



**Title: Feasibility study as required in Article 10 of Directive 2010/63/EU on the protection of animals used for scientific purposes**

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## **Feasibility study as required in Article 10 of Directive 2010/63/EU on the protection of animals used for scientific purposes**

### **1. Executive Summary**

Directive 2010/63/EU on the protection of animals used for scientific purposes (replacing Directive 86/609/EEC) acknowledges animal welfare, animal health as well as ethical problems arising from the capture of non-human primates (NHP) from the wild. To end the capturing of animals from the wild for both scientific and breeding purposes, the Directive has set as one of its aims to allow, after an appropriate transition period, only the use of NHP that are the offspring of animals which have been bred in captivity (F2/F2+ generation), or that are sourced from self-sustaining colonies (SSC).

The Commission is also required to conduct a feasibility study to consider the implementation of this requirement as set out in Article 10, and the related dates set out in Annex II of the Directive, which require the transition to be provisionally completed five years after the publication of this feasibility study, that is by November 2022. The feasibility study is also to take into account animal welfare and animal health impacts in the context of the transition to F2/F2+.

#### **1.1. Progress towards the use of F2/F2+ non-human primates**

In 2014, 6227 NHP were reported as being used in the EU for the first time. The main users are in UK, Germany and France, which together account for between 80% and 90% of all NHP used in the EU. Five other MS reported the use of NHP in 2014. Two further MS reported only re-use of NHP in 2014.

Since the initial 2006 Impact Assessment and the related Prognos Report (1) for the Commission proposal to revise Directive 86/609/EEC, and the policy change introduced by Directive 2010/63/EU to progress towards the use of only purpose-bred animals, there has been significant progress made towards the use of F2/F2+ NHP within EU. There are no official statistics at EU level available, as information on the generation of animals used was not required to be collected before 2014. However, to illustrate the progress that has been made, drawing from national statistics in UK and information from the Impact Assessment, in 2004, around 80% of NHP used in UK (2) were of F1 generation, but by 2014, all animals used in the UK were either F2/F2+ or acquired from self-sustaining colonies.

In relation to the species used, users have been required to use F2/F2+ Marmosets (*Callithrix jacchus*) since 1 January 2013 with no additional transitional period. No issues have been identified with this requirement, and no further consideration is given to this species within this report.

The other commonly used species are the Cynomolgus macaque (*Macaca fascicularis*) accounting for 82% of all NHP first used in 2014, the Rhesus macaque (*Macaca mulatta*) (5.6%), Baboon (*Papio sp*) (2.9%) and Prosimians (2.2%).

In 2014, the greater majority of animals used were of F2/F2+ generation or originated from self-sustaining colonies: 82% of animals used for the first time were either F2/F2+ (38%) or from self-sustaining colonies (44%). 1134 (18%) of the animals were of F1 generation.

Of those reported as F1, 98% were *Cynomolgus* macaques, almost all of which were sourced from Africa (all from Mauritius). A small number of Rhesus macaques and baboons were reported as F1 generation.

The other species reported (Vervet, Squirrel monkey) were used in much smaller numbers and all of these animals used for the first time in 2014 were at least F2 generation.

### **1.2. Scientific needs**

The responses from users indicated that there were currently no specific scientific reasons which required the use of F1 animals instead of F2/F2+ generations. However, the importance of genetic status was highlighted, whether it be diversity or specificity, and that there may be circumstances in the future where a scientific justification could be made to use specific F1 or wild-caught animals. Concerns which were also raised from the scientific community related to the non-availability of sufficient scientifically suitable F2 animals after full implementation of Article 10, and requested that exemptions from the F2 requirement on scientific grounds should continue to be permissible. Current global availability would, however, suggest that there are sufficient F2 animals to meet the current and future demands, unless there is, for example, a specific scientific need to use a species not yet bred for research purposes. Article 10(3) provides for this exemption. Should a specific scientific need arise to use wild-caught animals, this is also provided for within Article 9(2) of the Directive.

A further issue of concern raised by the users was the continued need for access to specific types of animals such as animals for ageing studies or for animals with natural clinical disease such as diabetes. It is not yet always possible to obtain sufficient F2 animals with such specific criteria, and until the self-sustaining colonies are well established (and F2 animals have reached the appropriate age), there is likely to be a continued, albeit limited, scientific need to use F1 animals in such circumstances.

### **1.3. Animal welfare**

Animal welfare and health quality will be improved by moving from wild-caught animals to those reared and bred in captivity. This is supported by SCAHAW report (3) of 2002 which also stated that only animals of the second or subsequent generation bred in captivity should be accepted as being classified as 'purpose-bred' and supplied for research.

The Prognos report (1) indicated potential welfare problems in moving to F2 animals until such colonies were established – the issues identified included poor breeding success with F1 animals, and the unnecessary culling of unsaleable surplus F1 males.

The main Mauritian breeders did provide information to the effect that reproductive success was reduced and breeding life was shortened in F1 animals when compared with wild-caught breeders. However, breeders from Asia and EU indicated that they had not experienced these problems, and have had good success rates with captive-bred stock using their management and breeding strategies.

Care is needed in any transitional breeding programme from wild-caught (F0) to F2 animals, to minimize the potential consequences of inbreeding.

One Mauritian breeder highlighted the potential effect of surplus males with a rapid change to F1 breeding stock, but to date such animals have been supplied for use, with no avoidable culling reported either by breeders in Mauritius or in Asia.

#### **1.4. Health status**

The availability of animals of particular health status, in particular Herpes B free, was raised as justification to continue the sourcing of animals from Africa rather than Asia, and as a consequence extending the period for implementation of requiring the use of F2/F2+ should insufficient F2 animals be available to meet EU demand for such animals from Africa. However, many EU users source animals from Asian colonies and are content with the testing and biosecurity strategies at their suppliers that can ensure health status and minimize risk of infection with this zoonotic pathogen. Increased biosecurity is often put in place until post-arrival health screenings confirm the status of the imported animals, but this is not considered to negatively affect the care or welfare practices for these animals.

#### **1.5. Cost of Animals**

The Prognos report (1) suggested that a move to F2 animals would result in increased costs for the scientific community. During the negotiations on the new Directive the UK also suggested that costs for moving to F2 animals could be as much as a ten-fold increase (4).

This has not turned out to be the case with little, or no, price differential reported between F1 and F2/F2+ generations since 2007 (confirmed by two overseas breeders).

#### **1.6. Definitions – self-sustaining colony (SSC)**

Although the intention within the Directive, as reflected in Recital 19, is eventually to move to a situation where all the animals in a breeding colony would be at least F2, Article 10 provides for a gradual progression to that goal. The understanding of SSC is that once closed, the colony no longer can be reopened. It is also implicit from the intentions of the legislators that "other colonies" from which animals can be sourced, must be considered to be also self-sustaining captive-bred colonies, and from which no F0 can be obtained as breeders.

Many SSC have been closed for many years, but these may still contain F0 animals, from which F1 offspring are still produced, in addition to F2/F2+ animals from captive-bred parents. Responses to the questionnaires and enquiries confirmed that some "SSC" supplying into EU still contain F0 animals and that both F1 and F2/F2+ animals are supplied into EU from such colonies.

The new statistical reporting requirements as set out in Commission Implementing Decision 2012/707/EU (and as amended in 2014/11/EU) do not currently distinguish the generation of the animal when sourced from SSC. However, the information provided from users and suppliers in the questionnaires has indicated that the production of F2 animals in SSC continues to increase as the F0 breeders are retired.

## **2. Continued use of FO/F1 NHP beyond the implementation date set out in Annex II**

It has been noted that there is likely to be some F1 NHP still in use on procedures beyond the implementation date of 2022 (almost exclusively *Cynomolgus* macaques). For animals

already in use, it should be permissible for these animals to complete the respective projects to prevent loss of data and avoid unnecessary animal wastage.

## **2.1. Supply**

The only species with uncertainty over whether or not there would be a sufficient supply of F2s by 2022 is the *Cynomolgus* macaque. Only 4.5% of *Cynomolgus* used in 2014 were obtained from EU breeders, with the remainder supplied from breeders in Mauritius (60%) and Asia (35%). On the basis of responses from the three overseas breeders from whom answers were received directly, their current global annual supply of F2/F2+ is around 7835 which comfortably exceeds the current total EU use of *Cynomolgus* macaques (5135). Taking into account also information provided by those overseas breeders who currently do not supply into EU, the combined global availability of F2/F2+ exceeds 13,000 animals annually.

## **2.2. Conclusions**

Considering the current and projected demand and supply of the species used, and impacts on the animal welfare and health, the conclusions of this study do not support altering the dates set out in Annex II of the Directive.

The main species of concern is the *Cynomolgus* macaque. Their global availability in F2/F2+ generation already today exceeds the current and projected EU demand. However, the additional five years (2017-2022) are required to further facilitate the complete transition to F2/F2+ Herpes B-virus free *Cynomolgus* macaques from those suppliers in Mauritius who are not yet able to fully meet demand. This would allow continuity of supply and allay scientific concerns on, for example availability of historical data/results from previous studies, should animals be required to be sourced elsewhere.

Competent authorities can continue to grant exemptions beyond 2022 on the basis of scientific justification as provided in Article 10(3) should specific scientific needs so require, such as studies for aged animals which are not yet available as F2s.

The Directive sets as the ultimate goal of sourcing of animals from SSC, where animals supplied are offspring of animals who themselves have been bred in captivity, with the interim possibility to obtain F2/F2+ animals which do not yet come from such a colony. The policy objective, which is gradual in nature, does not, however, exclude the possibility that during the transitional phase, a SSC may still house animals that were originally caught from the wild nor that such animals may be used as breeders until the end of their reproductive cycle.

To facilitate accurate reporting, Commission Implementing Decision 2012/707/EU should be adjusted to obtain annual information on the generation of animals supplied from SSC as this is currently not recorded. The expectations as set out in Recital 19, need to be clearly communicated to users, breeders and suppliers to ensure that efforts towards the final goal are being made. With accurate information on the generation of each animal and its origin, the progress can then be assessed during the subsequent feasibility study on sourcing animals only from SSC as required in Article 10(2).

It is noteworthy that within only a few years of implementation of the Directive, good progress has already been made towards the policy objective set out in the Directive to use only NHP that are offspring of purpose-bred animals



### 3. Introduction

The use of animals for scientific purposes in the EU is governed by Directive 2010/63/EU on the protection of animals used for scientific purposes. This Directive includes controls on the origin, breeding, care and accommodation of animals.

Recital 19 of the Directive states that *“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.”*

The respective Article 10 of the Directive requires that the Commission shall, in consultation with the Member States and stakeholders, conduct a feasibility study, which shall include an animal health and welfare assessment, of the obligation to ensure that non-human primates (NHP), listed in Annex II of the Directive may be used in procedures only where they are the offspring of NHP which have been bred in captivity (F2 / F2+) or where they are sourced from self-sustaining colonies (SSC - colonies in which animals are bred only within the colony, or sourced from other colonies, but not taken from the wild, and kept in a way that ensures that they are accustomed to humans).

Annex II states that marmosets (*Callithrix jacchus*) shall meet this requirement by 1 January 2013 and other NHP by 5 years after the publication of the feasibility study, provided the study does not recommend an extended period.

Furthermore, Article 28 requires that authorised breeders of NHP within the EU have a strategy in place for increasing the proportion of animals that are the offspring of NHP that have been bred in captivity.

This feasibility study is designed to assess whether or not the full requirements of Article 10 (using only F2/F2+ animals) can be met within 5 years of the publication of this study (that is by November 2022), earlier than that date, or if longer, by what feasible date. The feasibility study shall be published no later than 10 November 2017.

