GID-HTE10082 Technologies for the rapid diagnosis of endometriosis

Final Protocol

Produced by: **Coreva Scientific, External Assessment Group**

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1. Decision problem

In this early use assessment, the EAG will address the following key decision questions:

1) Does offering the new diagnostic tests described in the scope have the potential to be clinically and cost-effective within the NHS?
2) Are there gaps in the evidence base, and if so, what are the key gaps?

Table 1 summarises elements of the decision problem to be addressed. Further detail on each element can be found in the scope document for this assessment.

Table 1. Summary table of the decision problem

Item	Description	EAG comments
Type of assessment	Early use assessment	
Population(s)	People who have or have had female reproductive organs (including women, trans men and non-binary people) with recurrent symptoms of suspected endometriosis with normal clinical examination and either negative imaging results for endometriosis or no imaging results because imaging is unacceptable.	
Subgroups	• Young people and adolescents • Perimenopausal and postmenopausal people • People who have fertility as a priority • People with higher body mass index • People who find transvaginal ultrasound unacceptable	These subgroups will be considered if the evidence allows. The EAG acknowledges that some of these subgroups are not eligible to receive two of the three technologies included in this assessment due to the age restrictions set by medical device regulatory bodies. The subgroup of people for whom a transvaginal ultrasound may not be appropriate should still be

		offered this diagnostic method to support equitable access and uphold individual choice
Intervention(s)	• EndoSure • DotEndo • EndoTest	
Comparators	Current practice, including clinical examination and imaging without the technologies	The novel diagnostic tests included in this assessment will not be used to replace established tests within the diagnostic pathway
Setting	Primary care	

Outcomes eligible for inclusion	**Clinical outcomes:**
	• Diagnostic accuracy
	  ○ Test sensitivity
	  ○ Test specificity
	  ○ Positive and negative predictive values
	• Time taken from initial presentation to referral to specialist services
	• Impact of false positives
	• Time taken to diagnosis
	• Time taken to starting treatment
	• Number of hospital attendances including admissions and emergency department attendances
	• Number of primary care consultations
	• Number of referrals for laparoscopy
	Patient-reported outcomes:
	• Overall pain
	• Symptom burden
	• Quality of life
	• Level of daily function
	• Patient experience
	• Ease of use and acceptability for patients and carers
	Other
	• Adverse events
		The EAG will prioritise outcomes in consultation with NICE and clinical experts based on the availability of evidence
		
		If the evidence base is large, the EAG will prioritise the highest quality and most generalisable evidence
		
		Any additional outcomes relevant to the decision problem outlined in the scope (if reported and available) may be summarised by the EAG

	Costs and resource use:
	• Costs of equipment
	• Costs of staff and associated training
	• Cost of testing, including time requesting, reviewing and communicating results
	• Cost of follow up appointments, including
	  ○ Further investigations
	  ○ Further treatment
	• Costs of appointments, investigations and treatments avoided	

Economic analysis	• A health-economic model will be developed comprising a cost-utility or cost-comparison analysis. • Costs will be considered from an NHS and Personal Social Services perspective. • Sensitivity and scenario analysis should be undertaken to address the relative effect of parameter or structural uncertainty on results. • The time horizon should be long enough to reflect all important differences in costs or outcomes between the technologies being compared.	

1.1 Objectives

The purpose of this early use assessment is to summarise and critically appraise the evidence for the health technologies outlined in the scope document. The aim is to evaluate the clinical- and cost-effectiveness of these technologies, highlight evidence gaps, and identify any risks associated with the adoption of these technologies by the NHS while further evidence is generated. The objectives listed below have been proposed based on the scope published by NICE.

Clinical effectiveness:

- Identify and critically appraise the available evidence on the use and clinical effectiveness of the technologies included within the project scope.

- Describe any potential safety concerns associated with the use of these technologies.
- Highlight gaps in the current evidence base and indicate what further data may be required to address these uncertainties.

