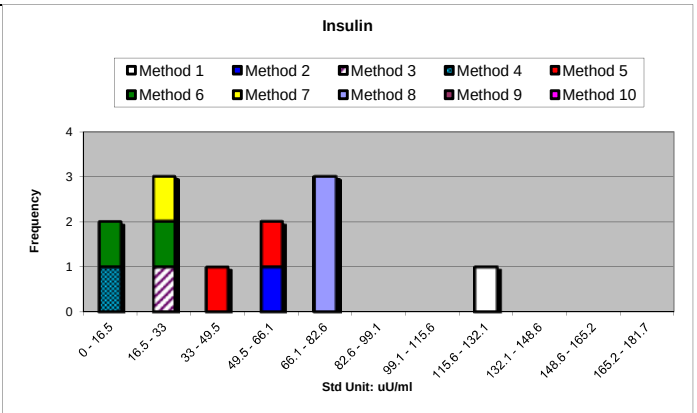
	n	Mean	StDev	%CV
Method 1	1	312		
Method 2	5	315	8.2	2.6
Method 3	3	478	87.3	18.3
Method 4	1	549		
Method 5	3	340	14.3	4.2
Method 6	1	383		
Method 7	1	210		
Method 8	2	410	112.6	27.4
Method 9	7	310	31.9	10.3
Method 10	0			
All Methods	**24**	**353**	**85.8**	**24.3**



Note: Reported results ranged from 210 to 555 umol/L

Insulin

	n	Mean	StDev	%CV
Method 1	1	117.3		
Method 2	1	59.0		
Method 3	1	30.0		
Method 4	1	7.2		
Method 5	2	49.1	8.4	17.2
Method 6	2	18.6	3.4	18.3
Method 7	1	17.8		
Method 8	3	79.7	1.9	2.3
Method 9	0			
Method 10	0			
All Methods	**12**	**50.5**	**33.83**	**67.0**



Note: A conversion factor of 101 was used for the 2 participating laboratories that reported in "ug/L Canine insulin"
A conversion factor of 0.101 for 1 that measured "ng/L Equine insulin"

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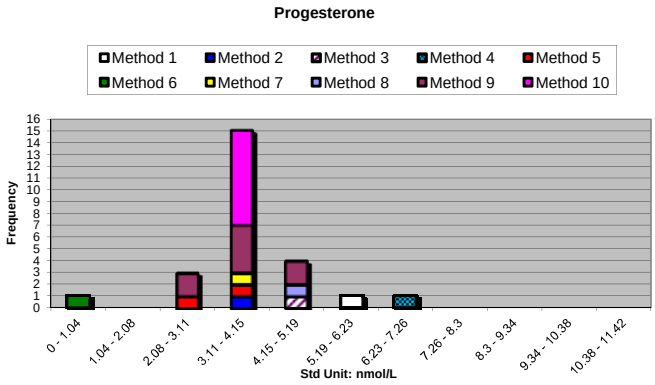
Progesterone

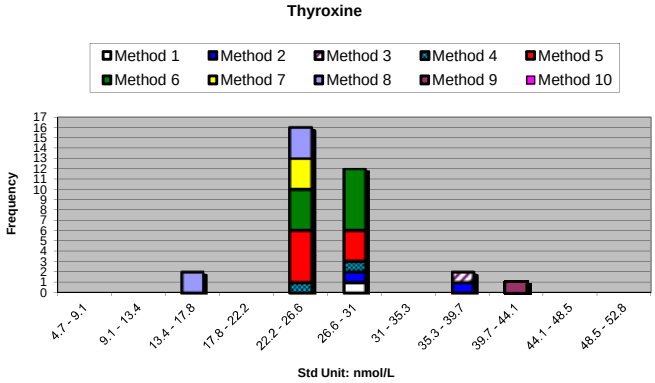
	n	Mean	StDev	%CV
Method 1	1	5.34		
Method 2	1	3.20		
Method 3	1	5.16		
Method 4	1	6.95		
Method 5	2	2.90	1.0	33.5
Method 6	1	0.03		
Method 7	1	3.40		
Method 8	1	5.09		
Method 9	8	3.55	0.8	23.7
Method 10	8	3.52	0.2	6.4
All Methods	**25**	**3.70**	**1.28**	**34.6**



Note: Reported results ranged from 0.03 to 6.95 nmol/L

Thyroxine

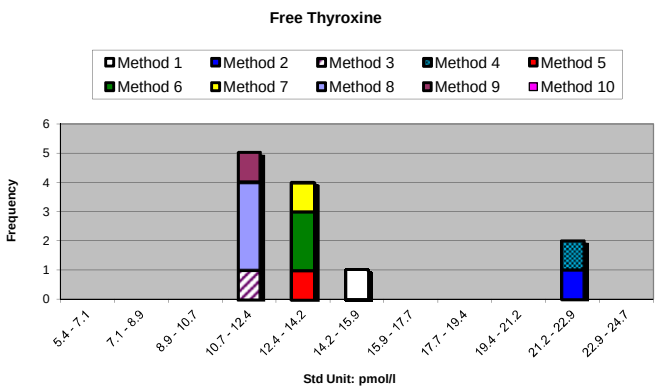
	n	Mean	StDev	%CV
Method 1	1	27.00		
Method 2	2	33.41	6.265	18.8
Method 3	1	37.00		
Method 4	2	25.20	1.973	7.8
Method 5	8	26.10	1.777	6.8
Method 6	10	26.67	2.081	7.8
Method 7	3	24.76	1.448	5.8
Method 8	5	20.64	4.853	23.5
Method 9	1	42.78		
Method 10	0			
All Methods	**33**	**26.60**	**5.180**	**19.5**



