EU PROPOSALS FOR A NEW DIRECTIVE ON THE PROTECTION OF ANIMALS USED FOR SCIENTIFIC PURPOSES	
Q1: What are your views on the proposed inclusion of animals bred for their tissues and organs within the scope of the proposal and our estimate of its impact?	• In order to increase transparency around the total number of animals used in research it is desirable to include them in annual returns. This is already done in a number of Member States. At least two UK establishments already account for these animals within their internal systems, which shows that it is feasible for some – although each establishment will of course have its own specific circumstances. • It is very important that the Directive does not regulate the use of tissue or organs from animals killed for reasons unrelated to scientific research. This includes, for example, sampling tissues and organs from animals killed in abattoirs for consumption, euthanased by veterinarians for animal welfare reasons or killed using "pest control" methods because they are regarded as vermin. Use of these organs and tissues can contribute to animal welfare research as well as the development and use of alternatives and there would be no welfare benefit in regulating their collection. • Animals euthanased solely so that their tissues and organs can be used in research and testing could be within the scope of the Directive but be excluded from the need for Project Licences. In this scenario, someone would have to be designated as responsible for collecting the data.
Q2: What are your views on the provisions regarding the protection of immature forms and our estimate of their impact?	• Evidence for the precise stage at which immature forms develop the capacity to experience pain, suffering, or distress is not clear, although their capacity to be viable and in some cases their active behaviour prior to birth or hatching indicates that they should be protected in the later stage. • Protection for immature forms has worked in current UK legislation without undue problems. • Moving to two thirds of the way through gestation or incubation, from the current UK dividing line of half way, is likely to have a negligible impact on welfare. It might have the advantages of being more in accord with the concept of "trimesters" in humans and might be of practical help, since the gestation/incubation of the most commonly used laboratory species of both mammals and birds (21 days) divides more conveniently into three parts than two. • The Parish amendment 30 proposes to insert the words "of species of mammals". This is

	misleading, as it appears to exclude the other non-larval classes of animals, i.e. birds and reptiles. This amendment should not be supported. • The proposed provisions otherwise should be supported.
Q3: What are your views on the inclusion of cyclostomes, cephalopods and crustacean decapods within the scope of the proposal? Can you provide any information on their current use in the UK for experimental or other scientific purposes?	• Cyclostomes (Agnatha) lie within the Subphylum Vertebrata according to the National Biodiversity Network (http://nbn.nhm.ac.uk/nhm/animalia.shtml). Cyclostomes should thus be included within the scope unless there is scientific justification for excluding them. • There is debate about the ability of cephalopods and decapod crustaceans to experience pain, suffering and distress. A number of studies on cognition and pain in these species have concluded that either these animals can suffer, or the criteria for determining this are wrong or insufficient. If decapod crustacea and cephalopods are to be given the benefit of the doubt, then scientific procedures on them should be regulated. • Publications regarding the ability of decapods to feel pain are few and very recent and there has not been time for a scientific consensus to develop. However, this does not mean that it is right to ignore this group as there is certainly not sufficient evidence to exclude them. • We propose that the Directive should provide a mechanism to include cephalopod and decapods as and when there is sufficient evidence. This might be decided by an expert committee which should include those who work with the species, ethologists and animal welfare scientists. It should be understood that, as for any other animal including those currently protected, it is not possible to conclusively prove the ability to suffer and therefore ultimately decisions have to be made on the balance of the evidence (see also Q66). • Including cephalopods and decapods in the Directive would clearly require resources, e.g. bureaucratic costs in terms of counting and reporting, and could detract from their use in developing alternatives. However, if these animals are capable of suffering, their use cannot be regarded as an alternative. • If some invertebrate species are included in the new Directive, concerns about counting these animals could be addressed by regulating their care and use but not requiring statistics on procedures to be submitted centrally. • The APC cannot provide any information on the use of cyclostomes, cephalopods or decapods in the UK.
Q4: Do you have any views on the proposed exemption affecting veterinary clinical trials?	• This exemption would currently affect few UK licences but could potentially leave some studies unregulated. If veterinary clinical trials are exempted, it is essential that appropriate controls be in place to ensure the welfare of the animals in the trials. An alternative mechanism to regulate

	veterinary clinical trials could be analogous to that which exists for human clinical trials. • The Royal College of Veterinary Surgeons and Veterinary Medicines Directorate could be involved in this process in the UK, with the equivalent bodies having oversight in other Member States. • If alternative safeguards to ensure that the Three Rs are implemented and safeguard animals against avoidable suffering are not feasible throughout Member States, veterinary clinical trials should be subject to the same level of scrutiny and authorisation as other animal studies (see also our response to Q35).
Q5: Do you have any views on the proposed "marking" exemption? Do you support the proposition that the most appropriate humane methods should be used?	• The APC supports the proposition that the most appropriate humane methods should be used. We are not aware of reasons why such a requirement would not apply. The term "appropriate" is presumably defined as the best balance between harms and benefits to the animal associated with the marking technique. • We welcome the use of the term "primary purpose", as this would allow some refinements to be implemented more easily. An example would be the ability to change to using microchips for identification that also include temperature transponders without the need for licensing this as a technique. These chips can provide body temperature data to assist with welfare assessment and the implementation of humane endpoints with no additional welfare cost to the animal. It would also allow tissue from ear notching for identification to be used to genotype animals without the need for additional authorisation.
Q6: Do you have any comments on our approach to the proposed exemption of non-invasive practices?	• This Article is in need of more explicit wording. The term "invasive" is commonly used to describe procedures involving surgery, yet there are many procedures that do not involve surgical interventions that can cause pain, suffering, distress and lasting harm. Even observation of animals can cause harms if animals are subjected to stress or habitat damage or prevented from feeding, for example. • The exemption should only apply to practices that do not cause pain, suffering, distress or lasting harm, such as simple observation of animals that has been fully refined to ensure that no disturbance is caused to the experimental subjects or any other animals. The APC supports the suggested approach.
Q7: Do you have any comments on any of proposed definitions set out in Article 3 and their implications? Are there any other terms used in the proposal that should be defined in this article? How would you define those	• *Procedure* – the important departure from ASPA here seems to be in relation to genetically altered (GA) lines. Their creation would be regulated but not their subsequent breeding, unless the alteration were known to involve pain, suffering, distress or lasting harm. Unregulated