#### 3.1. Methodology and consultation strategy

- Preliminary background information was requested from the Member States who reported use of NHP in 2014 (Annex I) to inform the development of a detailed questionnaire on NHP acquisition and use for EU user, breeding and supplying establishments, and a separate questionnaire for breeders and suppliers from outside EU, who provide NHP for use in EU.

Member States that have establishments using or breeding NHP for scientific purposes were requested through this initial questionnaire to provide information on breeding, supplying or use, including progress towards meeting the requirements of Article 28, information on any measures taken to obtain reassurance on accommodation, welfare and care practices in overseas establishments which supply into the MS and information on progress towards the supply of higher generation (F2/F2+) purpose-bred animals. These MS were also requested to provide contact details of organisations or overseas

breeding/supplying establishments who could be invited to contribute to the feasibility study.

- A stakeholder organisation, Eurogroup for Animals, had previously requested similar information from MS in a survey in October 2015. With the permission of the relevant MS and Eurogroup for Animals, this information was made available to the EC for consideration within the feasibility study. A summary of the relevant findings is presented in Annex II of this report.
- The initial questionnaire was followed by a meeting hosted by the EC in Brussels on 24 June with MS that have establishments using, breeding and/or supplying NHP for scientific purposes, and stakeholder organisations with interests in the use, breeding, supply or care of NHP in scientific procedures. A discussion document was circulated prior to the meeting (Annex III).

The purpose of this meeting was to agree elements for inclusion in a questionnaire which would generate suitable information on which an informed decision could be developed on a timetable for full implementation of Article 10 and to develop proposals, as necessary, for changes to Annex II to the Directive.

The considerations at the meeting included:

- Numbers of NHP used, including source and generation of animals and availability of the commonly used species;
- The evolution on the availability of and demand for F2 NHP since the adoption of the Directive; consideration of the findings and recommendations in the Prognos report (1);
- Estimation of future needs and predicted availability of animals to meet this demand;
- The identification of relevant information required to assess the time needed to fulfil the anticipated demand;
- The aspects of animal health and welfare which may be impacted in meeting the objectives and timescales set out in the Directive;
- Identification of relevant stakeholders for the targeted questionnaire.

Although other aspects of NHP welfare, care and accommodation were raised at the meeting, the scope was confirmed as set out in Article 10.3, namely the feasibility of moving to the use in procedures only of F2/F2+ NHP in procedures, having regard for animal health and welfare consequences that may result from this approach.

The meeting agreed the elements necessary to be covered in the feasibility study questionnaires.

- Subsequent to the meeting, two questionnaires were prepared for distribution using "EU Survey"<sup>1</sup>. The first was targeted towards all users, breeders and suppliers of NHP (Annex IV) in the EU and the second intended for breeders of NHP who supply animals into the EU (Annex V).

As the Commission does not have direct contacts with establishments within MS, the National Contact Points (NCP) were asked to circulate the request to the respective NHP users, breeders and suppliers in their MS to contribute to the study. A link was provided

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<sup>1</sup> <https://ec.europa.eu/eusurvey/home/welcome>

to each establishment to complete the EU survey electronically. The EU Survey was open 30 August 2016 – 31 October 2016.

- As not all MS were aware of details of overseas suppliers of NHP, the invitation to the EU users, breeders and suppliers also contained a request to provide contact details for their overseas suppliers.
- Links to the EU survey were sent to all the overseas breeders/suppliers for whom details were provided. The EU Survey was open 21 November 2016 – 15 February 2017.
- Following receipt and review of the responses further bilateral contacts were made for clarification and some additional information, as appropriate.
- On the basis of the analysis of the surveys and other background material provided by stakeholders, the Prognos Report (1) and available statistical data, a public consultation meeting was held in Brussels on 30 March 2017 to present and discuss the draft findings. Additional feedback provided during the meeting was taken into account in the final results of this feasibility study.

#### **4. Preliminary results and discussion at June 2016 MS/Stakeholder meeting**

##### **4.1. Initial Information from Member States on NHP use**

Eleven MS responded with information on NHP supply and use, which encompasses all MS which authorise the use and breeding of NHP within EU. One of these MS has authorised a programme of work which involves NHP use, but no work had been undertaken at the time of the survey.

All EU authorised breeders are already meeting the requirements of Article 28, having in place a strategy for increasing the proportion of animals that are the offspring of NHP that have been bred in captivity.

Some MS already require that NHP being sourced outside EU are already F2/F2+, others indicated that this was still a direction of travel, but that there were as yet insufficient numbers of F2 animals to meet demand, and a further view was that the MS was unaware of any measures being made by users to progress to F2/F2+.

##### **4.2. June 2016 Meeting**

In preparation for the meeting, an analysis of the recent source and use of NHP was made using EU and national published statistics and, with the agreement of the relevant MS, the data gathered in 2014 under the new statistical reporting requirements set out in Commission Implementing Decision 2012/63/EU<sup>2</sup>. The new requirements provide additional information on the source of animals and on the generation of NHP supplied into EU. There are other differences in the new reporting requirements, in particular that animals are reported at the end of a procedure rather than, as previously, when the procedure started.

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<sup>2</sup> OJ L 320, 17.11.2012, p. 33



Table 1 - Non-human primate use in EU 1999-2014

	1999	2002	2005	2008	2011	2014
<b>Prosimians</b>	455	1 095	677	1 261	83	140
<b>New World</b>	1 353	1 192	1 564	904	700	417
<b>Old World</b>	5 199	8 075	8 208	7 404	5 312	5 682
<b>Total</b>	7 007	10 362	10 449	9 569	6 095	6 239 <sup>3</sup>

The statistical reporting requirements under the previous Directive 86/609/EC provided information on the source of animals, whether coming from registered breeding or supplying establishments within EU, or member countries of Council of Europe parties to Convention ETS 123, or from other origins.

As NHP purchased through registered suppliers in EU could have themselves been sourced from outside the EU, it is impossible from the data to determine the geographical origins (i.e. birth place) of the animals. Neither did the reporting include information on the generation of animals supplied (F0; F1; F2/F2+).

The data on origins from the statistical reports are reproduced below.

Table 2 – Source of NHP species 1999-2014

	From EC	Other Origins	Total	% other origins
<b>Prosimians</b>				
1999	323	123	455	27%
2002	1095	0	1095	0%
2005	677	0	677	0%
2008	1261	0	1261	0%
2011	83	0	83	0%
2014	140	0	140	0%
<b>New World Monkeys</b>				
1999	1294	56	1353	4%
2002	1064	128	1192	11%
2005	1504	60	1564	4%
2008	904	0	904	0%
2011	649	51	700	7%
2014	415	4	419	1%
<b>Old World Monkeys</b>				
1999	2463	2736	5199	53%
2002	1763	6312	8075	78%
2005	2216	5994	8210	73%
2008	4068	3336	7404	45%
2011	3522	1796	5312	34%
2014	653	5027	5680	88%

<sup>3</sup> This figure includes 12 animals (7 marmosets (all F2/F2+) and 5 cynomolgus (1F1;4F2) macaques) killed for tissue (These should have been excluded from the data reported under Commission Implementing Decisions 2012/707EU). The total number of animals used for the first time under the Directive in 2014 was 6227.

The numbers of Prosimians obtained from other origins have been very low, and in 2014 all such animals were obtained from breeding colonies within EU.

Few New World NHP are obtained from outside EU.

The number of Old World NHP coming from other origins has reduced over time, but as stated above, under the previous statistical reporting rules, it is likely that many animals obtained from EU suppliers will have originated from outside EU, but reported correctly under the previous requirements as sourced from EU. This interpretation seems to be further confirmed when examining data from 2014.

The new statistical reporting format (Commission Implementing Decision 2012/63/EU<sup>4</sup>) provides much more information than the requirements under EC/86/609 on the origins of the animals coming into the EU for use in procedures, and provides a greater breakdown in species. For example, Old World Monkeys are now subdivided to include reporting on Rhesus macaques, Cynomolgus macaques, Vervet monkeys, Baboons and “other species of old world NHP”.

### 4.3. Non-human primate use in 2014

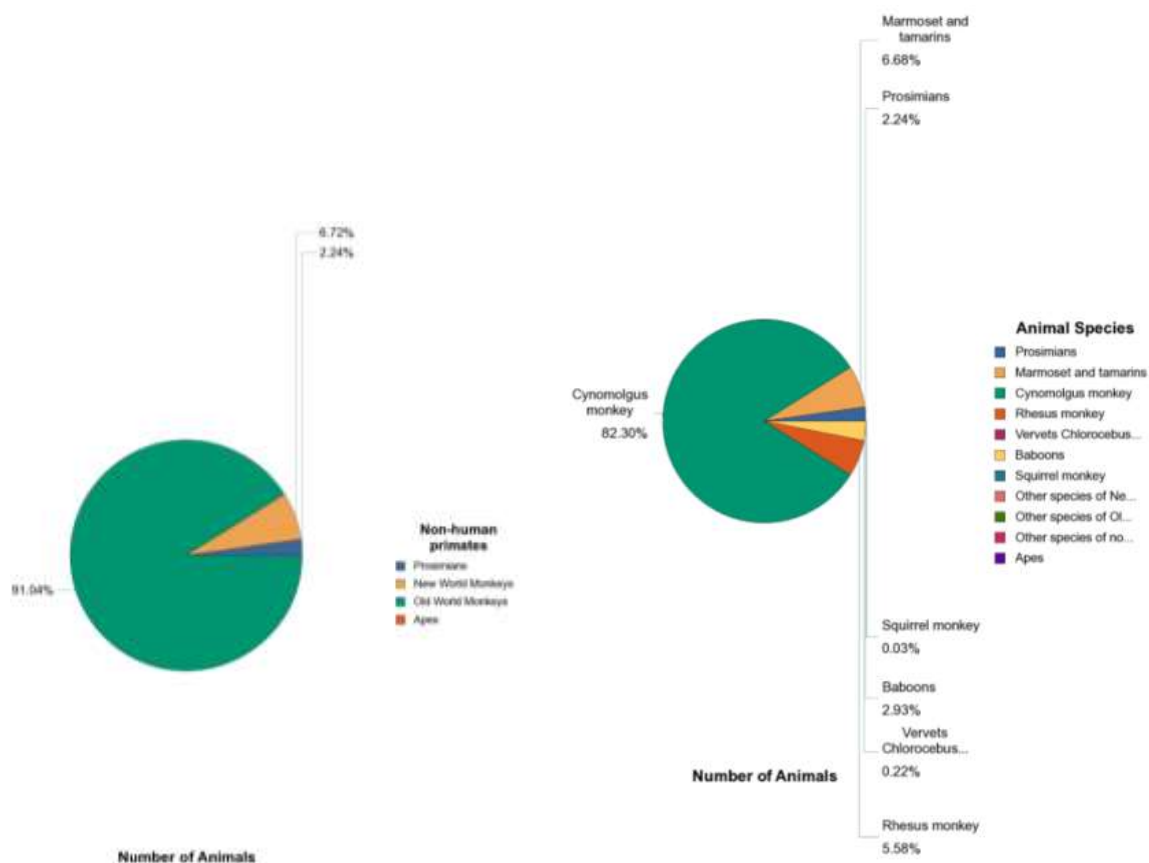
The number and species of NHP used for the first time in 2014 are listed below in Table 3 and Figure 1.