Note: Reported results ranged from 13.6 to 42.8 nmol/L
Methods 4, 5 and 6 were "canine" methods

Free T4

	n	Mean	StDev	%CV
Method 1	1	15.3		
Method 2	1	22.5		
Method 3	1	12.2		
Method 4	1	21.8		
Method 5	1	12.7		
Method 6	2	12.9	0.02	0.2
Method 7	1	13.1		
Method 8	3	11.9	0.71	5.9
Method 9	1	10.8		
Method 10	0			
All Methods	**12**	**14.2**	**3.89**	**27.4**



Note: Reported results ranged from 10.8 to 22.5 pmol/L
A FT4 result by equilibrium dialysis was reported by one laboratory (Method 1; 15.3 pmol/l)
Methods 8 and 9 were "veterinary" methods

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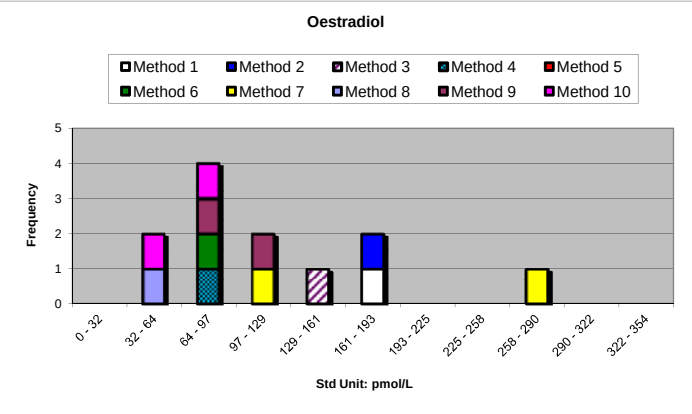
Oestradiol

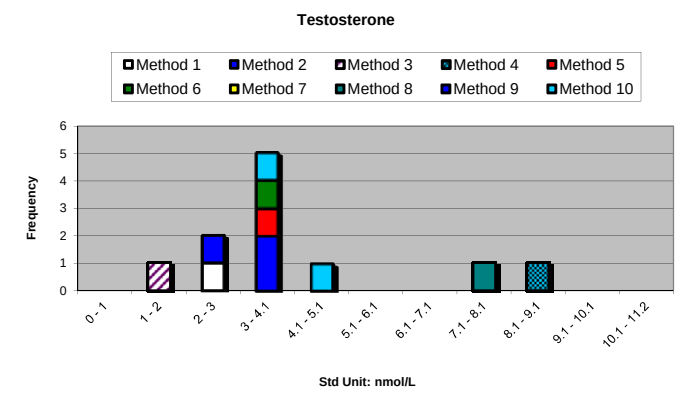
	n	Mean	StDev	%CV
Method 1	1	179.9		
Method 2	1	179.4		
Method 3	1	140.6		
Method 4	1	74.0		
Method 5	0			
Method 6	1	82.5		
Method 7	2	188.5	120.26	63.8
Method 8	1	58.7		
Method 9	2	101.7	9.33	9.2
Method 10	2	66.0	4.24	6.4
All Methods	**12**	**119**	**64.1**	**53.9**



Note: Reported results ranged from 59 to 552 pmol/L
One extreme result was excluded from statistical analysis (Method 5; 552 pmol/L; 150pg/ml)

Testosterone

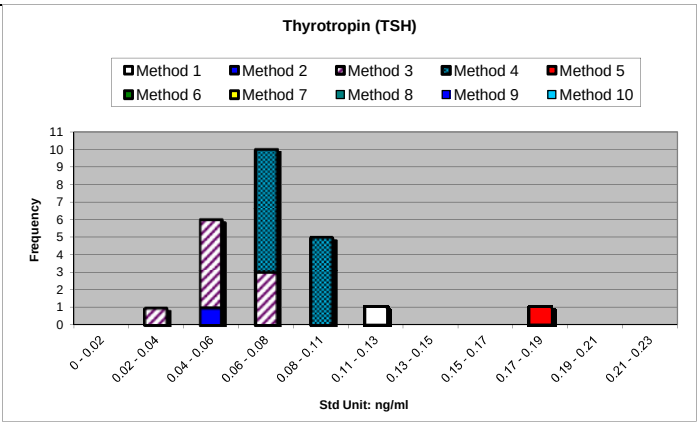
	n	Mean	StDev	%CV
Method 1	1	3.0		
Method 2	2	3.8	0.00	0.0
Method 3	1	2.0		
Method 4	1	8.4		
Method 5	1	3.1		
Method 6	1	3.4		
Method 7	1	8.8		
Method 8	1	7.2		
Method 9	1	2.9		
Method 10	2	3.7	0.61	16.6
All Methods	**12**	**4.5**	**2.29**	**50.9**



Note: Reported results ranged from 2 to 8.8 nmol/L

TSH

	n	Mean	StDev	%CV
Method 1	1	0.11		
Method 2	1	0.06		
Method 3	9	0.05	0.01	21.3
Method 4	12	0.09	0.01	6.0
Method 5	1	0.2		
Method 6	0			
Method 7	0			
Method 8	0			
Method 9	0			
Method 10	0			
All Methods	**24**	**0.08**	**0.028**	**35.0**



Note: Reported results ranged from 0.04 to 0.18 ng/ml
Methods 2, 3 and 4 represent the same manufacturer's chemiluminescent assay on 3 platforms
Method 5 is the same manufacturer's IRMA method

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