Cost effectiveness:

- Identify and assess economic evidence relating to the use of the technologies included within the project scope.
- Develop a conceptual economic model that can be used to inform future research and data collection.
- Summarise the available model inputs and identify areas where evidence is lacking.
- Describe the key uncertainties within the economic model, outline their potential implications for decision-making, and explore the impact of alternative plausible assumptions via sensitivity and scenario analyses.
- Present the estimated costs and effects of the technologies and provide an early indication, based on the currently available evidence, of whether their use could be a cost-effective addition to the current care within the NHS.

2. Evidence review methods

The EAG will conduct an independent search of evidence relevant to the scope of this assessment. The primary aim of the evidence review will be to conduct a rapid literature review to identify and summarise published evidence on the clinical- and cost-effectiveness of the technologies for the rapid diagnosis of endometriosis included in the project scope. Its secondary aim will be to identify and summarise any gaps in the evidence. This review will follow the NICE HealthTech programme manual.

Missing or incomplete information may be supplemented with information available in the public domain, such as company websites or grey literature, or information supplied by the companies or other stakeholders (e.g., unpublished studies), provided that they are complete enough to enable critical appraisal.

2.1 Inclusion criteria

The inclusion and exclusion criteria are outlined in Table 2. Based on initial scoping searches, the EAG does not expect there to be a large body of published evidence for

the included technologies. If the literature search does not identify sufficient evidence directly relevant to the decision problem for a given technology, the EAG will review whether elements of the scope can be broadened. The EAG will also consult with clinical experts to consider the extent to which the available evidence and findings may be generalisable to NHS practice.

Table 2. Inclusion and exclusion criteria

	Inclusion Criteria	**Exclusion Criteria**
Population	People who have or have had female reproductive organs (including women, trans men and non-binary people) with recurrent symptoms of suspected endometriosis	People who are not suspected of having endometriosis or who are not eligible for a diagnostic test for endometriosis
Intervention	The included interventions: • EndoSure, including tests manufactured by EndoSure or related generic descriptors (e.g., gastrointestinal myoelectical activity, electroviscerogram, electroviscerography) • DotEndo, including tests manufactured by DotLab or related generic descriptors (e.g., blood-based microRNA test) • EndoTest, including tests manufactured by Ziwig or related generic descriptors (e.g., saliva-based microRNA test)	• Studies on technologies other than those listed in the scope • Studies that do not explicitly disclose the technology in the full-text version of the manuscript and were not submitted by the company or located on the company's website, where the technology used could otherwise be inferred • Studies that only name the technology of interest incidentally
Comparators	As in Table 1	No exclusion based on comparator
Setting	As in Table 1	No exclusion based on setting
Outcomes	As in Table 1	Studies that do not include any outcomes relevant to the decision problem outlined in the scope
Study design	Study types reporting primary data, including: • Randomised controlled trials	Studies not reporting original data (e.g., narrative reviews, opinion pieces, editorials, commentaries, and letters) or not adhering to the listed PICO

	• Prospective cohort studies • Retrospective cohort studies • Real-world studies • Database studies • Case-control studies • Cross-sectional studies • Single-arm studies • Qualitative and mixed-methods studies • Case series • Care reports Studies reporting secondary data (e.g., health-economic evaluations, systematic reviews, and meta-analyses) or those reporting preliminary data (e.g., protocols or trial registrations) will also be considered if appropriate	criteria (e.g., animal or pre-clinical studies)
Other	The literature search will be restricted to articles published in English	

2.2 Search strategy

A structured search strategy will be developed to identify articles reporting both clinical and health-economic outcomes on the relevant technologies for the rapid diagnosis of endometriosis. Search terms will be structured around the population and interventions as detailed in the inclusion criteria (Section 2.1) and use controlled vocabulary from database thesauri such as MeSH (MEDLINE) or EMTREE (EMBASE), as well as free-text terms derived from target references and terms specific to the technologies of interest (such as brand names, company names, and generic descriptors of the technologies included in the project scope).

Where appropriate, the EAG will consider applying limits to the literature search (e.g., English language publications and/or date of publication). Additional studies may be identified from hand searching relevant references of included papers.

In addition to the structured literature search that will be used to find evidence on the new technologies, the EAG may perform supplementary pragmatic searches of the broader literature on endometriosis for evidence on health-related quality of life (HRQoL), resource use, and treatment costs in order to inform the health-economic model.