*Table 3 – Species of NHP used in 2014 in EU*

Animal Species	Number of Animals
Prosimians	140
Marmoset and tamarins	417
Cynomolgus monkey	5,135
Rhesus monkey	348
Vervets Chlorocebus spp.	14
Baboons	183
Squirrel monkey	2
Other species of New World Monkeys (Ceboidea)	
Other species of Old World Monkeys (Cercopithecoidea)	
Other species of non-human primates	
Apes	
Total:	6,239

<sup>4</sup> OJ L 320, 17.11.2012, p. 33

Figure 1 – Species of NHP used in 2014 in EU



The most commonly used species was the Cynomolgus macaque (82%), followed by Marmoset (& Tamarin) (7%), Rhesus macaque (5%), Baboons (3%), Prosimians (2%) with the remainder, Squirrel monkeys and Vervet monkeys making up less than 1% of the total. No animal of any other NHP species was used for the first time in 2014.

#### 4.4. Species to be included in the feasibility study

With regard to the species listed in Annex II of the Directive, the requirement is to consider specifically Marmoset (*Callithrix jacchus*), Cynomolgus monkey (*Macaca fascicularis*) and the Rhesus monkey (*Macaca mulatta*).

##### Marmoset (*Callithrix jacchus*)

The requirements of Article 10 with regard to F2 use has applied to Marmosets from 1 January 2013. An analysis of statistical data combined with feedback from users and stakeholders confirm that this has been achieved and is current practice. **As a consequence, no further consideration will be given to this species in the context of this study.**

##### Cynomolgus monkey (*Macaca fascicularis*) and Rhesus monkey (*Macaca mulatta*)

Specific consideration will be given to the Cynomolgus monkey (*Macaca fascicularis*) and Rhesus monkey (*Macaca mulatta*).

“Other species of non-human primates”

Within the context of this study, consideration will be given to the other species reported in the 2014 figures, these are Prosimians (140), Baboons (*Papio sp*) (183), Vervets (14) and Squirrel Monkeys (2).

NHP were used in procedures for the first time in 2014 in 8 MS (in a further two MS only re-use was reported).

*Table 4 – Species of NHP used in 2014, by MS*

	BE	CZ	DE	ES	FR	HU	IT	NL	SE	UK	Total uses
Prosimians			85		55						140
Marmoset and tamarins			234				6	77		100	417
Cynomolgus monkey	8		1,475	382	547		443	18		2,262	5,135
Rhesus monkey	3		111	2	25	2	5	96		104	348
Vervets <i>Chlorocebus spp.</i>					14						14
Baboons			2	32	149						183
Squirrel monkey					2						2
Other species of New World Monkeys (Ceboidea)											
Other species of Old World Monkeys (Cercopithecoidea)											
Other species of non-human primates											
<b>Total uses</b>	<b>11</b>		<b>1,907</b>	<b>418</b>	<b>792</b>	<b>2</b>	<b>454</b>	<b>191</b>		<b>2,486</b>	<b>6,239</b>
<b>%</b>	<b>0%</b>		<b>31%</b>	<b>7%</b>	<b>13%</b>	<b>0%</b>	<b>7%</b>	<b>3%</b>		<b>40%</b>	

The origins of the animals are included in Table 5 and the generation of the animals used in Table 6 and Figure 2.

*Table 5 – Source of NHP in 2014*

NHP Source (origin)	Number of Animals
Animals born at a registered breeder within EU	1,151
Animals born in rest of Europe	57
Animals born in Asia	1,935
Animals born in America	14
Animals born in Africa	3,081
Animals born elsewhere	1
<b>Total:</b>	<b>6,239</b>

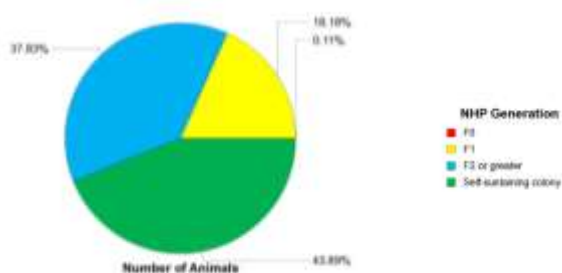
Around 20% of the NHP used for the first time in 2014 were born in Europe, 31% in Asia and 50% born in Africa (entirely from Mauritius).



Table 6 – Generation of NHP used in 2014

NHP Generation	Number of Animals
F0	7
F1	1,134
F2 or greater	2,360
Self-sustaining colony	2,738
<b>Total:</b>	<b>6,239</b>

Figure 2 – Generation of NHP used in 2014



For the first time within the EU statistical reporting of animals used for scientific procedures there is information on the generation of NHP used.

Of the seven wild-caught animals reported, further enquiries elicited that four Marmosets were incorrectly reported and were confirmed as F2/F2+.

18% of animals were reported as F1, 38% as F2/F2+ and 44% from self-sustaining colonies.

The origins of the different NHP species used in 2014 are included below.

Table 7 – Source of NHP by species in 2014

	Animals born at a registered breeder within EU	Animals born in rest of Europe	Animals born in Asia	Animals born in America	Animals born in Africa	Animals born elsewhere	Total
Primates	87	50					140
Marmoset and tamarins	413				4		417
Cynomolgus monkey	231	4	1,810		3,075	1	5,135
Rhesus monkey	231		117				348
Vervets Chlorocebus spp.					14		14
Baboons	181				2		183
Squirrel monkey	2						2
Other species of New World Monkeys (Cebidae)							
Other species of Old World Monkeys (Cercopithecoidea)							
Other species of non-human primates							
Apes							
<b>Total</b>	<b>1,151</b>	<b>57</b>	<b>1,935</b>	<b>14</b>	<b>3,091</b>	<b>1</b>	<b>6,239</b>

The generations of the different NHP species used in 2014 are included below

Table 8 – Generation of NHP by species in 2014

	F0	F1	F2 or greater	Self-sustaining colony	Total
Primates					140
Marmoset and tamarins		4		101	417
Cynomolgus monkey	3		1,125	2,147	5,135
Rhesus monkey			4	94	348
Vervets Chlorocebus spp.				14	14
Baboons			2	2	179
Squirrel monkey				2	2
Other species of New World Monkeys (Cebidae)					
Other species of Old World Monkeys (Cercopithecoidea)					
Other species of non-human primates					
Apes					
<b>Total</b>	<b>7</b>	<b>1,134</b>	<b>2,360</b>	<b>2,738</b>	<b>6,239</b>

Excluding the three wild caught Cynomolgus macaques used for the first time 38% of NHP used in 2014 were F2 or greater, 44% were from self-sustaining colonies and 18% were F1.

Looking in more detail at the breakdown per species, the only significant use of F1 animals evidenced from the 2014 data is with the *Cynomolgus macaque* (22% F1; 42% F2; 36% SSC).

Further analysis indicates that the majority of the F1 *Cynomolgus macaques* used in 2014 were born in Africa (98%).

*Table 9 – Source and generation of Cynomolgus macaques used in 2014*

*Cynomolgus macaques sourced from Africa; sourced from Asia*

NHP Source (origin)	Number of uses	Percentage
Animals born in Africa	3,075	100.00%
<b>Total uses</b>	<b>3,075</b>	<b>100.00%</b>

NHP Source (origin)	Number of uses	Percentage
Animals born in Asia	1,818	100.00%
<b>Total uses</b>	<b>1,818</b>	<b>100.00%</b>

NHP Generation	Number of uses	Percentage
F0	1	0.03%
F1	1,102	35.84%
F2 or greater	519	16.88%
Self-sustaining colony	1,453	47.25%
<b>Total uses</b>	<b>3,075</b>	<b>100.00%</b>

NHP Generation	Number of uses	Percentage
F0	2	0.11%
F1	25	1.38%
F2 or greater	1,622	89.22%
Self-sustaining colony	169	9.30%
<b>Total uses</b>	<b>1,818</b>	<b>100.00%</b>

*Cynomolgus macaques sourced in EU*

NHP Source (origin)	Number of uses	Percentage
Animals born at a registered breeder within EU	237	98.34%
Animals born in rest of Europe	4	1.66%
<b>Total uses</b>	<b>241</b>	<b>100.00%</b>

NHP Generation	Number of uses	Percentage
F0		
F1		
F2 or greater	8	2.49%
Self-sustaining colony	235	97.51%
<b>Total uses</b>	<b>241</b>	<b>100.00%</b>

All *Cynomolgus macaques* sourced from within the EU were either F2/F2+ or from SSC.

Note: Table 9 above excludes one *Cynomolgus macaque* that was from an origin other than EU, Africa or Asia.

In contrast to the results for *Cynomolgus macaques*, the great majority (99%) of animals of the second most commonly used species, the Rhesus macaque, were obtained either as F2 or from SSCs (Table 10).

*Table 10 – Source and generation of Rhesus macaques used in 2014*

NHP Source (origin)	Number of uses	Percentage
Animals born in Asia	117	100.00%
<b>Total uses</b>	<b>117</b>	<b>100.00%</b>

NHP Source (origin)	Number of uses	Percentage
Animals born at a registered breeder within EU	231	100.00%
Animals born in rest of Europe		
<b>Total uses</b>	<b>231</b>	<b>100.00%</b>

NHP Generation	Number of uses	Percentage
F0		
F1	3	2.56%
F2 or greater	60	51.28%
Self-sustaining colony	54	46.15%
<b>Total uses</b>	<b>117</b>	<b>100.00%</b>

NHP Generation	Number of uses	Percentage
F0		
F1	1	0.43%
F2 or greater	34	14.72%
Self-sustaining colony	196	84.65%
<b>Total uses</b>	<b>231</b>	<b>100.00%</b>

For the other species used less frequently almost all of the animals were either F2/F2+ generation or from a self-sustaining colony in EU (Tables 11-13).

Table 11 – Source and generation of Baboons used in 2014

NHP Source (origin)	Number of uses	Percentage
Animals born at a registered breeder within EU	181	98.91%
Animals born in rest of Europe		
Animals born in Asia		
Animals born in America		
Animals born in Africa	2	1.09%
Animals born elsewhere		
<b>Total uses</b>	<b>183</b>	<b>100.00%</b>

NHP Generation	Number of uses	Percentage
F0		
F1	2	1.09%
F2 or greater	2	1.09%
Self-sustaining colony	179	97.81%
<b>Total uses</b>	<b>183</b>	<b>100.00%</b>

Table 12 – Source and generation of Prosimians used in 2014

NHP Source (origin)	Number of uses	Percentage
Animals born at a registered breeder within EU	87	62.14%
Animals born in rest of Europe	53	37.86%
Animals born in Asia		
Animals born in America		
Animals born in Africa		
Animals born elsewhere		
<b>Total uses</b>	<b>140</b>	<b>100.00%</b>

NHP Generation	Number of uses	Percentage
F0		
F1		
F2 or greater		
Self-sustaining colony	140	100.00%
<b>Total uses</b>	<b>140</b>	<b>100.00%</b>

Table 13 – Source and generation of Vervet monkeys used in 2014

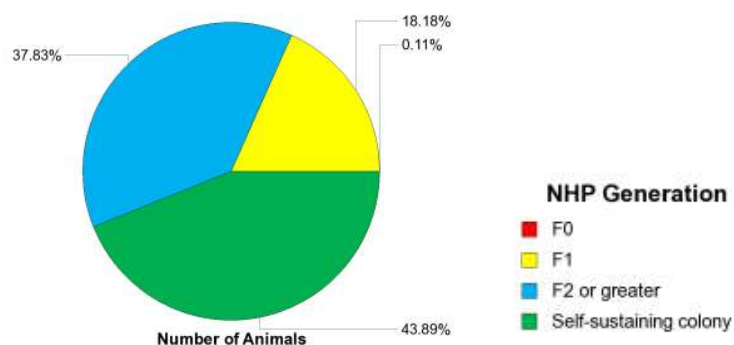
NHP Source (origin)	Number of uses	Percentage
Animals born at a registered breeder within EU		
Animals born in rest of Europe		
Animals born in Asia		
Animals born in America	14	100.00%
Animals born in Africa		
Animals born elsewhere		
<b>Total uses</b>	<b>14</b>	<b>100.00%</b>

NHP Generation	Number of uses	Percentage
F0		
F1		
F2 or greater	14	100.00%
Self-sustaining colony		
<b>Total uses</b>	<b>14</b>	<b>100.00%</b>

Further analysis of the data from 2014, indicates significant differences in the proportions of F1/F2 generations of animals used among MS (Figures 3 and 4).