terms?	breeding of GA lines could follow the creation of the line in as little as 6 weeks in mice, compared with two full lifespan generations (at least 2 years) under the current ASPA criterion for discharge of GA lines from legal control. Whilst removing large numbers of animals that do not suffer any adverse effects from unnecessary legal control would be widely welcomed, the APC's Working Group on the discharge of GA lines from ASPA highlighted practical difficulties associated with such a proposal and advised the need for a formally agreed welfare screening programme to provide assurances that animal welfare would not be compromised. • *Project & Establishment* - definitions are appropriate. • *Breeding and Supplying Establishments* – whilst Article 10 makes it clear that Annex II lists the species that must be bred specifically for use in procedures, the definition of breeding and supplying establishments does not refer to Annex II. This should be included to avoid the potential problems noted by the Home Office. • There is no definition of the Three Rs of replacement, reduction and refinement in the Directive proposal. This is a serious omission given that there is considerable variation in the interpretation of the Three Rs and some interpretations of the concept are regressive[1]. The APC suggests that the following be added to this Article: - *Replacement* refers to methods that avoid or replace the use of protected animals in regulated procedures. - *Reduction* refers to methods that minimise animal use and enable researchers to obtain comparable levels of information from fewer animals. Reduction also means obtaining more information from the same number of animals, thereby reducing future use of animals. - *Refinement* refers to improvements to husbandry and procedures that minimise pain, suffering, distress or lasting harm and improve animal welfare. Refinement is applied to the lifetime experience of the animal, which includes not only husbandry and procedures but also sourcing, breeding transport, identification, handling, welfare assessment and euthanasia.
Q8: Do you have any comments on the provisions of Article 4 relating to replacement, reduction and refinement?	• The APC strongly supports the inclusion of an Article on the Three Rs. • It is important that paragraph 4 (1) is understood to refer to replacement in the full range of animal use disciplines, not just regulatory toxicology. It is also important that alternatives are used wherever possible, and in this context the phrase "reasonably and practically available" is open to interpretation. To take these issues into account, paragraph 4 (1) should read "*Where*

[1] Buchanan-Smith HM *et al.* (2005) Harmonising the definition of refinement. *Animal Welfare* **14:** 379-384

	a scientifically satisfactory and internationally accepted method or testing strategy exists, by means of which the information sought may be obtained without the use of a procedure, Member States shall ensure that the alternative method or strategy is used." • Paragraph (3) on ensuring refinement should be expanded to encompass the entire lifetime experience of the animal, including transport, identification, handling, humane killing, reuse and rehoming. • There should also be a requirement for Member States to encourage the development of refinements to all of the above.
Q9: Do you have any comments on the proposed permissible purposes?	• The protection of human health in the context of workers' or consumers' exposure to chemicals should be included. • The breeding (as opposed to creation) and maintenance of GA animals with harmful defects, or animals with other harmful genetic defects, should also be included.
Q10: What are your views on the implications of the requirements relating to humane killing? Is there evidence-based alternative provision you believe should be considered?	• Methods of humane killing should be controlled on animal welfare grounds and built on evidence-based knowledge. Annex V broadly provides a basis for doing this in the same way as does Schedule 1 to ASPA, but the APC has deep concerns regarding both the approach of the Annex and some of the techniques included in it (see Q70). • Parish Amendment 52 would allow non-Annex V methods to be used where they are scientifically demonstrated to be at least as humane. This would allow a degree of flexibility but it is essential that the humane nature of the method is evidence-based and controlled by other animal welfare legislation. It would be better to have a more flexible Annex that would provide relevant parties such as regulatory bodies, veterinarians and researchers with guidance on making decisions about techniques. • The Parish Amendment 52 also adds that non-Annex V methods that are *more* humane would be allowed, but apparently without the need for this to be scientifically demonstrated. This should have to be evidence based as well. • The Directive should require that animals are killed by a person who is both authorised and competent.
Q11: What are your views on the provisions protecting endangered species? Are you aware of any current classes of animal use in the UK that would be affected?	• There does not seem justification within a harm-benefit analysis to use endangered species in experimentation related to "avoidance, prevention, diagnosis or treatment of disease or other abnormality" related to plants. The phrase "for translational or applied" suggests that basic research that by necessity needs to be performed in endangered species, will be excluded and