The search strategies will be developed in MEDLINE (PubMed; see Appendix A for the search strings used) and translated specifically for each database, keeping as many of the key terms as possible while adapting database-specific keywords and thesaurus terms according to the configuration of each database. Filters may be applied to identify relevant clinical and health-economic publications, as appropriate.

The following databases will be searched to identify published literature on clinical and health-economic evidence:

- MEDLINE (PubMed)
- EMBASE (Elsevier)
- Cochrane Database of Systematic Reviews (CDSR)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Epistemonikos
- International HTA database (INAHTA)

The following databases will be searched to identify unpublished and ongoing trials:

- ClinicalTrials.gov
- EU Clinical Trials Register
- International Clinical Trials Registry Platform (ICTRP)

2.3 Study selection

All retrieved references will be imported into PICO Portal (https://picoportal.org) for deduplication and screening; the platform will record the screening decisions of all reviewers involved.

The titles and abstracts of all identified references will be screened by one reviewer, and the first 10% of screened abstracts will be checked by a second reviewer against the pre-specified selection criteria (Section 2.1). Selection at title and abstract level will be more inclusive as the technologies used in the study are often not mentioned by name in the abstract but described in more generic terms. This approach will ensure that all relevant literature on the technologies included in the scope is identified.

Full-text articles will be obtained for all eligible references and screened by one reviewer, with a second reviewer checking the first 20% of screened full texts. At full-text level, articles that do not explicitly name the technology or where the technology used cannot be inferred (e.g., from the manufacturing company sponsoring the study, or the paper being sent by the company) will be excluded.

All disagreements in screening decisions will be settled by a third reviewer. All studies excluded during full-text screening will be presented in the appendix of the report, including the reason for their exclusion.

PICO Portal includes an artificial intelligence (AI) function that is meant to support the human reviewer and speed up the screening and data extraction processes but not replace the human researchers. During screening, it predicts which articles are likely to be included and shows these to the reviewers first. There is no risk associated with its use as all abstracts will be screened by human reviewers; the only impact the AI has is in the order in which the abstracts are screened.

Unpublished evidence will be considered and handled according to the NICE HealthTech programme manual. Any unpublished evidence should ideally be structured and presented in the form of a research publication and has to be accompanied by sufficient details to enable judgement on whether it meets the required standards and to determine potential sources of bias.

Evidence provided by companies and other stakeholders will be considered and included if it is relevant to the decision problem (Section 1), fulfils the inclusion criteria (Section 2.1), and was submitted to NICE before 9th March 2026. For more details, refer to Section 5.

2.4 Data extraction strategy

Data from the included studies will be extracted by one independent reviewer using a customised Microsoft Excel spreadsheet. A second reviewer will check the data extraction sheet. A third reviewer may be brought in to resolve any disagreements between the first and second reviewer by consensus or discussion. The extracted data will include information about the study reference (e.g., authors, date, title) and the study characteristics (e.g., design, population, intervention, comparator [if applicable], and outcomes listed in the project scope). Any additional outcomes reported in the included evidence and relevant to the decision problem will also be extracted.

The PICO Portal AI may be used to support data extraction, where the AI highlights potentially relevant text passages containing the data to be extracted, but the task will ultimately be performed and completed by human researchers.

2.5 Quality assessment strategy

A formal risk of bias assessment will not be undertaken, as this is not required for an early value assessment according to NICE's HealthTech programme manual. However, the EAG will provide a narrative discussion of potential sources of bias within the included studies and consider how these may influence key outcomes. The discussion of potential risk of bias in real-world evidence may consider the reporting on methods used to minimise risk of bias section of the NICE's real-world evidence framework. The assessment report will discuss possible biases, such as major confounding factors, and will also comment on how far the available evidence can be generalised to routine clinical practice within the NHS.

2.6 Methods of synthesis and analysis

Data from the published evidence will be extracted into a customised Microsoft Excel spreadsheet and be grouped by technology and population (if subgroup analyses are

performed) for each of the outcomes included in the project scope. The results will be synthesised narratively, and evidence gaps will be summarised.

