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Commission of advice from the Animals in Science Committee

Non-human primates bred for use in scientific procedures

DATE:	23 June 2022
SUMMARY:	The capture of non-human primates (NHPs) from the wild gives rise to animal welfare, health, and ethical issues. The UK government wishes to clarify its policy on the use of NHPs bred for use in scientific procedures. This is in the context of European Directive 2010/63/EU, which the UK was committed to prior to its exit from the European Union and which from November 2022 is set to require EU Member States to use only non-human primates that are the offspring of animals which have themselves been bred in captivity, or that are sourced from self- sustaining colonies. The UK does not have this requirement in legislation, however, the government wishes to review this policy with due consideration to the animal protection imperative and in order to provide clarity and certainty for the UK science sector. Data shows that all NHPs used in the UK in 2020 were second generation captive and/or from self-sustaining colonies. However, new challenges have arisen in the international supply of NHPs for scientific purposes, in particular the ongoing export ban from China following Covid. The Committee is therefore requested to provide advice to the UK government on the policy questions set out, after carefully considering relevant factors.

1. Policy issue

The UK policy on non-human primates (NHPs) bred for use in scientific procedures requires review. The UK is no longer bound to align with the European Union's approach. However, noting that the UK was until recently on the same trajectory as the EU, which is expected to implement a significant policy change in November, clarity is needed for the UK science sector and interested stakeholders on the UK's policy position; specifically with respect to Article 10 of European Directive 2010/63/EU.

2. Context

The use of non-human primates (NHPs) in scientific procedures

NHPs (Marmosets, Cynomologus monkeys, Rhesus monkeys and other species) are used in scientific research for basic research, translational and applied research and for regulatory purposes. This has also included understanding the coronavirus infection process and testing for various health strategies/therapies. NHP models have provided a number of scientific step changes in human research and treatments and are a regulatory requirement for the testing of medicines. This latter requirement comes from '2nd species testing' where an NHP is a usual animal of choice due to its similarity to humans.

Non-endangered NHPs are specially protected species. This confers higher levels of protection under the Animals (Scientific Procedures) Act (1986) (ASPA) than other protected animals. The use of non-endangered NHPs can only be for:

- basic research;
- translational or applied research; or
- research aimed at preserving the species of primate being used.

Translational or applied research must be for the avoidance, prevention, diagnosis or treatment of debilitating or potentially life-threatening clinical conditions or their effects in humans, or the development, manufacture or testing of the quality, effectiveness and safety of drugs for the same purposes.

The use of endangered NHPs in research can only be for:

- translational or applied research (same limitations as non-endangered NHPs); or
- research aimed at preserving the species of primate being used.

The genetic proximity of NHPs to human beings and highly developed social skills gives rise to animal welfare, health, and ethical issues. The capture of NHPs from the wild is highly stressful for the animals and carries an elevated risk of suffering during capture and transport. Using NHPs born in captivity and familiar with human interaction can reduce animal suffering, in line with the 3Rs (Replacement, Reduction and Refinement); specifically refinement.

Background to European Directive 2010/63/EU

To end the capturing of animals from the wild for both scientific and breeding purposes, European Directive 2010/63/EU (the Directive)[1] set as one of its aims to allow, after an appropriate transition period, only the use of NHPs bred in captivity. See Annex 1 for recitals 17-19 of the Directive.

Specifically, Article 10(1) of the Directive requires, following the adoption by the European Commission of its feasibility study on 8 November 2017[2], that from November 2022 member states will ensure that all NHPs used in scientific procedures, as listed in Annex II of the Directive[3], would only be used where they are the offspring of NHPs bred in captivity (second generation or F2[4]), or from a self-sustaining colony.

Annex II is an integral part of the Directive adopted in 2010. Annex II cannot be amended through delegated / implementing (Member State) acts as it was specifically excluded in Article 50 on the adaptation of Annexes to technical progress by the Council when the Directive was negotiated. We understand there are currently no plans to open the Directive for amendments, therefore it is expected to come into force for EU Member States in November 2022.

The Directive only allows granting of exemptions to Article 10(1) on the basis of scientific justification.

The Commission is currently carrying out a second feasibility study on the sourcing of NHPs exclusively from self-sustaining colonies, as required under Article 10(2) to be published by 10 November 2022.