	this may negatively impact on subsequent development of translational or applied research. • The APC is aware of research using endangered species in the UK, but this is carried out with the purpose of preserving the species which would be permissible under the proposal.
Q12: What are your views on the provisions limiting the use of non-human primates?	• Proposals to limit primate research to that which could ameliorate “life-threatening or debilitating” conditions may lead to some fundamental studies being done in non EU countries. • However, the term “debilitating” literally means “weakening” or “incapacitating”. On that basis, it is not clear whether or to what extent the current wording of the proposal would have an impact on primate research in the EU. The APC therefore believes that this Article is not meaningful as currently drafted. • Regarding restrictions on primate use *per se*, some APC members believe that these are justified on animal welfare and ethical grounds. Those in the proposal are proportionate to the level at which primates can suffer and public concerns about the acquisition and use of these animals. • Most members believe that instead of restrictions on primate use, authorisation requirements and ethical reviews should be sufficiently robust to ensure that primate experiments are appropriately challenged as a "built in" part of the process. This should take into account the cognitive abilities of these animals and possible links between these and their ability to suffer. This approach does not devalue concerns about primate use, but instead argues that appropriate ethical review is required for all species. However, it also assumes that all Member States and establishments will have appropriate review mechanisms in place to achieve this, and some APC members doubt whether this will be uniformly possible. • All APC members recognise that the use of primates is controversial and respect the view that their use should be proportionate and very well justified. Authorisation for such use must be well controlled, particularly when the severity band is more than mild, and any limits on primate use must be clear and enforceable. The authority to use primates should be evaluated according to criteria that include: the applicant's track record of implementation of the Three Rs; the ability to provide high standards of welfare and minimise suffering within the project; the institutional track record of compliance with the law and its “culture of care”; and the effectiveness of its ERB.
Q13: What are your views on the provisions relating to Great apes?	• The draft proposal is pragmatically worded. Even if Great Ape experiments were banned, any scenario requiring their use would probably be exceptionally serious and urgent, such that these animals would be used regardless of the Directive and national laws. We hope that the

	likelihood of this would be extremely small.
Q14: What are your views on the provisions limiting the use of animals taken from the wild? Would there ever be justification for the use of such animals on the grounds that suitable purpose-bred animals were not available?	• There are serious animal welfare issues associated with capture in the field with respect to stress caused to the trapped individual, the potential for injury and the disruption that may be caused to other animals and the environment. These harms may be underestimated in the harm-benefit assessment. The APC therefore agrees that there should be an assumption against using wild-caught animals in the Directive. • The clause relating to exemptions is sensible and precautionary. The circumstances that could arise and provide scientific justification for the use of animals taken from the wild are not always predictable.
Q15: Do you have any comments on the proposed requirements regarding the use of purpose-bred animals? Are you aware of any potential problems with the likely availability of sufficient, suitable, purpose-bred animals?	• Exemption should only be allowed on the basis of a rigorous scientific justification when purpose-bred animals are not available. This should also be subject to a rigorous harm-benefit assessment to take account of any animal welfare issues or public concerns.
Q16: What are your views on the proposed timetable(s) for the switch to the use of F2+ non-human primates? Do you agree that a feasiblity study should be carried out to identify the best way forward?	• Time lines for the switch for macaques should be unspecified until it has been demonstrated that self-sustaining colonies can be established. There could be both welfare issues and supply implications unless this switch is carefully managed. • The process should be informed by conducting a study into both the feasibility of developing self-sustaining colonies and the full, direct and indirect, implications for primate welfare in the short and long term.
Q17: Do you have any comments on proposed prohibition of the use of stray and feral domestic animals?	• The use of stray or feral animals could: (a) lose public confidence that missing pets cannot be used in experiments; (b) undermine the general use of consistently high quality animals in procedures; (c) have very little application in practice because of the limited use of the species that would be appropriate. • Therefore, the proposal not to normally allow their use should be supported. The only exception to this should be where the use of stray or feral animals is scientifically justified in order to conduct studies that could directly improve the welfare of these animals and where purpose-bred animals would not be suitable for scientific reasons.

Q18: Do you have any comments on the provisions of Article 12 relating to the conduct of procedures?	• We agree with the Home Office views on this Article.
Q19: Do you have any comments on the proposed requirements regarding the selection of methods to be used in procedures?	• The majority APC view is that the requirements are in line with current UK practice under ASPA and broadly in accord with the 3Rs principle. The proposal should be supported. • One APC member believes that the term "reasonably and practically available" presents too much of a loophole for establishments to interpret this as not having to use alternatives if they do not have the facilities and/or it will be too expensive to change.
Q20: Do you have any comments on the proposed requirements regarding death as an endpoint?	• We agree with the Home Office view. • One APC member believes that death as an endpoint is totally unacceptable and that humane endpoints should always be applied. If this is not possible, the study should not be permitted.
Q21: Do you have any comments on the proposed requirements regarding anaesthesia? Or our concerns about the inadequate provision made for post-operative animals?	• To imply that anaesthesia is the general default for all procedures may be unwise. Other approaches to alleviation of pain may be more suited (e.g. analgesics) and should be considered on a case-by-case basis. • Paragraph 2 (b) would permit anaesthesia to be withheld for scientific reasons for all but "serious injuries that may cause severe pain". One member believes that this is unacceptable and the paragraph should be deleted. Others take the view that the member's objection is too sweeping and would prevent research into some debilitating diseases; this issue should be addressed by an effective system for harm-benefit analysis. In any case, the term "serious injuries" is ill-advised; the phrase "involves serious injuries that" should be deleted. • Regarding post-operative care, it is difficult to envisage how 'considerable pain' as opposed to 'any pain' can be defined and used for decision-making. Appropriate treatment to minimise and alleviate any level postoperative pain should be the default, not least for reasons of animal welfare. • In some cases there may be scientific justification for the use of neuromuscular blocking agents (NMBA) in some protected species without anaesthesia. For example, NMBA may be used solely for the purpose of restraint in tadpoles. This should only be permitted if there is no evidence that the animal will suffer as a consequence (e.g. some animals may experience distress due to being paralysed while conscious). Paragraph (4) should therefore forbid the use of drugs that stop or restrict animals from showing pain without an adequate level of anaesthesia or analgesia *if potentially painful or distressing procedures are subsequently to be carried out*.

