Unpublished Report

Document ID:	SheepCRC_3_5
Title:	Parasite Diagnostic Tests
Author:	Ian Colditz, I.; Gray, D.; Page, S.
Key words:	sheep; parasite; diagnostic test; evaluation

CRC FOR SHEEP INDUSTRY INNOVATION

PARASITE DIAGNOSTIC TESTS

Review

Report prepared by

Ian Colditz
Douglas Gray
Stephen Page

Edited: Brown Besier

December 2008

TABLE OF CONTENTS

CRC FOR SHEEP INDUSTRY INNOVATION

PARASITE DIAGNOSTIC TESTS

1. INTRODUCTION

The need for more sustainable approaches to sheep nematode control has led to the development of programs that seek to minimize the frequency of anthelmintic treatment. To provide an objective basis for treatment decisions, periodic assessments of worm burdens by worm egg counts are recommended. However, the disadvantages of worm egg counts have long been recognised, and tests that are more cost and time efficient and improve the accuracy of worm burden estimation would significant enhance the effectiveness of worm control. Improved detection methods for other parasites, including blowflies, would also be of major benefits.

With this background, the Australian Sheep Industry CRC has supported research into a number of prospective diagnostic tests for sheep parasites, several with co-funding from Meat and Livestock Australia and Australian Wool Innovations. At the time of this review, one test was in the final validation stage before commercialization, and several other tests at various stages of development. With the termination of the Australian Sheep Industry CRC, it is appropriate to review progress within each project to guide further action, and this is incorporated into the Operational Plan of the CRC for Sheep Industry Innovation as an activity within Project 1.7.

The parasite detection capability has been proven for most of the tests within the CRC portfolio, in some cases quantitatively, though the proximity to a field testing stage varies greatly. Of particular interest is whether with a small amount of additional work, any test may become attractive to an animal health or diagnostics company. Due to changes in the strategic directions under the second Sheep CRC (CRC for Sheep Industry Innovation), it is unlikely that further diagnostic test development will continue, except for the finalisation of tests considered by the Review to warrant this support. However, interest by scientific, industry funding or commercial organizations may be facilitated for particular test projects where favourable prospects are indicated by scores against the assessment criteria.

1.1 OBJECTIVES

CRC Test Project Review

- To develop a general basis for the comparative evaluation of existing, in-development and putative parasite diagnostic tests (especially for sheep), on the basis of
    - technical performance (including precision, sensitivity, specificity)
    - operational advantages (including simplicity, time, equipment need)
    - likely industry benefit (including cost, user acceptance and adoption)

- To apply relevant criteria to candidate tests within the Sheep CRC portfolio to indicate the relevance to industry and justification for continued effort

- To make recommendations or provide guidance to progress research into these tests, and possible sources of support.

Diagnostic Test references

- To provide a comprehensive database of recent research or review publications relevant to animal parasite diagnostic test development.

1.2 CURRENT PROGRAM

The Projects funded by the CRC are listed below, with technical presentations at the Review made by the Project Leaders (underlined).

1 ON-FARM HAEMONCHUS DIPSTICK TEST

Ian Colditz, Leo le Jambre, Brown Besier, Deborah Maxwell, Maxine Lyndall-Murphy, Gareth Hutchinson

2 FAECAL ANTIGEN DIAGNOSIS OF NEMATODES

Mark Sandeman, Peyman Mehrpouian, Steve Cotton (Post-grad. Student)

3 FAECAL ANTIGENS FOR WORM EGG DETECTION

Dieter Palmer, Amy Tay, Eva Mowe, Heather Mc Letchie

4 ELECTRONIC NOSE FOR BLOWFLY STRIKE DETECTION

Peter James, Andrew Cramp, Jae Ho Sohn, Les Zeller, Rudolf Urech, Michael Atzeni and Wayne Ehrlich, Ian Colditz

5 ANALYSIS OF ODOUR FOR THE DIAGNOSIS OF GASTROINTESTINAL NEMATODES

Jacqueline Burgess (Post-grad. Student), John Traeger, Mark Sandeman

6 LECTIN BINDING ASSAY FOR WORM EGG GENUS IDENTIFICATION

Dieter Palmer, Amy Tay, Eva Mowe, Heather Mc Letchie

7 DEVELOPMENT OF FAECAL NIRS TO DIAGNOSE PARASITE BURDEN

Rob Dixon, Ian Colditz, Leo le Jambre

(Leader for the CRC Program “Improved Sheep Parasite Management”: Brown Besier)

1.3 ASSESSMENT OF DIAGNOSTIC TESTS

The following models provide a theoretical basis for decisions on the applicability of putative test technologies in relation to disease occurrence and test result, in terms of relevance and precision.

Figure 1. Applicability of testing in relation to probability that disease is present.

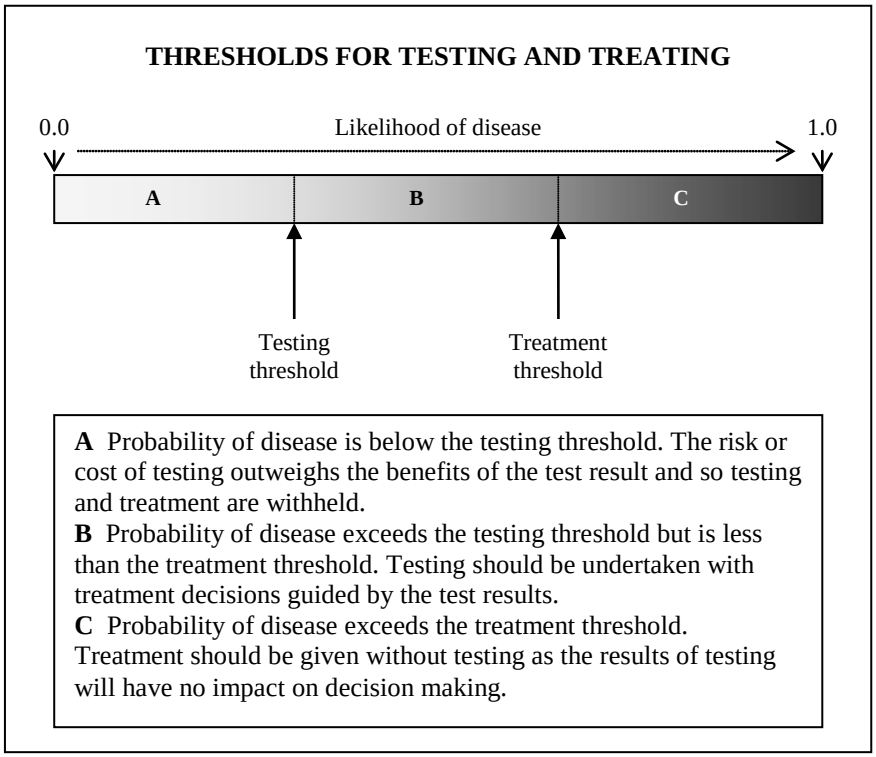
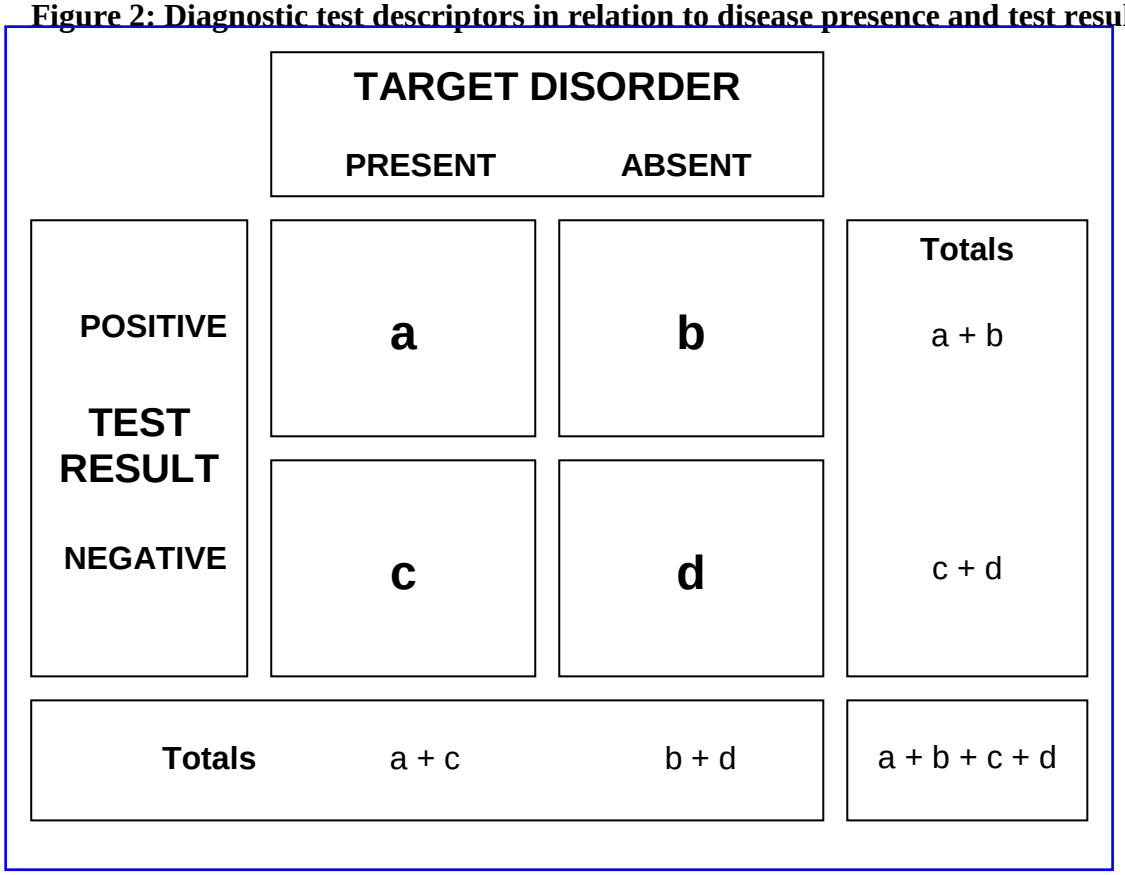


Figure 2: Diagnostic test descriptors in relation to disease presence and test result



Test characteristic	**Question addressed**	**Formula and calculation**
Prevalence (Pre-test probability)	How common is the disease in the test population?	(a +c)/(a + b + c + d)
Sensitivity (Sn) (True positive rate)	What is the proportion of patients with disease who have a positive test?	a/(a + c)
Specificity (Sp) True negative rate	What is the proportion of patients without disease who have a negative test?	d/(b + d)
Positive predictive value (PPV) (Post-test probability of disease with a positive test)	What is the probability of disease if a patient has a positive test?	a/(a + b)
Negative predictive value (NPV) (Post-test probability of no disease with a negative test)	What is the probability of not having disease if a patient has a negative test?	d/(c + d)
Diagnostic accuracy	What proportion of all tests have given the correct result? (True positives + true negatives as a proportion of all tests)	(a + d)/(a + b + c + d)
Likelihood ratio of a positive test (LR+)	How much more likely is a positive test to be found in a patient with the disease than in a patient without disease?	[a/(a + c)]/[b/(b + d)] = (Sensitivity)/(1-specificity) (true positive rate/ false positive rate)
Likelihood ratio of a negative test (LR-)	How much more likely is a negative test to be found in a patient with the disease than in a patient without disease?	[c/(a + c)]/[d/(b + d)] = (1-sensitivity)/specificity (false negative rate/true negative rate)
Number needed to diagnose (NND)	How many patients have to be tested to give one correct positive test?	1/true positive rate-false positive rate = 1/[sensitivity-(1-specificity)]

2. CURRENT DIAGNOSTIC APPROACHES TO SHEEP PARASITOSES

Parasitoses are diagnosed for a number of reasons. In commercial sheep enterprises, information gained from the attempt to diagnose parasitoses is used for:

- quarantine purposes
- management of sheep health, including differential diagnosis of parasitoses from other diseases
- management of pasture contamination with larvae
- identification of the genetic merit of individuals for breeding programs

Information sought through diagnosis can include:

- species presence and their distribution and abundance both in the host population and in the environment
- parasiticide resistance status of the parasite

In research settings, information gained through diagnosis can be used for many purposes, principally focused around gaining new knowledge of host and pathogen biology.

2.1 Internal parasites

2.1.1 Techniques available

2.1.1.1 Counting parasites and their eggs

Worm egg in faeces

The modified McMaster method (Whitlock, 1948) for counting strongyle worm eggs in faeces (WEC) is the gold standard method for quantifying the burden of gastrointestinal strongyles in sheep on commercial properties. A SOP is provided in Appendix 1. WEC is used as a proxy for parasite burden, and by further inference, the risk to the host of pathology and loss of production from the infection. WEC can be measured either on individual animal or group samples.

Real and potential sources of error in the method include:

- Parasite species – egg laying capacity differs between parasite species, and may differ between field isolates within species (Dr Peter Hunt, personal communication). The approximate egg laying potential of worms is:
  - *Haemonchus* – 5,000 to 10,000 per day
  - *Oesophagostomum* and *Chabertia* – 3,000 to 5,000 per day
  - *Trichostrongylus* and *Ostertagia* – 100 to 200 per day
  - *Nematodirus* – 50 per day (Gordon, 1967)
- Interactions between parasite species – some parasite species affect egg laying capacity of co-infecting parasites. For example, infection with *Haemonchus contortus* increases the rate of egg production by *Trichostrongylus colubriformis* during co-infection with the two parasites (J. Lello and S.J. McClure, personal communication).
- Host immune status – immunity of the host can suppress egg laying especially by *Trichostrongylus spp*.. In addition, damage to eggs by immune effector mechanisms of the host can reduce the buoyant density of eggs thus leading to underestimation of egg numbers in a sample (L.F. Le Jambre, personal communication)
- Recent exposure to anthelmintics – some members of a parasite population that has a degree of resistance to an anthelmintic will survive exposure to the anthelmintic but reduce or cease their egg production during the recovery phase following anthelmintic exposure
- Fecal moisture – moisture content of faeces affects the dilution of eggs (expressed as eggs per gram (wet weight) of faeces). The correction factors proposed by Gordon (1967) for

adjusting WECs to a common faecal moisture content have recently been confirmed (Le Jambre et al., 2007).

- Circadian variations in egg output by parasites
- Circadian variations in digesta passage within the host
- Variation between faecal pellets in egg content
- Death of eggs in transit affecting their buoyant density and hence recovery in the lab
- Number of eggs in the sample. The WEC method counts the number of eggs in a fixed dilution of faeces. Sampling theory indicates that the number of eggs estimated to be in samples with a low real number of eggs will be less accurate than the number estimated to be in a sample with a high real number of eggs.
- Technical sources of error in labs, eg between operator errors. When samples were allocated at random to laboratory staff within a single lab, the repeatability of WEC counts performed on duplicate aliquots from a single egg dilution in salt solution was found to be between 0.80 and 0.91 (S.J. Eady, personal communication)

Speciation of larvae

Faecal culture and larval differentiation on morphological criteria are the standard methods for identifying the species of nematode present in a faecal sample. A SOP is provided in the appendix. The sample may be from an individual or a group. Sources of error include:

- Loss of viability of eggs in transit from property to lab
- Competition between species during larval culture
- Differential sensitivity of species to culture temperature
- Differential hatching time between species – eg *Nematodirus spp* take at least 8 days to hatch whereas *Haemonchus spp, Ostertagia spp* and *Trichostrongylus spp* hatch by 7 days.
- Technical sources of error in labs, eg between operator errors

Identification of the genus and species of parasite eggs

A research method for the identification of the genus of parasite eggs by lectin staining characteristics was described by Palmer and McCombe (1996) and further developed by Colditz et al. (2002). Fluorochrome labelled peanut agglutinin has been used to identify *Haemonchus spp* eggs in faecal samples as a service to sheep producers by WADA for several years. The genus classification of eggs can be performed on the day a sample arrives in the lab and has the potential to be more accurate than larval differentiation due to retention of the staining characteristics by dead and non-viable eggs.

Research by Dr Peter Hunt in Sheep CRC I parasite program on a quantitative PCR method for detection of larvae on pasture showed the potential for speciation of larvae and parasite eggs. Identification of the genus of gastrointestinal nematode eggs by PCR identification has been demonstrated in cattle (Zarlenga et al., 2001). Work on quantitative estimation of the number and species of strongyle eggs in sheep faeces by real time PCR continues with MLA funding by Peter Hunt in collaboration with Robin Gasser (University of Melbourne).

Post mortem examination of sheep

Slaughter of sheep and inspection of the gastrointestinal tract for semi-quantitative or quantitative enumeration of parasite burdens and the genera present is used both on farm and in research facilities and is a service provided by some diagnostic laboratories.

2.1.1.2 Measurement of the host response to parasite infection

Measurement of the host reaction to infection can be used for diagnosis of parasitoses and has also been used as a method for assessing the resistance of sheep to parasites.

Antibody to parasite antigens
The presence of antibody in serum, milk or faeces has been used as a diagnostic test, at least in experimental settings for most gastrointestinal nematode infections and for liver fluke infections in sheep. An ELISA for fluke antibodies is commercially available (Molloy 2005) and a test for the antibody to *Trichostrongylus spp* has been used to estimate breeding values for resistance to gastrointestinal nematodes in New Zealand. This test is no longer offered commercially in New Zealand. ELISAs for diagnosis of *Haemonchus* infections have been described (Schallig et al., 1995; Gomez-Munoz et al., 1996) as has an ELISA for *Ostertagia* infections (Johnson et al., 2004).

Circulating eosinophil count
The number of eosinophils in peripheral blood has been observed to increase during the expression of acquired immunity to *T. colubriformis* and *H. contortus* in sheep (Dawkins et al., 1989); however, the accuracy of circulating eosinophil numbers as a selection criterion for resistance to these parasites was found by Woolaston et al. (1996) to be less than WEC.

2.1.1.3 Measurement of host pathology

Gastrointestinal enzymes
Change in permeability of abomasal and duodenal mucosae has been used as a measure of the severity of *Ostertagia* infection in sheep and cattle. Both gastrin and pepsinogen have been used as indicators of infection (Berghen et al., 1993). Serum pepsinogen is measured by some veterinary pathology laboratories.

Anaemia
Anaemia and the presence of bottle jaw (dependent oedema) due to hypoproteineamia have been used as indicators of liver fluke and *H. contortus* infections in sheep by veterinary practitioners and graziers for many years (Gordon, 1967). A five point scale for anaemia has been standardised as the FAMACHA test and is offered to sheep and goat owners in South Africa and the US for on farm use following training (Vatta et al., 2001). Estimates of sensitivity, specificity and predictive value of the test have not been performed in Australia and could differ from values observed in the United States (Vatta et al., 2001) due to differences in prevalence of anaemia due to causes other than *H. contortus* infection.