Methods and findings synthesised from the included economic evidence will be presented in a table and summarised narratively for each technology included in the project scope.

3. Economic analysis methods

The primary aim of this economic analysis is to examine the cost-effectiveness of using the three technologies outlined in the scope (see Table 1) to diagnose endometriosis in people presenting with typical disease-related symptoms as described in the current NICE Endometriosis diagnosis and management guidelines. A decision-analytic model will be developed to compare the costs and consequences of using these novel diagnostic tests to current care. The secondary aim of this analysis is to identify and summarise current evidence gaps.

3.1 Model development

For this early use assessment, the EAG will develop a *de novo* economic model to appropriately reflect the NHS setting in accordance with the reference case. Published economic evaluations performed in various settings will be examined when conceptualising the model.

The model structure will consider the diagnostic pathway of people with suspected endometriosis and will reflect a time horizon long enough to capture relevant costs and consequences. The model structure will be informed by the current clinical evidence and subsequently validated by NICE-appointed experts.

Three interventions, as outlined in the project scope, will be examined against current care. Given that endometriosis is a chronic condition and that its delayed diagnosis is expected to impact patient outcomes (e.g., HRQoL), the EAG would prefer to undertake a cost-utility analysis if the available evidence permits.

Clinical and cost data inputs for the model will be derived from the literature search undertaken for the evidence review portion of the external assessment report. Further data will be obtained from published literature using pragmatic, targeted searches, as

well as from the manufacturers of the included technologies and clinical experts assigned by NICE.

Costs will be considered from an NHS and PSS perspective in line with the reference case. Costs anticipated to be included in the model are:

- Costs of implementation (e.g., staff training, laboratory setup).
- Costs of the technologies included in the scope.
- Costs of current care (e.g., costs related to diagnostic laparoscopy and previous imaging tests, depending on the positioning of the tests in the diagnostic pathway).
- Costs of pharmaceutical treatment prior to a definitive diagnosis being made.
- Costs of general and specialist care appointments both in primary and secondary care.
- Costs of hospital emergency department visits due to symptoms of endometriosis.

The EAG expects that the development of a health-economic model will be feasible but may have to rely on assumptions.

3.2 Methods of health-economic analysis

The EAG will develop the decision-analytic model using Microsoft Excel. The model will be developed and reported according to the Good Practice Guidelines for Health-Economic Modelling and Reporting (Caro et al. 2012).

Depending on data availability, the EAG will undertake either a cost-utility or a cost-comparison analysis. If a cost-utility analysis is pursued, the incremental cost-effectiveness ratio (ICER) will be derived and compared to the willingness-to-pay threshold. In addition, the net monetary benefit for each diagnostic strategy may be calculated. Additional outcomes such as the time to definite diagnosis, the number of diagnostic tests performed, and the impact on resource use will be captured to inform decision-making.

Given that an early use health-economic model design is proposed, the EAG will address any anticipated data gaps and uncertainties around the model conceptualisation, structure, and inputs. Transparent reporting of all modelling assumptions and limitations will be ensured within the external assessment report by

adhering to the Consolidated Health-Economic Evaluation Reporting Standards (CHEERS) checklist (Husereau et al. 2022). Uncertainty around the assumptions will be explored through expert validation and sensitivity analyses. Structural uncertainty (e.g., alternative pricing options or potential subgroup analyses) will be examined using scenario analyses if evidence allows. Parameter uncertainty will be assessed through probabilistic sensitivity analysis, implemented as a 10,000-iteration Monte Carlo simulation. To identify the key drivers of model outcomes, deterministic one-way sensitivity analyses will be conducted.

3.3 Cost of reversing a decision

The EAG will consider, if possible and depending on data availability, the impact of reversing the decision to introduce the included technologies into NHS practice. Implementation costs, such as equipment, one-off training costs, or necessary changes to the organisational pathway, will be estimated, validated by expert opinion, and tested in sensitivity analyses.