Q22: Do you have any comments on the proposed severity classification requirements? Or our belief that fuller details must be agreed before a new directive is adopted?	• It is essential that a severity classification be established before the Directive is finalised. A number of provisions, including this one, cannot be interpreted until this is in place. • See also our response to Meg Hillier, February 2009 (Section 2).
Q23: Do you have any comments on the proposed limitation on the performance of "severe" procedures? Or our belief that it may prohibit important areas of research?	• The majority view within the APC is that prohibiting procedures that are "severe" and prolonged is likely to limit investigation into diseases such as neurodegenerative conditions and chronic fibrotic disease and those associated with ageing. Redrafting is essential. • One member believes that the onus should be on animal users to endeavour to reduce either severity or duration – preferably both – so as to avoid causing these levels of suffering to animals.
Q24: Do you have any comments on the provisions for re-use or the impact it would have on current UK practice?	• The re-use of animals is a contentious area. Allowing re-use can be a means of implementing reduction, but there must be safeguards to prevent individual animals bearing an undue degree of suffering for reasons of financial or other expedience. The proposals provide a means to balance these considerations. • However, the Home Office concerns that the proposals could result in unnecessary use of additional animals by disallowing re-use involving moderate severity procedures seems justified, and the proposed balance of considerations should be reviewed. • The APC therefore concurs with the Home Office concerns around the assessment of animals in re-use situations.
Q25: Do you have any comments on the provisions regarding the end of procedures? Or the reservations set out above?	• We agree with the Home Office views on this Article. • It takes a positive approach in that death following procedures is not the default fate of the animal, notwithstanding the fact that tissues or organs may be required. This proviso should be added to the text, but in such a way that it is clear experimental animals should not routinely be euthanased following procedures. • There would have to be a sound support framework for the veterinarian if s/he is to bear responsibility for deciding on whether or not animals should remain alive.
Q26: Do you have any comments on the proposed requirement regarding the sharing of organs and tissues and how it might be implemented in practice?	• We agree with the Home Office appraisal of the Article. We suggest a more realistic wording that Member States should 'encourage the establishment' of programmes for sharing organs and tissues of animals killed by humane methods.

Q27: Do you have any comments on the proposed requirement regarding the setting free and re-homing of animals?	• This is a positively worded Article that values the lives of research animals. It needs some further clarification to bring it more in line with standard practice under the ASPA. • A veterinarian or other suitably qualified person should certify that any animal to be rehomed or set free is in good health and is not likely to suffer as a result of having been used in procedures (if applicable). Animals to be set free should not have learned any inappropriate behaviours in captivity that may compromise their welfare or survival in the field. • Presumably "the environment" in paragraph 19 (b) includes other animals in the environment, such that the released animal(s) would not present a health or ecological hazard to existing populations[2].
Q.28: What are your views on the proposed provisions for personal authorisation? And the specific issues highlighted in our analysis?	• To achieve effective harmonisation of practices in the EU, more prescription is required in content and processes relating to training, supervision, assessment and maintenance of personal documented training competence record. In essence, this would provide a common framework. • Member States should recognise and mutually accept authorised documented training competence, which should be effective for fixed time periods. • Without overall governance of training providers in respect of authorisation of persons (Article 20) the Directive becomes little more than guidance. This will not lead to harmonisation. • We have also provided you with our views on this Article in our initial response to Meg Hillier, submitted in February 2009 (Section 1).
Q29: Do you have any comments on the proposed requirement for authorisation of establishments? Or our analysis of their impact?	• It is important that this Article clarifies what is meant by "all breeding, supplying and user establishments". In the case of breeding and supply facilities, it should apply only to those establishments that breed and/or supply the species listed in Annex II and this should be made clear in the text. Otherwise, this could be interpreted as all experimental animals having to be obtained from designated facilities. This could have negative implications for resources and the Three Rs, if there is a requirement to maintain stocks of rarely used animals.
Q.30: What are your views on the proposed provisions for the mandatory suspension and withdrawal of	• Suspension and withdrawal of authorisation for minor technical infringements of non-compliance allows no flexibility and would require an establishment to stop all work, requiring

[2] Association for the Study of Animal Behaviour (ASAB) (2006) Guidelines for the treatment of animals in behavioural research and teaching. *Animal Behaviour* **71:** 245-253

authorisation of establishments for non-compliance with the provisions of the directive and on our preference for a more proportionate approach?	animals to be killed. • This would be a disproportionate response and with no mechanism for appeal it is unreasonable. It would also be a very strong disincentive to self-reporting, to the detriment of animal welfare. • We agree with the proportionate approach suggested by the Home Office, and also consider that Article 55 adequately addresses this issue. • However, we note that there is a significant risk that a proportionate approach may become an ineffective approach if there are inadequate sanctions to deal with infringements in organisations that do not have the necessary internal management structures operating alongside regulatory mechanisms. The public needs to be confident that the law is being enforced.
Q31: Do you have any comments on the proposed requirement for installations and equipment?	• The reference to 'obtaining consistent results' should be deleted from Article 23.2. The important point is the minimum use of animals with the minimum degree of pain, suffering, distress or lasting harm. Intrinsic biological variation can lead to inconsistent results on occasions.
Q32: Do you have any comments on the proposed requirement for personnel in establishments?	• We agree with the Home Office proposal for "other suitably qualified experts" under certain circumstances. • There is widespread concern in establishments that the Parish Amendment 86 requires at least one trained person to be available in establishments at all times to look after the animals' welfare and summon the vet if necessary. This would be impractical for a number of reasons. There would need to be several such staff in the case of staff quarantine restrictions between areas, staff could run up against EU working time restrictions, and overly frequent or unnecessary checking can be disruptive to animals. It would be more feasible, and better for animal welfare, to require that personnel should be available in circumstances where the veterinarian deems it necessary.
Q33: Do you have any comments on the roles proposed for the animal welfare and care person and designated veterinarian?	• It is not appropriate to place a responsibility for identifying and rectifying non-compliance on the NACWO equivalent. They of course should report non-compliance if they come across it, but the level of responsibility within the proposal is unfair and will negatively affect their relationship with researchers. • Under the current ASPA, if an infringement affects welfare, the NACWO must notify the personal licensee if an animal gives cause for concern (if the licensee is not available, they