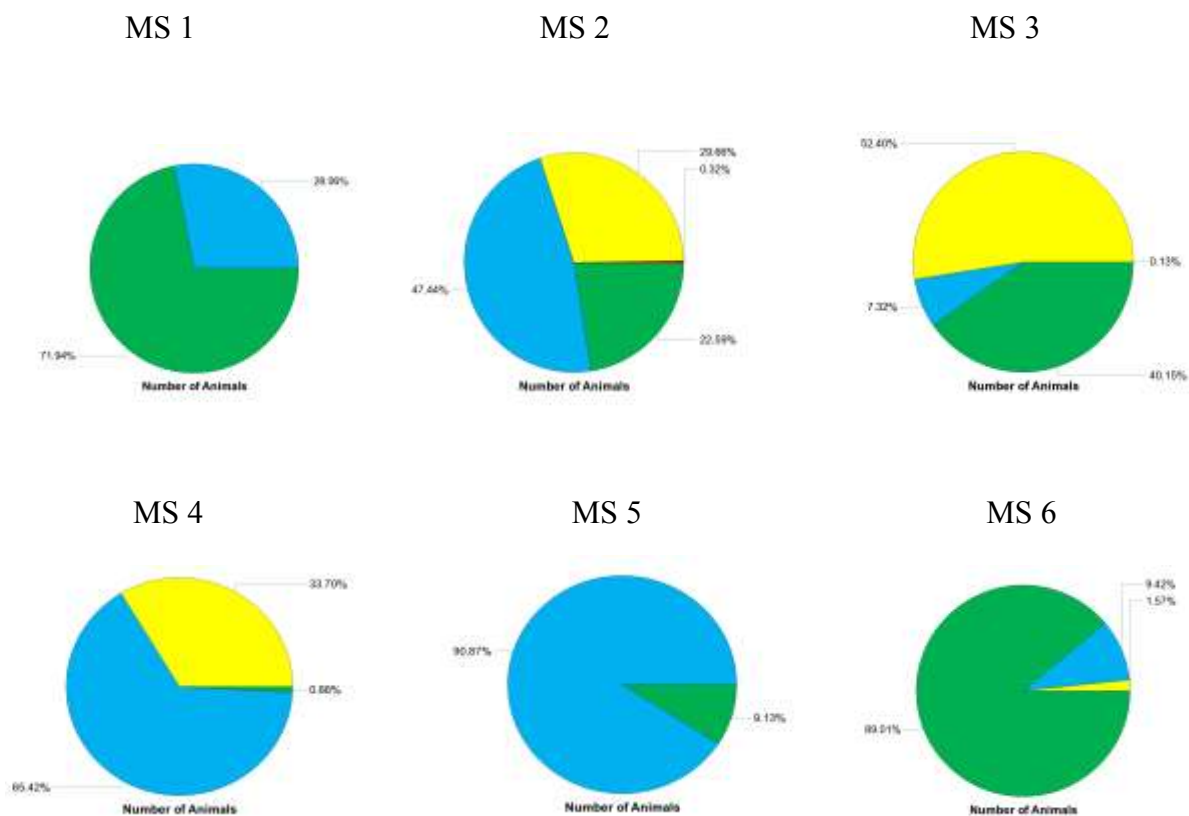
#### 4.5. Distribution of NHP generations of animals used by MS in 2014

Figure 3 - Distribution of NHP generations of animals used in EU in 2014



The combined EU figures indicate that 39% of animals are F2/F2+, 44% from SSCs, and 18% as F1 generation.

Figure 4 - Distribution of NHP generations of animals used, by the six largest MS NHP users in 2014



There are clear differences in the use of animals of different generations across MS. In 2 MS only F2/F2+ animals or those from self-sustaining colonies are used. In three others, the percentage of F1 animals used in 2014 are 30%, 33% and 52%, suggesting that MS are at differing stages of progress towards achieving the Directive objective of using only F2/F2+ animals in procedures.

#### 4.6. Definition of self-sustaining colony (SSC) and collection of statistical data

On first review of the figures from the 2014 statistical submission, there seems to have been considerable progress made from the time of the pre-Directive Prognosis report (1) towards the use of F2/F2+ NHP in scientific procedures.

The Prognosis report indicated that only small numbers of F2 were available. For example, 70–80% of the *Cynomolgus macaques* imported into the UK in the years 2001–2004 were the F1 (2). The Prognosis report (1) acknowledged however that more F1 breeding females were being brought into production in both Mauritius and Asian breeding centres.

Since the introduction of the Directive and the revised policy objectives, there has been an increase in the production and availability of F2 animals, as evidenced by experts at the June 2016 meeting.

However, it was clear from discussions at the MS/Stakeholder meeting, that there were differing interpretations of the definition of a “self-sustaining colony”, and it became apparent that some F1 animals are still being supplied from SSC to EU.

**The intention of the legislative framework is to firstly move away from the use of wild-caught NHP to purpose bred animals, then move from wild-caught animals as breeding animals to using breeding stock that were themselves bred in captivity, and finally to have independent self-sustaining colonies which do no longer either obtain, or have animals from the wild as breeding stock.**

This intention is set out clearly in Recital 19 [emphasis added] "*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.*"

Article 10 further defines that a “self-sustaining” colony means a colony in which animals are bred only within the colony or sourced from other colonies but not taken from the wild, and where they are accustomed to humans.

The experts at the June 2016 meeting suggested that the definition within the Directive should be clarified by the Commission and that information be sought in the questionnaire from the commercial breeders who supply EU on their understanding of the term “self-sustaining colony”.

A further issue was identified during discussions on SSC concerning the reporting of the origins and generations of NHP as required under Commission Implementing Decision 2012/707/EU. Animals sourced from SSC should be reported under the SSC option regardless of the generation derived from the maternal line; the generation of animals sourced from SSC is not reported separately. The discussions on the reliability of the 2014 statistical data in separating F1 and F2 generations led to the further conclusion that with current statistical reporting it cannot be assumed that all animals reported from a SSC are F2/F2+.

#### **4.7. Outcome of June 2016 MS/stakeholder meeting**

The draft questionnaires were revised following the discussions with the stakeholder and MS representatives to include additional questions, including a request for further information on the definition of self-sustaining colonies by breeders/suppliers of NHP.

The key information to be requested from the questionnaires included:

1. Current and predicted use
2. Availability of suitable animals
3. Health quality, including Herpes B virus
4. Animal welfare issues of moving to F2/F2+ generation
5. Differential costs of F1/F2 animals

MS were requested to provide users, breeders and suppliers with information on the questionnaire requests and an electronic link to the EU Survey.

Where contact details were provided either by MS or establishments, an invitation was sent to overseas breeders and suppliers who supply animals to users within EU.

Following initial analysis of the responses from the questionnaires, a number of supplementary questions were made to individual respondents, primarily to clarify aspects of their initial response.

## **5. Results and analysis of questionnaire responses**

### **5.1. Definition of self-sustaining colony (SSC) and collection of statistical data on animal use**

Review of the responses obtained through the surveys indicated that all animals supplied from EU breeding colonies are either F2/F2+ or from SSC.

However, the interpretation of “SSC” does differ slightly in responses provided by attendees at the June 2016 meeting and in responses from the three overseas breeders.

#### **5.2. EFPIA/FELASA (5)**

*“Self-sustaining colony means a colony in which animals are bred only within the colony or sourced from other colonies, where they have been bred, but not taken from wild, and where these animals are kept in a way that ensures that they are accustomed to humans. This means that F1 generation from self-sustaining colonies can still be used in research as no further animals are taken from the wild.”*

#### **5.3. International Primatological Society (IPS) Guidelines (6)**

*“Captive primate collections should not rely on the import of wild caught primates for the continuation of their programs, but rather use alternative means to introduce new stock into their breeding populations (e.g., exchange individuals with other known breeding colonies; accept legally rescued or confiscated individuals” = a self-sustaining but not closed colony.”*

#### **5.4. Overseas breeders**

##### **a. Mauritius breeder 1**

*"A SSC is one where all new breeders are derived from F1 or F1+ generations animals only. Once a particular SSC is established, no new F0 breeder may be introduced into it. Once no more newly caught F0 animals are being introduced, a colony can be deemed to be self-sustaining."*

##### **b. Mauritius breeder 2**

*"A SSC is a colony that use the monkeys born in its colony as breeders. In our definition, no external source is accepted. No satellite farm is accepted."*

##### **c. Asia breeder**

*"A self-sustaining colony is a colony which has a sustainable capability to produce enough animals to serve both breeding and commercial needs, whether these needs are only short term or continually in the medium to long run."*

The common thread through these interpretations is, however, that when closed, no replacement breeding stock is taken from the wild.

The Directive sets as the ultimate goal of sourcing of animals from SSC, where animals supplied are offspring of animals who themselves have been bred in captivity, with the interim possibility to obtain F2/F2+ animals which do not yet come from SSC. However, the understanding of SSC is that once closed, the colony can no longer be reopened. It is also implicit from the intentions of the legislators that "other colonies" from which animals can be sourced, must be considered to be also self-sustaining captive-bred colonies, and from which no F0 can be obtained as breeders. The policy objective, which is gradual in nature, does not, however, exclude the possibility that during the transition phase a SSC may still today house animals that were originally caught from the wild (F0) nor that such animals may be used as breeders until the end of their reproductive cycle.

At the time of the Directive negotiations, a number of uncertainties over the feasibility of the proposed EU policy were voiced, including concerns on isolated EU demands in a global market in which EU plays no prominent role. However, it seems that since the adoption of the EU policy increasing efforts to end the capture of NHP from the wild and to move toward fully established SSC are being successfully made by those supplying to the EU.

To facilitate accurate reporting, Commission Implementing Decision 2012/707/EU should be adjusted to obtain annual information on the generation of animals supplied from SSC as this is currently not recorded. The expectations as set out in Recital 19, need to be clearly communicated to users, breeders and suppliers to ensure that efforts towards the final goal are being made. With accurate information on the generation of each animal and its origin, the progress can then be assessed during the subsequent feasibility study on sourcing animals only from SSC as required in Article 10(2).

## 6. EU establishment questionnaire responses

### 6.1. Respondent background and NHP use

NCP were invited to circulate the link to the questionnaire to user, breeding and supplying establishments involved in the use, breeding or supply of NHP for scientific purposes.

Thirty-six responses were received from establishments in 8 MS.

#### 1.2 My organisation operates in

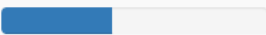
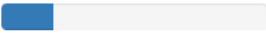
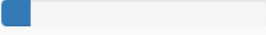
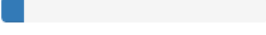
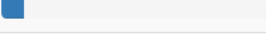
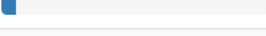
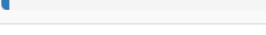

		Answers	Ratio
France		15	41.67 %
Germany		7	19.44 %
Spain		4	11.11 %
Netherlands		3	8.33 %
United Kingdom		3	8.33 %
Belgium		2	5.56 %
Italy		1	2.78 %
Sweden		1	2.78 %

Table 4 below (reproduced here for clarity) illustrates the NHP use in 2014 for each MS. No figures are available on the number of establishments which are authorized to breed, supply or use NHP within EU.