Current UK policy position

The UK transposed the Directive on 1st January 2013 through amending the Animals (Scientific Procedures) Act 1986 (ASPA). Prior to its exit from the EU, the UK was bound to follow the Directive and implement Article 10(1) in line with all EU member states.

The UK transposed into ASPA the Directive's Article 10(1) Annex II requirement for one species of NHP – marmosets (which came into force at that time) – but not for the other species of NHPs listed in Annex II of the Directive (due to the uncertainty at that time about when or if they would come into effect, pending the Commission's feasibility study).

The UK has no legal obligation to implement Article 10(1) of the Directive (beyond what has already been transposed into ASPA) or to change current policy on the use of NHPs.

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[1] https://www.legislation.gov.uk/eudr/2010/63
[2] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52017DC0631&from=EN
[3] Marmosets – from 1 January 2013; all other species of NHP – from November 2022.
[4] The 'F' refers to the filial generation; F1 is 'first filial generation (in this case the first offspring from wild-caught) and F1 then reproduce to form F2. An 'F0' denotes wild caught.

Nevertheless, there is likely to be public and sector expectation that the intent of Article 10(1) will be delivered in the UK given the animal protection benefits, the world-leading progress made in the UK already, and the leading role the UK played in the design of the Directive.

The current relevant UK government policy positions are:

- Marmosets are specifically named in ASPA Schedule 2C Section 25(d) as NHPs that *"must not be subjected to a regulated procedure as part of the specified programme of work unless it is the offspring of marmosets bred in captivity (F2) or it has been obtained from a self-sustaining colony of marmosets"*.

- For other species of NHPs there is a prohibition on using animals taken from the wild (F0) in scientific procedures but no prohibition on using F1 as long as they are purpose bred.

- Exceptions to the above are possible where there is scientific justification (ASPA Schedule 2C 25(3)).

- ASPA requires the UK government to ensure compliance with the principles of the 3Rs, notably Refinement in this context: *"the principle of refinement is the principle that the breeding, accommodation and care of protected animals and the methods used in regulated procedures applied to such animals must be refined so as to eliminate or reduce to the minimum any possible pain, suffering, distress or lasting harm to those animals."* (ASPA Section 2A(2)(c))

- ASPA also requires as a condition of project licences, the holder to ensure that the regulated procedures: *"involve animals with the lowest capacity to experience pain, suffering, distress or lasting harm"*. (ASPA Schedule 2C paragraph 18(1)(b)

- UK breeders are required to comply with the ASPA requirement (Schedule 2C paragraph 7) to have a strategy in place to increase the proportion of second generation NHPs.

- Self-sustaining colonies are defined in ASPA (ASPA Schedule 2C 25(6)) as a colony that:

    - is kept in captivity in a way that ensures the animals are accustomed to humans;
    - consists only of animals that have been bred in captivity (noting that this can include F1); and
    - is sustained only by animals being bred within the colony or animals being sourced from other self-sustaining colonies.

3. Evidence

The European Commission feasibility study

The Commission has, in consultation with member states and stakeholders, conducted a feasibility study on the requirement in the Directive to only use NHPs that are the offspring of animals which have been bred in captivity (F2+), or that are sourced from self-sustaining colonies. The feasibility study was produced on 31 July 2017[5]. The study found:

- significant progress made towards the use of F2+ NHPs within EU, citing the UK as an example;
- no specific scientific reasons not to use F2+ NHPs but feedback from the scientific community on the need to retain the exemption to the F2 requirement where there was scientific justification including in the case of non-availability of F2 (e.g. for animals with a specific health status such as Herpes B free);
- animal welfare and health quality will be improved by moving from wild-caught animals to those reared and bred in captivity, although risks of inbreeding and reduced reproductive success were noted;
- no observable cost impact with little or no price differential reported between supply of F1 or F2+ animals since 2007;
- that the transition dates set out in the Directive should remain, meaning an implementation date of November 2022.

UK statistics

The published statistics[6] show that of the 1,718 NHPs used in the UK for the first time in experimental procedures in 2020 (Table 2.3 of the data tables):

- all were from self-sustaining colonies;
- 1,354 were second generation (F2);
- 364 were first generation (F1) (from self-sustaining colonies);
- no wild caught (F0) animals were used.