Haematocrit has proved more highly heritable than WEC as a selection criterion for resistance to nematode infections in some studies (Albers et al., 1987)

Faecal blood
Measurement of blood in faeces for diagnosis of the presence of blood feeding parasites has been described in several host species. The faecal occult blood test developed in the Sheep CRC employs this principle and can detect infection around 10 days before eggs appear in faeces (Colditz and Le Jambre, 2007). A limitation is the need to heat samples to remove interference from non-haem peroxidases. This problem could be overcome with an antibody to haem as recently demonstrated in horses www.SucceedFBT.com. Field validation in commercial environments is required and in progress.

2.1.1.4 Estimation of genetic merit for phenotypic resistance to gastrointestinal nematodes

WEC is the currently employed measure of phenotypic resistance to gastrointestinal nematodes. As noted above, serum antibody, haematocrit and circulating eosinophil counts have been examined as selection criteria for resistance. It is noteworthy that the goal of the current Parasite Program of

Sheep Genomics is a gene product (protein) marker of genetic resistance. Other research in this program and elsewhere is investigating gene markers for resistance. A gene marker diagnostic test for identifying animals with resistance to internal parasites in sheep was released on 23rd October 2007 and Catapult Genetics (http://www.catapultsystems.co.nz/products/55_wormstar.cfm)

2.1.1.5 Differential diagnosis of anaemia in sheep

Parasite infections need to be differentiated from a number of other diseases which can present with similar signs. A potential guide for on-farm diagnosis of gastrointestinal parasitism and anaemia follows (table shading does not print well in B&W)

Differential Diagnosis of anaemia and gastrointestinal parasitism – On Farm

Diagnostic indicator	Haemonchus	Liver Fluke	Other GIN	Mycoplasma ovis	Coccidiosis & salmonellosis	Anaemia trace element
Bottle neck	+	+	-			?
FAMACHA (Pale ocular membranes)	+	+	-	+	?	+
Faecal occult blood test	+	+	-	-	- or +	-
Failure to walk 100 m	+	+	+ or -	+		+
Diarrhoea	-	-	+ or -	-	+	-
Bloody faeces	-	-	-	-	+ or -	-
Distribution	Summer rainfall / irrigation	Temperate	Temperate high rainfall	Widespread	High rainfall, high stocking rates, housed	Regional
Prevalence	Very common	Locally prevalent	Very common	Common in weaners	Common in weaners	Local history

2.1.2 SWOT analysis

SWOT anlaysis

Test	Validated	Commercially available	Use on farm	Species identification	Time	Cost	Strengths	Weaknesses	Opportunities	Threats
WEC	Yes	Yes	With training	Fluke and Stronglyes	15 minutes to one day	$32.30 for 2 pooled WEC from 10 samples (NSW DPI)	Industry gold standard for estimation of parasite burden, cheap, fast	Lack of accuracy Variability between labs	Many methods for automation, egg flow cytometry, particle size analysis, image analysis have been explored and all remain technically feasible but probably not financially viable	
Larval diff	Yes	Yes	No	Haemonchus, Trichostrongylus Ostertagia Nematodirus	Around 8 days	$29.10 (NSW DPI)	Industry gold standard for species identification	Time delay in diagnosis		
Lectin stain	Yes or No?	DAWA only	No	Haemonchus only in currently offered format	One day		Speed for species identification	Need fluorescent microscope	Extend to other genera	Availability of reliable supplies of lectins
Necropsy	Yes	Yes	Yes	Yes	20 minutes for qualitative assessment	NSW DPI - $108.35 Farmer's time plus value of animal	Speed	Usually a sample size of 1 is used	Could be more widely employed	

Test	Validated	Commercially available	Use on farm	Species identification	Time	Cost	Strengths	Weaknesses	Opportunities	Threats
FAMACHA	Yes	Not in Australia	Yes	No	Same day	Farmer's time plus training	Potential for individual animal assessment	Low specificity and low predictive value of a positive.	Automated image analysis of membrane colour. Automated on farm Hb measuring device (eg hemocue)	Labour costs
Faecal occult blood test	No	No	Yes	Haemonchus and Liver fluke + other causes of blood in faeces	1 hr	$2	Leading indicator of severity of infection	Cross reactivity Boiling step	Second generation antibody body based test that avoids need for boiling	imitations
Pepsinogen	Yes or No?	Yes	No	Ostertagia	Same day	$27.50 then $16.50 ea	Not affected by variability of Oster WEC		Dipstick format for on farm use	
Immunoassay (eg Antibody) **Fluke ELISA**	No Yes	No Yes	No	Can be species specific	Same day	xxx $19.50 then $14.95 ea	Potential for Specificity	Continuity of antibody supplies	Dipstick format for on farm use	
Gene markers	Yes	Yes	no	Possible but probably not desirable	Not an issue	~$30 per head	Freedom from phenotypic variation	Requires frequent re-validation of association with phenotype		
Gene products	No	no	No	Possible but probably not desirable	Not an issue			Influenced by parasite exposure		
Egg PCR	No	No	No	Yes	Same day	~$30 per sample			PCR diagnosis of other faecal attributes – eg gene markers in host cells in faeces,	

2.2 External parasites

2.2.1 Techniques available

Blowflies

Blow fly infection is usually identified by inspection of sheep. Much anecdotal evidence reports the occurrence of occasional sheep dogs and some horses that can identify struck sheep, presumably by odours released from the struck animal. In bad cases of fly strike, people can smell struck sheep before the animal is caught.

Environmental monitoring of blowfly populations can be performed with commercially available Lucitraps.

Identification of fly species present in a strike lesion on commercial properties is rarely performed.

Identification of insecticide resistance status of flies on commercial properties is rarely undertaken by producers, but can be assessed by diagnostic laboratories.

Lice and mites

Presence of lice is typically indicated by presence of plucked wool and confirmed by observation of lice, though this is not easy. An immunoassay for detection of lice antigens on shearing combs remains under commercialisation. In one format under consideration it will be commercialised by NanoVic using the RMIT gold nanoparticle platform. In a second format under consideration, it will be a race-side dipstick immunoassay.

It has been demonstrated that immunoassays can detect antibodies to sheep mite in infected sheep (Ochs et al., 2001).

2.2.2 SWOT analysis

SWOT anlaysis

Test	Validated	Commercially available	Use on farm	Species identification	Time	Cost	Strengths	Weaknesses	Opportunities	Threats
Fly strike observation		Not a commercial test	yes	No	Farmer's time for mustering	Cost of farmer's time	Direct observation	Misses occult strike	Automation – eg odour detection	Welfare perception
Lucitrap	Yes	Yes	yes	Yes	Time for monitoring traps			High density of traps needed plus experience in appropriate location of traps	Automated monitoring of trap contents	
Lice observation		Not a commercial test	yes	No	Farmer's time for mustering	Cost of farmer's time	Direct observation	Not reliable for detecting low density infections		
Lice EIA	Yes?	No	yes	yes	Use integrated with shearing. Test about 15 minutes	Cost unkown. One test per property per year	Detects low level infections	Predicted cost of test?		
Mite EIA		Not in Australia		yes						

2.3 Summary of opportunities for improved diagnostic approaches

The standard diagnostic tests for strongyle infections, WECs and larval diffs are currently offered at a price that does not provide a strong economic argument for entrepreneurs to offer parasite diagnostic services. Despite the low price, uptake of the service by producers is weak. The low price of the tests creates substantial difficulties for competing technologies attempting to enter the market. Presumably underpinning the low uptake is a perception that the tests provide limited value to producers and a lingering agrarian socialist viewpoint that such services will or should be provided at cost or less by state Departments of Primary Industries. Research and development costs for a new test are not likely to be less than $500,000 and are quite likely to be in excess of $1 million, an investment that would be difficult to recover through sale of tests in the same price range as WECs and larval diffs. Field validation of a novel test for use in the field that has completed proof of principle and manufacturing R&D could be in excess of $100,000 and take up to 3 years to encompass seasonal variations. The current WEC market is estimated to be less than 100,000 tests per year. Tests for use in the field could substantial increase this market size.

Tests fall into 3 main classes:

1. measurement of parasite burden through presence of eggs, worm antigens or worms themselves;
2. measurement of components of host immunity (eg antibodies, eosinophils, other immune mediators) and
3. measurement of host pathology (wool growth, body growth, appetite, blood loss, digestive enzymes, anaemia, hypoproteinaemia, odours).

Desirable features of new diagnostic tests have been assumed, without thorough consumer validation, to include:

- Similar or lower price than current tests
- Faster provision of information to farmers
- Suitable for implementation by farmers on-farm
- At least as accurate as WECs and larval diffs
- At least as precise as WECs and larval diffs
- Applicable to other hosts including humans

Most diagnostic tests used in human and veterinary medicine aim to detect the presence or absence of infection. In contrast, diagnostic tests for internal parasitoses usually aim to determine the severity of infection. In most instances sheep management practices aim not to eliminate the internal parasite but to treat when infections reach a level that threatens or reduces productivity of sheep. Thus tests need accuracy and precision around the decision points associated with risk of production loss. Validating a new test designed to detect the severity of infection is a more demanding task than validating a test designed only to detect the presence or absence of infection. A further challenge is the lack of uniformity in decision points and treatment goals for minimising the production losses associated with internal parasitoses. Thus a new test for internal parasitoses would typically need to be validated against a suite of decision points (or test goals) rather than a single test objective, infected or not infected. Decision points may differ for stage of infection, parasite species, breed of sheep, class of sheep, physiological status of sheep, gender of sheep, resistance status of sheep, climatic region, feed type, body condition and so on. Validation of the test for each of these variables could be necessary.

Tests that measure the host antibody response to infection are not attractive for making decisions to treat or not treat sheep for stronglye infections because the half life of antibody (around 30 days) does not match the dynamics of parasite infection and re-infection after treatment. In addition,

ingested larvae stimulate antibody production in some infections but fail to mature into adults. In contrast, assessment of the presence of liver fluke, which is typically based on monitoring and treatment twice per year, is well suited to antibody testing.

Measures of parasite burden such as eggs or worm antigens are in principle attractive because they quantitatively reflect the presence of worms, and in the instance of eggs, the presence of mature worms. Reliance on egg counts is not desirable when pathology (or the risk of pathology) is associated with prepatent stages of infection such as severe *Haemonchus* infections (blood feeding by immature adults) and the hypobiotic phase of infection, eg Ostertagiasis in cattle and *Haemonchus* infections in sheep although the latter risk may have changed since the widespread adoption of anthelmintics (L.F. Le Jambre, personal communication). Tests such as the *Ostertagia* ELISA in cattle that can predict the impending severity of infection during the prepatent period are therefore attractive. A strength of the faecal occult blood test for *Haemonchus* infections in sheep is its capacity to predict the severity of subsequent mature infection. This test is thus a predictive or "leading" indicator of the severity of *Haemonchus* infection.

A weakness of measures of pathology, such as weight loss, anaemia and hypoproteinemia is the fact that production losses are incurred before positive test results are obtained. These measures are thus "lagging" indicators of the severity of infection.

References

Albers, G.A.A., Gray, G.D., Piper, L.R., Barker, J.S.F., Le Jambre, L.F., Barger, I.A., 1987. The genetics of resistance and resilience to *Haemonchus contortus* in young Merino sheep. International Journal for Parasitology 17, 1355-1363.

Berghen, P., Hilderson, H., Vercruysse, J., Dorny, P., 1993. Evaluation of pepsinogen, gastrin and antibody response in diagnosing ostertagiasis. Veterinary Parasitology 46.

Colditz, I.G., Le Jambre, L.F., 2007. Development of a faecal occult blood test to determine the severity of *Haemonchus contortus* infections in sheep. Veterinary Research, submitted.

Colditz, I.G., Le Jambre, L.F., Hosse, R., 2002. Use of lectin binding characteristics to identify gastrointestinal parasite eggs in faeces. Vet. Parasitol. 105, 219-227.

Dawkins, H.J.S., Windon, R.G., Eagleson, G.K., 1989. Eosinophil responses in sheep selected for high and low responsiveness to *Trichostrongylus colubriformis*. Int. J. Parasitol. 19, 199-205.

Gomez-Munoz, M., Cuquerella, M., Alunda, J., 1996. Identification and partial purification of a 26 kilodalton antigen of adult Haemonchus contortus. International Journal for Parasitology 26.

Gordon, H.M., 1967. The diagnosis of helminthosis in sheep. Veterinary Medical Review 67, 140-168.

Johnson, D., Behnke, J., Coles, G., 2004. Copro-antigen capture ELISA for the detection of Teladorsagia (Ostertagia) circumcincta in sheep: improvement of specificity by heat treatment. Parasitology 129.

Le Jambre, L.F., Dominik, S., Eady, S.J., Henshall, J.M., Colditz, I.G., 2007. Adjusting worm egg counts for faecal moisture in sheep. Vet. Parasitol. 145, 108-115.

Ochs, H., Lonneux, J., Losson, B., Deplazes, P., 2001. Diagnosis of psoroptic sheep scab with an improved enzyme-linked immunosorbent assay. Veterinary Parasitology 96.

Palmer, D.G., McCombe, I.L., 1996. Lectin staining of trichostrongylid nematode eggs of sheep: rapid identification of *Haemonchus contortus* eggs with peanut agglutinin. International Journal for Parasitology 26, 447-450.

Schallig, H., Hornok, S., Cornelissen, J., 1995. Comparison of two enzyme immunoassays for the detection of Haemonchus contortus infections in sheep. Veterinary Parasitology 57.

Vatta, A.F., Letty, B.A., van der Linde, M.J., van Wijk, E.F., Hansen, J.W., Krecek, R.C., 2001. Testing for clinical anaemia caused by Haemonchus spp. in goats farmed under resource-poor conditions in South Africa using an eye colour chart developed for sheep. Vet. Parasitol. 99, 1-14.

Whitlock, H.V., 1948. Some modifications of the McMaster helminth egg-counting technique and apparatus. Journal of the Council for Scientific and Industrial Research 21, 177-180.

Woolaston, R.R., Manueli, P., Eady, S.J., Barger, I.A., LeJambre, L.F., Banks, D.J.D., Windon, R.G., 1996. The value of circulating eosinophil count as a selection criterion for resistance of sheep to trichostrongyle parasites. International Journal for Parasitology 26, 123-126.

Zarlenga, D., Chute, M., Gasbarre, L., Boyd, P., 2001. A multiplex PCR assay for differentiating economically important gastrointestinal nematodes of cattle. Veterinary Parasitology 97.

3. PROJECT ASSESSMENT CRITERIA

Fifteen criteria have been developed to assess the novel diagnostic tests under consideration. The criteria are designed to construct a comprehensive overview of the research and development status of each test, their probability of succeeding in achieving their research objectives, how the test might be put into operation and the benefits of the tests to the Australian sheep industry. There are criteria that mainly address the question "What is the likelihood of successful commercialisation and adoption ? (marked with an "L") and others that are directed mainly at the benefits to the industry (marked with a "B"). Scores for each of the 15 criteria have been combined to develop composite scores for "Likelihood of Success" and "Benefits to Industry". The timeframe for the assessment is to achieve significant commercialisation or adoption within the lifetime of the current CRC (2014), but the criteria are relevant to test assessment generally.

3.1 Assessment Criteria

The assessment criteria are described here in terms of the questions that can be asked of the test.

1 Test Description:
What will the test do and how does it work?

2 Diagnostic Need:
What information will the test provide and what decisions will that information support?

3 Research Maturity:
Is there a well organised and supported research effort making steady progress? (L)

4 Research Complexity:
How many problems need to be solved before reaching 'proof of concept' and how complex are these problems? (L)

5 Operating Characteristics:
How complex are the reagents and materials for the test? (L)

6 Accuracy:
What is the expected sensitivity, specificity and predictive value of the test? (L)

7 Reliability:
Will the test be reliable when applied many times by the same, by different operators and between laboratories (L)

8 Implementation:
How will the test be used, samples collected, assays completed, results delivered etc). (L)

9 Skills and Training:
How much training will be needed for each aspect of test implementation. (L)

10 Customers:
Who will sell the tests and who are the target customers?

11 Competition:
Are there likely to be other test on the market and what are they?

12 Capital Investment:

How much capital investment is likely to be needed: production laboratory, machines to make reagents, containers etc. (B)

13 Value Proposition:

What will the price be relative to other tests and how much greater will the benefits be? Who will be the beneficiaries? (B)

14 Transformation:

To what extent will the adoption of the diagnostic transform the way that sheep are managed? (B)

15 **External Opportunities**:

What are the opportunities for use of the diagnostic outside the sheep industry, and for other parasites and diseases? (B)

16 Likelihood of Success:

What is the overall assessment of the likelihood of successful commercialisation and adoption?

17 Benefits to Industry

What is the overall assessment of the magnitude of benefits to the sheep industry.

4. ASSESSMENT OF CURRENT PROJECTS AGAINST THE FRAMEWORK

The core of this section is a tabulation of the framework criteria against each of the novel diagnostics which have been supported by the CRC. Using these criteria each test has been scored and an evaluation made of their potential impact in the sheep industry and the probability of their successful implementation in the seven year lifetime of the current CRC (2014). In all cases a single star indicates the least favourable condition for the test and three stars the most favourable condition. The *Haemonchus* dipstick test has been included in the analysis for comparison. It may be useful to include the PCR test being developed with MLA funding for completeness.