	must ensure that the animal is cared for and euthanase if necessary). We believe that this is an appropriate level of responsibility for the NACWO equivalent in relation to infringements.
Q34: Do you have any comments on the proposed requirement for permanent ethical review bodies (PERBs)? What are your views on their proposed membership? Is there a need to involve lay or external members?	• Local ERPs under ASPA have been generally accepted as a valuable means of propagating a culture in which animal welfare and the best scientific use of animals are under continual review and improvement. The proposed PERBs will fulfil a broadly similar function and should be welcomed. • The proposed mandatory membership is minimal, presumably in consideration of the widely differing nature and scale of establishments, but the types of member named are appropriate and should be supported. • Lay members can challenge the assumptions of a scientific advisory committee, scrutinise its processes and witness the quality and objectivity of scientific decision-making, serving both to ensure the maintenance of high-quality scientific advice and to improve public confidence[3]. The lack of a requirement for an external or lay member on PERBs is likely to raise public suspicion of a bias toward self-serving expedience from the establishment, and an objective, disinterested voice as a mandatory member of the PERB should be reconsidered. However, it would be important clearly to define what constitutes a "lay" or "external" member. In the view of the APC, this is someone who is not involved in animal experimentation and is independent of the establishment (i.e. unaffiliated). • It would also be useful to give guidance on other types of members whose inclusion or advice would be valuable, such as experts in statistics and experimental design or ethicists. • Please see also our views on the PERB in response to Meg Hillier, February 2009 (Section 3).
Q35: What are your views on the proposed tasks of permanent ethical review bodies?	• The proposed tasks are largely in line with those of the current LERPs under ASPA, and therefore should be broadly supported for reasons given in bullet point 1 in the previous question. • The requirement to review all projects over 12 months in duration annually would add considerably to the current burden in many establishments where large numbers of projects are carried out. This would introduce the risk that PERBs would tend to carry out the reviews superficially, as an administrative task, without adding real value by the exercise. A better basis might be less frequent but more thorough and valuable project reviews, for example at the half

[3] House of Lords Select Committee on Science and Technology (2000) *Third Report: Science and Society.* London: The Stationery Office. http://www.publications.parliament.uk/pa/ld199900/ldselect/ldsctech/38/3801.htm

	way stage or, in the case of longer projects, at roughly one third and two thirds of its duration. The timing of these reviews should be at the discretion of the PERB. • The proposed requirement for records of recommendations and subsequent responses from PERBs is welcome, since defined output of such bodies is good practice and would help to avoid PERBs acting more as discussion groups than as a means of effective management. • Further definition is required relating to specialist skills input to institutional PERBs. It is essential for optimal study design and proper evaluation of projects that expert statistical input is available, and this input is documented, e.g. by having each study 'signed off' by a statistician before submission to the Competent Authority. Otherwise, inappropriately designed experiments may be conducted unless they are identified by statistical experts in the Competent Authority (Article 37, Ethical Evaluation). • Statistical input to clinical trial design, analysis and interpretation is required for both regulatory bodies and the responsible institutions running trials. It is equally important, ethically, that animal studies are planned and executed with the same diligence to ensure both good science and minimum harm to animals. Hence the need for statistician input at both user institutions (PERBs) and the regulatory body (Competent Authority). • It is also essential that user establishments access appropriate statistical input to optimise and monitor performance of animal models throughout the life of a project licence (as part of Three Rs improvements and scientific review). For example, it is possible that animal models used on multiple occasions, e.g. as part of a screening cascade, stop working. This needs to be detected and resolved. Otherwise results are not reproducible, leading to less confidence in data and decisions, animals are wasted, and additional scientific effort is required for avoidable re-work.
Q36: What are your views on the proposed requirement that establishments breeding and supplying non-human primates shall have a strategy for increasing the supply of F2 animals?	• We agree with the Home Office position. Any legislation could only apply to breeders in the EU. Even supplying establishments within the EU cannot force a breeder outside of this territory to provide a breeding strategy to increase the proportion of animals that are F2+. • The need to change to F2+ primates is not in dispute. A number of authoritative reports have stated that moving to F2+ is desirable due to the pressing animal welfare, health and scientific concerns, such as the reports by SCAHAW[4] and the APC Primates Sub-committee[5]. Trapping

[4] European Commission (EC) Scientific Committee on Animal Health and Animal Welfare (SCAHAW) (2002) *The Welfare of Non-human primates Used in Research.* EC: Brussels