Of the 1,718 NHPs used in the UK in 2020 (see Table 2.2 of the data tables):

- All (n=255) marmosets and tamarins and rhesus monkeys were born in the UK at a licensed establishment
- Whereas 98% of cynomolgus monkeys (n=1,463 total) were born in either Africa or Asia.

Thus, in 2020, the UK only used NHPs from self-sustaining colonies. This would indicate that prohibiting the use of all NHPs not either F2 or from a self-sustaining colony would have little impact on the UK science sector. However, recent developments mean this may not be the case (see below on international supply issues).

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[5] https://ec.europa.eu/environment/chemicals/lab_animals/pdf/related_topics/Article%2010%20Feasibility%20Study%20Final%20report%2031%20July%202017.pdf

[6] https://www.gov.uk/government/statistics/statistics-of-scientific-procedures-on-living-animals-great-britain-2020

The latest statistics for 2021 will be published on 30 June 2022 and the Committee will wish to consider these as part of the evidence base.

UK regulation

The Animals in Science Regulation Unit (ASRU) regulate the sector in accordance with the current ASPA legislation and associated guidance. Applications involving the use of NHPs are required to answer detailed questions about the origin of the NHPs and their generational status, and to justify their use. Applications that propose the use of wild-caught (F0) NHPs are currently referred to the Animals in Science Committee for additional advice[7].

The ASPA guidance[8] indicates that regulation of a wider range of NHPs is to be expected in future, stating: *"Other species of primate may, in due course, be subject to the same additional restrictions as marmosets"*.

Recent international supply issues

Recent events have changed the international landscape for NHP supply. There is a shrinking global supply of NHPs, caused by China's ongoing export ban on NHPs since 2020 following Covid and increasing research demand. Although exports from China were a relatively small proportion of the European market, it has a knock-on effect on global supply. This has resulted in an international shortage of Macaque monkeys (the key species used in EU and US laboratories) resulting in increased demand and rising costs for the remaining global supply, and greater pressure on other providers (particularly Mauritius).

Evidence gap

Further evidence is needed to inform the Committee's advice to the UK government to support consideration of the policy including:

- Impact on UK science sector of EU member states implementing Directive e.g. availability of animal products, global supply and cost, availability of NHPs to refresh UK colonies.
- Impact of the wider global supply challenges on availability of NHPs on supply for use in the in the UK, balanced against forecast UK demand.
- Assessment of the impact of policy choices on the harm and suffering to NHPs used in the UK.
- Other relevant evidence identified by the Committee or stakeholders.

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[7] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/871022/Annotated_PPL_v2.0_171221.pdf - guidance note D11.10

[8] https://www.gov.uk/guidance/guidance-on-the-operation-of-the-animals-scientific-procedures-act-1986 - Section 5.18.6

4. Policy choices

The government's primary objective is to improve animal welfare by stopping the use of use wild-caught NHPs in favour of NHPs bred in captivity (with exemptions possible where there is scientific justification); whilst ensuring that UK science continues to thrive.

With regard to both the legitimate requirements of science and industry and to the protection of animals against avoidable suffering and unnecessary use in scientific procedures, the Committee is requested to provide advice to inform four broad policy questions:

1. Should new requirements be applied to the use of NHPs in scientific procedures in the UK, such that they must be the offspring of NHPs bred in captivity (F2) or from a self-sustaining colony?

2. Which NHPs should any new requirements apply to – all species, or only some?

3. When should any new requirements come into force?

4. Where new requirements are applied for NHPs, what exemptions should be permissible, with what justification, and should certain exemptions be limited for a certain time period?

Depending on the answers to these questions, illustrative potential policy options could include (but are not limited to):

- Require or encourage **all** NHPs used in scientific procedures to be the offspring of NHPs bred in captivity (F2), or from a self-sustaining colony, with defined (and potentially time-bound) exemptions for scientific justification, from November 2022 or at a different time.

- Require or encourage **some** NHPs used in scientific procedures to be the offspring of NHPs bred in captivity (F2), or from a self-sustaining colony, with defined exemptions for scientific justification, coming into force on varying dates according to species.