	BE	CZ	DE	ES	FR	HU	IT	NL	SE	UK	Total uses
Prosimians			85		55						140
Marmoset and tamarins			234				6	77		100	417
Cynomolgus monkey	8		1,475	382	547		443	18		2,262	5,135
Rhesus monkey	3		111	2	25	2	5	96		104	348
Vervets Chlorocebus spp.					14						14
Baboons			2	32	149						183
Squirrel monkey					2						2
Other species of New World Monkeys (Ceboidea)											
Other species of Old World Monkeys (Cercopithecoidea)											
Other species of non-human primates											
<b>Total uses</b>	<b>11</b>		<b>1,907</b>	<b>416</b>	<b>792</b>	<b>2</b>	<b>454</b>	<b>191</b>		<b>2,486</b>	<b>6,239</b>
<b>%</b>	<b>0%</b>		<b>31%</b>	<b>7%</b>	<b>13%</b>	<b>0%</b>	<b>7%</b>	<b>3%</b>		<b>40%</b>	

Although, the survey responses from the EU establishments relate to 2015 data, if a comparison is made with the 2014 MS data, an approximate estimate of the relative response rate for each MS can be determined, by comparing the total use of NHP given in the establishment responses with the individual MS statistical reports.

Table 14 – Comparison of 2014 data from MS and 2015 data from users

	2014 stats (4 species)	User responses for 2015 (total numbers used)				Total	Percentage of Total use 2015 vs 2014
		Cynos	Rhesus	Prosimians	Baboons		
France	776	1000	21	10	15	1046	104%
Germany	1673	1400	130	50	4	1584	94%
Spain	216	37	5			42	20%
NL	114	26	105			131	114%
UK	2366	750	110			860	36%
Belgium	11		38			38	345%
Italy	448		5			5	1%
Sweden	0						0%
Hungary	2						0%

Proportionately, there seems to have been a high response rate from France when compared with UK, the largest user of NHP in EU in 2014.

There seems to be a good representation from users in Germany.

The responses were mainly from NHP users in science and academia, although there were also responses from breeders and suppliers (a number were both users and breeders).



1.4 The area(s) of activity of my organisation is(are)

		Answers	Ratio
Animal user in science or academia		24	66.67 %
Animal user in industry		10	27.78 %
Animal breeder		7	19.44 %
Animal supplier		5	13.89 %

The species used or bred by the respondents to the survey are illustrated below.

		Answers	Ratio
2.2.3 Cynomolgus ( <i>M fascicularis</i> )		24	66.67 %
2.2.4 Rhesus ( <i>M mulatta</i> )		18	50.00 %
2.2.9 Other New World NHPs		5	13.89 %
2.2.6 Baboons ( <i>Papio sp</i> )		4	11.11 %
No Answer		3	8.33 %
2.2.1 Prosimians		2	5.56 %
2.2.5 Vervets ( <i>Chlorocebus sp</i> )		1	2.78 %
2.2.8 Other Old World NHPs		1	2.78 %
2.2.2 Tamarins		0	0.00 %
2.2.7 Squirrel Monkeys		0	0.00 %

Note – All the responses indicating use of “Other New World NHP” were actually referring to the use of “Marmosets” which had been deliberately excluded from the Questionnaire as the F2 requirement has been in force since 01 January 2013.

The additional “Other Old World NHP” species reported was the Southern Pig-tailed macaque (*Macaca Nemestrina*).

**6.2. Availability of suitable animals**

Over 70% of respondents indicated that they had no difficulties sourcing suitable animals for their scientific studies.

2.1.4 Do you have any difficulties at present in sourcing suitable animals for your studies e.g. due to company/Member State policy on NHP sourcing, restrictions on the use of F1s or transport issues?

		Answers	Ratio
No		26	72.22 %
Yes		7	19.44 %
No Answer		3	8.33 %

For those responding “Yes”, 5/7 indicated difficulties with transport, 1/7 acquiring aged F2 animals, and 1/7 obtaining animals of an appropriate genetic background (requiring specific MHC - major histocompatibility complex).

### 6.3. Establishment policy on use of F2 or higher generation for studies using NHP

2.1.5 Do you have a policy on the use of F2 or higher generation for your studies?

		Answers	Ratio
No		19	52.78 %
Yes		14	38.89 %
No Answer		3	8.33 %

40% of Establishments who responded have policies in place to use only F2/F2+ generations, although exemptions from the establishment policy would be considered should no suitable F2 animals be available.

On further analysis, it became apparent that there was a significant difference in responses from one MS than from the others.

2.1.5 Do you have a policy on the use of F2 or higher generation for your studies?

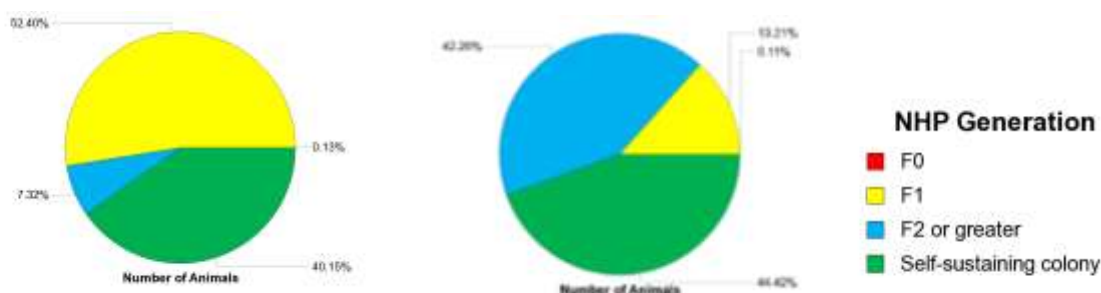


This absence of any policy to progress to F2/F2+ generations seems to have had an impact on the generation of animals used in that MS, as illustrated in Figure 5.

Figure 5 – Comparative distribution of NHP generations of animals used by MS in 2014

One MS

Combined – all *other* MS reporting use in 2014



## 6.4. Obligation on suppliers to supply F2/F2+ NHP

### 2.1.6 Do you have a policy in place requiring your suppliers to only supply F2/F2+?

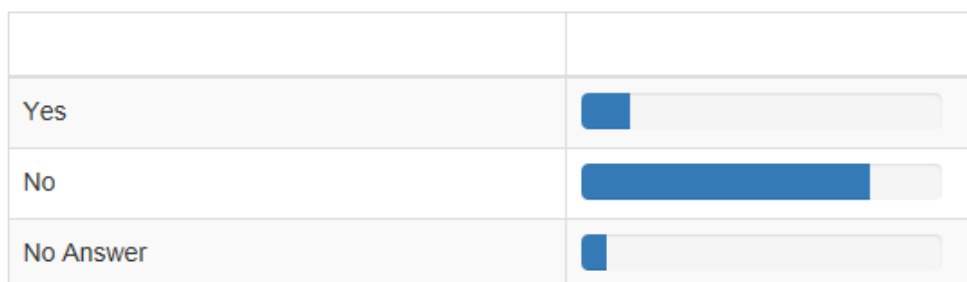
		Answers	Ratio
No		17	47.22 %
Yes		16	44.44 %
No Answer		3	8.33 %

17/35 users have an agreement with their suppliers of NHP to supply only F2/F2+ animals.

Of those answering no, the majority indicated that there were still occasions where there are insufficient F2 animals (exclusively Cynomolgus macaques) of a suitable age and sex to meet their needs, and a further few indicated that their policy would be unchanged until it became a firm legal requirement.

There was also a significant difference here in responses from one MS, which, as shown above in Figure 5, seems to have had an impact on the proportion of the generations of animals used in that MS.

### 2.1.6 Do you have a policy in place requiring your suppliers to only supply F2/F2+?



## 6.5. Regulatory blocks on transition to F2/F2+ generation

### 2.1.7 Are there any regulatory demands that hinder the transition to F2/F2+?

		Answers	Ratio
No		32	88.89 %
No Answer		3	8.33 %
Yes		1	2.78 %

Only one respondent indicated that there was a regulatory block on transition to F2. However, the reason given was related to availability of F2 animals rather than concerns over any regulatory demand.

## 6.6. Assurance on animals supplied

All users have measures in place to confirm the provenance of the animals.

These measures include a combination of review of individual health and production records, colony health and serological screening reports, information on accommodation and care practices, confirmation of compliance with national legislation, accreditation by recognized organization, such as the American Association for Accreditation of Laboratory Animal Care (AAALAC), and visits/audits conducted by individual EU user establishments.

The nature and extent of these measures seem largely to reflect the numbers of animals being sourced.

## **6.7. Herpes B virus**

Herpes B virus (Cercopithecine herpesvirus 1[CHV-1]), is closely related to the human herpes simplex virus. The virus is an infectious agent that is found in populations of macaque monkeys, including rhesus, pig-tailed, and cynomolgus macaques. Monkeys infected with this virus usually have no symptoms or only mild symptoms, including oral or genital lesions, but the virus can also be shed in the absence of lesions.

Infection of humans is rare in the research environment, but is associated with close contact with infected animals and tissues, and can be fatal.

Macaques from Mauritius are virus free, but many breeding colonies in Asia have virus positive animals.

To minimise the zoonotic risk, establishments may choose to source from Mauritius to ensure virus free status, or require animals from other sources to be screened as negative before purchase. Biosecurity precautions remain in place until health status is confirmed. A number of EU establishments are not virus free and minimise transmission risk through biosecurity measures.

To minimise risk of human infection, some indicated a preference for Mauritius suppliers as animals are Herpes B free. Others manage the risk by serological screening and biosecurity measures.

## **7. User views on progress towards F2/F2+ generation for individual species**

### **7.1. Summary of key issues raised by users**

#### **7.1.1. General issues**

- Concerns over difficulties in transporting animals as few airline companies will transport NHP.
- Ensuring a sufficient genetic pool to minimise in-breeding problems.
- Concern over continuity of supply if there are future significant fluctuations in demand.

One example illustrates these concerns:

*"Science in Europe critically depends on the availability of non-human primates. Given the grade of uncertainty on the effective availability of F2 monkeys (low number of European breeders, lack of experience, long breeding time, lack of reserve capacities, etc.), it seems necessary to have a fall-back regulation which allows using F1, if European breeders are not*

*able to meet the demands. Otherwise, future European science in the public as well as the private sector will not be competitive to research in the US and Asia."*

## **8. Availability of different species of non-human primates used in research in EU**

### **8.1. Marmosets**

Although not included in the questionnaire, some responses were received. These merely confirmed that marmosets are being supplied as F2/F2+ . This obligation has been in place since 01 January 2013 and no further action is needed.

### **8.2. Prosimians**

All Prosimians used in 2014 (total use 140 animals) were F2/F2+ sourced from self-sustaining colonies in EU.

**Movement to F2:** user responses indicated that there was sufficient supply of F2/F2+ animals available today to meet scientific needs.

### **8.3. Baboons**

98% of baboons used in 2014 (total use 183 animals) were F2/F2+ sourced from self-sustaining colonies in EU.

**Movement to F2:** user responses indicated that there was sufficient supply of F2/F2+ animals available today to meet scientific needs.

### **8.4. Vervet monkeys**

100% of Vervets used in 2014 (total use 14) were F2/F2+ sourced from America.