[5] APC Primates Sub-committee (2006) *Acceptance of Overseas Centres Supplying Non-human Primates to UK Laboratories*. APC: http://www.apc.gov.uk/reference/primate-sources-report.pdf

	wild primates can cause significant distress, suffering and physical injury. There are also a number of scientific implications, e.g. using animals only one generation away from the wild would be unthinkable in other species such as rats or mice for scientific reasons. • We note that the EU is a relatively small user of primates on a global scale, and that breeding establishments of non-human primates are mostly located outside the EU. The requirement to have a strategy to increase supply of F2+ animals to the EU, which is not a major customer of these suppliers, is likely to increase the costs of undertaking this type of research in the EU. This is because F2+ animals are more expensive and the cost is passed on to the customer requesting them, which has led to a two tier price structure at some breeding centres. • Notwithstanding this, the APC Primates Sub-committee suggested that breeding centres accepted to supply primates to the UK should have a strategy in place for moving to F2+ animals[4]. • Balancing the financial costs to primate users against the welfare implications of trapping from the wild, we agree that the Directive should include a strategy for "increasing the proportion of animals that are the offspring of non-human primates that have been bred in captivity". We recommend that the role of the NAWEC should include advising the Competent Authority on the suitability of overseas primate suppliers and monitoring progress towards supplying F2+ animals only. • It would be desirable within this Article that the Commission and Member States take all necessary measures to refine the breeding and supply process with immediate effect, including ensuring appropriate transport conditions.
Q37: What are your views on the requirement for re-homing schemes?	• The APC supports the requirement for re-homing schemes, as a means of increasing the likelihood of successful re-homing, which benefits both animal welfare and staff morale. • The word "ensures" could be changed to "includes", as appropriate habituation to stimuli that the animals may encounter when re-homed should also be provided wherever possible.
Q38: Do you have any comments on the recording requirements?	• The HO position should be supported on the understanding that, as under ASPA, it is often not practical to identify individuals of some species, e.g. rats and mice, for recording purposes.
Q39: Do you have any comments on the information on dogs, cats and non-human primates requirements?	• All establishments should keep adequate records on all species that go into appropriate detail depending on the numbers used and the length of time that projects run for. This is especially useful for retrospective analysis of projects and breeding strategies. • This Article simply sets out good practice for dogs, cats and non-human primates, although the

	reason for restricting the requirements to these animals is not clear. • The APC welcomes the requirement for individual history files, including social information, in non-human primates.
Q40 Do you have any comments on the requirements for marking?	• We agree with the Home Office comments on marking of animals.
Q41: Do you have any comments on the requirements for care and accommodation? Should the UK retain present standards where they exceed the recommendations in Annex IV?	• There needs to be greater flexibility in the requirements for care and accommodation and an allowance for deviation from the stated "standards" if this can be justified by the scientific question under investigation. The UK should not relax its present standards where it is felt they exceed the recommendations in Annex IV. • We make more detailed comments in our answer to Q69.
Q42: Do you have any comments on the requirements for national inspections?	• The APC broadly agrees that transparency, accountability, and comparability are key principles • Inspections need to be conducted uniformly across Member States to achieve harmonisation. This raises the question of whether there should be either minimal agreed criteria and a process with a single EU governance structure, or devolution of principles to be left to individual Member States to implement.
Q43: Do you have any comments on the provisions for audit of the operation of national inspections?	• It is important for the Directive to be applied consistently across Member States, and efficient audit of this would be needed to ensure harmonisation. The proposal should be supported. • The Home Office consultation document raises the issue of information disclosure, on which APC members also have some concerns. For example: - What information will be available to the Commission and its auditors? - How will information on individual institutes and their work be distributed, used and protected for academic, commercial and individual confidentiality and protection of competitiveness? • Clarification on these issues is required before the Directive becomes law.
Q44: What are your views on the proposal for authorisation of projects and on possible provision for notification of projects?	• In principle, the extent of control (authorisation) should be proportional to the potential harm caused by the procedures and therefore the potential welfare gains of regulation. • Projects containing moderate or severe procedures and all those involving non-human primates should be submitted to the competent authority together with the outcome of the ethical review process. A decision of the competent authority should be available within 30 or

	60 days depending upon the complexity of the project ("Submit & Wait"). • Projects containing only mild procedures should be submitted to the Competent Authority together with the outcome of the ethical review process and with notice of the intended start date. Authorisation by the Competent Authority can be made retrospectively ("Tell & Wait"). This should be undertaken on a risk based system taking into account the organisation, the individual, the species and the type of project. Below a certain defined threshold such projects could then be approved. This should not be applied in academia where there is much less internal management control. For commercial premises there should first be an assessment of the effectiveness of the PERB. • The Home Office suggests that, where projects are assessed at the parent establishment only, Competent Authority inspectors are likely to be reduced to focussing principally on monitoring compliance rather than engaging in discussion and assessment of projects. The APC believes that this would be a detrimental step. The current sanctions for non-compliance are relatively ineffective, and without engagement and discussion, inspectors would be reduced to being merely "tick box auditors" having little input to good science and welfare. • One member disagrees with the proportionate approach and believes that all projects should be subject to the same authorisation process by the Competent Authority. Mild procedures can involve large numbers of animals and there will inevitably be "grey areas" where procedures are of borderline moderate severity yet not authorised by the Competent Authority. This member considers that the level of authorisation set out in the proposal is the baseline for all levels of severity, and that more severe procedures should receive greater scrutiny. • It should also be noted that severity limits are yet to be defined within the Directive proposal.
Q45: Do you have any comments on the proposed content of applications for project authorisation?	• The majority of APC members agree with the Home office appraisal of this Article. • There appears to be considerable overlap between the requirements for Article 36 (project authorisation) and Article 37 (ethical evaluation). Both of these articles need redrafting to clarify that applicants need only provide one body of information that will be used for both authorisation and ethical evaluation, including the harm-benefit analysis. • Some members welcomed the opportunity for a reduced project proposal for mild projects not involving non-human primates, but the majority of the Committee believes that the same level of detail should be required for all regulated procedures. • It seems strange that the user establishment submits the application, rather than the researcher leading the project.
Q46: Do you have any comments on the proposals for	• The APC agrees with the Home Office analysis of this Article.