4. Evidence gap analysis

Outcomes outlined in the scope will be prioritised based on how they may impact clinical decision-making, patient-relevant benefits, and/or health-economic modelling. A table will be used to classify the strength of the available evidence. The accompanying narrative will describe priority areas relating to elements of the scope where further research may be required, including population characteristics, clinical settings, and comparators. To help guide future research, the EAG will also outline potential study designs capable of addressing the identified uncertainties, drawing on clinical expert judgement to assess the practicality of the proposed approaches.

5. Handling information from the companies and other stakeholders

All data submitted by the companies in evidence and information requests by NICE, or data submitted by other stakeholders will be considered by the EAG if received by 13th March 2026. Information arriving after this date will not be considered. If the data included in the information provided meets the inclusion criteria for the review, they will be extracted and quality assessed following the procedures outlined in this

protocol. The EAG may seek clarification or additional information from companies and other stakeholders where necessary. All correspondence between the EAG and companies will happen through NICE.

Any 'commercial in confidence' data provided by a company and specified as such will be highlighted in blue and underlined in the assessment report. Any 'academic in confidence' data provided by company(s), and specified as such, will be highlighted in yellow and underlined in the assessment report. If confidential information is included in the economic model, the EAG will provide a copy of the model with 'dummy variable values' for the confidential values (using non-confidential values).

6. Additional information sources.

The EAG will engage with clinical experts appointed by NICE to clarify issues related to model design and execution, including clinical pathways, model structure, model inputs, and underlying assumptions. These experts will also provide feedback on the validity and suitability of the conceptual economic model.

7. Competing interests of authors

The authors declare no competing interests.

8. References

Caro, J. Jaime; Briggs, Andrew H.; Siebert, Uwe; Kuntz, Karen M. (2012): Modeling good research practices--overview: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force--1. In *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research* 15 (6), pp. 796–803. DOI: 10.1016/j.jval.2012.06.012.

Hooijmans, Carlijn R.; Tillema, Alice; Leenaars, Marlies; Ritskes-Hoitinga, Merel (2010): Enhancing search efficiency by means of a search filter for finding all studies on animal experimentation in PubMed. In *Laboratory animals* 44 (3), pp. 170–175. DOI: 10.1258/la.2010.009117.

Husereau, Don; Drummond, Michael; Augustovski, Federico; Bekker-Grob, Esther de; Briggs, Andrew H.; Carswell, Chris et al. (2022): Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. In *Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research* 25 (1), pp. 3–9. DOI: 10.1016/j.jval.2021.11.1351.

Appendix A: Draft search strategy

The following search strategy (Table 3) is for illustrative purposes only and will be amended in line with input from clinical experts.

Table 3. Exemplary draft search strings for MEDLINE (PubMed)

#	Search string	Contextual detail
1	Endometriosis*[tiab] OR Endometrioma[tiab] OR Endometrioses[tiab] OR Endometriomas[tiab] OR Endometriosis[majr]	Search for population (people suspected of having endometriosis)
2	EndoSure[tw] OR EndoSure*[tw] OR "Endo Sure"[tw] OR Endo Sure*[tw] OR DotEndo*[tw] OR "Dot Endo"[tw] OR DotEndo[tw] OR Dot Endo*[tw] OR "Dot Lab"[tw] OR DotLab[tw] OR DotLab*[tw] OR Dot Lab*[tw] OR EndoTest[tw] OR Endo Test*[tw] OR EndoTest*[tw] OR "Endo Test"[tw] OR Ziwig[tw] OR Ziwig*[tw]	Search for brand names and manufacturers of the included technologies
3	Diagnosis[tiab] OR Test[tiab] OR Diagnose*[tiab] OR Testing[tiab] OR Diagnostic[tiab] OR Tests[tiab] OR Signature[tiab] OR Screening[tiab] OR Diagnose[tiab]	Search for studies on diagnostic tests
4	Non-invasive[tiab] OR non-invasively[tiab] OR "non invasive"[tiab] OR "non invasively"[tiab] OR "Gastrointestinal myoelectrical activity"[tiab] OR noninvasive[tiab] OR noninvasively[tiab] OR electroviscerography[tiab] OR GIMA[tiab] OR electroviscerogram[tiab] OR miRNA*[tiab] OR Salivary[tiab] OR microRNA*[tiab] OR miRNome[tiab] OR microRNome[tiab] OR miRNA[tiab] OR microRNA[tiab] OR Saliva[tiab] OR “blood test”[tiab:~3] OR “blood testing”[tiab:~3]	Search for generic terms related to the tests
5	#3 AND #4	Combining the generic terms for the technologies of interest with diagnostic application