Criteria	**A. On Farm *Haemonchus* Dipstick Test**	**B. Faecal Antigen Diagnosis of Nematodes**	**C. Faecal Antigens for Worm Detection**	**D. Electronic Nose for Blowlfly Strike Detection**	**E. Analysis of Odour for the Diagnosis of GI Nematodes**	**F. Lectin Binding Assay for Worm Genus Identification**	**G. Faecal NIRS to Diagnose Parasite Burden**
Test Description	Paper strip dipped in to slurry of faeces and water to detect blood.	Immunological detection of worm antigens in faecal extracts.	Immunological detection of worm antigens in faecal extracts.	Electronic sensors detect chemicals in air drawn from sheep struck with blowflies	Electronic sensors detect chemicals in air drawn from dung of worm-infected sheep.	Differential chemical labelling and counting of worm eggs isolated from faeces.	Detection on blood in faeces based on absorbance of Infra Red light.
Diagnostic Need (B)	Presence of *Haemonchus* and its contribution to WECs. ***	Rapid on-farm detection of worm burdens.***	Accurate laboratory quantification of worm burdens. **	Early warning of struck sheep in mobs at risk. ***	Rapid confirmation of worm infection and of pre-patent or sub-patent infections. *	Treatment of sheep worms is improved if genera can be identified accurately and quickly.***	Presence of *Haemonchus* and its contribution to WECs. ***

Criteria (cont.)	A. On Farm *Haemonchus* Dipstick Test	B. Faecal Antigen Diagnosis of Nematodes	C. Faecal Antigens for Worm Detection	D. Electronic Nose for Blowlfly Strike Detection	E. Analysis of Odour for the Diagnosis of GI Nematodes	F. Lectin Binding Assay for Worm Genus Identification	G. Faecal NIRS to Diagnose Parasite Burden
Research Maturity (L)	Problem solving for commercial partner. *******	Reliant on PhD students.*	Strong long-term research team.***	Good progress as small part of larger QDPI development group. *****	Reliant on PhD students.*	Research team and expertise is established.***	Experienced research group with range of interests in NIRS.**
Research Complexity (L)	No new reagents or materials. *******	Reagents need to be further developed and tests validate in lab and in field. *	Calibration ands sensitivity problems yet to be solved.**	Major problems of detection and deployment to be solved. *****	Major problems of detection and deployment to be solved. *****	All methods developed but need to be simplified and standardised. ***	Ca;librating and simplifying spectrometer are major tasks.**
Operating Characteristics (L)	On-farm, some mixing and heating of faeces, eyeball colour assessment. *******	On-farm, some mixing and sieving of faeces, eyeball colour assessment. ***	Laboratory, batch processing with quantitative colorimetric outputs.***	Options include race-side drafting to remote monitoring. *	On farm or laboratory use, monitor of sheep camps and holding yards.*	Counting with fluorescence microscope after sieving and centrifuging faeces.**	On-farm with mobile spectrometer with immediate result.**
Accuracy (L)	Subjective scale of 1-5. ******	Subjective scale of 1-3?. ******	Close correlation with egg counts (sometimes poorly reflects worm burden) **	Once developed should be highly specific. ***	Once developed should be highly specific. ***	Very accurate egg counts (which sometimes poorly reflect worm burden) **	Quantitative estimate of blood in faeces: equivalent to test A.*
Reliability (B)	May be confounded by blood loss for other reasons and feed components. ******	Not known. May be confounded by other immune components in faeces. *	Not known. May be confounded by other immune components in faeces. *	Technically complex, dependent on power source subject to accidents if remote.*	Not known. May be confounded by other metabolic components in faeces.*	Very reliable from faeces arrival to results delivery.***	May be confounded by blood loss for other reasons and feed components. ******
Implementation (B)	Sampling, test and results are all on farm or next day from lab. *******	Sampling, test and results are all on farm.***	Count by worm genus available on day of test.**	Instant results to manager or consultant. ***	Instant results to manager or consultant. ***	Permits 'same day' differentiation of egg counts to more genera than current tests.***	Sampling, test and results are all on farm or next day from lab. *******
Skills and Training (B)	Simple processes, no storage or preparation. ***	Skills to use are simple. ***	Skills available in modern diagnostic laboratories.***	Requires good local technical backup of trained technicians.*	Requires good local technical backup of trained technicians.*	Requires good lab skill but steps can be standardised easily.***	Spectrometer calibratrio and maintnance requires care**
Customers	Vets and resellers targeting other vets and graziers.	Vets and resellers targeting other vets and graziers.	Diagnostic laboratories which process over 1000 WECs per year.	Large operators, studs and graziers with high welfare priorities.	Large operators, studs and graziers with high priority for worm control.	Diagnostic laboratories which process over 1000 WECs per year.	Large operators, vets and sheep consultants.
Competition (B)	None now. B, C, E and G all potential competitors. *******	WEC with A and potentially C.*	Combination of WEC and Test F. **	Stock monitoring by trained staff. ***	WECs and tests A, B, C.*	There is no equivalent test. Current test need 7 days.***	Mostly Test A. unless other use found for spectrometer (feed analysis?) *

Criteria (cont.)	A. On Farm *Haemonchus* Dipstick Test	B. Faecal Antigen Diagnosis of Nematodes	C. Faecal Antigens for Worm Detection	D. Electronic Nose for Blowlfly Strike Detection	E. Analysis of Odour for the Diagnosis of GI Nematodes	F. Lectin Binding Assay for Worm Genus Identification	G. Faecal NIRS to Diagnose Parasite Burden
Capital Investment (B)	Almost none: all materials *off the shelf*. ***	High to develop reagents and Quality Control. *.	High to develop reagents and Quality Control.*	Likely to be expensive: equivalent to ATV or large weighing crate. *	Likely to be expensive: equivalent to ATV or large weighing crate. *	Most laboratories have capital items. ***	High for end user*
Value Proposition (B)	'Same-day' diagnosis of Hc reduces risk and increases drug effectiveness. **	Quick diagnosis but quantitative enough? **	Quick and quantitative estimates of worm burden for existing users.**	Provide welfare or non-chemical 'edge' for marketing. Reduced monitoring labour. **	Could provide 'hands-off' estimates of worm burdens.**	Same day diagnosis of Hc, accumulation of accurate worm data, better genetic evaluations. Cheaper than current test.***	Provide instant estimate of *Haemonchus* problem but at high cost for most users. *
Transformation (B)	May enable continued sheep raising in some summer rainfall zones. *	May enable continued sheep raising in some summer rainfall zones. *	May enable continued sheep raising in some summer rainfall zones. *	'ticket to play' some zones? *	May enable continued sheep raising in some summer rainfall zones.*	May enable continued sheep raising in some summer rainfall zones. *	May enable continued sheep raising in some summer rainfall zones. *
External Opportunities (B)	South Africa, parts of South America *	Global but there may be other players. *	Could be applied to all species where nematode eggs are passed in faeces. SA, NZ for sheep**.	Global for screw worm in cattle, NZ for strike especially if remote. **	Global for sheep and could extend to many gastrointestinal parasites.***	Global market for laboratories for sheep and cattle nematode parasites. **	Global for blood loss in faeces (other parasites and diseases).*
Likelihood / 18	14	10	12	10	7	13	10
Benefit / 24	18	13	14	14	13	21	12

SUMMARY OF ASSESSMENTS

A. On Farm *Haemonchus* Dipstick test.

This test benefits from 'off the shelf' availability of reagents and materials so there is only a limited amount of technical development required. Markets are limited to those areas where *Haemonchus* poses a high risk to graziers and is likely to be limited to those clients who currently use WECs as a means to monitor worm burdens. Technical development is almost complete and a commercial partner is on the point of signing a commercial agreement. It is significant that the partner will not use the test on its own to generate profit but as an entry point to differentiate it from other providers of worm advisory services.

B. Faecal Antigen Diagnosis of Nematodes.

This on-farm or laboratory test is distinguished from Test C by aiming to detect free antigens which are dispersed within the faeces of infected sheep and can be detected by an immune reaction in a slurry of faecal material. If developed to a dipstick format it has application across all of the sheep industry where nematodes (not just *Haemonchus*) are a constraint. In order to justify their development, which is still at the early stages, there would need to be an expansion of the market

for their use; much wider that the current market for WECs. Development costs and ongoing QA for reagents is likely to be expensive. It is unlikely that the Australian sheep market alone is large enough to justify this type of test when WEC tests (plus current larval differentiation or test F) could provide similar information at around the same cost. The research team currently working on this test would need to be stabilised and receive substantial funding before technical development could be completed within the life of the CRC.

C. Faecal Antigens for Worm Detection

Test C has similarities to Test B except that it requires laboratory processing of faeces and eggs to release egg antigens. It has proved to have specificity across the important worm species but there have been problems in calibrating the test to reflect the numbers of eggs in faeces and, indirectly, the worm burden. The strong technical team is in a position to take the research forward and the test would provide a quantitative species-specific estimate of worm burden. However, without a substantial increase in the size of the market for worm burden testing the cost is likely to be much higher than current practice, and as a laboratory-based test it would need to have advantages over the existing worm egg counts/larval differentiation (or Test F), or of possible on-farm tests such as Tests A and B).

D. Electronic Nose for Blowfly Strike Detection

There is a large amount of global research in the technology of odour detection and its associated software and hardware. There is also increasing concern about the welfare of sheep exposed to the risk of blowflies (and of other species exposed to other flies, including the presently-exotic Screw Worm Fly). Demand for, and potential to supply a method for early detection are both increasing rapidly. The current research team has partly integrated into a larger group at Toowoomba (QDPI) with substantial expertise in odour detection. While technology development is likely to move most rapidly with a large research and development group, the development of new applications requires the innovative capacity of the whole sheep industry, possibly through the CRC. It is certain there is a need for this technology and that it can be used. But how it can be used most effectively is very uncertain: power supply, cost, accuracy and potential other applications are the major variables.

E. Analysis of Odour for the Diagnosis of GI Nematodes

This test would use similar technology as Test D but the need for its use and application would be different (and, as yet, not fully explored). It has proved possible to detect worm infected from non-infected sheep on the basis of odours in faecal masses. The need for information on worm burden is rarely, however, of a quantum nature: ‘worm-infected’ or ‘non-infected’, in contrast to the presence of a single fly-blown sheep in a mob being of critical interest. Current research is based on the excellent work of a PhD student and therefore is a preliminary to the extended research and development that would be needed to validate a product as useful for worm control.

F. Lectin Binding Assay for Worm Genus Identification

This test is in current commercial use in one laboratory in Australia (DAFWA) as an alternative to larval differentiation of nematode larvae by microscopy. Technically therefore there are few barriers between the current state of research and its wider use by major laboratories throughout the country. The major feature for ‘real-time’ worm control is the ability to count *Haemonchus* eggs at the same time as total worm egg counts, giving a ‘same-day’ result back to advisors and farmers. Small but significant improvements in methods for preparing eggs are required before uptake by other major labs is likely. This test gives a very precise answer which is, like all estimates of worm burden based on egg counts, of very variable accuracy dependent on size of worm burden, species mix, faecal moisture and conditions for faecal collection and transport.

G. Faecal NIRS to Diagnose Parasite Burden

Near Infra-red Spectroscopy can analyse faecal masses for changes associated with infectious and metabolic diseases and diet. Spectrometers are relatively expensive devices, even in basic handheld versions, although many are available in grain receiving centres throughout Australia. Research has focused on the changes associated with blood in the faeces and therefore is an alternative approach to test A, the *Haemonchus* dipstick. The whole range of on-farm uses of a spectrometer needs to be evaluated as a commercial option (feed analysis, weaned animals not eating). The possible research uses of these devices, for example in the Information Nucleus, could be considered.

5. FINAL ASSESSMENT AND RECOMMENDATIONS

RECOMMENDATION 1: ROLE OF DIAGNOSTIC TESTS IN IMPROVING DECISIONS

o Note that diagnostic test development and decisions on use are most soundly based on need and value rather than on elegance and sophistication of the technology.
o Before introduction, diagnostic tests should be subject to appropriate laboratory validation to demonstrate fitness for proposed use and field assessment to establish reliability and value of elicited information.
o After introduction and use, test performance should be monitored as part of routine quality assurance and to determine positive or negative impacts of test use on decision making.
o There is likely to be a substantial benefit to farmers if an objective assessment is made of the accuracy and appropriateness of diagnosis and treatment decisions based on information obtained by farmers from local parasite epidemiology, flock history and physical examination. The results observed in such a study should form the baseline against which the value of using an additional diagnostic test is made.
o Cost effectiveness and economic consequences of the use of special diagnostic tests should be modeled and investigated to identify those situations (in time and place) likely to benefit most from the use of such tests.
o The establishment of contact with CRC for Diagnostics to explore shared objectives and opportunities for collaboration should be considered.

RECOMMENDATION 2: SHEEP CRC INVOLVEMENT IN PROPOSED DIAGNOSTIC TESTS

The following recommendations are presented in the context of projects that could have outcomes within the lifetime of the current Sheep CRC. Projects not supported may still have great merit and potential to improve parasite control decisions but may have a longer development and validation horizon than is consistent with CRC strategies.

SUPPORT
1. ***Haemonchus* dipstick (A):** Proceed as planned with development to a commercial test product through an animal health company. Make enquiries regarding overseas markets.
2. **Lectin-binding assay (F):** Support packaging of the assay for major Australian laboratories, and investigate commercialisation into global markets. Note that *Haemonchus* differentiation offers a stand alone test method to which multiple species identification and differentiation can be added.

FURTHER INVESTIGATION
3. **Odour detection, blowflies (D):** A scoping study of all possible uses of in the sheep industry should be considered. An option to be considered as part of that study is for the CRC to retain interest in e-nose for blowflies because of strong and increasing demand for early detection of fly infestation, through collaboration of Programs 1 and 6 with a strong existing technical group such as the QDPI team.

4. **NIRS (G):** Consider further exploration of the use of as a research tool to look at relationships between pasture, feed, worms and genetics.

ABANDON
5. **Faecal antigen tests (B and C):** These have encountered considerable technical difficulties which would require significant basic research to resolve, and even if the research goes well.
6. **E-nose for worms (F):** The concept in relation to worm detection is at an early stage, and development to a testable technology would be outside the CRC's timeframe for research commercialization..

6. BRIEF OVERVIEW OF DIAGNOSTIC TECHNOLOGIES UNDER DEVELOPMENT IN OTHER VETERINARY AND MEDICAL FIELDS

6.1 SUMMARY OF DIAGNOSTIC TECHNOLOGIES

6.1.1 Detector dogs

Substance	Reference
Accelerants	Armstrong et al 2004; Gialamas 1996; Kurz et al 1994; Tindall and Lothridge 1995
Bear, grizzly or black	Akenson et al 2004; Wasser et al 2004
Brown tree snakes (Boiga irregularis)	Engeman et al 1998a, b
Cancer, bladder, breast, lung, melanoma, ovarian carcinoma	Gordon et al 2008; Horvath et al 2008; McCulloch et al 2006; Willias et al 2004; Williams and Pembroke 1989; Church and Williams 2001;Pickel et al 2004
Desert tortoise (Gopherus agassizii)	Cablk and Heaton 2006
Drugs, cocaine	Furton et al 2002
Drugs, narcotics	Lorenzo et al 2003
Oestrus-related odours in cows or milk	Kiddy et al 1978, 1981, 1984; Hawk et al 1984
Explosives	Furton and Myers 2001; Gazit and Terkel 2003
Gypsy moth eggs	Wallner and Ellis 1976
Human, cadavers and remains	Komar 1999; Oesterhelweg et al 2008
Human, living	Fenton 1992
Human, perpetrators from crime scene odours	Schoon 1998
Residues, organochlorine in soil	Anon 2008
San Joaquin kit fox	Smith et al 2003
Screwworms (Diptera: Calliphoridae)	Welch 1990
Smuggled food	Eastwood 1990
Termites	Brooks et al 2003
Nematode infection in sheep	Richards et al 2008
Hypoglycaemia	Anon (2008)

6.1.2 Etongue

Etongue sensors	Toko 1998; Vlasov et al 2002; Sohn et al 2005; Olsson et al 2006; Ahluwalia and De Rossi 2007; Wang et al 2007; Ipatov et al 2008
Bovine mastitis detection	Mottram et al 2007
Bacterial species identification	Söderström et al 2003

6.1.3 Urine odours of parasitism

Mice	Kavaliers et al 1998a, b, 2006
Mice, detection by of parasitised individual	Kavaliers et al 2005a,b
Mice, Eimeria vermiformis	Kavaliers and Colwell 1993, 1995b; Kavaliers et al 1997
Mice, Heligmosomoides polygyrus	Ehman and Scott 2001, 2002; Kavaliers et al 2004; Kavaliers and Colwell 1995a
Mice, Polyplax serrata (louse)	Kavaliers et al 2003a,b
Mice, Taenia crassiceps	Morales et al 1996
Rats, Hymenolepis diminuta	Willis and Poulin 2000
Vole, Trichinella spiralis	Klein et al 1999

6.1.4 Enose

Situation	Species	Detection	Reference
Anaerobic bacteria (Clostridium spp. (14 strains) and Bacteroides fragilis (12 strains))	In vitro	Enose	Pavlou et al 2002b
Asthma	Human (exhaled breath)	Enose	Alving et al 2006; Gill et al 2006; Dragonieri et al 2007
Bacterial classification	In vitro	Enose	Gibson et al 1997; Gardner et al 1998; Moens et al 2006
Bacterial sinusitis	Human	Enose	Mohamed et al 2003, Thaler 2002; Thaler and Hanson 2006; Bruno et al 2008
Bacterial vaginosis	Human (swabs)	Enose	Chandiok et al 1997; Hay et al 2003; Persaud et al 2003, 2006; Chaudry et al 2004
Bacteriuria	Human (urine)	Enose	Aathithan et al 2001
Biofilm-producing Pseudomonas & Staphylococcus	in vitro	Enose	Thaler et al 2008
Blood culture bacteria	Human (ex vivo)	Enose	Lykos et al 2001; Yates et al 2005
Blood in urine	Human (urine)	Enose	Di Natale et al 1999; Mantini et al 2000
Bovine ketosis	Cattle (nasal)	Enose	Elliott-Martin et al 1997
Bovine oestrus	Cattle (perineal odour swab)	Enose	Lane and Wathes 1998
Breast cancer	Human (breath)	Enose	Phillips et al 2003, 2006
Cerebrospinal fluid differentiation from serum	Human (fluid)	Enose	Thaler et al 2000; Thaler 2002; Aronzon et al 2005
Cyanobacteria in water	In aqua	Enose	Gardner et al 2000; Shin et al 2000
Diabetes (exhaled acetone and urine volatile analysis)	Human (breath, urine)	Enose	Wang et al 1997; Ping et al 1997; Zhang et al 2000; Mohamed et al 2002; Dalton et al 2004
Diarrhoea (C difficile, Campylobacter, rotavirus, small rounded structured virus (SRSV), adenovirus, astrovirus, giardiosis)	Human (faeces)	Enose	Probert et al 2004
Ear, nose and throat bacteria (*Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa)*	In vitro (ex vivo swabs)	Enose	Boilot et al 2002; Dutta et al 2004; Shykhon et al 2004; Dutta and Dutta 2006

Eye infection bacteria	In vitro	Enose	Dutta et al 2002
Haemodialysis fluid monitoring	Human (in line fluid)	Enose	Fend et al 2004
Helicobacter pylori	Human	Enose	Pavolu et al 2000
Intrapulmonary infection	Human	Enose	Hanson and Steinberger 1997; Hockstein et al 2004, 2005; Hanson and Thaler 2005
Lung cancer	Human (breath)	Enose	Phillips et al 1999, 2003, 2007, 2008; Di Natale et al 2003; Machado et al 2005; Chen et al 2007;
Melanoma	Human (lesion in situ)	Enose	D'Amico et al 2008a, b
Mycobacterium bovis	Badger, cattle (serum)	Enose	Fend et al 2005
Mycobacterium tuberculosis infection	Human (sputum)	Enose	Pavlou et al 2004; Fend et al 2006
Renal dysfunction staging	Human (skin)	Enose	Voss et al 2005
Review		Enose	Gardner and Bartlett 1994; Harper 2001; Thaler et al 2001; Turner and Magan 2004; Thaler and Hanson 2005; Pavlou and Turner 2000; Röck et al 2008
Schizophrenia	Human (sweat)	Enose	D'Amico et al 2008a
Upper aerodigestive tract tumor cells	In vitro	Enose	Gendron et al 2007
Upper respiratory tract bacteria	In vitro	Enose	Lai et al 2002
Urinary tract cancers	Human (urine)	Enose	Bernabei et al 2008
Urinary tract infection	Human (urine)	Enose	Guernion et al 2001; Lin et al 2001; Pavlou et al 2002a, 2004; Kodogiannis and Wadge 2005; Yates et al 2005; Persaud et al 2006
Wound healing	Human (wound)	Enose	Parry et al 1995; Greenwood et al 1997
Wound infection	Human (wound)	Enose	Persaud 2005; Šetkus et al 2006