ethical evaluation of projects?	• With respect to "independent parties", It is essential that intellectual property and confidential information is safeguarded together with the safety of goods and persons (see Parish Amendment 116). • The Commission needs to clarify who the Competent Authority could be. A body like the Home Office is an independent party, but according to the proposals the Competent Authority could be the establishment itself. In this case the Competent Authority could not be independent without strong representation from an outside party.
Q47: Do you have any comments on the provisions for retrospective assessment of projects? Or our belief that further clarification is required?	• Retrospective assessment of project licences forms an integral part of the renewal or amendment process. The expectation is that this would only apply to project licences that are not renewed, which is likely to be small in number. • We agree that clarification of the body that would be responsible for this is needed. • The exemption of "up to mild" projects is not justified. Retrospective review of the actual adverse effects experienced by animals in such projects is vital for ensuring that harms are accurately predicted and appropriate judgements made on severity. All projects should be subject to the same level of review in any case. • One member believes that the basis for review should be proportionate to the severity of the work and that emphasis should be placed on those projects with moderate and severe procedures. This would allow more time for consideration and discussion of refinement.
Q48: Do you have any comments on the provisions relating to records of ethical evaluation?	• This seems confused. The proposals seem to say that it is the Competent Authority that would carry out ethical evaluations, but this article requires that the establishment would hold the records of these and submit them to the Competent Authority on request. • The proposal needs clarification or reviewing.
Q49: Do you have any comments on the requirement for project summaries and its impact on current UK practice?	• Non-technical project summaries (subject to IP safeguards) can be helpful ways of providing information about animal use to the general public. • Including comments relating to retrospective assessment with specified deadlines could be problematic, as time frames can change during the course of a scientific investigation, which limits the value of a stated deadline. • The majority of APC members believe that project summaries are an essential descriptive tool for ensuring transparency and fulfilling the public's right to know what animals experience in research and testing (most of which the public directly or indirectly funds). • One member feels that retrospective reviews would have to be so sanitised to avoid

	compromising IP or commercial confidentiality that their value would be considerably diminished. Peer review and publication of animal work would be a better mechanism to share learning.
Q50: Do you have any comments on the provisions for granting of project authorisations? Or our preference for retaining a five-year maximum duration for project authorisations?	• We concur with the Home Office view. Project authorisations should be granted for a 5 year period. • Authorisation of multiple projects, when these are carried out to fulfil legal requirements, removes unnecessary burden for routine regulatory and other safety testing without compromising animal welfare, provided that there are robust internal controls and ethical review. • One member disagreed with this, as it does not require the level of benefit of each substance under test, which can vary widely, to be taken into account.
Q51: Do you have any comments on the provisions for the amendment, renewal and withdrawal of project authorisations?	• Amendments to mild and moderate procedures that do not increase the severity of the procedure may be made by the permanent ERB but must be communicated to the competent authority within one week of such change. All decisions are open for scrutiny by the inspectorate and at project licence review stage. • Some members take the view that all levels of severity should be subject to the same scrutiny throughout the licensing process, including amendments.
Q52: Do you have any comments on the proposed provisions relating to authorisation decisions?	• EU Member States are likely to have different time frames for reaching decisions on project submissions - this should be properly investigated as it would be helpful to have evidence based clear understanding, state by state, of current practice. It would then be feasible to set out a workable time scale. • Once a workable time frame for a Competent Authority response has been agreed then there should be no non-responses from Competent Authorities. If a decision cannot be made due to complexity or other reasons then this should be communicated as a 'response'. These 'delayed' response should be dealt with on a case by case basis and numbers monitored with strict Key Performance Indicators for Competent Authorities • Delays are costly for all concerned and need to be avoided. • Authorisation by default could undermine confidence in the compliance approach.
Q53: Do you have any comments on the provisions relating to the sharing of data and any practical	• We agree with the Home Office position that widespread unnecessary duplication of procedures is not backed up by evidence.

suggestions how data sharing might be implemented in practice?	• Compulsory sharing of data generated by procedures would not be workable. There are no objections to sharing data per se, but there are intellectual property issues that must be respected in order to ensure protection from competitors. This would require properly set out standards and defined procedures for sharing pre-clinical data, which do not currently exist. Even with these safeguards, simply loading data onto a platform without a structure to ensure that it is searchable is unlikely to result in reductions in animal use. • Where there is evidence that duplication of procedures could take place, a number of focused initiatives are underway to avoid this. Examples include the RSPCA/FRAME/EFPIA database of toxicity information on excipients, the International Life Science Institute consortium of pre-clinical toxicology and the Innovative Medicines Initiative project.
Q54: Do you have any comments on the provisions to encourage the development of alternative approaches?	• Clearer definition of what is meant by a 'contribution' to the Three 3Rs by Member States is required before further informed comment can be made. • The desired outcome is presumably alternative approaches that are validated and accepted by the scientific and/or regulatory communities. A central reference laboratory or individual state/establishments are not likely to achieve this outcome alone. • New approaches gain acceptable scientific validation through publication and peer critique. The publication of more animal work, and more stringent journal reviews processes, will contribute here.
Q55: What are your views on the proposed requirements for the designation and functions of national reference laboratories?	• We agree with the Home office analysis of the value of National Reference Laboratories and share its concerns over the operation of such a venture.
Q56: What are your views on the proposed requirement for a national animal welfare and ethics committee and how it might be staffed and resourced?	• The APC supports this proposal in principle. • We have provided you with our views on this Article in our initial response to Meg Hillier, submitted in February 2009 (Section 4).
Q57: What are your views on the proposed arrangements for updating the technical annexes?	• The APC agrees that regular updates are essential. We note that Annex I is excluded, which is strange given the controversy over including these species.
Q58: Do you have any comments on the proposed reporting requirements?	• The Home Office position on this proposal should be supported.