**Movement to F2:** user responses indicated that there was sufficient supply of F2/F2+ animals available today to meet scientific needs.

### **8.5. Rhesus macaque**

99% of Rhesus macaques used in 2014 (total use 348 animals) were obtained either as F2/F2+ or from SSC. 231 (66%) were obtained from EU sources, the remaining 117 animals from Asia.

#### **8.5.1. Scientific needs**

Examples of response provided:

- *Different age and weight ranges are required.*
- *Specific MHC profile necessary for some immune studies.*
- *Specific serological profile - antibody negative for certain viruses which may interfere with scientific programme.*

### 8.5.2. Health requirements

Examples of responses provided:

- *Animals required to meet FELASA health screening standards (7).*
- *Herpes B-virus negative (or from colony free of virus) – to minimise risk of zoonotic disease.*
- *Negative serology for Simian Retroviruses (SRV), such as Simian Immunodeficiency Virus (SIV) and Simian T-cell Lymphotropic Virus (STLV).*

### 8.5.3. Future need for wild caught and/or F1 generation

Examples of responses provided:

- *May be scientific need in future to use wild-caught animals – for example specific haplotype unavailable from captive-bred animals; investigation of disease outbreaks; conservation studies using animals reared under natural conditions.*
- *Genetic drift in captive-bred populations.*

### 8.5.4. Difficulties with obtaining F2s

Examples of responses provided:

- *Limited availability of full range of age and sex.*
- *Insufficient B-virus negative animals*

### 8.5.5. Impact of move to F2/F2+

Examples of responses provided:

- *Unpredictable effects of genetic and behavioural drift on models.*
- *Research less competitive - increased costs (housing and breeding) to secure availability (animals are “reserved” and held for a particular customer until required).*

### 8.5.6. Concerns over 2022 deadline

2.2.4.13 By what date do you consider that there will be sufficient suitable F2/F2+ Rhesus (M mulatta) to meet your needs?

		Answers	Ratio
Earlier than 2022		12	66.67 %
2022		3	16.67 %
2025		0	0.00 %
2028		1	5.56 %
Later than 2028		2	11.11 %

Of those who responded that implementation be later than 2022:

- *Unknown capability of the breeders to fulfil F2 requirements.*
- *Concerns over genetic drift, health issues (B-virus, sanitary and differences in behaviour/cognitive abilities if forced to change supplier).*

### 8.5.7. Movement to F2 - Rhesus macaque

In 2014, 99% of the Rhesus macaques used in EU were of F2/F2+ generation or from SSCs.

- **Movement to F2:** Although the F2 requirement is already largely being met, users have requested that the possibility of exemption to this requirement be retained should there be an unexpected change in demand and no other species would scientifically suffice.

### 8.6. Cynomolgus macaques

In 2014, 82% of the total NHP used for the first time in EU were Cynomolgus macaques.

Of the 5136 Cynomolgus used, 1,128(22%) were F1, 2147 (42%) were F2/F2+ and 1857 (36%) were obtained from a self-sustaining colony.

The majority (98%) of F1 animals used were born in Africa (exclusively in Mauritius). Confirmation was given that a number of the SSC colonies in Mauritius have been “closed” for around 10 years, but that these colonies still contain FO breeders, and also continue to supply F1 animals to Europe.

**The present EU statistical reporting system does not distinguish the generation of an animal born in a SSC, and therefore the number of F1 Cynomolgus macaques used in EU may be higher than those reported (that is animals sourced from SSC could be either F1 or F2/F2+).**

#### 8.6.1. Scientific needs

Examples of responses provided:

- *Varied weight range, sexual mature/immature, adult ethogram and full cognitive abilities, MHC compatibility between animals.*
- *Animals free from Herpes B virus, tuberculosis.*

#### 8.6.2. Health requirements

Examples of responses provided:

- *Animals to be of a suitable health status, for example meeting the FELASA Health screening requirements (7)*
- *Animals to be Herpes B-virus free. **Note** – Mauritius is B-virus free.*

#### 8.6.3. Future need for wild caught and/or F1 generation

Examples of responses provided:

- *Wild-caught animals may be required in the future for some studies.*
- *Investigation into new or emerging diseases.*
- *Genetic variability – specific genetic profile required*
- *F1 generation may be required – concerns raised over possible fecundity issues in reproductive studies in long established captive breeding colonies.*

#### 8.6.4. Difficulties with obtaining F2s

Examples of responses provided:

- *Genetic drift.*
- *Changes in cognitive responses/behaviour if have to change suppliers.*
- *Concerns re different health status between Mauritius and Asia.*

#### 8.6.5. Impact

Examples of responses provided:

- *Unpredictable effects of changed sources on science.*
- *Relocation of science outside EU if no suitable animals.*
- *Welfare concerns over alleged different standards of care in overseas breeding establishments*

#### 8.6.6. Concerns over 2022 deadline

Examples provided:

- *Unknown capability of breeders to meet all requirements for animals – age, disease model, behaviour, reproducibility of research.*
- *F1 generation animals have poorer fecundity.*
- *There could be inbreeding/genetic diversity issues.*
- *European market small compared with USA (in 2015 USA imported 22,300 Cynomolgus vs 4893 in EU in 2014) – no requirements for change to F2 purpose-bred animals in USA. Breeders may preferentially supply other markets.*

From the User responses received regarding implementation dates for Cynomolgus macaques 15/24 were of the view that the 2022 date was achievable.

2.2.3.13 By what date do you consider that there will be sufficient suitable F2/F2+ Cynomolgus (M fascicularis) to meet your needs?

		Answers	Ratio
Earlier than 2022		9	37.50 %
2022		6	25.00 %
2025		2	8.33 %
2028		5	20.83 %
Later than 2028		2	8.33 %

- All user responses from 7/8 Member States confirmed the feasibility of the 2022 timeline set out in Annex II with no negative impact on research.

Of those who responded that implementation be later than 2022:

Users in only one MS indicated difficulties in meeting the 2022 timeline. However, further analysis showed that in that particular MS, those users that were using more than 50% of the total number of NHP in that MS indicated that the timeline of 2022 was feasible.



## Views from users in one MS

2.2.3.13 By what date do you consider that there will be sufficient suitable F2/F2+ Cynomolgus (M fascicularis) to meet your needs?

		Answers	Ratio
Earlier than 2022		2	15.38 %
2022		2	15.38 %
2025		2	15.38 %
2028		5	38.46 %
Later than 2028		2	15.38 %

The main reasons given by those who were of the view that further time was needed were as follows:

### 8.6.7. Later than 2028

- "I don't know"
- *We don't know the breeders' capability to supply our need if only F2 is required"*

### 8.6.8. By 2028

- *According to discussion with supplier"*
- *Time would be needed for the suppliers to increase their stock and organize their work"*
- *All F1 animals are used in research therefore not available for breeding. Accelerated switch would have major economic consequences for breeders"*
- *Mostly due to breeding capacity and current population of F1 animals available for breeding (most of them are used in research), a long period of time shall be anticipated before 100% F2/F2+ animals are available, with an appropriate genetic diversity among this population."*
- *[the same response by two different users]*

### 8.6.9. By 2025

- *A sufficient number of animals might not be available before 2025 because of decreased fertility of F1 females and potential genetic diversity issue with F2 animals"*
- *difficult to know, please see with breeders"*

### 8.6.10. Movement to F2 – Cynomolgus macaque

This is the species used most commonly in EU, and the majority of animals are sourced from overseas breeding colonies in Mauritius and Asia. Progress has been made in recent years towards increased numbers of F2 animals, but the views expressed by users is that it will take some years for the current suppliers in Mauritius to meet demand using only F2 animals. The majority of users were of the view that 2022 is achievable, but there will be a continued need for exemptions for scientific reasons for some time thereafter, for example when aged animals are needed, or animals with natural disease, such as diabetes, as it will be some time until F2 animals of that age are available for supply.

In one MS, the majority of users suggested an extended timeline for implementation. However, this seems to be based either on lack of information or on information provided by their current overseas suppliers. In order to assess the actual supply, the analysis of the responses from the overseas suppliers are summarized in the next section.

- **Movement to F2:** Although good progress has been made already, significant concerns have been raised by users in one MS on insufficient availability of F2/F2+ to meet the requirements by 2022 by overseas suppliers.

**This will be further explored below in the analysis of the supplier questionnaire.**

### **8.7. Additional species**

Information was provided on the use of one additional species, which is not listed as a separate species in the statistical reporting.

**Macaca nemestrina** (Southern pig-tailed macaque) – used in very small numbers. No information provided on commercial breeding colonies.

### **8.8. Summary of responses from overseas breeders /suppliers of NHP into EU**

Information was obtained from three *Cynomolgus* breeders (two from Mauritius and one from Asia), who completed the EU questionnaire.

Further, additional information was supplied by an EU supplier on a further five Asian breeding centres supplying *Cynomolgus* and Rhesus macaques.

The majority of these breeders supply to a global market, but only two of the Asian centres supply at present into EU.

For reasons of confidentiality, information on supply can only be provided in a consolidated manner.

### **8.9. Suppliers from Asia**

The majority of sales from the Asian breeders from whom information was gathered indicated that many animals were destined for markets other than EU. The US market is significantly greater than the EU market – in 2014, 47930 NHP were used in USA (8) compared with 6239 in EU.

In 2014 in EU, 2035 NHP (1915 *Cynomolgus*; 117 Rhesus) were used which had been born in Asia. Only a very few (30) were not of F2/F2+ generation. Two respondents supplied around 90% of these animals, both of whom have no F0 animals in their colony and only supply F2 to EU.

### **8.10. Suppliers from Africa**

The suppliers from Africa are based in Mauritius.

In 2014, 3075 NHP (all *Cynomolgus*) were used which had been born in Africa. 1,102 were F1 animals (36%) and a further 1453 (47%) were from SSC, which supplied both F1 and F2 animals. 519 (17%) were sold as F2 animals.

The two suppliers who responded accounted for the great majority of animals supplied for use in the EU. The data provided for supply in 2015 indicated that the generations supplied were 56% F1 and 44% F2.

### 8.11. Availability of F2/F2+ Cynomolgus macaques

*Table 15 - Combined data on Cynomolgus macaque annual availability from the three completed questionnaire responses*

<b>Availability of Cynomolgus Macaques</b>		
<b>Number of animals</b>		
<b>F0</b>	<b>F1</b>	<b>F2/F2+</b>
<b>28</b>	<b>3763</b>	<b>7835</b>

The availability of F2/F2+ Cynomolgus macaques which could be supplied into EU from current overseas suppliers significantly exceeds demand (7835 available vs 5135 used in 2014). It is important to note that one of the suppliers to the EU provided only information on their EU sales, not their global sales, and F2 availability could therefore be significantly higher.

From information received from all sources, it is estimated that around 13,500 F2/F2+ cynomolgus macaques are available for sale annually.

## 9. Summary

Unlike Rhesus macaques where all animals are born in EU or Asia, and more than 99% used are already F2/F2+ generation, the situation with Cynomolgus is more complex. In 2014, around 5% of Cynomolgus were born in EU, 35% in Asia and the remaining 60% in Africa (Mauritius).

The Asian supplier who responded to the questionnaire indicated that there was no difficulty at present in meeting the demand for F2/F2+ animals.

It is acknowledged that this analysis is premised on the view that all animals could be sourced from any available supplier, but there are likely to be factors making this problematic, for example continuity of genetic background, and of historical data in behavioural studies.