#	Search string	Contextual detail
6	#1 AND (#2 OR #5)	Combining all searches for intervention and population
7	English[la]	English language publications
8	2015/01/01:2026/02/23[edat] AND 2015/01/01:2026/02/23[dp]	Time frame in which the technologies in question have been in use (the final end date will be the day the search is performed and stated in the report)
9	#6 AND #7 AND #8	Limiting results to relevant language and time frame
10	"ex vivo"[tw] OR ex-vivo[tw] OR cadaver[tw] OR cadaveric[tw] OR "deceased donor"[tw]	Search for non-clinical studies to be excluded
11	Address[pt] OR Autobiography[pt] OR Biography[pt] OR Bibliography[pt] OR "Clinical Trial, Veterinary"[pt] OR "Collected Work"[pt] OR Comment[pt] OR Dictionary[pt] OR Directory[pt] OR "Duplicate Publication"[pt] OR Editorial[pt] OR "Expression of Concern"[pt] OR Festschrift[pt] OR "Historical article"[pt] OR "Interactive tutorial"[pt] OR Interview[pt] OR "Introductory Journal Article"[pt] OR Lecture[pt] OR "Legal Case"[pt] OR Legislation[pt] OR Letter[pt] OR News[pt] OR "Newspaper Article"[pt] OR "Observational Study, Veterinary"[pt] OR "Patient Education Handout"[pt] OR "Periodical Index"[pt] OR Portrait[pt] OR "Published Erratum"[pt] OR "Randomized Controlled Trial, Veterinary"[pt] OR "Retracted Publication"[pt] OR "Retraction of Publication"[pt] OR "Twin Study"[pt] OR "Video-Audio Media"[pt] OR Webcast[pt] OR Review[pt]	Search publication types to be excluded
12	"animal experimentation"[mh] OR "models, animal"[mh] OR invertebrates[mh] OR Animals[mh:NoExp] OR "animal population	Search for animal studies, adapted from Hooijmans

#	Search string	Contextual detail
	groups"[mh] OR chordata[mh:NoExp] OR "chordata, nonvertebrate"[mh] OR vertebrates[mh:NoExp] OR amphibians[mh] OR birds[mh] OR fishes[mh] OR reptiles[mh] OR mammals[mh:NoExp] OR primates[mh:NoExp] OR artiodactyla[mh] OR carnivora[mh] OR cetacea[mh] OR chiroptera[mh] OR elephants[mh] OR hyraxes[mh] OR Eulipotyphla[mh] OR lagomorpha[mh] OR marsupialia[mh] OR monotremata[mh] OR perissodactyla[mh] OR rodentia[mh] OR scandentia[mh] OR sirenia[mh] OR xenarthra[mh] OR haplorhini[mh:NoExp] OR strepsirhini[mh] OR platyrrhini[mh] OR tarsii[mh] OR catarrhini[mh:NoExp] OR cercopithecidae[mh] OR hylobatidae[mh] OR hominidae[mh:NoExp] OR "gorilla gorilla"[mh] OR "pan paniscus"[mh] OR "pan troglodytes"[mh] OR "pongo pygmaeus"[mh] OR ((animals[tiab] OR animal[tiab] OR mice[tiab] OR mus[tiab] OR mouse[tiab] OR murine[tiab] OR woodmouse[tiab] OR rats[tiab] OR rat[tiab] OR murinae[tiab] OR muridae[tiab] OR cottonrat[tiab] OR cottonrats[tiab] OR hamster[tiab] OR hamsters[tiab] OR cricetinae[tiab] OR rodentia[tiab] OR rodent[tiab] OR rodents[tiab] OR pigs[tiab] OR pig[tiab] OR swine[tiab] OR swines[tiab] OR piglets[tiab] OR piglet[tiab] OR boar[tiab] OR boars[tiab] OR "sus scrofa"[tiab] OR ferrets[tiab] OR ferret[tiab] OR polecat[tiab] OR polecats[tiab] OR "mustela putorius"[tiab] OR "guinea pigs"[tiab] OR "guinea pig"[tiab] OR cavia[tiab] OR callithrix[tiab] OR marmoset[tiab] OR marmosets[tiab] OR cebuella[tiab] OR hapale[tiab] OR octodon[tiab] OR chinchilla[tiab] OR chinchillas[tiab] OR gerbillinae[tiab] OR gerbil[tiab] OR gerbils[tiab] OR jird[tiab] OR jirds[tiab] OR merione[tiab] OR meriones[tiab] OR rabbits[tiab] OR rabbit[tiab] OR hares[tiab] OR hare[tiab] OR diptera[tiab] OR flies[tiab] OR fly[tiab] OR dipteral[tiab] OR drosphila[tiab] OR	et al. 2010(Hooijmans et al. 2010), to be excluded