6.1.5 Near-Infrared Reflectance Spectroscopy

Clinical applications of NIRS	**Reference**
Clinical tissue oxygen saturation (shock and resuscitation; compartment syndrome; necrotising fasciitis; peripheral vascular disease; free flaps; cerebral oxygenation)	Cohn 2007
Clinical optical mammography to provide functional information about breast cancer lesions	Leff et al 2008
clinical burns distinguishing shallow injuries from deeper burns that require surgery	Sowa et al 2001; 2006
clinical cancer diagnosis	Kondepati et al 2008

clinical cerebral blood oxygen changes during stroke or brain tumours	Sakatani et al 2007
clinical cerebral oxygen saturation monitoring	Farouk et al 2008
clinical cerebral oxygenation in the neurointensive care unit	Wright 2007
clinical circulation in transplanted tissues	Cai et al 2008
clinical continuous monitoring of central venous oxygen saturation (unreliable)	Baulig et al 2008
clinical detection of lipid-rich plaque and possibly of vulnerable plaque in the coronary arterial wall	Waxman et al 2007
clinical diagnosis and severity evaluation in patients with peripheral vascular disease	Vardi and Nini 2008
clinical faecal composition in coeliac disease	Rivero et al 2000
clinical glucose (not clinically useful)	Tura et al 2007
clinical hemodynamic monitoring and early detection of inadequate tissue perfusion and oxygenation	Creteur 2008
clinical malabsorption faecal fat and N	Neumeister et al 1997
clinical migraine and cerebral haemo-dynamics	Vernieri et al 2008
clinical muscle oxygenation and oxidative metabolism in healthy and diseased humans	Hamaoka et al 2007
clinical neonatal brain optical tomography	Hebden and Austin 2007
clinical neuroimaging	Hoshi 2007
clinical neuro-monitoring in cardiac surgery: patients	Saidi and Murkin 2005
clinical neuro-monitoring to prevent and reduce brain injury in cardiovascular surgery	Guarracino 2008
clinical non-invasive glucose monitoring	Heise et al 2000
clinical noninvasive imaging of tissue hypoxia	Vikram et al 2007
clinical skin classification	Bodén et al 2008
clinical tissue oxygenation	McVeigh 2006
clinical tissue oxygentation and intra-abdominal hypertension	Widder et al 2008
clinical tissue pH	Soller et al 1996
clinical transcranial perfusion monitoring	Smith 2007
clinical tumour measurement	Steinberg et al 1997
Faecal analysis by NIRS	
Faecal analysis and prediction of botanical composition of diet	Walker et al 2007
faecal composition and prediction of feed composition	Tolleson et al 2005
faecal composition review	Landau et al 2006
faecal composition used to determine diet quality in sheep	Li et al 2007
Faecal nutrients	Lyons et al 1993; Stuth and Tolleson 2000
Faecal output and PEG poly-ethylene glycol	Landau et al 2002
Discrimination between physiologically different groups of cattle	Tolleson et al 2000a
Feed analysis and NIRS	
feed analysis and prediction of sheep response	Eckman et al 1983
feed fatty acid analysis in forages	Foster et al 2006
feed nutrient composition	Mentink et al 2006
feed prediction of effective degradation of DM, CP and NDF in ruminant feeds	Ohlsson et al 2007
feed surveillance and monitoring in the manufacture, processing, and marketing of compound feeds	Fernández-Ahumada et al 2008
feed utilization by faecal NIRS analysis	Glasser et al 2008
quality of browsing for herbivores	DeGabriel et al 2008
Pharmaceutical industry applications of NIRS	
pharmaceutical active pharmaceutical ingredient monitoring	Feng and Hu 2006
pharmaceutical analysis of solid, liquid and biotechnological pharmaceutical forms	Roggo et al 2007
pharmaceutical herb extracts	Rager et al 2002

pharmaceutical herb identification	Kudo et al 2000
pharmaceutical herbal medicine discrimination	Woo et al 1999; Xie et al 2006
pharmaceutical illicit ecstasy tablet profiling	Baer et al 2007
pharmaceutical intermediate quality control	Andre 2003
pharmaceutical polymorph determination	Patel et al 2000; 2001
pharmaceutical QC	Corti et al 1993; Reich 2005; Räsänen and Sandler 2007; Gowen et al 2008
pharmaceutical tablet blend homogeneity, content uniformity, coating thickness QC	Moes et al 2008
pharmaceutical tablet formulation development	Hilden et al 2008
pharmaceutical tablet hardness QC	Morisseau and Rhodes 1997
Parasitism detection and NIRS	
Faecal NIRS of cattle and tick infestation	Tolleson et al 2000b, 2002, 2007

6.1.6 Point of care tests (POCTs)

Test subject	reference
Cancer	
Cancer, bladder carcinoma	Dey P 2004; Tomera 2004
Cancer, cell screening	Kang et al 2007
Cancer, lung, epidermal growth factor receptor mutations	Hoshi et al 2007
Cancer, oral squamous cell carcinoma	Mauk et al 2007; Ziober et al 2006
Cancer, profiling	Dufva and Christensen 2005
Cancer, prostate-specific antigen	Healy et al 2007; Lin et al 2008
Clinical Chemistry	
Cholesterol	Warnick and Remaley 2001
Complete blood count	Rao et al 2008
Electrolytes, blood gases, haematocrit	Steinfelder et al 2008; Steinmetz et al 2007; Vos et al 2006
Glucose	Armor and Britton 2004; Desachy et al 2008; Meex et al 2006; Morris et al 2008; Rust et al 2008
Haemoglobin	Gupta et al 2008; Myers and Browne 2007; Nguyen-Khac et al 2006
Lactate	Acierno and Mitchell 2007; Ferasin and Nguyenba 2008; Stevenson et al 2007; Tennent-Brown et al 2007; Thorneloe et al 2007
Lipids	Shephard et al 2007
Nerve growth factor	Tang et al 2007
Parathyroid hormone	Sokoll et al 2004
Pregnancy	Eichner and Timpe 2004
Protein	Johnston et al 2007
Pulmonary function	Tovar and Gums 2004
RNA (saliva)	Wei et al 2008
Coagulation	
Coagulation (international normalized ratio INR)	Fancher and White 2004; Murray et al 2004
Platelet function	Gaál et al 2007; Harle 2007; Seegmiller and Sarode 2007
Drug detection	
Drug monitoring, antiepileptics	Yang et al 2007
Drug monitoring, lithium	Vrouwe et al 2007
Drug monitoring, tricyclic antidepressants (urine)	Melanson et al 2007

Drugs of abuse	George and Braithwaite 2002; Lewandrowski et al 2008; Wilson et al 2007
Smoking (urine test)	Payne and Southern 2006
Genomics	
Genetic testing	Dobson et al 2007
Imaging	
Acute compartment syndrome (IR imaging)	Katz et al 2008
Cerebral perfusion (laser Doppler, thermal diffusion, oximetry, microdialysis)	De Georgia and Deogaonkar 2005
Lower extremity arterial disease (Doppler flow)	Bonham 2006
Ultrasonography	Hillingsø et al 2008
Immune function	
CD4+ T cells	Cheng et al 2007; Peter et al 2008
Infectious agents	
Anthrax PA IgG	Bienek et al 2008
Babesia-bovis	Nascimento et al 2007
Botulinum neurotoxin type A	Gessler et al 2007
Brucella	Abdoel and Smits 2007
Chlamydia	Mahilum-Tapay et al 2007; Olshen and Shrier 2005; Peeling et al 2006
Dengue virus IgG	Aytur et al 2006
Entamoeba histolytica	Leo et al 2006
Feline leukaemia virus, Feline immunodeficiency virus	Goldkamp et al 2008
Helicobacter	Basset et al 2003; Cardenas et al 2008; Opekun et al 2006
Herpes simplex type 2 IgG	Laderman et al 2008
HIV	Anon 2007; Curtis et al 2008; Dewsnap and Mcowan 2006; Pai et al 2007
Influenza, avian	Zarkov 2008
Influenza, human	Shimasaki et al 2001; Turner et al 2006; Uphoff Metzger 2002; Weitzel et al 2007; Oh et al 2008
Legionella pneumophila	Diederen and Peeters 2007
Leprosy	Bührer-Sékula et al 2007
Leptospira	Doungchawee et al 2008
Loa loa	Burbelo et al 2008
Malaria	Wongsrichanalai et al 1008; Ratnawati et al 2008; Reyburn et al 2007; Wiese et al 2006
MRSA (meticillin resistant Staphylococcus aureus)	Jeyaratnam et al 2008
Pneumococcal antigen (urine)	Weatherall et al 2008
Schistosoma japonicum antibodies	Wang et al 2006
Streptococcus, group A (Rapid Streptococcal Antigen Test RSAT)	Humair et al 2006; Sheeler and Little 2006
Streptococcus, group B	Edwards et al 2008; Gavino and Wang 2007
Syphilis	Benzaken et al 2008; Peeling and Ye 2004
Trachoma (Chlamydia trachomatis)	Michel et al 2006
Tuberculosis	Dinnes et al 2007; Steingart et al 2007
Typhoid	Pastoor et al 2008
Viruses (influenza virus, respiratory syncytial virus, rotavirus and adenovirus)	Kayaba 2002
Kidney disease	

Albumin:creatinine ratio	Shephard et al 2006
Creatinine	Schenk et al 2007
Microalbuminuria	Garner and Wiedmeyer 2007; Goldstein et al 2007
Tissue injury, Pathology	
Acid-base balance	Story 2004
Ammonia, blood	Goggs et al 2008
B-type natriuretic peptide	Ancheta 2006
Cardiac Injury Biomarkers (myoglobin, creatinine kinase myocardial band [CKMB],and cardiac troponin I [cTnI])	Giannitsis et al 2008; Kost and Tran 2005; Stubbs Collinson 2001
C-reactive protein	Melbye Stocks 2006; Miyazaki 2002; Monteny et al 2006
D-dimer (assay for the diagnosis of pulmonary embolism)	Runyon et al 2008
Fatty acid binding proteins (tissue injury)	Chan et al 2005
Liver function (breath tests)	Ilan 2007
Trypsinogen (urine testing for the diagnosis of pancreatitis)	Jang et al 2007
Errors	
POCT error	Ehrmeyer and Laessig 2007

6.1.7 New Technology Reviews

Technology	**Reference**
Aptamers	Kirby et al 2004; Mairal et al 2008
DNA chip	Marchand et al 2008
Immunoassays	Chan et al 2008
immunotesting	von Lode 2005
IR	Hoşafçi et al 2007
Lectinomics	Gemeiner, P., D. Mislovicová, et al. (2009).
Metabolic profiling	Mansfield et al 2006
Microbiology	Robertson and Nicholson 2005
Microfluidics	Situma et al 2006
Molecular Dx	Holland and Kiechle 2005
Nanobiotechnology	Jain 2007
Pathogens	Yeung et al 2006
Protein microarrays, antibody arrays	Dufva and Christensen 2005
Review	Price 2001
Saliva	Pesce and Spitalnik 2007; Christodoulideset al 2005; Gutiérrez et al 2008; Parra et al 2005; Wright and Bickle 2005

6.2 REFERENCES

CATEG.	**REFERENCE**
Enose	Aathithan S, Plant JC, Chaudry AN, French GL (2001): Diagnosis of bacteriuria by detection of volatile organic compounds in urine using an automated headspace analyzer with multiple conducting polymer sensors. J Clin Microbiol 39: 2590-2593
POCT	Abdoel TH, Smits HL (2007). Rapid latex agglutination test for the serodiagnosis of human brucellosis. Diagn Microbiol Infect Dis 57(2): 123-128
POCT	Acierno MJ, Mitchell MA (2007). Evaluation of four point-of-care meters for rapid determination of blood lactate concentrations in dogs. J Am Vet Med Assoc 230(9): 1315-1318
Etongue	Ahluwalia A, De Rossi D (2007). Artificial Noses and Tongues. Encyclopedia of Materials: Science and Technology, pp 344-347
Dog	Akenson JJ, Henjum MG, Wertz TL, Craddock TJ (2004). Use of dogs and mark–recapture techniques to

	estimate American black bear density in northeastern Oregon. Ursus 12: 203–210
Enose	Alving K, Janson C, Nordvall L (2006). Performance of a new hand-held device for exhaled nitric oxide measurement in adults and children. Respir Res 7: 67
POCT	Ancheta IB (2006). B-type natriuretic peptide rapid assay: a diagnostic test for heart failure. Dimens Crit Care Nurs 25(4): 149-154
NIRS	Andre M (2003). Multivariate analysis and classification of the chemical quality of 7-aminocephalosporanic acid using near-infrared reflectance spectroscopy. Anal Chem 75(14): 3460-3467
POCT	Anon (2007). Point-of-care HIV testing using rapid HIV test kits: guidance for health-care professionals. Can Commun Dis Rep 33 Suppl 2: 1-22
Dog	Anon (2008) Use of detector dogs in residue-management programs. Queensland Department of Primary Industries and Fisheries. http://www.dpi.qld.gov.au/cps/rde/dpi/hs.xsl/4790_6603_ENA_HTML.htm
Dog	Anon (2008). Dogs trained to alert owners to onset of hypoglycaemia. Vet Rec 162: 428
POCT	Armor BL, Britton ML (2004). Diabetes mellitus non-glucose monitoring: point-of-care testing. Ann Pharmacother 38(6):1039-47. Epub 2004 Apr 30. Review.
Dog	Armstrong A, Babrauskas V, Holmes DL, Martin C, Powell R, Riggs S, Young LD (2004). The evaluation of the extent of transporting or "tracking" an identifiable ignitable liquid (gasoline) throughout fire scenes during the investigative process. J Forensic Sci 49(4): 741-748
Enose	Aronzon A, Hanson CW, Thaler ER (2005). Differentiation between cerebrospinal fluid and serum with electronic nose. Otolaryngol Head Neck Surg 133: 16-19
POCT	Aytur T, Foley J, Anwar M, Boser B, Harris E, Beatty PR (2006). A novel magnetic bead bioassay platform using a microchip-based sensor for infectious disease diagnosis. J Immunol Methods 314(1-2): 21-29
NIRS	Baer I, Gurny R, Margot P (2007). NIR analysis of cellulose and lactose--application to ecstasy tablet analysis. Forensic Sci Int 167(2-3): 234-241
POCT	Basset C, Holton J, Ricci C, Gatta L, Tampieri A, Perna F, Miglioli M, Vaira D (2003). Review article: diagnosis and treatment of Helicobacter: a 2002 updated review. Aliment Pharmacol Ther 17 Suppl 2: 89-97
NIRS	Baulig W, Dullenkopf A, Hasenclever P, Schmid ER, Weiss M (2008). In vitro evaluation of the CeVOX continuous central venous oxygenation monitoring system. Anaesthesia 63(4): 412-417
POCT	Benzaken AS, Sabidó M, Galban EG, Pedroza V, Vasquez F, Araújo A, Peeling RW, Mayaud P (2008). Field evaluation of the performance and testing costs of a rapid point-of-care test for syphilis in a red-light district of Manaus, Brazil. Sex Transm Infect
Enose	Bernabei M, Pennazza G, Santonico M, Corsi C, Roscioni C, Paolesse R, Di Natale C, D'Amico A (2008). A preliminary study on the possibility to diagnose urinary tract cancers by an electronic nose. Sensors Actuators B: Chemical 131: 1-4
POCT	Bienek DR, Biagini RE, Charlton DG, Smith JP, Sammons DL, Robertson SA (2008). Rapid point-of-care test to detect broad ranges of protective antigen-specific immunoglobulin G concentrations in recipients of the U.S.-licensed anthrax vaccine. Clin Vaccine Immunol 15(4): 644-649
NIRS	Bodén I, Nilsson D, Naredi P, Lindholm-Sethson B (2008). Characterization of healthy skin using near infrared spectroscopy and skin impedance. Med Biol Eng Comput [Epub ahead of print]
Enose	Boilot P, Hines EL, Gardner JW, Pitt R, John S, Mitchell J, Morgan DW (2002). Classification of bacteria responsible for ENT and eye infections using the cyranose system. IEEE Sens J 2: 247-253
POCT	Bonham PA (2006). Get the LEAD out: noninvasive assessment for lower extremity arterial disease using ankle brachial index and toe brachial index measurements. J Wound Ostomy Continence Nurs 33(1): 30-41
Dog	Brooks SE, Oi FM, Koehler PG (2003). Ability of canine termite detectors to locate live termites and discriminate them from non-termite material. Journal of Economic Entomology 96: 1259-1266
Enose	Bruno E, Alessandrini M, Ottaviani F, Delfini A, Di Pierro D, Camillo A, De Lorenzo A (2008). Can the electronic nose diagnose chronic rhinosinusitis? A new experimental study. Eur Arch Otorhinolaryngol 265: 425-428
POCT	Bührer-Sékula S, Visschedijk J, Grossi MA, Dhakal KP, Namadi AU, Klatser PR, Oskam L (2007). The ML flow test as a point of care test for leprosy control programmes: potential effects on classification of leprosy patients. Lepr Rev 78(1): 70-79
POCT	Burbelo PD, Ramanathan R, Klion AD, Iadarola MJ, Nutman TB (2008). Rapid, Novel, Specific, High-throughput Diagnostic for Loa loa Infection. J Clin Microbiol
Dog	Cablk ME, Heaton JS (2006). Accuracy and reliability of dogs in surveying for desert tortoise (Gopherus agassizii). Ecol Appl 16(5): 1926-1935
NIRS	Cai Z, Zhang J, Zhang J, Zhao F, Yu G, Li Y, Ding H (2008). Evaluation of near infrared spectroscopy in monitoring postoperative regional tissue oxygen saturation for fibular flaps. Journal of Plastic, Reconstructive & Aesthetic Surgery 61: 289-296
POCT	Cardenas VM, Dominguez DC, Puentes FA, Aragaki CC, Goodman KJ, Graham DY, Fukuda Y (2008). Evaluation of a novel stool native catalase antigen test for Helicobacter pylori infection in asymptomatic North American children. J Pediatr Gastroenterol Nutr 46(4): 399-402
New tech	Chan CP, Cheung YC, Renneberg R, Seydack M (2008). New trends in immunoassays. Adv Biochem Eng