### 9.1. Responses by overseas breeders/suppliers to questionnaire

In Mauritius, until around 2008, breeding stock was sourced from the wild – the Cynomolgus macaque is classified as a pest in this country. Since then, the colonies have been “closed”, and F1 breeders have been building up slowly. However, concerns have been expressed that moving too quickly towards F2 production will have negative welfare impacts, including surplus of males and poorer reproductive performance in F1 breeding stock.

These concerns were not expressed in the detailed response from the large Asian supplier, but this supplier has been evolving a closed SSC for a longer period of time.

### **9.1.1. Insufficient supply to meet demand**

Examples of responses provided:

- *There have been fluctuating demands and it is not always possible to match supply and demand.*
- *One response noted that the move towards production of F2 only, has impacted on sales as increased number of females are held back as breeding stock and a number of males are unsold.*
- *It can be difficult to supply special requests for, in particular, aged animals or of a specific disease status.*

### **9.1.2. How do you match supply and demand for Cynomolgus (M. fascicularis)?**

Examples of responses provided:

- *It is challenging. Longer lead in times for orders would help.*
- *Trapping of wild-caught animals offered some greater flexibility in supply but this is not currently an option.*

### **9.1.3. Strategy for replacement breeding stock**

Examples of responses provided:

- *Additional F1 females are being retained to increase F2 production.*

### **9.1.4. Under what circumstances, if any, you would capture animals from the wild**

Examples of responses provided:

- *In Mauritius, Cynomolgus macaques are considered a pest species. Capture would be considered only in very specific circumstances where no purpose-bred animals are available or suitable for the study.*

### **9.1.5. Are there any impacts on breeding performance of using only breeding stock which themselves are offspring of animals bred in captivity when compared with wild caught or F1 generation?**

Both Mauritian breeders indicated that they had concerns over the breeding performance of F1 animals. These included reduced numbers of offspring, higher pre-weaning mortality rates (between 2-5%) reduced breeding life (late onset maturity and earlier retirement) and early onset of age-related diseases. One breeding centre has published information on the differences in reproductive success between wild-caught and captive-bred Cynomolgus macaques (9).

In contrast, the Asian breeder was of the view that there was no adverse impact on breeding performance of F1s, taking into consideration the overall productivity and infant mortality rate. This breeder believes that captive-bred dams are healthier than wild-caught dams and indeed have improved performance when compared with wild caught animals.

Similar findings to that of the Asian breeder were expressed from breeding establishments within the EU. Although they did not have experience of F0 animals, they found reproductive performance to be satisfactory. All commented that the management of replacement breeders was very important, in terms of selection and husbandry practices, to ensure some exposure to rearing practices for potential replacement breeding animals. Placement with experienced breeding groups, both males and females, is considered very important to success. Still births and pre-weaning losses were reported as very low.

**9.1.6. Are there any impacts on animal health or welfare of using only breeding stock which themselves are offspring of animals bred in captivity when compared with wild caught or F1 generation?**

Both Mauritian breeders were of the view that F1 animals seem to age more quickly than the wild caught animals.

Their views were that F1+ breeders have a higher tendency to obesity than wild-caught breeding animals. These animals are also considered much less active in a breeding group and are more susceptible to boredom than F0 breeders. This is considered to impact negatively on their welfare.

Another concern with the rapid expansion of an F1 colony is to ensure appropriate genetic variability and minimise the potential adverse effects of in-breeding (3).

These observations again differed from those of the Asian breeder, where no adverse impact on animal health or welfare has been observed. In fact, the response noted that captive-bred breeders tended to exhibit higher tolerance in the captive breeding environment than wild-caught animals and integrated better into breeding groups.

**9.1.7. Breeding strategy in place to increase the proportion of F2 and higher generation (F2+)**

The Mauritian breeders have since 2009 been accelerating the number of F1 replacement breeders to increase the numbers of F2 animals available for sale.

This strategy has been put in place to meet the expectations of the Directive, without being required by EU customers.

**9.1.8. Please estimate the date by which all animals supplied from your organisation to EU can be F2 or F2+ (in accordance with the projected demands) - broken down by species. If you do not consider it feasible, please explain reasons why - broken down by species).**

One Mauritian breeder expects to be able to supply EU customers with F2 animals within the next two to three years, the other by between 2023-2026.

Asian breeders have today sufficient capacity to supply EU with F2/F2+.

**9.1.9. Has the EU policy to increase the demand to F2 and F2+ resulted in surplus of F1 animals?**

One Mauritian breeder commented that this policy has resulted in a surplus of around 250 males per year. Although a market has to date been found for these, there is a risk that some animals may need to be euthanised.

The other responses indicated that sales had been secured for any surplus males generated by the breeding strategy.

When the F1 colony is well established this risk should recede.

**9.1.10. What would be the impacts on your business of EU requiring that only F2 or F2+ animals be supplied from 2022 onward to EU?**

Impact will be dependent on reliance on EU market. USA market is much greater and if no change in their requirements, then ensuring F2 animals for EU should be achievable.

However, an approximate increase in costs of around 20% was suggested by one breeder.

In contrast, however, information provided from users and other breeders indicated that the anticipated increase and differential costing between F1 and F2 costs (Prognos report (1)) has not materialised.

**9.1.11. Are there any special customer requirements, other than age and sex, which you have to fulfil, for example providing aged or diabetic NHP?**

There continue to be requests for older animals for ageing research, including osteoporosis, obesity and diabetes.

F2 animals to meet these needs will not be available for some years, and there should be the possibility to continue to use F1 animals, for example retired breeding stock.

**Comment** – The ethical issues of killing animals as pests versus capture and maintaining as breeding stock was raised as an issue, but acknowledged that in the present political climate, acceptance of the capture, breeding and use of wild-caught animals was unlikely to change.

**9.1.12. Do your self-sustaining colonies contain F0 animals? Please specify by species and an estimate of the date until when the colony will continue to contain F0 animals.**

Both Mauritian breeders continue to have F0 breeding animals within their SSC. It is not expected that they will be fully replaced until around 2026.

**9.2. Rationale for continued exemptions for use of F0/F1 animals**

Reasons were given for retention of the option for MS to authorise a scientific exemption from the F2 requirement.

Exemption from F2 requirement may be necessary for:

- *Aged animals or animals with specific natural disease, such as diabetes. It is unlikely that such F2 animals will be available for a number of years.*
- *Unforeseen disease outbreaks in the animals might mean that a particular and large supplier, or even an entire country, can no longer supply European states.*

- *A severe human disease outbreak might result in the need to use extraordinarily large numbers of non-human primates for vaccine or other treatment options in the face of a potential international disaster, for example recent epidemics such as SARS virus, Ebola virus, Zika virus.*

**In this context, it is important to note that Article 10(3) foresees a possibility for an exemption on basis of a scientific justification**

### **Movement to F2 - Cynomolgus macaque**

This is the most commonly used species in EU, and although progress is being made towards the supply and use of only F2/F2+ animals, this objective has not yet been fully achieved.

Although there are sufficient F2 animals now available within the global market, an early deadline would require users to move from their current suppliers with potential concerns raised over continuity of historical scientific data.

- **Movement to F2:** By 2022, it is expected that there will be sufficient animals from existing sources to implement the requirement for use of only F2/F2+ animals, although there will continue to be for some time beyond that date a potential need for scientific exemption where certain requirements need to be met, and no scientifically suitable F2/F2+ animals are available.

## 10. References

1. Study on the impacts of different options for the Revision of the Directive 86/609/EEC on the Protection of Laboratory Animals Final report. Prognos AG 2007 ([http://ec.europa.eu/environment/chemicals/lab\\_animals/pdf/prognos\\_summary.pdf](http://ec.europa.eu/environment/chemicals/lab_animals/pdf/prognos_summary.pdf) )
2. Hansards. House of Commons written answer to a parliamentary question for 4 October 2004 by Elliot Morley MP (Secretary of State for Environment, Food and Rural Affairs). Hansards' question 188717, UK House of Commons: Hansard, Vol. 424, Column 1933W, 4 October 2004
3. European Commission - The welfare of non-human primates used in research, Report of the Scientific Committee on Animal Health and Animal Welfare. Adopted on 17 December 2002 [ec.europa.eu/food/sites/food/files/.../sci-com\\_scah\\_out83\\_en.pdf](http://ec.europa.eu/food/sites/food/files/.../sci-com_scah_out83_en.pdf)
4. Hansard - (A) 2009 and (B) 2010. [*Official Report, 4 November 2010, Vol. 517, c. 876-77W.*] <https://www.publications.parliament.uk/pa/cm200809/cmgeneral/euro/090203/90203s01.htm>
5. Criteria for feasibility, health and welfare assessment of requirement to use second and subsequent generations of non-human primates or animals from self-sustaining colonies in research. Extract from an expert group report endorsed by EFPIA, FELASA, ESLAV and ECLAM, 2010 Thierry Decelle, Lars Friis Mikkelsen, David Smith and Magda Chlebus ; *Primatologie.revues.org* 3:2011
6. IPS International Guidelines for the acquisition, care and breeding of non-human primates ( <http://internationalprimatologicalsociety.org/>)
7. Recommendations for health monitoring of non-human primate colonies (1999) <http://www.felasa.eu/recommendations/recommendation/recommendations-for-health-monitoring-of-non-human-primate-colonies>
8. USDA/APHIS Annual Report Animal Usage by Fiscal Year 2014 [https://www.aphis.usda.gov/animal\\_welfare/downloads/7023.pdf](https://www.aphis.usda.gov/animal_welfare/downloads/7023.pdf)
9. Reproductive success of wild-caught and captive-bred cynomolgus macaques at a breeding facility Levallois L, de Marigny SD, Noveprim Group, Le Vallon, Vieux Grand Port, Mauritius, *Lab Anim (NY)*. 2015 Oct;44(10):387-93.



## 11. Glossary of terms

**AAALAC** – American Association for Accreditation of Laboratory Animal Care

**Breeder** - establishment which breeds and supplies animals for scientific procedures

**Commission Implementing Decision 2012/707/EU** (revised in 2014 to 2014/11/EU) indicates the information which needs to be reported on animal use

**Directive 2010/63/EU** – Directive on the protection of animals used for scientific purposes.

**EU** - European Union

**EC** - European Commission

**EU Survey** – EUSurvey is the Commission's online survey management tool used to create and conduct multilingual surveys.

**F0** - wild caught animals

**F1** – offspring bred in captivity from wild caught parent(s)

**F2** – first generation of animals whose parents themselves were bred in captivity

**F2+** - subsequent generations of animals whose parents themselves were bred in captivity

**Fecundity** - the state of being fertile; capable of producing offspring

**Haplotype** - the genetic constitution of an individual at a set of linked genes.

**Herpes B virus** – Herpes B virus (Cercopithecine herpesvirus 1[CHV-1]), is an infectious agent that is found in populations of macaque monkeys. Monkeys infected with this virus usually have no symptoms or only mild symptoms, but if the virus infects humans it is life-threatening.

**MS** – Member State

**MHC** - major histocompatibility complex (MHC) is a set of cell surface proteins essential for the immune system to recognise foreign molecules. The MHC determines compatibility of donors for organ transplant as well as susceptibility to autoimmune diseases.

**NCP** – National Contact Point – main contact point in MS for implementation of the Directive

**NHP** – non-human primate

**SRV** – Simian Retroviruses

**SIV** – Simian Immunodeficiency Virus

**SSC** – a "self-sustaining colony" colonies in which animals are bred only within the colony, or sourced from other colonies, but not taken from the wild and kept in a way that ensures that they are accustomed to humans (Article 10(2)).