#	Search string	Contextual detail
	drosophilidae[tiab] OR cats[tiab] OR cat[tiab] OR carus[tiab] OR felis[tiab] OR nematoda[tiab] OR nematode[tiab] OR nematodes[tiab] OR sipunculida[tiab] OR dogs[tiab] OR dog[tiab] OR canine[tiab] OR canines[tiab] OR canis[tiab] OR sheep[tiab] OR sheeps[tiab] OR mouflon[tiab] OR mouflons[tiab] OR ovis[tiab] OR goats[tiab] OR goat[tiab] OR capra[tiab] OR capras[tiab] OR rupicapra[tiab] OR chamois[tiab] OR haplorhini[tiab] OR monkey[tiab] OR monkeys[tiab] OR anthropoidea[tiab] OR anthropoids[tiab] OR saguinus[tiab] OR tamarin[tiab] OR tamarins[tiab] OR leontopithecus[tiab] OR hominidae[tiab] OR ape[tiab] OR apes[tiab] OR pan[tiab] OR paniscus[tiab] OR "pan paniscus"[tiab] OR bonobo[tiab] OR bonobos[tiab] OR troglodytes[tiab] OR "pan troglodytes"[tiab] OR gibbon[tiab] OR gibbons[tiab] OR siamang[tiab] OR siamangs[tiab] OR nomascus[tiab] OR symphalangus[tiab] OR chimpanzee[tiab] OR chimpanzees[tiab] OR prosimians[tiab] OR "bush baby"[tiab] OR prosimian[tiab] OR "bush babies"[tiab] OR galagos[tiab] OR galago[tiab] OR pongidae[tiab] OR gorilla[tiab] OR gorillas[tiab] OR pongo[tiab] OR "pongo pygmaeus"[tiab] OR orangutans[tiab] OR pygmaeus[tiab] OR lemur[tiab] OR lemurs[tiab] OR lemuridae[tiab] OR horse[tiab] OR horses[tiab] OR equus[tiab] OR cow[tiab] OR calf[tiab] OR bull[tiab] OR chicken[tiab] OR chickens[tiab] OR gallus[tiab] OR quail[tiab] OR bird[tiab] OR birds[tiab] OR quails[tiab] OR poultry[tiab] OR poultries[tiab] OR fowl[tiab] OR fowls[tiab] OR reptile[tiab] OR reptilia[tiab] OR reptiles[tiab] OR snakes[tiab] OR snake[tiab] OR lizard[tiab] OR lizards[tiab] OR alligator[tiab] OR alligators[tiab] OR crocodile[tiab] OR crocodiles[tiab] OR turtle[tiab] OR turtles[tiab] OR amphibian[tiab] OR amphibians[tiab] OR amphibia[tiab] OR frog[tiab] OR frogs[tiab] OR	