	Biotechnol 109: 123-154
POCT	Chan CP, Wan TS, Watkins KL, Pelsers MM, Van der Voort D, Tang FP, Lam KH, Mill J, Yuan Y, Lehmann M, Hempel A, Sanderson JE, Glatz JF, Renneberg R (2005). Rapid analysis of fatty acid-binding proteins with immunosensors and immunotests for early monitoring of tissue injury. Biosens Bioelectron. 20(12): 2566-2580
Enose	Chandiok S, Crawley BA, Oppenheim BA, Chadwick PR, Higgins S, Persaud KC (1997). Screening for bacterial vaginosis: a novel application of artificial nose technology. J Clin Pathol 50: 790-791
Enose	Chaudry AN, Travers PJ, Yuenger J, Colletta L, Evans P, Zenilman JM, Tummon A (2004). Analysis of vaginal acetic acid in patients undergoing treatment for bacterial vaginosis. J Clin Microbiol 42: 5170-5175
Enose	Chen X, Xu F, Wang Y, Pan Y, Lu D, Wang P, Ying K, Chen E, Zhang W (2007). A study of the volatile organic compounds exhaled by lung cancer cells in vitro for breath diagnosis. Cancer 110: 835-844
POCT	Cheng X, Irimia D, Dixon M, Sekine K, Demirci U, Zamir L, Tompkins RG, Rodriguez W, Toner M (2007). A microfluidic device for practical label-free CD4(+) T cell counting of HIV-infected subjects. Lab Chip 7(2): 170-178
Saliva	Christodoulides N, Mohanty S, Miller CS, Langub MC, Floriano PN, Dharshan P, Ali MF, Bernard B, Romanovicz D, Anslyn E, Fox PC, McDevitt JT. Application of microchip assay system for the measurement of C-reactive protein in human saliva. Lab Chip. 2005 Mar;5(3):261-9
Dog	Church J, Williams H (2001). Another sniffer dog for the clinic? Lancet 358: 930
NIRS	Cohn SM (2007). Near-infrared spectroscopy: potential clinical benefits in surgery. J Am Coll Surg 205(2): 322-332
NIRS	Corti P, Dreassi E, Leonardi S (1993). Near infrared reflectance analysis: features and applications in pharmaceutical and biomedical analysis. Farmaco 48(1): 3-20
NIRS	Creteur J (2008). Muscle StO2 in critically ill patients. Curr Opin Crit Care 14(3): 361-366
POCT	Curtis KA, Rudolph DL, Owen SM (2008). Rapid detection of HIV-1 by reverse-transcription, loop-mediated isothermal amplification (RT-LAMP). J Virol Methods
Enose	D'Amico A, Bono R, Pennazza G, Santonico M, Mantini G, Bernabei M, Zarlenga M, Roscioni C, Martinelli E, Paolesse R, Di Natale C (2008b). Identification of melanoma with a gas sensor array. Skin Res Technol 14: 226-236
Enose	D'Amico A, Di Natale C, Paolesse R, Macagnano A, Martinelli E, Pennazza G, Santonico M, Bernabei M, Roscioni C, Galluccio G, Bono R, Agrò EF, Rullo S (2008a). Olfactory systems for medical applications. Sensors Actuators B: Chemical 130: 458-465
Enose	Dalton P, Gelperin A, Preti G (2004). Volatile metabolic monitoring of glycemic status in diabetes using electronic olfaction. Diabetes Technol Ther 6: 534-544
POCT	De Georgia MA, Deogaonkar A (2005). Multimodal monitoring in the neurological intensive care unit. Neurologist 11(1): 45-54
NIRS	DeGabriel JL, Wallis IR, Moore BD, Foley WJ (2008). A simple, integrative assay to quantify nutritional quality of browses for herbivores. Oecologia 156: 107-116
POCT	Desachy A, Vuagnat AC, Ghazali AD, Baudin OT, Longuet OH, Calvat SN, Gissot V (2008). Accuracy of bedside glucometry in critically ill patients: influence of clinical characteristics and perfusion index. Mayo Clin Proc 83(4): 400-405
POCT	Dewsnap CH, Mcowan A (2006). A review of HIV point-of-care tests. Int J STD AIDS. 17(6): 357-359
POCT	Dey P (2004). Urinary markers of bladder carcinoma. Clin Chim Acta 340(1-2): 57-65
Enose	Di Natale C, Macagnano A, Martinelli E, Paolesse R, D'Arcangelo G, Roscioni C, Finazzi-Agro A, D'Amico A (2003). Lung cancer identification by the analysis of breath by means of an array of non-selective gas sensors. Biosens Bioelectron 18: 1209-1218
Enose	Di Natale C, Mantini A, Macagnano A, Antuzzi D, Paolesse R, D'Amico A (1999). Electronic nose analysis of urine samples containing blood. Phyisiological Measurements 20: 377-384
POCT	Diederen BM, Peeters MF (2007). Evaluation of the SAS Legionella Test, a new immunochromatographic assay for the detection of Legionella pneumophila serogroup 1 antigen in urine. Clin Microbiol Infect 13(1): 86-88
POCT	Dinnes J, Deeks J, Kunst H, Gibson A, Cummins E, Waugh N, Drobniewski F, Lalvani A (2007). A systematic review of rapid diagnostic tests for the detection of tuberculosis infection. Health Technol Assess 11(3)
POCT	Dobson MG, Galvin P, Barton DE (2007). Emerging technologies for point-of-care genetic testing. Expert Rev Mol Diagn 7(4): 359-370
POCT	Doungchawee G, Kositanont U, Niwetpathomwat A, Inwisai T, Sagarasaeranee P, Haake DA (2008). Early diagnosis of leptospirosis by immunoglobulin M immunoblot testing. Clin Vaccine Immunol 15(3): 492-498
Enose	Dragonieri S, Schot R, Mertens BJ, Le Cessie S, Gauw SA, Spanevello A, Resta O, Willard NP, Vink TJ, Rabe KF, Bel EH, Sterk PJ (2007). An electronic nose in the discrimination of patients with asthma and controls. J Allergy Clin Immunol 120: 856-862
New tech	Dufva M, Christensen CB (2005). Diagnostic and analytical applications of protein microarrays. Expert

	Rev Proteomics 2(1): 41-48
POCT	Dufva M, Christensen CB (2005). Diagnostic and analytical applications of protein microarrays. Expert Rev Proteomics 2(1): 41-48
Enose	Dutta R, Dutta R (2006). Intelligent Bayes Classifier (IBC) for ENT infection classification in hospital environment. Biomed Eng Online 5: 65
Enose	Dutta R, Gardner JW, Hines EL (2004). ENT bacteria classification using a neural network based Cyranose 320 electronic nose. Sensors 1: 324-325
Enose	Dutta R, Hines EL, Gardner JW, Boilot P (2002). Bacteria classification using Cyranose 320 electronic nose. Biomed Eng Online 1: 4
Dog	Eastwood B (1990). Beagles bag contraband foodstuffs. Dog World. 75: 144-149
NIRS	Eckman DD, Shenk JS, Wangsness PJ, Westerhaus MO (1983). Prediction of sheep responses by near infrared reflectance spectroscopy. J Dairy Sci 66(9): 1983-1987
POCT	Edwards RK, Novak-Weekley SM, Koty PP, Davis T, Leeds LJ, Jordan JA (2008). Rapid group B streptococci screening using a real-time polymerase chain reaction assay. Obstet Gynecol 111(6): 1335-1341
Urine para	Ehman KD, Scott ME (2001). Urinary odour preferences of MHC congeric female mice, Mus domesticus. implications for kin recognition and detection of parasitized males. Anim Behav 62: 781-789
Urine para	Ehman KD, Scott ME (2002). Female mice mate preferentially with non-parasitized males. Parasitology 125: 461- 466
New tech	Ehrmeyer SS, Laessig RH (2007). Point-of-care testing, medical error, and patient safety: a 2007 assessment. Clin Chem Lab Med 45(6): 766-773
POCT	Eichner SF, Timpe EM (2004). Urinary-based ovulation and pregnancy: point-of-care testing. Ann Pharmacother 38(2): 325-331
Enose	Elliott-Martin RJ, Mottram TT, Gardner JW, Hobbs PJ, Bartlett PN (1997). Preliminary Investigation of Breath Sampling as a Monitor of Health in Dairy Cattle. Journal of Agricultural Engineering Research 67: 267-275
Dog	Engeman RM, Rodriquez DV, Linnell MA, Pitzler ME (1998a). A review of the case histories of the brown tree snakes (Boiga irregularis) located by detector dogs on Guam. International Biodeterioration and Biodegradation 42: 161–165
Dog	Engeman RM, Vice DS, Rodriquez DV, Gruver KS, Santos WS, Pitzler ME (1998b). Effectiveness of the detector dogs used for deterring the dispersal of brown tree snakes. Pacific Conservation Biology 4: 256–260
POCT	Fancher TL, White RH (2004). Patient self-management of oral anticoagulation. Curr Hematol Rep 3(5): 368-374
NIRS	Farouk A, Karimi M, Henderson M, Ostrowsky J, Siwik E, Hennein H (2008). Cerebral regional oxygenation during aortic coarctation repair in pediatric population. Eur J Cardiothorac Surg [Epub ahead of print]
Enose	Fend R, Bessant C, Williams AJ, Woodman AC (2004). Monitoring haemodialysis using electronic nose and chemometrics. Biosens Bioelectron 19: 1581-1590
Enose	Fend R, Geddes R, Lesellier S, Vordermeier HM, Corner LA, Gormley E, Costello E, Hewinson RG, Marlin DJ, Woodman AC, Chambers MA (2005). Use of an electronic nose to diagnose Mycobacterium bovis infection in badgers and cattle. J Clin Microbiol 43: 1745-1751
Enose	Fend R, Kolk AH, Bessant C, Buijtels P, Klatser PR, Woodman AC (2006). Prospects for clinical application of electronic-nose technology to early detection of Mycobacterium tuberculosis in culture and sputum. J Clin Microbiol 44: 2039-2045
NIRS	Feng YC, Hu CQ (2006). Construction of universal quantitative models for determination of roxithromycin and erythromycin ethylsuccinate in tablets from different manufacturers using near infrared reflectance spectroscopy. J Pharm Biomed Anal 41(2): 373-384
Dog	Fenton V (1992). The use of dogs in search, rescue and recovery. Journal of Wilderness Medicine 3: 292–300
POCT	Ferasin L, Nguyenba TP (2008). Comparison of canine capillary and jugular venous blood lactate concentrations determined by use of an enzymatic-amperometric bedside system. Am J Vet Res 69(2): 208-211
NIRS	Fernández-Ahumada E, Garrido-Varo A, Guerrero-Ginel JE (2008). Feasibility of diode-array instruments to carry near-infrared spectroscopy from laboratory to feed process control. J Agric Food Chem 56(9): 3185-3192
NIRS	Foster JG, Clapham WM, Fedders JM (2006). Quantification of fatty acids in forages by near-infrared reflectance spectroscopy. J Agric Food Chem 54(9): 3186-3192
Dog	Furton KG, Hong YC, Hsu YL, Luo T, Rose S, Walton J (2002). Identification of odor signature chemicals in cocaine using solid-phase microextraction-gas chromatography and detector-dog response to isolated compounds spiked on US paper currency. J Chromatogr Sci 40(3): 147-155

Dog	Furton KG, Myers LJ (2001). The scientific foundation and efficacy of the use of canines as chemical detectors for explosives. Talanta 54: 487-500
POCT	Gaál T, Halmay D, Kocsis R, Abonyi-Tóth Z (2007). Evaluation of the effect of ketoprofen and carprofen on platelet function in dogs studied by PFA-100 point-of-care analyser. Acta Vet Hung 55(3): 287-294
Enose	Gardner JW, Craven M, Dow C, Hines EL (1998). The prediction of bacteria type and culture growth phase by an electronic nose with a multi-layer perceptron network. Measurement Sci Technol **9:** 120–127
Enose	Gardner JW, Shin HW, Hines EL (2000). An electronic nose system to diagnose illness. Sensors Actuators B: Chemical 70: 19-24
POCT	Garner BC, Wiedmeyer CE (2007). Comparison of a semiquantitative point-of-care assay for the detection of canine microalbuminuria with routine semiquantitative methods for proteinuria. Vet Clin Pathol 36(3): 240-244
POCT	Gavino M, Wang E (2007). A comparison of a new rapid real-time polymerase chain reaction system to traditional culture in determining group B streptococcus colonization. Am J Obstet Gynecol 197(4): 388.e1-4.
Dog	Gazit I, Terkel J (2003). Explosives detection by sniffer dogs following strenuous physical activity. Appl Anim Behav Sci 81: 149-161
Enose	Gendron KB, Hockstein NG, Thaler ER, Vachani A, Hanson CW (2007). In vitro discrimination of tumor cell lines with an electronic nose. Otolaryngol Head Neck Surg 137: 269-273
POCT	George S, Braithwaite RA (2002). Use of on-site testing for drugs of abuse. Clin Chem 48(10): 1639-1646
POCT	Gessler F, Pagel-Wieder S, Avondet MA, Böhnel H (2007). Evaluation of lateral flow assays for the detection of botulinum neurotoxin type A and their application in laboratory diagnosis of botulism. Diagn Microbiol Infect Dis 57(3): 243-249
Dog	Gialamas DM (1996). Enhancement of fire scene investigations using accelerant detection canines. Sci Justice 36(1): 51-54
POCT	Giannitsis E, Baum H, Bertsch T, Juchum M, Müller-Bardorff M, Jørgensen B, Böhmer A, Rebmann M, Schäffler J, Schwab M, Zerback R (2008). Multicentre evaluation of a new point-of-care test for the determination of CK-MB in whole blood. Clin Chem Lab Med
Enose	Gibson TD, Prosser O, Hulbert J, Marshall RW, Li Z (1997). Detection and simultaneous identification of microorganisms from headspace samples using and electronic nose. Sensors Actuators B **44:** 413–422
Enose	Gill M, Graff GR, Adler AJ, Dweik RA (2006). Validation study of fractional exhaled nitric oxide measurements using a handheld monitoring device. J Asthma 43: 731-734
NIRS	Glasser T, Landau S, Ungar ED, Perevolotsky A, Dvash L, Muklada H, Kababya D, Walker JW (2008). A fecal NIRS-aided methodology to determine goat dietary composition in a Mediterranean shrubland. J Anim Sci [Epub ahead of print]
Lectins	Gemeiner, P., D. Mislovicová, et al. (2009). "Lectinomics: II. A highway to biomedical/clinical diagnostics." Biotechnology Advances 27(1): 1-15.
POCT	Goggs R, Serrano S, Szladovits B, Keir I, Ong R, Hughes D (2008). Clinical investigation of a point-of-care blood ammonia analyzer. Vet Clin Pathol 37(2): 198-206
POCT	Goldkamp CE, Levy JK, Edinboro CH, Lachtara JL (2008). Seroprevalences of feline leukemia virus and feline immunodeficiency virus in cats with abscesses or bite wounds and rate of veterinarian compliance with current guidelines for retrovirus testing. J Am Vet Med Assoc 232(8): 1152-1158
POCT	Goldstein RE, Cordner AP, Sandler JL, Bellohusen BA, Erb HN (2007). Microalbuminuria and comparison of serologic testing for exposure to Borrelia burgdorferi in nonclinical Labrador and Golden Retrievers. J Vet Diagn Invest 19(3): 294-297
Dog	Gordon RT, Schatz CB, Myers LJ, Kosty M, Gonczy C, Kroener J, Tran M, Kurtzhals P, Heath S, Koziol JA, Arthur N, Gabriel M, Hemping J, Hemping G, Nesbitt S, Tucker-Clark L, Zaayer J (2008). The use of canines in the detection of human cancers. J Altern Complement Med 14(1): 61-67
NIRS	Gowen AA, O'Donnell CP, Cullen PJ, Bell SE (2008). Recent applications of Chemical Imaging to pharmaceutical process monitoring and quality control. Eur J Pharm Biopharm 69(1): 10-22
Enose	Greenwood JE, Crawley BA, Clark SL, Chadwick PR, Ellison DA, Oppenheim BA, McCollum CN (1997). Monitoring wound healing by odour. J Wound Care 6: 219-221
NIRS	Guarracino F (2008). Cerebral monitoring during cardiovascular surgery. Curr Opin Anaesthesiol 21(1): 50-54
Enose	Guernion N, Ratcliffe NM, Spencer-Phillips PT, Howe RA (2001). Identifying bacteria in human urine: current practice and the potential for rapid, near-patient diagnosis by sensing volatile organic compounds. Clin Chem Lab Med 39: 893-906
POCT	Gupta A, Wrench IJ, Feast MJ, Alderson JD (2008). Use of the HemoCue near patient testing device to measure the concentration of haemoglobin in suction fluid at elective caesarean section. Anaesthesia 63(5): 531-534
Saliva	Gutiérrez AM, Martínez-Subiela S, Eckersall PD, Cerón JJ. C-reactive protein quantification in porcine saliva: A minimally invasive test for pig health monitoring. Vet J. 2008 May 12. [Epub ahead of print]
NIRS	Hamaoka T, McCully KK, Quaresima V, Yamamoto K, Chance B (2007). Near-infrared