Q59: Do you have any views on the safeguard clause? And its likely impact on current practice in the UK?	• See our answer to Q13 above.
Q60: Do you have any views on the proposal for the Commission to be assisted by a committee and of the need for the directive to contain more information on its terms of reference and composition?	• We share the Home Office views on the establishment of such a committee.
Q61: Do you have any views on Article 52?	• The APC agrees with the Home Office comments
Q62: Do you have any views on the proposal for review of the directive?	• The APC agrees that a 10 year review is essential. We also agree that regular and early review of the operation of the Directive is vital, as is a capacity to amend the Directive should any serious problems with application and/or compliance be identified.
Q63: Do you have any views on the provisions for competent authorities?	• It can be argued that under UK arrangements, the control of scientific use of animals has never sat comfortably within the Home Office remit, so flexibility in the selection of a Competent Authority could have benefits. • There is no regional basis to animal-based science in the UK, so no benefit is seen from having regional Competent Authorities. The need for consistency would seem to be better served by a national authority, at least in the UK. • The suggestion of self-regulation would present a serious risk to public confidence in the control of science's use of animals and be burdensome on establishments, possibly implying the need for two separate bodies within the establishment (PERB and Competent Authority).
Q64: Do you have any views on the provisions for penalties?	• Nothing to add to HO comments on this.
Q65: Do you have any views on Articles 56, 57, 58, 59 or 60?	• No comment.
Q66: Do you have any views on Annex I?	• As set out in the answer to Q3 above, Cyclostomes are a Class within the Subphylum Vertebrata, so they should not be listed here. • The Technical Expert Working Group on Scope proposed an Annex listing invertebrate species that were sentient and able to feel pain, on the basis of scientific evidence assessed by an

	expert Scientific Committee appointed by the EC (applying the precautionary principle). The APC supports this proposal. • More information is needed on the species of invertebrates used in research and testing, what type of procedures are conducted on them and what potential suffering may be caused in order to construct a meaningful Annex. A Scientific Committee should be set up to explore these questions. • We question why this Annex is not open to comitology, as it is clear that research into invertebrate sentience and cognition is ongoing and is likely to provide results that will inform decisions on which species should come under the Directive. Annex I should be flexible and capable of being updated as new knowledge becomes available.
Q67: Do you have any views on Annex II?	• Rabbits, ferrets and zebra fish should all be included in Annex II. • GA animals should be included in order to ensure that breeding GA animals, limiting any suffering, transporting them, assessing their welfare etc. are all properly regulated.
Q68: Do you have any views on Annex III?	• We do not understand how timescales can be set for the various species without first obtaining the results of the proposed study into the feasibility of switching to F2+. It is essential that this study be completed within the proposed timescale of eighteen months. • The switch to F2+ should then be accomplished within whichever time periods are recommended by the study, even if these differ from the estimates in the original draft.
Q69: Do you have any comments on Annex IV?	• The care and accommodation standards in Annex IV are largely appropriate, if somewhat inexplicit and lacking detail in some aspects. • The standards of care and accommodation in Annex IV should be usually mandatory, but open to exceptions by scientific or animal welfare justification to the Competent Authority. • The Annex is an abridged version of Appendix A to Council of Europe Convention ETS123, in which much of the explanatory text is missing. It would have been preferable for Annex IV to incorporate both the text and tables from Appendix A. The full text encouraged good practice, with advisory qualifications. It is a great pity from the point of view of animal welfare that so much of this text was removed when producing Annex IV. • The full text, plus tables, should be reinstated to provide a basic understanding of animals' welfare requirements and how to fulfil them in a flexible way. It would also re-establish the links to the important supplementary information in "Part B" to the species-specific guidelines. • Facilities should have the option to adopt additional provisions demonstrated to improve

	welfare, with advice from the Ethical Review Body. • Annex IV is not prescriptive on air conditions for any species other than reptiles and amphibians, merely stating that temperature and humidity should be "adapted to species housed" and that "the air in the room shall be renewed at frequent intervals". This is open to interpretation.
Q70: Do you have any comments on Annex V?	• The APC strongly agrees with the Home Office concerns over the inclusion and omission of some methods In Annex V. We also agree with the suggestion that the Annex be reconsidered and revised, preferably with reference to the APC report on Schedule 1 methods. • In particular, the Annex should emphasis that humane killing is a process that can be refined at a number of different stages. It should set out a framework for humane euthanasia, including the aim to minimise distress and why this is so important, and it should also be minimally prescriptive, flexible and easy to update. • The use of neuro-muscular blocking agents alongside anaesthetic agents for killing animals presents an unnecessary risk to welfare and would currently require specific justification and Project Licence authority under ASPA. There is no justification for its inclusion in Annex V.
Q71: Do you have any comments on Annex VI?	• It seems odd that element 6 uses the term "species-specific", but it would seem just as necessary in elements 3, 4, 5 and 7.
Q72: Do you have any comments on Annex VII?	• The elements listed are appropriate and promote the application of the 3Rs. • There are two serious omissions, however: (i) no requirement for the severity classification and (ii) no requirement for the proposal to have undergone local ethical review by the PERB. These should both be added to the Annex.
Section C: impact assessment	
	• The APC is not in a position to answer most of the specific questions in this section. • Many of the questions concern the monetary values of potential benefits to science, welfare, transparency and harmonisation. • There are important non-monetary benefits to better science, welfare, transparency and harmonisation that also deserve due consideration and weighting. These are set out in the Recitals to the Directive and include improved wellbeing of sentient animals, maintaining the confidence and trust of the public, and better science with respect to research directions and

	efforts. These advantages should not be downgraded or sacrificed in the name of monetary benefit.