#	Search string	Contextual detail
	bombina[tiab] OR salientia[tiab] OR toad[tiab] OR toads[tiab] OR "epidalea calamita"[tiab] OR salamander[tiab] OR salamanders[tiab] OR eel[tiab] OR eels[tiab] OR fish[tiab] OR fishes[tiab] OR pisces[tiab] OR catfish[tiab] OR catfishes[tiab] OR siluriformes[tiab] OR arius[tiab] OR heteropneustes[tiab] OR sheatfish[tiab] OR perch[tiab] OR perches[tiab] OR percidae[tiab] OR perca[tiab] OR trout[tiab] OR trouts[tiab] OR char[tiab] OR chars[tiab] OR salvelinus[tiab] OR "fathead minnow"[tiab] OR minnow[tiab] OR cyprinidae[tiab] OR carps[tiab] OR carp[tiab] OR zebrafish[tiab] OR zebrafishes[tiab] OR goldfish[tiab] OR goldfishes[tiab] OR guppy[tiab] OR guppies[tiab] OR chub[tiab] OR chubs[tiab] OR tinca[tiab] OR barbels[tiab] OR barbus[tiab] OR pimephales[tiab] OR promelas[tiab] OR "poecilia reticulata"[tiab] OR mullet[tiab] OR mullets[tiab] OR seahorse[tiab] OR seahorses[tiab] OR "mugil curema"[tiab] OR "atlantic cod"[tiab] OR shark[tiab] OR sharks[tiab] OR catshark[tiab] OR anguilla[tiab] OR salmonid[tiab] OR salmonids[tiab] OR whitefish[tiab] OR whitefishes[tiab] OR salmon[tiab] OR salmons[tiab] OR sole[tiab] OR solea[tiab] OR "sea lamprey"[tiab] OR lamprey[tiab] OR lampreys[tiab] OR pumpkinseed[tiab] OR sunfish[tiab] OR sunfishes[tiab] OR tilapia[tiab] OR tilapias[tiab] OR turbot[tiab] OR turbots[tiab] OR flatfish[tiab] OR flatfishes[tiab] OR sciuridae[tiab] OR squirrel[tiab] OR squirrels[tiab] OR chipmunk[tiab] OR chipmunks[tiab] OR suslik[tiab] OR susliks[tiab] OR vole[tiab] OR voles[tiab] OR lemming[tiab] OR lemmings[tiab] OR muskrat[tiab] OR muskrats[tiab] OR lemmus[tiab] OR otter[tiab] OR otters[tiab] OR marten[tiab] OR martens[tiab] OR martes[tiab] OR weasel[tiab] OR badger[tiab] OR badgers[tiab] OR ermine[tiab] OR mink[tiab] OR minks[tiab] OR sable[tiab] OR sables[tiab] OR	

#	Search string	Contextual detail
	gulo[tiab] OR gulos[tiab] OR wolverine[tiab] OR wolverines[tiab] OR mustela[tiab] OR llama[tiab] OR llamas[tiab] OR alpaca[tiab] OR alpacas[tiab] OR camelid[tiab] OR camelids[tiab] OR guanaco[tiab] OR guanacos[tiab] OR chiroptera[tiab] OR chiropteras[tiab] OR bat[tiab] OR bats[tiab] OR fox[tiab] OR foxes[tiab] OR iguana[tiab] OR iguanas[tiab] OR "xenopus laevis"[tiab] OR parakeet[tiab] OR parakeets[tiab] OR parrot[tiab] OR parrots[tiab] OR donkey[tiab] OR donkeys[tiab] OR mule[tiab] OR mules[tiab] OR zebra[tiab] OR zebras[tiab] OR shrew[tiab] OR shrews[tiab] OR bison[tiab] OR bisons[tiab] OR buffalo[tiab] OR buffaloes[tiab] OR deer[tiab] OR deers[tiab] OR bear[tiab] OR bears[tiab] OR panda[tiab] OR pandas[tiab] OR "wild hog"[tiab] OR "wild boar"[tiab] OR fitchew[tiab] OR fitch[tiab] OR beaver[tiab] OR beavers[tiab] OR jerboa[tiab] OR jerboas[tiab] OR capybara[tiab] OR capybaras[tiab]) NOT medline[SB])	
13	#9 NOT (#10 OR #11 OR #12)	Relevant studies minus exclusions