	spectroscopy/imaging for monitoring muscle oxygenation and oxidative metabolism in healthy and diseased humans. J Biomed Opt 12(6): 062105
Enose	Hanson CW, Steinberger HA (1997). The use of a novel electronic nose to diagnose the presence of intrapulmonary infection. Anesthesiology 87: A269
Enose	Hanson CW, Thaler ER (2005). Electronic nose prediction of a clinical pneumonia score: biosensors and microbes. Anesthesiology 102:63-8
POCT	Harle CC (2007). Point-of-care platelet function testing. Semin Cardiothorac Vasc Anesth 11(4): 247-251
Enose	Harper WJ (2001). The strengths and weaknesses of the electronic nose. Adv Exp Med Biol 488: 59-71
Dog	Hawk HW, Conley HH, Kiddy CA (1984). Estrus-related odors in milk detected by trained dogs. J Dairy Sci 67(2): 392-397
Enose	Hay P, Tummon A, Ogunfile M, Adebiyi A, Adefowora A (2003). Evaluation of a novel diagnostic test for bacterial vaginosis: 'the electronic nose.' Int J STD AIDS 4: 114-118
POCT	Healy DA, Hayes CJ, Leonard P, McKenna L, O'Kennedy R (2007). Biosensor developments: application to prostate-specific antigen detection. Trends Biotechnol 25(3): 125-131
NIRS	Hebden JC, Austin T (2007). Optical tomography of the neonatal brain. Eur Radiol 17(11): 2926-2933
NIRS	Heise HM, Bittner A, Marbach R (2000). Near-infrared reflectance spectroscopy for noninvasive monitoring of metabolites. Clin Chem Lab Med 38(2): 137-145
NIRS	Hilden LR, Pommier CJ, Badawy SI, Friedman EM (2008). NIR chemical imaging to guide/support BMS-561389 tablet formulation development. Int J Pharm 353(1-2): 283-290
POCT	Hillingsø JG, Svendsen LB, Nielsen MB (2008). Focused bedside ultrasonography by clinicians: experiences with a basic introductory course. Scand J Gastroenterol 43(2): 229-233
Enose	Hockstein NG, Thaler ER, Lin Y, Lee DD, Hanson CW (2005). Correlation of pneumonia score with electronic nose signature: A prospective study. Ann Otol Rhinol Laryngol 114: 504-508
Enose	Hockstein NG, Thaler ER, Torigian D, Miller WT Jr, Deffenderfer O, Hanson CW (2004). Diagnosis of pneumonia with an electronic nose: correlation of vapor signature with chest computed tomography scan findings. Laryngoscope 114: 1701-1705
New tech	Holland CA, Kiechle FL (2005). Point-of-care molecular diagnostic systems--past, present and future. Curr Opin Microbiol. Oct;8(5): 504-509
POCT	Holland CA, Kiechle FL (2005). Point-of-care molecular diagnostic systems--past, present and future. Curr Opin Microbiol 8(5): 504-509
Dog	Horvath G, Järverud GA, Järverud S, Horváth I (2008). Human ovarian carcinomas detected by specific odor. Integr Cancer Ther 7(2): 76-80
New tech	Hoşafçi G, Klein O, Oremek G, Mäntele W (2007). Clinical chemistry without reagents? An infrared spectroscopic technique for determination of clinically relevant constituents of body fluids. Anal Bioanal Chem 387(5): 1815-1822
POCT	Hoshi K, Takakura H, Mitani Y, Tatsumi K, Momiyama N, Ichikawa Y, Togo S, Miyagi T, Kawai Y, Kogo Y, Kikuchi T, Kato C, Arakawa T, Uno S, Cizdziel PE, Lezhava A, Ogawa N, Hayashizaki Y, Shimada H (2007). Rapid detection of epidermal growth factor receptor mutations in lung cancer by the SMart-Amplification Process. Clin Cancer Res 13(17): 4974-4983
NIRS	Hoshi Y (2007). Functional near-infrared spectroscopy: current status and future prospects. J Biomed Opt 12(6): 062106
POCT	Humair JP, Revaz SA, Bovier P, Stalder H (2006). Management of acute pharyngitis in adults: reliability of rapid streptococcal tests and clinical findings. Arch Intern Med 166(6): 640-644
POCT	Ilan Y (2007). Review article: the assessment of liver function using breath tests. Aliment Pharmacol Ther 26(10):1293-302
Etongue	Ipatov A, Abramova N, Bratov A, Domínguez C (2008). Sensors Actuators B Chemical 08 Integrated multisensor chip with sequential injection technique as a base for "electronic tongue" devices. Sensors and Actuators B: Chemical 131: 48-52
New tech	Jain KK (2007). Applications of nanobiotechnology in clinical diagnostics. Clin Chem 53(11): 2002-2009
POCT	Jang T, Uzbielo A, Sineff S, Naunheim R, Scott MG, Lewis LM (2007). Point-of-care urine trypsinogen testing for the diagnosis of pancreatitis. Acad Emerg Med 14(1):29-34
POCT	Jeyaratnam D, Whitty CJ, Phillips K, Liu D, Orezzi C, Ajoku U, French GL (2008). Impact of rapid screening tests on acquisition of meticillin resistant Staphylococcus aureus: cluster randomised crossover trial. BMJ 336(7650): 927-930
POCT	Johnston MS, Rosenthal KL, Shofer FS (2007). Assessment of a point-of-care biochemical analyzer and comparison with a commercial laboratory for the measurement of total protein and albumin concentrations in psittacines. Am J Vet Res 68(12): 1348-1353
POCT	Kang CC, Chang CC, Chang TC, Liao LJ, Lou PJ, Xie W, Yeung ES (2007). A handheld device for potential point-of-care screening of cancer. Analyst 132(8): 745-749
POCT	Katz LM, Nauriyal V, Nagaraj S, Finch A, Pearlstein K, Szymanowski A, Sproule C, Rich PB, Guenther BD, Pearlstein RD (2008). Infrared imaging of trauma patients for detection of acute compartment syndrome of the leg. Crit Care Med 36(6): 1756-1761

Urine para	Kavaliers M, Choleris E, Agmo A, Braun WJ, Colwell DD, Muglia LJ, Ogawa S, Pfaff DW (2006). Inadvertent social information and the avoidance of parasitized male mice. a role for oxytocin. Proc Natl Acad Sci USA 103. 4293-4298
Urine para	Kavaliers M, Choleris E, Agmo A, Pfaff DW (2004). Olfactory-mediated parasite recognition and avoidance. linking genes to behavior. Horm Behav 46. 272-283
Urine para	Kavaliers M, Choleris E, Pfaff DW (2005). Genes, odours and the recognition of parasitized individuals by rodents. Trends Parasitol 21. 423-429
Urine para	Kavaliers M, Choleris E, Pfaff DW (2005). Recognition and avoidance of the odors of parasitized conspecifics and predators. differential genomic correlates. Neurosci Biobehav Rev 29. 1347-1359
Urine para	Kavaliers M, Colwell DD (1993). Aversive responses of female mice to the odors of parasitized males. neuromodulatory mechanisms and implications for mate choice. Ethology 95: 206-212
Urine para	Kavaliers M, Colwell DD (1995a). Odours of parasitized males induce aversive response in female mice. Anim Behav 50: 1161- 1169
Urine para	Kavaliers M, Colwell DD (1995b). Discrimination by female mice between the odours of parasitized and non-parasitized males. Proc Biol Sci 261(1360). 31-35
Urine para	Kavaliers M, Colwell DD, Braun WJ, Choleris E (2003a). Brief exposure to the odour of a parasitized male alters the subsequent mate odour response of female mice. Anim Behav 65: 59- 68
Urine para	Kavaliers M, Colwell DD, Choleris E (1998). Analgesic responses of male mice exposed to the odors of parasitized females. effects of male sexual experience and infection status. Behav Neurosci 112. 1001-1011
Urine para	Kavaliers M, Colwell DD, Choleris E (1998). Parasitized female mice display reduced aversive responses to the odours of infected males. Proc Biol Sci 265(1401). 1111-1118
Urine para	Kavaliers M, Colwell DD, Ossenkopp KP, Perrot-Sinal TS (1997). Altered responses to female odors in parasitized male mice. neuromodulatory mechanisms and relations to female choice. Behav Ecol Sociobiol 40: 373- 384
Urine para	Kavaliers M, Fudge MA, Colwell DD, Choleris E (2003b). Aversive and avoidance responses of female mice to the odors of males infected with an ectoparasite and the effects of prior familiarity. Behav Ecol Sociobiol 54: 423- 430
POCT	Kayaba H (2002). Rapid detection tests for viruses available in pediatric clinics. Rinsho Byori 50(11): 1047-1054
Dog	Kiddy CA, Mitchell DS (1981). Estrus-related odors in cows: time of occurrence. J Dairy Sci 64(2): 267-271
Dog	Kiddy CA, Mitchell DS, Bolt DJ, Hawk HW (1978). Detection of estrus-related odors in cows by trained dogs. Biol Reprod 19(2): 389-395
Dog	Kiddy CA, Mitchell DS, Hawk HW (1984). Estrus-related odors in body fluids of dairy cows. J Dairy Sci 67(2): 388-391
New tech	Kirby R, Cho EJ, Gehrke B, Bayer T, Park YS, Neikirk DP, McDevitt JT, Ellington AD (2004). Aptamer-based sensor arrays for the detection and quantitation of proteins. Anal Chem 76(14): 4066-4075
Urine para	Klein SL, Gamble HR, Nelson RJ (1999). Trichinella spiralis alters female odor preferences, but not mate preferences, in voles. Behav Ecol Sociobiol 45: 323- 329
Enose	Kodogiannis V, Wadge E (2005). The use of gas-sensor arrays to diagnose urinary tract infections. Int J Neural Syst 15: 363-376
Dog	Komar D (1999). The use of cadaver dogs in locating scattered, scavenged human remains: preliminary field test results. Journal of Forensic Sciences 44: 405–408
NIRS	Kondepati VR, Heise HM, Backhaus J (2008). Recent applications of near-infrared spectroscopy in cancer diagnosis and therapy. Anal Bioanal Chem 390(1): 125-139
POCT	Kost GJ, Tran NK (2005). Point-of-Care Testing and Cardiac Biomarkers: The Standard of Care and Vision for Chest Pain Centers. Cardiol Clin 23(4): 467-490
NIRS	Kudo M, Watt RA, Moffat AC (2000). Rapid identification of Digitalis purpurea using near-infrared reflectance spectroscopy. J Pharm Pharmacol 52(10): 1271-1277
Dog	Kurz ME, Billard M, Rettig M, Augustiniak J, Lange J, Larsen M, Warrick R, Mohns T, Bora R, Broadus K (1994). Evaluation of canines for accelerant detection at fire scenes. J Forensic Sci 39(6): 1528-1536
POCT	Laderman EI, Whitworth E, Dumaual E, Jones M, Hudak A, Hogrefe W, Carney J, Groen J (2008). Rapid, sensitive, and specific lateral-flow immunochromatographic point-of-care device for detection of herpes simplex virus type 2-specific immunoglobulin G antibodies in serum and whole blood. Clin Vaccine Immunol 15(1): 159-163
Enose	Lai SY, Deffenderfer OF, Hanson W, Phillips MP, Thaler ER (2002). Identification of upper respiratory bacterial pathogens with the electronic nose. Laryngoscope 112: 975-979
NIRS	Landau S, Friedman S, Devash L, Mabjeesh SJ (2002). Polyethylene glycol, determined by near-infrared reflectance spectroscopy, as a marker of fecal output in goats. J Agric Food Chem 50(6): 1374-1378
NIRS	Landau S, Glasser T, Dvash L (2006). Monitoring nutrition in small ruminants with the aid of near infrared

	reflectance spectroscopy (NIRS) technology: A review. Small Ruminant Research 61: 1-11
Enose	Lane AJ, Wathes DC (1998). An electronic nose to detect changes in perineal odors associated with estrus in the cow. J Dairy Sci 81: 2145-2150
NIRS	Leff DR, Leong JJ, Warren O, Athanasiou T, Yang GZ, Darzi A (2008). Near-infrared spectroscopy: potential clinical benefits in surgery. J Am Coll Surg 206(4): 761-762
POCT	Leo M, Haque R, Kabir M, Roy S, Lahlou RM, Mondal D, Tannich E, Petri WA Jr (2006). Evaluation of Entamoeba histolytica antigen and antibody point-of-care tests for the rapid diagnosis of amebiasis. J Clin Microbiol 44(12): 4569-4571
POCT	Lewandrowski K, Flood J, Finn C, Tannous B, Farris AB, Benzer TI, Lee-Lewandrowski E (2008). Implementation of point-of-care rapid urine testing for drugs of abuse in the emergency department of an academic medical center: impact on test utilization and ED length of stay. Am J Clin Pathol 129(5): 796-801
NIRS	Li H, Tolleson DR, Stuth J, Bai K, Mo F, Kronberg S (2007). Faecal near infrared reflectance spectroscopy to predict diet quality for sheep. Small Ruminant Research 68: 263-268
Enose	Lin YJ, Guo H, Chang Y (2001). Application of the electronic nose for uraemia diagnosis. Sens Actuators B 76: 177-180
POCT	Lin YY, Wang J, Liu G, Wu H, Wai CM, Lin Y (2008). A nanoparticle label/immunochromatographic electrochemical biosensor for rapid and sensitive detection of prostate-specific antigen. Biosens Bioelectron 23(11): 1659-1665
Dog	Lorenzo N, Wan TL, Harper RJ, Hsu YL, Cho M, Rose S, Furton KG (2003). Laboratory and field experiments used to identify Canis lupus var. familiaris active odor signature chemicals from drugs, explosives, and humans. Analytical and Bioanalytical Chemistry 376: 1212-1224
Enose	Lykos P, Patel PH, Morong C, Joseph A (2001). Rapid detection of bacteria from blood culture by an electronic nose. J Microbiol. 39: 213-218
NIRS	Lyons RK, Stuth JW, Huston JE, Angerer JP (1993). Predictions of the nutrient composition of the diets of supplemented versus unsupplemented grazing beef cows based on near-infrared reflectance spectroscopy of feces. J Anim Sci 71(2): 530-538
Enose	Machado RF, Laskowski D, Deffenderfer O, Burch T, Zheng S, Mazzone PJ, Mekhail T, Jennings C, Stoller JK, Pyle J, Duncan J, Dweik RA, Erzurum SC (2005). Detection of lung cancer by sensor array analyses of exhaled breath. Am J Respir Crit Care Med 171: 1286-1291
POCT	Mahilum-Tapay L, Laitila V, Wawrzyniak JJ, Lee HH, Alexander S, Ison C, Swain A, Barber P, Ushiro-Lumb I, Goh BT (2007). New point of care Chlamydia Rapid Test--bridging the gap between diagnosis and treatment: performance evaluation study. BMJ 335(7631): 1190-1194
New tech	Mairal T, Özalp C, Sánchez PL, Mir M, Katakis I, O'Sullivan CK (2008). Aptamers: molecular tools for analytical applications. Anal Bioanal Chem 390: 989-1007
New tech	Mansfield CD, Man A, Shaw RA (2006). Integration of microfluidics with biomedical infrared spectroscopy for analytical and diagnostic metabolic profiling. IEE Proc Nanobiotechnol 153(4):74-80.
Enose	Mantini A, Di Natale C, Macagnano A, Paolesse R, Finazzi-Agrò A, D'Amico A (2000). Biomedical application of an electronic nose. Crit Rev Biomed Eng 28: 481-485
New tech	Marchand G, Broyer P, Lanet V, Delattre C, Foucault F, Menou L, Calvas B, Roller D, Ginot F, Campagnolo R, Mallard F (2008). Opto-electronic DNA chip-based integrated card for clinical diagnostics. Biomed Microdevices 10(1): 35-45
POCT	Mauk MG, Ziober BL, Chen Z, Thompson JA, Bau HH (2007). Lab-on-a-chip technologies for oral-based cancer screening and diagnostics: capabilities, issues, and prospects. Ann N Y Acad Sci 1098: 467-475
Dog	McCulloch M, Jezierski T, Broffman M, Hubbard A, Turner K, Janecki T (2006). Diagnostic accuracy of canine scent detection in early- and late-stage lung and breast cancers. Integr Cancer Ther 5: 30-39
NIRS	McVeigh ER (2006). Emerging imaging techniques. Circ Res 98(7): 879-886
POCT	Meex C, Poncin J, Chapelle JP, Cavalier E (2006). Analytical validation of the new plasma calibrated Accu-Chek Test Strips (Roche Diagnostics). Clin Chem Lab Med 44(11): 1376-1378
POCT	Melanson SE, Lewandrowski EL, Griggs DA, Flood JG (2007). Interpreting tricyclic antidepressant measurements in urine in an emergency department setting: comparison of two qualitative point-of-care urine tricyclic antidepressant drug immunoassays with quantitative serum chromatographic analysis. J Anal Toxicol 31(5): 270-275
POCT	Melbye H, Stocks N (2006). Point of care testing for C-reactive protein - a new path for Australian GPs? Aust Fam Physician 35(7): 513-517
NIRS	Mentink RL, Hoffman PC, Bauman LM (2006). Utility of near-infrared reflectance spectroscopy to predict nutrient composition and in vitro digestibility of total mixed rations. J Dairy Sci 89(6): 2320-2326
POCT	Michel CE, Solomon AW, Magbanua JP, Massae PA, Huang L, Mosha J, West SK, Nadala EC, Bailey R, Wisniewski C, Mabey DC, Lee HH (2006). Field evaluation of a rapid point-of-care assay for targeting antibiotic treatment for trachoma control: a comparative study. Lancet 367(9522): 1585-1590
POCT	Miyazaki M (2002). The relevance of a simultaneous measurement of WBC and CRP as a POCT(point of care testing) of the inflammatory markers running title: the POCT(point of care testing) of WBC and CRP.

	Rinsho Byori 50(11): 1029-1034
Enose	Moens M, Smet A, Naudts B, Verhoeven J, Ieven M, Jorens P, Geise HJ, Blockhuys F (2006). Fast identification of ten clinically important micro-organisms using an electronic nose. Lett Appl Microbiol 42: 121-126
NIRS	Moes JJ, Ruijken MM, Gout E, Frijlink HW, Ugwoke MI (2008). Application of process analytical technology in tablet process development using NIR spectroscopy: Blend uniformity, content uniformity and coating thickness measurements. Int J Pharm 357(1-2): 108-118
Enose	Mohamed EI, Bruno E, Linder R, Alessandrini M, Di Girolamo A, Poppl SJ, Puija A, De Lorenzo A (2003). A novel method for diagnosing chronic rhinosinusitis based on an electronic nose. An Otorrinolaringol Ibero Am 30: 447–457
Enose	Mohamed EI, Linder R, Perriello G, Di Daniele N, Pöppl SJ, De Lorenzo A (2002). Predicting Type 2 diabetes using an electronic nose-based artificial neural network analysis. Diabetes Nutr Metab 15: 215-221
POCT	Monteny M, ten Brinke MH, van Brakel J, de Rijke YB, Berger MY (2006). Point-of-care C-reactive protein testing in febrile children in general practice. Clin Chem Lab Med 44(12): 1428-1432
Urine para	Morales J, Larralde C, Artega M, Govezensky T, Romano MC (1996). Inhibition of sexual behavior in male mice infected with Taenia crassiceps cysticerci. J Parasitol 82: 689- 693
NIRS	Morisseau KM, Rhodes CT (1997). Near-infrared spectroscopy as a nondestructive alternative to conventional tablet hardness testing. Pharm Res 14(1): 108-111
POCT	Morris AH, Orme J Jr, Truwit JD, Steingrub J, Grissom C, Lee KH, Li GL, Thompson BT, Brower R, Tidswell M, Bernard GR, Sorenson D, Sward K, Zheng H, Schoenfeld D, Warner H (2008). A replicable method for blood glucose control in critically Ill patients. Crit Care Med 36(6): 1787-1795
Etongue	Mottram T, Rudnitskaya A, Legin A, Fitzpatrick JL, Eckersall PD (2007). Evaluation of a novel chemical sensor system to detect clinical mastitis in bovine milk. Biosensors and Bioelectronics 22: 2689-2693
POCT	Murray ET, Fitzmaurice DA, McCahon D (2004). Point of care testing for INR monitoring: where are we now? Br J Haematol 127(4): 373-378
POCT	Myers GJ, Browne J (2007). Point of care hematocrit and hemoglobin in cardiac surgery: a review. Perfusion 22(3): 179-183
POCT	Nascimento E, Silva T, Oliva A (2007). Identification, characterization and manipulation of Babesia-bovis-infected red blood cells using microfluidics technology. Parassitologia 49 Suppl 1: 45-52
NIRS	Neumeister V, Henker J, Kaltenborn G, Sprössig C, Jaross W (1997). Simultaneous determination of fecal fat, nitrogen, and water by near-infrared reflectance spectroscopy. J Pediatr Gastroenterol Nutr 25(4): 388-393
POCT	Nguyen-Khac E, Gournay N, Tiry C, Thevenot T, Skaf CE, Leroy MH (2006). Portable hemoglobinometer for bedside monitoring of capillary blood hemoglobin in patients with acute gastrointestinal hemorrhage] Presse Med 35(7-8): 1131-1137
Dog	Oesterhelweg L, Kröber S, Rottmann K, Willhöft J, Braun C, Thies N, Püschel K, Silkenath J, Gehl A (2008). Cadaver dogs--a study on detection of contaminated carpet squares. Forensic Sci Int 174(1): 35-39
POCT	Oh SY, Cornell B, Smith D, Higgins G, Burrell CJ, Kok TW (2008). Rapid detection of influenza A virus in clinical samples using an ion channel switch biosensor. Biosens Bioelectron 23(7): 1161-1165
NIRS	Ohlsson C, Houmøller LP, Weisbjerg MR, Lund P, Hvelplund T (2007). Effective rumen degradation of dry matter, crude protein and neutral detergent fibre in forage determined by near infrared reflectance spectroscopy. J Anim Physiol Anim Nutr (Berl) 91(11-12): 498-507
POCT	Olshen E, Shrier LA (2005). Diagnostic tests for chlamydial and gonorrheal infections. Semin Pediatr Infect Dis 16(3):192-198
Etongue	Olsson J, Winquist F, Lundström I (2006). A self polishing electronic tongue. Sensors and Actuators B: Chemical 118: 461-465
POCT	Opekun AR, Luu P, Gotschall AB, Abdalla N, Torres E, Rudd SB, Graham DY, Nurgalieva ZZ, Tsuchiya K (2006). Point-of-care Helicobacter pylori urine antibody detection in a multi-ethnic adult population in the United States. Transl Res 148(1): 13-18
POCT	Pai NP, Tulsky JP, Cohan D, Colford JM Jr, Reingold AL (2007). Rapid point-of-care HIV testing in pregnant women: a systematic review and meta-analysis. Trop Med Int Health 12(2): 162-173
Saliva	Parra MD, Tecles F, Martínez-Subiela S, Cerón JJ. C-reactive protein measurement in canine saliva. J Vet Diagn Invest. 2005 Mar;17(2):139-44
Enose	Parry AD, Chadwick PR, Simon D, Oppenheim B, McCollum CN. (1995). Leg ulcer odour detection identifies β-haemolytic streptococcal infection. J Wound Care 4: 404-406
POCT	Pastoor R, Hatta M, Abdoel TH, Smits HL (2008). Simple, rapid, and affordable point-of-care test for the serodiagnosis of typhoid fever. Diagn Microbiol Infect Dis 61(2): 129-134
NIRS	Patel AD, Luner PE, Kemper MS (2000). Quantitative analysis of polymorphs in binary and multi-component powder mixtures by near-infrared reflectance spectroscopy. Int J Pharm 206(1-2): 63-74
NIRS	Patel AD, Luner PE, Kemper MS (2001). Low-level determination of polymorph composition in physical mixtures by near-infrared reflectance spectroscopy. J Pharm Sci 90(3): 360-370