- Do nothing.

There are three broad ways in which the UK government can look to implement any policy change (which will require further consideration of legal and practical issues depending on the policy choices):

- Amend ASPA to include further NHP species in addition to marmosets at Schedule 2C Section 25(d), noting that securing change to primary legislation is likely to be very slow to implement.

- Set policy position in guidance and implement through regulator guidance as part of 3Rs requirement, including guidance on grounds for exemptions.

- Set expectation and encourage as leading practice with sector self-regulating.

5. Advice sought from the Animals in Science Committee

The Committee is asked to provide written advice on the four policy questions set out above, after carefully considering relevant factors including:

- the need to reduce animal harm and suffering in line with the 3Rs;
- the impact on the UK science sector and consequential outcomes (e.g. delivery of new medicines, new scientific discoveries, ability to conduct regulatory testing);
- the global context on the supply and regulation of the use of NHPs, including the impact of the implementation of the EU Directive in EU countries and global supply issues on the UK science sector;
- any unintended consequences;
- what, if any, exemptions may be required, what may constitute acceptable scientific justification, and for what timeframe any exemptions should be in place.

The written advice is requested no later than 12 September 2022.

6. Process

How will the Committee provide advice?

The Committee will provide written advice to the UK government in line with its statutory remit, as set out in ASPA Section 20:

> *(1)* ***The Committee must provide advice to the Secretary of State*** *and the Animal Welfare and Ethical Review Bodies* ***on such matters relating to the acquisition, breeding, accommodation, care and use of protected animals*** *as the Committee may determine or* ***as may be referred to the Committee by the Secretary of State****.*
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> *(2) In its consideration of any matter* ***the Committee shall have regard both to the legitimate requirements of science and industry and to the protection of animals against avoidable suffering and unnecessary use in scientific procedures****.*
>
> *(3) The Committee must take such steps as it considers appropriate to ensure the sharing of best practice in relation to the acquisition, breeding, accommodation, care and use of protected animals.*

In developing advice, the Committee will wish to gather relevant evidence including by engaging with relevant stakeholders concerned with science and industry, animal protection, and regulated establishments.

How will the Committee's advice be used?

The UK government will carefully consider the Committee's advice, alongside wider policy, legal and political considerations, before reaching a policy decision. If necessary, the Government may revert to the Committee for further advice or clarification.

The government will continue to engage with the Committee to support the implementation of any policy decision and to monitor the impacts.

Annex 1.

Recitals 17-19 of Directive 2010/63/EU

(17) Having regard to the present state of scientific knowledge, the use of non-human primates in scientific procedures is still necessary in biomedical research. Due to their genetic proximity to human beings and to their highly developed social skills, the use of non-human primates in scientific procedures raises specific ethical and practical problems in terms of meeting their behavioural, environmental and social needs in a laboratory environment. Furthermore, the use of non-human primates is of the greatest concern to the public. Therefore the use of non-human primates should be permitted only in those biomedical areas essential for the benefit of human beings, for which no other alternative replacement methods are yet available. Their use should be permitted only for basic research, the preservation of the respective non-human primate species or when the work, including xenotransplantation, is carried out in relation to potentially life-threatening conditions in humans or in relation to cases having a substantial impact on a person's day-to-day functioning, i.e. debilitating conditions.

(18) The use of great apes, as the closest species to human beings with the most advanced social and behavioural skills, should be permitted only for the purposes of research aimed at the preservation of those species and where action in relation to a life-threatening, debilitating condition endangering human beings is warranted, and no other species or alternative method would suffice in order to achieve the aims of the procedure. The Member State claiming such a need should provide information necessary for the Commission to take a decision.

(19) The capture of non-human primates from the wild is highly stressful for the animals concerned and carries an elevated risk of injury and suffering during capture and transport. In order to end the capturing of animals from the wild for breeding purposes, only animals that are the offspring of an animal which has been bred in captivity, or that are sourced from self-sustaining colonies, should be used in procedures after an appropriate transition period. A feasibility study should be carried out to that effect and the transition period adopted if necessary. The feasibility of moving towards sourcing non-human primates only from self-sustaining colonies as an ultimate goal should also be examined.