**Supplier** – establishment which sources animals from breeders and supplies on to user establishment

**STLV** - Simian T-cell Lymphotropic Viruses

**User** - establishment/organisation in which animals are used in scientific procedures

## **12.List of Annexes**

Annex I – Request for information from Member States which have establishments using or breeding non-human primates for scientific purposes

Annex II - Eurogroup for Animals Survey on the implementation of Directive 2010/63/EU – presented at 11<sup>th</sup> NCP meeting on 17 February 2016

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## **Annex I: Request for information from Member States which have establishments using or breeding non-human primates for scientific purposes**

### **Survey on acquisition of NHPs for use in procedures** February 2016

#### **Legal Background**

The Commission shall, in consultation with the Member States and stakeholders, conduct a feasibility study, which shall include an animal health and welfare assessment, of the obligation to ensure that non-human primates, listed in Annex II of the Directive, may be used in procedures only where they are the offspring of non-human primates which have been bred in captivity or where they are sourced from self-sustaining colonies.

Annex II states that marmosets (*Callithrix jacchus*) shall meet this requirement by 1 January 2013 and other non-human primates by 5 years after the publication of the feasibility study, provided the study does not recommend an extended period

The feasibility study shall be **published no later than 10 November 2017**. It shall be accompanied, where appropriate, by proposals for amendments to Annex II.

#### **Initial questionnaire to provide background information for the feasibility study**

1. If non-human primates are currently ***not bred, supplied or used in your Member State***, are you aware of any future plans to initiate a breeding or use programme?

2. If non-human primates ***are bred in your Member State***, what measures have been taken to provide reassurances that breeding strategies have been set up in all relevant breeding establishments for increasing the proportion of animals that are offspring of animals bred in captivity?

3. Please list the key elements of such strategies established by your breeders to meet this requirement?

By what date do you expect to use only animals which are offspring of captive-bred animals? Please provide the information by species bred in your MS as the timeline may

differ between species.

4. Please list the key elements of such strategies established by your breeders to meet this requirement? \*)

By what date do you expect to use only animals which are offspring of captive-bred animals? Please provide the information by species bred in your MS as the timeline may differ between species

**5. If NHPs are sourced from outside the EU**, what measures, if any, are taken to obtain reassurance over the accommodation, welfare and care practices in overseas establishments, and on a breeding strategy to move toward higher generation purpose bred animals? \*)

By what date do you expect to use only animals which are offspring of captive-bred animals or from self-sustaining colonies obtained outside the EU? Please provide the information by species used in your MS as the timeline may differ between species.

6. Information will be sought from breeders, suppliers and users of non-human primates in the EU. Please provide the contact details for each of the establishments authorised to breed, supply and/or use non-human primates in your MS \*\*)

7. Are there any other relevant organisations in the EU that should be contacted with a request to provide information on this issue? If so, please provide their details.

8. Are there any other relevant organisations in third countries that supply animals into EU that should be contacted with a request to provide information on this issue. If so, please provide/attach their details.

**\*) Please note that there is no need to answer question marked with \*) if you have already responded to the Eurogroup Questionnaire. Commission has already received copies of these answers.**

**\*\*\*) Please note that all contact details, as well as details of the organisations, will remain strictly confidential. Furthermore, information provided by respondents will remain anonymous and/or consolidated at EU level.**

Finally, please indicate whether you agree to the use of statistical information submitted to ALURES on non-human primates. Please note that no formal EU report is published at the time of this study. However, national data should have been published annually. Information from ALURES would be consolidated at EU level without any MS specific references.

**YES / NO**

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## Annex II: Eurogroup for Animals Survey on the implementation of Directive 2010/63/EU – presented at 11<sup>th</sup> NCP meeting on 17 February 2016

# EUROGROUP FOR ANIMALS

Survey on the implementation of Directive 2010/63/EU  
11th NCP meeting

Date 17 February 2016



## Overview

- Eurogroup contacted Member State NCPs initially in October 2015 through a [questionnaire](#) (responses are still welcomed)

## Reasons for the Survey

- To develop some [understanding](#) on how the issues have been implemented across the Member States.
- We require this information so we can better understand where there are [gaps](#) and where improvements may be necessary through the [sharing of best practices](#).
- The intention is to start a [multi-stakeholder project](#) on the sharing of best practices involving critical stakeholders such as animal welfare, industry, research institutes, breeders, EU agencies and national authorities.



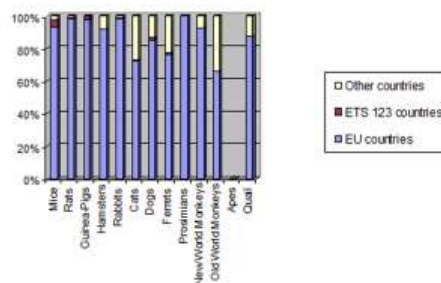
## Focus of the Questions

- The requirements for inspections laid out in Section 2, Article 34: **Inspections by the Member States**
- Article 28 requires Member States ensure that **breeders of non-human primates** have a system in place to increase the proportion of captive bred NHP
- **Project authorisation** process as laid out in Section 3 – *Requirements for projects*. All projects are required to go through a **project evaluation** as an integral part of the authorisation process

## Non-human primates

- **6095** primates in total from 2011 statistics
- **9 MS (+ 1)** used NHP in 2011 (2010 for France), **3 (+1)** of the MS who responded
- There is an **increase** in the use of old world monkeys of EU origin from 54% to 66%
- There is a **decrease** in use of new world monkeys of EU origin from 99% to 92%

Figure 1.2: Origin of species



## Article 28 - Breeding strategy for non-human primates

Member States shall ensure that breeders of non-human primates have a **strategy in place for increasing the proportion** of animals that are the offspring of non-human primates that have been bred in captivity.

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## Article 28 - Breeding strategy for non-human primates

- MS (who responded) with specific reference in their legislation:
  - **The Hungarian legislation concerning the use of NHPs is stricter than the Directive**
    - '...all species of NHPs (except two Macaque spp) have to be the offspring of NHPs which have been bred in captivity.'
    - '...all NHPs may only be used in procedures where those animals have been bred for use in experiments (without exemption),
    - '...the NHPs cannot previously been kept in a zoo, '
    - '... the conditions for the accommodation of NHPs are stricter than in the Directive.
  - **In The Netherlands: The only institute that breed NHPs for research purposes in the NL is the Biomedical Primate Research Centre (BPRC)**
    - is a self-sustaining colony that breeds sufficient numbers of animals (for internal use), using a system that mimics the natural situation as optimal as possible.
    - BPRC is a main partner in EUPRIM, a European network of primate research facilities. EUPRIM (waiting on project submission in March 2016). An important issue for guidance (to be disseminated) is breeding strategy (peer groups versus natural groups, weaning of animals etc).
  - **Sweden: use NHP but do not breed, however site visits (outside Sweden) have been made to the breeding facilities.**
    - Information has been given about the requirements of the Directive, and it is noticeable that animal welfare has been prioritized over the years. All animals delivered are at least F2 generation.

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## Views from Member States on NHP Breeding strategies

- MSs who **do not** use NHP presently would like to **seek best practices** to house and manage them should they use them in the future.
- MSs with system in place (in legislation) feel they don't require guidance however their **expertise may be valuable** to other MSs.
- **Guidance can come through EUPRIM** and could be provided to others, including focus on peer groups versus natural groups, weaning of animals etc.
- One MS noted there are **concerns** that the requirement of sourcing only from **self-sustaining breeding** colonies may create a lack of females for use in research. Waiting for outcome of the feasibility study (Article 10) (Deadline 17 November 2017).

## Next Steps

- **Thank you** to the NCPs who have sent us information
- If others still wish to **respond** (or confirm the information we have gathered is accurate) then this is welcomed
- The information will be gathered into a **report** with recommendations to move forward in **sharing good practices**

## **Annex III: Summary points for discussion at June 2016 Stakeholder Meeting**

### **Feasibility study as required in Article 10 of Directive 2010/63/EU on the protection of animals used for scientific purposes**

#### **Meeting of experts on Friday 24th June 2016, Brussels**

#### **Development of questionnaires on the acquisition of non-human primates (NHPs)**

##### Background

Recital 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.”*

The respective Article 10 of the Directive requires that the Commission shall, in consultation with the Member States and stakeholders, conduct a feasibility study, which shall include an animal health and welfare assessment, of the obligation to ensure that non-human primates, listed in Annex II of the Directive may be used in procedures only where they are the offspring of non-human primates which have been bred in captivity (F2 / F2+) or where they are sourced from self-sustaining colonies.

Annex II states that marmosets (*Callithrix jacchus*) shall meet this requirement by 1 January 2013 and other non-human primates by 5 years after the publication of the feasibility study, provided the study does not recommend an extended period. The feasibility study shall be published no later than 10 November 2017.

As stated in the invitation, **the purpose of this meeting is to define what information will be required to facilitate an informed decision on progress towards this requirement of Article 10.**

Having determined the information necessary, finalised questionnaires will be sent to all relevant stakeholders, including identified overseas breeders and suppliers of non-human primates into the EU.

The aspects which require to be considered include

- Current numbers of non-human primates used, including source and generation of animals and availability of all the commonly used species;
- The evolution on the availability and demand of F2 non-human primates since the adoption of the Directive;

- Estimation of future needs and predicted availability of animals to meet this demand;
- The identification of relevant information to assess the time needed to fulfil the anticipated demand – presently 5 years after publication of the feasibility study i.e. November 2022;
- The aspects of animal health and welfare which may be impacted in meeting the objectives and timescales set out in the Directive;
- Identification of relevant stakeholders for the targeted questionnaire.

### **Topics to be covered during the meeting**

1. Presentation of background data
  - Current use and availability on the basis of 2014 draft data
  - Previous trends/evolution on availability and demand for NHPs on the basis of the limited data available
2. Discussion of areas for consideration for inclusion within the study
  - Estimate of future needs (users)
  - Availability of suitable animals (breeders/suppliers).
  - Animal health and welfare considerations to be covered
  - Identification of information relevant to setting a date to meet Article 10 and Annex II requirements

Against the above background, two initial draft questionnaires have been developed to be used as the basis for discussion at the meeting.

### **Current status**

Summary of key points on current practices/strategies supplied in response to an earlier questionnaire circulated to the National Contact Points of the Member States

- Very few F0s reported – purpose and source yet to be confirmed.
- All prosimians, New world NHPs and majority (80%) of Old World NHPs used in 2014 are either F2/F2+ or from self-sustaining colonies.
- 18% of total use is of F1 animals, the majority of which are sourced from Africa.
- The number of NHPs used in EU seems to have increased by around 2% from 2011 to 2014;
- Although there are no hard figures on trends from F1 to F2/F2+/SSC, information in the EC impact assessment would suggest that significant progress has been made towards using purpose-bred F2/F2+ animals.

### **Trends**

#### **NHP Use in EU (2002 – 2014)**

	<b>2002</b>	<b>2005</b>	<b>2008</b>	<b>2011</b>	<b>2014</b>
Prosimians	1095	677	1261	83	Some national data not yet published, in other cases first use not separated from re-use. First indications at around 6200 first uses.
New World	1192	1564	904	700	
Old World	8075	8208	7404	5312	
Total	10,362	10449	9569	6095	

**General question**

Should any information be gathered on Marmosets? The F2 obligation is already in force from 1.1.2013.

**Annex IV: EU Directive 2010/63/EU: Article 10 feasibility study –  
questionnaire for users, breeders and suppliers of non-human primates**



Art10Dir2010-63-EU  
Users-Breeders-Supp

**Annex V: EU Directive 2010/63/EU: Article 10 feasibility study –  
questionnaire for breeders of non-human primates**



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