Enose	Pavlou A, Turner APF, Magan N (2002b). Recognition of anaerobic bacterial isolates in vitro using electronic nose technology. Lett Appl Microbiol 35: 366–369
Enose	Pavlou AK, Magan N, Jones JM, Brown J, Klatser P, Turner AP (2004). Detection of Mycobacterium tuberculosis (TB) in vitro and in situ using an electronic nose in combination with a neural network system. Biosens Bioelectron 20: 538-544
Enose	Pavlou AK, Magan N, McNulty C, Jones J, Sharp D, Brown J, Turner AP (2002a). Use of an electronic nose system for diagnoses of urinary tract infections. Biosens Bioelectron 17: 893-899
Enose	Pavlou AK, Magan n, Meecham Jones J, Brown J, Klatser PR, Turner APF (2004). Use of an electronic nose system for diagnoses of urinary tract infections. Biosens Bioelectron 20: 538-544
Enose	Pavlou AK, Magan N, Sharp D, Brown J, Barr H, Turner APF (2000). An intelligent rapid odour recognition model in discrimination of Helicobacter pylori and other gastroesophageal isolates in vitro. Biosen Bioelectron 15: 333–342
Enose	Pavlou AK, Turner AP (2000). Sniffing out the truth: clinical diagnosis using the electronic nose. Clin Chem Lab Med 38: 99-112
POCT	Payne CE, Southern SJ (2006). Urinary point-of-care test for smoking in the pre-operative assessment of patients undergoing elective plastic surgery. J Plast Reconstr Aesthet Surg 59(11): 1156-1161
POCT	Peeling RW, Holmes KK, Mabey D, Ronald A (2006). Rapid tests for sexually transmitted infections (STIs): the way forward. Sex Transm Infect 82 Suppl 5: v1-6
POCT	Peeling RW, Ye H (2004). Diagnostic tools for preventing and managing maternal and congenital syphilis: an overview. Bull World Health Organ 82(6): 439-446
Enose	Persaud KC (2005). Medical Applications of Odor-Sensing Devices. International Journal of Lower Extremity Wounds 4: 50-56
Enose	Persaud KC, Pisanelli AM, Evans P (2003). Medical diagnostics and health monitoring. *In* Handbook of Machine Olfaction: Electronic Nose Technology, edited by TC Pearce, SS Schiffman, HT Nagle, JW Gardner, Wiley-VCH Verlag GmbH Co, Weinheim, pp 445-460
Enose	Persaud KC, Pisanelli AM, Evans P, Travers PJ (2006). Monitoring urinary tract infections and bacterial vaginosis. Sensors Actuators B: Chemical 116: 116-120
New tech	Pesce MA, Spitalnik SL (2007). Saliva and the clinical pathology laboratory. Ann N Y Acad Sci 1098: 192-199
POCT	Peter T, Badrichani A, Wu E, Freeman R, Ncube B, Ariki F, Daily J, Shimada Y, Murtagh M (2008). Challenges in implementing CD4 testing in resource-limited settings. Cytometry B Clin Cytom 74 Suppl 1: S123-130
Enose	Phillips M, Altorki N, Austin JH, Cameron RB, Cataneo RN, Greenberg J, Kloss R, Maxfield RA, Munawar MI, Pass HI, Rashid A, Rom WN, Schmitt P (2007). Prediction of lung cancer using volatile biomarkers in breath. Cancer Biomark 3: 95-109
Enose	Phillips M, Altorki N, Austin JH, Cameron RB, Cataneo RN, Kloss R, Maxfield RA, Munawar MI, Pass HI, Rashid A, Rom WN, Schmit P, Wai J (2008). Detection of lung cancer using weighted digital analysis of breath biomarkers. Clin Chim Acta [Epub ahead of print]
Enose	Phillips M, Cataneo RN, Cummin AR, Gagliardi AJ, Gleeson K, Greenberg J, Maxfield RA, Rom WN (2003). Detection of lung cancer with volatile markers in the breath. Chest 123: 2115-2123
Enose	Phillips M, Cataneo RN, Ditkoff BA, Fisher P, Greenberg J, Gunawardena R, Kwon CS, Rahbari-Oskoui F, Wong C (2003). Volatile markers of breast cancer in the breath. Breast J 9: 184-191
Enose	Phillips M, Cataneo RN, Ditkoff BA, Fisher P, Greenberg J, Gunawardena R, Kwon CS, Tietje O, Wong C (2006). Prediction of breast cancer using volatile biomarkers in the breath. Breast Cancer Res Treat 99: 19-21
Enose	Phillips M, Gleeson K, Hughes JM, Greenberg J, Cataneo RN, Baker L, McVay WP (1999). Volatile organic compounds in breath as markers of lung cancer: a cross-sectional study. Lancet 353(9168): 1930-1933
Dog	Pickel DP, Manucy GP, Walker DB, Hall SB, Walker JC (2004). Evidence for canine olfactory detection of melanoma. Appl Anim Behav Sci 89: 107–116
Enose	Ping W, Yi T, Xie HB, Shen FR (1997). A novel method for diabetes diagnosis based on electronic nose. Biosensors Bioelectron 12: 1031-1036
New tech	Price CP (2001). Point of care testing. BMJ 322(7297): 1285-1288
Enose	Probert CS, Jones PR, Ratcliffe NM (2004). A novel method for rapidly diagnosing the causes of diarrhea. Gut 53: 58–61
NIRS	Rager I, Roos G, Schmidt PC, Kovar KA (2002). Rapid quantification of constituents in St. John's wort extracts by NIR spectroscopy. J Pharm Biomed Anal 28(3-4): 439-446
POCT	Rao LV, Ekberg BA, Connor D, Jakubiak F, Vallaro GM, Snyder M (2008). Evaluation of a new point of care automated complete blood count (CBC) analyzer in various clinical settings. Clin Chim Acta 389(1-2): 120-125
NIRS	Räsänen E, Sandler N (2007). Near infrared spectroscopy in the development of solid dosage forms. J Pharm Pharmacol 59(2): 147-159

POCT	Ratnawati, Hatta M, Smits HL (2008). Point-of-care testing for malaria outbreak management. Trans R Soc Trop Med Hyg 102(7): 699-704
NIRS	Reich G (2005). Near-infrared spectroscopy and imaging: Basic principles and pharmaceutical applications. Advanced Drug Delivery Reviews 57: 1109-1143
POCT	Reyburn H, Mbakilwa H, Mwangi R, Mwerinde O, Olomi R, Drakeley C, Whitty CJ (2007). Rapid diagnostic tests compared with malaria microscopy for guiding outpatient treatment of febrile illness in Tanzania: randomised trial. BMJ 334(7590): 403
Dog	Richards KM, Cotton SJ, Sandeman RM (2008). The use of detector dogs in the diagnosis of nematode infections in sheep feces. Journal of Veterinary Behavior 3: 25-31
NIRS	Rivero A, Sánchez-Valverde F, Olivera JE, García Merlo S (2000). Measurement of stool composition in children with celiac disease using near-infrared reflectance spectroscopy. An Sist Sanit Navar 23(3): 433-439
New tech	Robertson BH, Nicholson JK (2005). New microbiology tools for public health and their implications. Annu Rev Public Health 26: 281-302
Enose	Röck F, Barsan N, Weimar U (2008). Electronic nose: current status and future trends. Chem Rev 108: 705-725
NIRS	Roggo Y, Chalus P, Maurer L, Lema-Martinez C, Edmond A, Jent N (2007). A review of near infrared spectroscopy and chemometrics in pharmaceutical technologies. J Pharm Biomed Anal 44(3): 683-700
POCT	Runyon MS, Beam DM, King MC, Lipford EH, Kline JA (2008). Comparison of the Simplify D-dimer assay performed at the bedside with a laboratory-based quantitative D-dimer assay for the diagnosis of pulmonary embolism in a low prevalence emergency department population. Emerg Med J 25(2): 70-75
POCT	Rust G, Gailor M, Daniels E, McMillan-Persaud B, Strothers H, Mayberry R (2008). Point of care testing to improve glycemic control. Int J Health Care Qual Assur 21(3): 325-335
NIRS	Saidi N, Murkin JM (2005). Applied neuromonitoring in cardiac surgery: patient specific management. Semin Cardiothorac Vasc Anesth 9(1): 17-23
NIRS	Sakatani K, Murata Y, Fujiwara N, Hoshino T, Nakamura S, Kano T, Katayama Y (2007). Comparison of blood-oxygen-level-dependent functional magnetic resonance imaging and near-infrared spectroscopy recording during functional brain activation in patients with stroke and brain tumors. J Biomed Opt 12(6): 062110
POCT	Schenk PW, Cransberg K, Wolff ED, de Rijke YB (2007). Point-of-care creatinine testing in children at risk for sudden deterioration of renal function. Clin Chem Lab Med 45(11): 1536-1541
Dog	Schoon GA (1998). A first assessment of the reliability of an improved scent identification line-up. J Forensic Sci 43(1): 70-75
POCT	Seegmiller A, Sarode R (2007). Laboratory evaluation of platelet function. Hematol Oncol Clin North Am 21(4): 731-742
Enose	Šetkus A, Galdikas AJ, Kancleris ZA, Olekas A, Senulienė D, Strazdienė V, Rimdeika R, Bagdonas R (2006). Featuring of bacterial contamination of wounds by dynamic response of SnO2 gas sensor array. Sensors Actuators B: Chemical 115: 412-420
POCT	Sheeler RD, Little P (2006). Rapid streptococcal testing for sore throat and antibiotic resistance. Clin Microbiol Infect (Suppl 9): 3-7
POCT	Shephard MD, Allen GG, Paizis K, Barbara JA, Batterham M, Vanajek A (2006). Results of an Aboriginal community-based renal disease management program incorporating point of care testing for urine albumin:creatinine ratio. Rural Remote Health 6(4): 591
POCT	Shephard MD, Mazzachi BC, Shephard AK (2007). Comparative performance of two point-of-care analysers for lipid testing. Clin Lab 53(9-12): 561-566
POCT	Shimasaki CD, Achyuthan KE, Hansjergen JA, Appleman JR (2001). Rapid diagnostics: the detection of neuraminidase activity as a technology for high-specificity targets. Philos Trans R Soc Lond B Biol Sci 356(1416): 1925-1931
Enose	Shin HW, Llobet E, Gardner JW, Hines EL, Dow CS: Classification of the strain and growth phase of cyanobacteria in potable water using an electronic nose system. IEE Proc – Sci Meas Technol 2000, 147:158-64
Enose	Shykhon ME, Morgan DW, Dutta R, Hines EL, Gardner JW (2004). Clinical evaluation of the electronic nose in the diagnosis of ear, nose and throat infection: a preliminary study. J Laryngol Otol 118: 706-709
New tech	Situma C, Hashimoto M, Soper SA (2006). Merging microfluidics with microarray-based bioassays. Biomol Eng 23(5): 213-231
Dog	Smith DA, Ralls K, Hurt A, Adams B, Parker M, Davenport B, Smith MC, Maldonado JE (2003). Detection and accuracy rates of dogs trained to find scats of San Joaquin kit foxes (Vulpes macrotic mutica). Animal Conservation 6: 339–346
NIRS	Smith M (2007). Perioperative uses of transcranial perfusion monitoring. Anesthesiol Clin 25(3): 557-577
Etongue	Söderström C, Winquist F, Krantz-Rülcker C (2003). Recognition of six microbial species with an electronic tongue. Sensors Actuators B: Chemical 89: Pages 248-255
Etongue	Sohn YS, Goodey A, Anslyn EV, McDevitt JT, Shear JB, Neikirk DP (2005). A microbead array chemical

	sensor using capillary-based sample introduction: toward the development of an “electronic tongue”. Biosensors and Bioelectronics 21: 303-312
POCT	Sokoll LJ, Wians FH Jr, Remaley AT (2004). Rapid intraoperative immunoassay of parathyroid hormone and other hormones: a new paradigm for point-of-care testing. Clin Chem 50(7): 1126-1135
NIRS	Soller BR, Micheels RH, Coen J, Parikh B, Chu L, Hsi C (1996). Feasibility of non-invasive measurement of tissue pH using near-infrared reflectance spectroscopy. J Clin Monit 12(5): 387-395
NIRS	Sowa MG, Leonardi L, Payette JR, Cross KM, Gomez M, Fish JS (2006). Classification of burn injuries using near-infrared spectroscopy. J Biomed Opt 11(5): 054002
NIRS	Sowa MG, Leonardi L, Payette JR, Fish JS, Mantsch HH (2001). Near infrared spectroscopic assessment of hemodynamic changes in the early post-burn period. Burns 27(3): 241-249
NIRS	Steinberg F, Röhrborn HJ, Otto T, Scheufler KM, Streffer C (1997). NIR reflection measurements of hemoglobin and cytochrome aa3 in healthy tissue and tumors. Correlations to oxygen consumption: preclinical and clinical data. Adv Exp Med Biol 428: 69-77
POCT	Steinfelder-Visscher J, Teerenstra S, Gunnewiek JM, Weerwind PW (2008). Evaluation of the i-STAT point-of-care analyzer in critically ill adult patients. J Extra Corpor Technol 40(1): 57-60
POCT	Steingart KR, Henry M, Laal S, Hopewell PC, Ramsay A, Menzies D, Cunningham J, Weldingh K, Pai M (2007). Commercial serological antibody detection tests for the diagnosis of pulmonary tuberculosis: a systematic review. PLoS Med 4(6): e202
POCT	Steinmetz HW, Vogt R, Kästner S, Riond B, Hatt JM (2007). Evaluation of the i-STAT portable clinical analyzer in chickens (Gallus gallus). J Vet Diagn Invest 19(4): 382-388
POCT	Stevenson CK, Kidney BA, Duke T, Snead EC, Jackson ML (2007). Evaluation of the Accutrend for lactate measurement in dogs. Vet Clin Pathol 36(3):261-6.
POCT	Story DA (2004). Bench-to-bedside review: a brief history of clinical acid-base. Crit Care 8(4): 253-258
POCT	Stubbs P, Collinson PO (2001). Point-of-care testing: a cardiologist's view. Clin Chim Acta 311(1): 57-61
NIRS	Stuth JW, Tolleson DR (2000). Monitoring the nutritional status of grazing animals using near infrared spectroscopy. Compend Contin Ed Pract Vet 22: S108–S115
POCT	Tang L, Oh YS, Li H, Song J, Chen PS, Lin SF (2007). Clinical validation of fiberoptic immunobiosensor for point-of-care analysis of plasma nerve growth factor. Heart Rhythm 4(9): 1208-1213
POCT	Tennent-Brown BS, Wilkins PA, Lindborg S, Russell G, Boston RC (2007). Assessment of a point-of-care lactate monitor in emergency admissions of adult horses to a referral hospital. J Vet Intern Med 21(5): 1090-1098
Enose	Thaler ER (2002). Candidate's thesis: the diagnostic utility of an electronic nose: rhinologic applications. Laryngoscope 112: 1533-1542
Enose	Thaler ER (2002). The diagnostic utility of an electronic nose: rhinologic applications. Laryngoscope 112: 1533-1542
Enose	Thaler ER, Bruney FC, Kennedy DW, Hanson CW (2000). Use of an electronic nose to distinguish cerebrospinal fluid from serum. Arch Otolaryngol Head Neck Surg 126: 71-74
Enose	Thaler ER, Hanson CW (2005). Medical applications of electronic nose technology. Expert Rev Med Devices 2: 559-566
Enose	Thaler ER, Hanson CW (2006). Use of an electronic nose to diagnose bacterial sinusitis. Am J Rhinol 20: 170-172
Enose	Thaler ER, Huang D, Giebeig L, Palmer J, Lee D, Hanson CW, Cohen N (2008). Use of an electronic nose for detection of biofilms. Am J Rhinol 22: 29-33
Enose	Thaler ER, Kennedy DW, Hanson CW (2001). Medical applications of electronic nose technology: review of current status. Am J Rhinol 15: 291-295
POCT	Thorneloe C, Bédard C, Boysen S (2007). Evaluation of a hand-held lactate analyzer in dogs. Can Vet J 48(3): 283-288
Dog	Tindall R, Lothridge K (1995). An evaluation of 42 accelerant detection canine teams. Journal of Forensic Sciences 40: 561–564
Etongue	Toko K (1998). Electronic tongue. Biosensors and Bioelectronics 13: 701-709
NIRS	Tolleson DR, Randel RD, Stuth JW, Neuendorff DA (2005). Determination of sex and species in red and fallow deer by near infrared reflectance spectroscopy of the faeces. Small Ruminant Research 57: 141-150
NIRS	Tolleson DR, Teel PD, Stuth JW, Strey OF (2000b). Discrimination of parasite burden in livestock via near infrared reflectance spectroscopy of feces. J. Anim. Sci. 78(Suppl II):
NIRS	Tolleson DR, Teel PD, Stuth JW, Strey OF (2002). Phase of external parasite feeding cycle affects NIRS predicted diet quality in cattle. J Anim Sci 80 (Suppl II):
NIRS	Tolleson DR, Teel PD, Stuth JW, Strey OF, Welsh TH Jr, Carstens GE (2007). Fecal NIRS: detection of tick infestations in cattle and horses. Vet Parasitol 144(1-2): 146-152
NIRS	Tolleson DR,Wilson TW, Randel RD, Neuendorff DA, Lewis AW, Stuth JW (2000a). Discrimination between physiologically different groups of cattle via near infrared reflectance spectroscopy of feces. J Anim Sci 78(Suppl. II):

POCT	Tomera KM (2004). NMP22 BladderChek Test: point-of-care technology with life- and money-saving potential. Expert Rev Mol Diagn 4(6): 783-794
POCT	Tovar JM, Gums JG (2004). Monitoring pulmonary function in asthma and COPD: point-of-care testing. Ann Pharmacother 38(1): 126-133
NIRS	Tura A, Maran A, Pacini G (2007). Non-invasive glucose monitoring: assessment of technologies and devices according to quantitative criteria. Diabetes Res Clin Pract 77(1): 16-40
Enose	Turner AP, Magan N (2004). Electronic noses and disease diagnostics. Nat Rev Microbiol 2: 161-166
POCT	Turner KS, Shaw KA, Coleman DJ, Misrachi A (2006). Augmentation of influenza surveillance with rapid antigen detection at the point-of-care: results of a pilot study in Tasmania, 2004. Commun Dis Intell 30(2): 201-204
POCT	Uphoff H, Metzger C (2002). The use of rapid tests for individual diagnosis of influenza. Dtsch Med Wochenschr 127(20): 1096-1101
NIRS	Vardi M, Nini A (2008). Near-infrared spectroscopy for evaluation of peripheral vascular disease. A systematic review of literature. Eur J Vasc Endovasc Surg 35(1): 68-74
NIRS	Vernieri F, Tibuzzi F, Pasqualetti P, Altamura C, Palazzo P, Rossini PM, Silvestrini M (2008). Increased cerebral vasomotor reactivity in migraine with aura: an autoregulation disorder? A transcranial Doppler and near-infrared spectroscopy study. Cephalalgia [Epub ahead of print]
NIRS	Vikram DS, Zweier JL, Kuppusamy P (2007). Methods for noninvasive imaging of tissue hypoxia. Antioxid Redox Signal 9(10): 1745-1756
Etongue	Vlasov Y, Legin A, Rudnitskaya A (2002). Electronic tongues and their analytical application. Anal Bioanal Chem 373(3): 136-146
New tech	von Lode P (2005). Point-of-care immunotesting: approaching the analytical performance of central laboratory methods. Clin Biochem 38(7): 591-606
POCT	Vos G, Engel M, Ramsay G, van Waardenburg D (2006). Point-of-care blood analyzer during the interhospital transport of critically ill children. Eur J Emerg Med 13(5): 304-307
Enose	Voss A, Baier V, Reisch R, von Roda K, Elsner P, Ahlers H, Stein G (2005). Smelling renal dysfunction via electronic nose. Ann Biomed Eng 33: 656-660
POCT	Vrouwe EX, Luttge R, Vermes I, van den Berg A (2007). Microchip capillary electrophoresis for point-of-care analysis of lithium. Clin Chem 53(1):117-123
NIRS	Walker JW, Campbell ES, Lupton CJ, Taylor CA Jr, Waldron DF, Landau SY (2007). Effects of breed, sex, and age on the variation and ability of fecal near-infrared reflectance spectra to predict the composition of goat diets. J Anim Sci 85(2): 518-526
Dog	Wallner W, Ellis T (1976). Olfactory detection of Gypsy Moth pheromone and egg masses by domestic canines. Environ Entomol 5: 183-186
POCT	Wang H, Zhang Y, Yan B, Liu L, Wang S, Shen G, Yu R (2006). Rapid, simple, and sensitive immunoagglutination assay with SiO2 particles and quartz crystal microbalance for quantifying Schistosoma japonicum antibodies. Clin Chem 52(11): 2065-2071
Etongue	Wang P, Liu Q, Xu Y, Cai H, Li Y (2007). Olfactory and taste cell sensor and its applications in biomedicine. Sensors and Actuators A: Physical 139: 131-138
Enose	Wang P, Tan Y, Xie H, Shen F (1997). A novel method for diabetes diagnosis based on electronic nose. Biosens Bioelectron 12: 1031-1036
POCT	Warnick GR, Remaley AT (2001). Measurement of cholesterol in plasma and other body fluids. Curr Atheroscler Rep 3(5): 404-411
Dog	Wasser S, Davenport B, Ramage E, Hunt K, Parker M, Clarke C, Stenhouse,G (2004). Scat detection dogs in wildlife research and management: application to grizzly and black bears in the Yellowhead Ecosystem, Alberta, Canada. Can J Zool 82: 475-492
NIRS	Waxman S, Ishibashi F, Caplan JD (2007). Rationale and use of near-infrared spectroscopy for detection of lipid-rich and vulnerable plaques. J Nucl Cardiol 14(5): 719-728
POCT	Weatherall C, Paoloni R, Gottlieb T (2008). Point-of-care urinary pneumococcal antigen test in the emergency department for community acquired pneumonia. Emerg Med J 25(3): 144-148
POCT	Wei F, Wang J, Liao W, Zimmermann BG, Wong DT, Ho CM (2008). Electrochemical detection of low-copy number salivary RNA based on specific signal amplification with a hairpin probe. Nucleic Acids Res 36(11): e65
POCT	Weitzel T, Schnabel E, Dieckmann S, Börner U, Schweiger B (2007). Evaluation of a new point-of-care test for influenza A and B virus in travellers with influenza-like symptoms. Clin Microbiol Infect 13(7): 665-669
Dog	Welch JB (1990). A detector dog for screwworms (Diptera: Calliphoridae). J Econ Entomol 83(5): 1932-1934
NIRS	Widder S, Ranson MK, Zygun D, Knox L, Laupland KB, Laird P, Ball CG, Kirkpatrick AW (2008). Use of near-infrared spectroscopy as a physiologic monitor for intra-abdominal hypertension. J Trauma 64(5): 1165-1168
POCT	Wiese L, Bruun B, Baek L, Friis-Møller A, Gahrn-Hansen B, Hansen J, Heltberg O, Højbjerg T, Hornstrup

	MK, Kvinesdal B, Gomme G, Kurtzhals JA (2006). Bedside diagnosis of imported malaria using the Binax Now malaria antigen detection test. Scand J Infect Dis 38(11-12): 1063-1068
Dog	Williams H, Pembroke A (1989). Sniffer dogs in the melanoma clinic? Lancet 333 (8640): 734
Dog	Willias C, Church S, Guest C, Cook A, McCarthy N, Bransbury A, Church M, Church J (2004). Olfactory detection of human bladder cancer by dogs: proof of principle study. Brit Med J 329: 1-6
Urine para	Willis C, Poulin R (2000). Preference of females for the odours of non-parasitized males. the smell of good genes. Folia Parasitol 47: 6 -10
POCT	Wilson L, Jehanli A, Hand C, Cooper G, Smith R (2007). Evaluation of a rapid oral fluid point-of-care test for MDMA. J Anal Toxicol 31(2): 98-104
POCT	Wongsrichanalai C, Barcus MJ, Muth S, Sutamihardja A, Wernsdorfer WH (2007). A review of malaria diagnostic tools: microscopy and rapid diagnostic test (RDT). Am J Trop Med Hyg 77(6 Suppl): 119-127
NIRS	Woo YA, Kim HJ, Cho JH, Chung H (1999). Discrimination of herbal medicines according to geographical origin with near infrared reflectance spectroscopy and pattern recognition techniques. J Pharm Biomed Anal 21(2): 407-413
Saliva	Wright V, Bickle Q. Immune responses following experimental human hookworm infection. Clin Exp Immunol. 2005 Nov;142(2):398-403
NIRS	Wright WL (2007). Multimodal monitoring in the ICU: when could it be useful? J Neurol Sci 261(1-2): 10-15
NIRS	Xie HP, Jiang JH, Chen ZQ, Shen GL, Yu RQ (2006). Chemometric classification of traditional Chinese medicines by their geographical origins using near-infrared reflectance spectra. Anal Sci 22(8): 1111-1116
POCT	Yang X, Janatova J, Juenke JM, McMillin GA, Andrade JD (2007). An ImmunoChip prototype for simultaneous detection of antiepileptic drugs using an enhanced one-step homogeneous immunoassay. Anal Biochem 365(2): 222-229
Enose	Yates JW, Chappell MJ, Gardner JW, Dow CS, Dowson C, Hamood A, Bolt F, Beeby L (2005). Data reduction in headspace analysis of blood and urine samples for robust bacterial identification. Comput Methods Programs Biomed 79: 259-271
New tech	Yeung SW, Lee TM, Cai H, Hsing IM (2006). A DNA biochip for on-the-spot multiplexed pathogen identification. Nucleic Acids Res 34(18): e118
POCT	Zarkov IS (2008). Use of a commercial immunoassay for rapid detection of influenza A antigen in experimentally infected turkeys. Vet Rec 162(4): 126-127
Enose	Zhang Q, Wang P, Li J, Gao X (2000). Diagnosis of diabetes by image detection of breath using gas-sensitive LAPS. Biosens Bioelectron 15: 249–256
POCT	Ziober AF, Patel KR, Alawi F, Gimotty P, Weber RS, Feldman MM, Chalian AA, Weinstein GS, Hunt J, Ziober BL (2006). Identification of a gene signature for rapid screening of oral squamous cell carcinoma. Clin Cancer Res 12(20 Pt 1): 5960-5971

7. APPENDICES

APPENDIX 1. WORKSHOP PARTICIPANTS

PARTICIPANT	ROLES	CONTACT DETAILS
Dr Ian Colditz	Assessment Report Author Presenter	Research scientist (CSIRO) (Immunology/parasitology) CSIRO Livestock Industries Ian.Colditz@csiro.au
Dr Doug Gray	Assessment Report Author, Project Leader	Consultant parasitologist/ project management (POB 290, Kingscote SA 5223) dougiegray@bigpond.com
Dr Stephen Page	Assessment Report Author	Consultant, animal health specialist Advanced Veterinary Therapeutics (PO Box 345 Berry NSW 2535) swp@advet.com.au
Dr Brown Besier	Sheep CRC, Assessment Report Editor	CRC Sub-Program Leader/ Principal Veterinary Parasitologist Department of Agriculture and Food WA BBesier@agric.wa.gov.au
Dr Rob Dixon	Project Leader	Research scientist Queensland Department of Primary Industries and Fisheries Rob.Dixon@dpi.qld.gov.au
Dr Peter James	Project Leader	Research scientist/ Head of Parasitology Queensland Department of Primary Industries and Fisheries Peter.James@dpi.qld.gov.au
Deborah Maxwell	Project member	Queensland Department of Primary Industries and Fisheries. Extension Coordinator, CRC for Sheep Industry Innovation deborah.maxwell@une.edu.au
Dr Dieter Palmer	Project Leader	Research scientist (Immunology / parasitology) Department of Agriculture and Food WA dpalmer@agric.wa.gov.au
Dr Mark Sandeman	Project Leader	Head of Agriculture/ Research scientist La Trobe University M.Sandeman@latrobe.edu.au
Dr James Rowe	Participant (Sheep CRC)	CEO Sheep CRC/ Professor, University of New England CRC for Sheep Industry Innovation james.rowe@csiro.au
Peter Silk	Participant (Sheep CRC)	CRC for Sheep Industry Innovation Program Manager Adoption and Commercialisation peter.silk@sheepcrc.org.au
Russell Barnett	Participant (Consultant)	Consultant on adoption and commercialization Australian Venture Consultants russell@ventureconsultants.com.au
Dr Johann Schroder	Participant (AWI)	Program Manager, Animal Health and Welfare Australian Wool Innovations johannschroder@woolinnovation.com
Dr Keith Walker	Participant (MLA)	Program Manager, Environment, Animal Health and Welfare Meat and Livestock Australia kwalker@mla.com.au
Dr Tim Wilson	Participant (MLA)	Acting Project Manager, Animal Health Meat and Livestock Australia twilson@mla.com.au

APPENDIX 2. ASSESSMENT CRITERIA

App. 2.1 FRAMEWORK TO ASSESS TECHNICAL AND PRACTICAL ATTRACTIVENESS OF NEW DIAGNOSTIC TEST METHOD

#	PARAMETER	DESCRIPTION	SCORING CONSIDERATIONS	SCORE 1Low 2 Med 3 High	COMMENTS
			UNMET NEED		
A	Diagnostic Need:	What information will the test provide and what decisions will that information support?	o New information allowing improved decision making: Decision not to treat Decision to reassess later Decision of which anthelmintic to use Decision on change to management practice o Information can already be obtained but proposed test: Reduces time to result Improves accuracy of result Reduces cost of obtaining information Provides simple race-side test		
B	Transformation:	To what extent will the adoption of the diagnostic transform the way that sheep are managed?	o Will the information provided by the test allow new or improved decisions that will result in significant benefits? o What number of sheep at risk could potentially benefit from the use of the test (eg all sheep at risk of Haemonchosis, all sheep at risk of GIN infection etc)?		

#	PARAMETER	DESCRIPTION	SCORING CONSIDERATIONS	SCORE 1Low 2 Med 3 High	COMMENTS
TECHNICAL COMPLEXITY AND RISKS					
C	Research Maturity:	Is there a well organised and supported research effort making steady progress?	o Does the diagnostic research team already have the experience and skills to complete the project o Are there technical support resources accessible by the research team? o Does the technology already have an established track record of reliable performance?		
D	Research Complexity:	How many problems need to be solved before reaching 'proof of concept' and how complex are these problems?	o How novel is the technology being applied? o Does the approach benefit from published and other experiences and represent an advance? o Does the technology already have commercial applications relevant to the current objective? o How many (ie few or many) critical hurdles need to be overcome to allow the test to be developed? o Are the hurdles known, well defined, or unknown? o Are there any constraints concerning freedom-to-operate or technology licensing.		
E	Method complexity	How complex are the reagents and materials for the test?	o Are the reagents and other critical components of the test method readily available from multiple sources? o Can the quality of these components be readily assessed? o Do the test components have any special storage requirements or a short shelf life?		
F	Operating characteristics	What are the expected sensitivity, specificity and predictive values of the test?	o Do the operating characteristics meet or exceed the minimal requirements of what is needed? o How do expected test results compare with what is currently available?		
G	Reliability:	Will the test be reliable when applied many times by the same, by different operators and between laboratories	o Does the technology have the capacity to produce reliable and reproducible results when used by different operators and in different field situations o Are there any test method factors that could cause reduced reliability and reproducibility?		

#	PARAMETER	DESCRIPTION	SCORING CONSIDERATIONS	SCORE 1Low 2 Med 3 High	COMMENTS
ADOPTION FACTORS					
H	Implementation:	How will the test be used, samples collected, assays completed, results delivered etc).	o How easy is sample collection? o Do samples require any processing? o Is the test on-farm or at laboratory? o Is information provided in immediately usable form?		
I	Skills and Training:	How much training will be needed for each aspect of test implementation?	o How different is the proposed test method to currently used procedures by operator? o How many steps are involved? o How complex and subject to variation are the steps? o Are there any special procedures or equipment needed (eg power source)? o How easy is it to read or calculate the result of the test?		
J	Customers:	Who will sell the tests and who are the target customers?	o Is there already a distribution network to supply the test to the proposed operator? o Will the test be race-side (preferred) or laboratory based (requiring transport of samples and delay in response)?		
K	Competition:	Are there likely to be other test on the market and what are they?	o Are there already tests available that provide the same information? o Are new tests expected that will provide the same or improved information? o Are existing or new tests superior with respect to any aspect of the test (ease of performance, speed, cost etc)?		
L	Capital Investment:	How much capital investment is likely to be needed: production laboratory, machines to make reagents, containers etc.	o What is the anticipated cost to set up test method? o How long will it take to recover the set up cost? o How high will running costs be?		
M	Value Proposition:	What will the price be relative to other tests and how much greater will the benefits be? Who will be	o What is the anticipated cost of sufficient tests on which to base a decision? o What is the expected benefit (economic and other) of using the test?		

		the beneficiaries?	o How cost effective will the test be (eg demonstrably and unequivocal benefits or difficult to measure benefit?		

#	PARAMETER	DESCRIPTION	SCORING CONSIDERATIONS	SCORE 1Low 2 Med 3 High	COMMENTS
FUTURE DEVELOPMENT					
N	External Opportunities:	What are the opportunities for use of the diagnostic outside the sheep industry, and for other parasites and diseases?	o Does test method lend itself to use in other situations? o Will increased use be associated with decreases in test cost?		
O	Ongoing test refinement	Does the test lend itself to improvements in response to field use feedback or changes in technology?	o Is the technology subject to continuous improvement? o Will the ease of use improve with time? o Will the cost decrease with time?		

App. 2.2 TOTAL SCORES

CATEGORY	DESCRIPTION	SCORE		COMMENTS
Benefits to Industry	What is the overall assessment of the magnitude of the benefits to the sheep industry?	A+B		Most critical score. If less than threshold (to be decided) no need to explore other parameters
Likelihood of technical success:	What is the overall assessment of the likelihood of successful technical development?	C+D+E+F+G		A threshold score could be proposed Needs to be reasonable likelihood of success to justify support If benefits are very high then lower likelihood could be acceptable
Likelihood of adoption	What is the overall assessment of the likelihood of successful commercialisation and adoption?	H+I+J+K+L+M		A threshold score could be proposed All tests will suffer a background of entrenched low level of adoption
Future development	Does the test lend itself to improvements in response to field use feedback or changes in technology? Can the test find applications beyond sheep	N+O		Future development can increased likelihood of test survival in a format that is increasingly useful to end-users
OVERALL SCORE		**Σ(A-O)**		