

CONVENTION ON INTERNATIONAL TRADE IN ENDANGERED SPECIES
OF WILD FAUNA AND FLORA



Joint sessions of the 30th meeting of the Animals Committee and
the 24th meeting of the Plants Committee
Geneva (Switzerland), 20-21 July 2018

Interpretation and implementation matters

General compliance and enforcement

SPECIMENS PRODUCED FROM SYNTHETIC OR CULTURED DNA

1. This document has been prepared by the Secretariat.
2. At its 17th meeting (CoP17, Johannesburg, 2016), the Conference of the Parties adopted Decisions 17.89 to 17.91 on *Specimens produced from synthetic or cultured DNA*, as follows:

Directed to the Secretariat

17.89 *The Secretariat, subject to external funding, is requested to:*

- a) *undertake a review of relevant CITES provisions, resolutions and decisions, including Resolution Conf. 9.6 (Rev. CoP16) on Trade in readily recognizable parts and derivatives, to examine how Parties have applied the interpretation of Resolution Conf. 9.6 (Rev. CoP16) to wildlife products produced from synthetic or cultured DNA, under what circumstances wildlife products produced from synthetic or cultured DNA meet the current interpretation, and whether any revisions should be considered, with a view to ensuring that such trade does not pose a threat to the survival of CITES-listed species; and*
- b) *report the findings and recommendations of this study to the 29th meeting of the Animals Committee, the 23rd meeting of the Plants Committee, and the 69th meeting of the Standing Committee.*

Directed to the Animals and Plants Committees

17.90 *At the 29th meeting of the Animals Committee and the 23rd meeting of the Plants Committee, the Animals and Plants Committees are requested to review the findings and recommendations of the Secretariat's report in Decision 17.89 and make recommendations for consideration at the 69th meeting of the Standing Committee, including appropriate revisions to existing resolutions.*

Directed to the Standing Committee

17.91 *At its 69th meeting, the Standing Committee is requested to review the findings and recommendations of the Secretariat's report in Decision 17.89 and the recommendations of the Animals and Plants Committees, and make recommendations for consideration at the 18th meeting of the Conference of the Parties, including appropriate revisions to existing resolutions.*

Background

3. At the joint session of the 29th meeting of the Animals Committee and the 23rd meeting of the Plants Committee (Geneva, July 2017), the members of the Committees reviewed document [AC29 Doc. 15/PC23 Doc. 16](#) prepared by the Secretariat. It was noted that the definitions of synthetic or cultured DNA were not self-evident and would need to be clarified.
4. The Animals and Plant Committees established an in-session drafting group, which finalized the terms of reference for the study on specimens produced from synthetic or cultured DNA called for under Decision 17.89, paragraph a) (see [AC29 summary record](#), item 15).
5. The Standing Committee, at its 69th meeting (Geneva, November 2017) reviewed the Secretariat's report (see document [SC69 Doc. 35](#)) on the progress made and provided further inputs into the terms of reference for the study. The final version is found as Annex 1 to the present document. The Standing Committee invited Parties and observers to provide relevant information on the issue of specimens produced from synthetic or cultured DNA to the Secretariat, including existing reports and literature, examples of specimens produced from synthetic or cultured DNA, etc.
6. Furthermore, the Standing Committee established an intersessional working group (chaired by Mexico) on synthetic or cultured DNA (see [SC69 summary record](#), item 35) with a mandate to:
 - a) review the findings and recommendations of the Secretariat's report in Decision 17.89 and the recommendations of the Animals and Plants Committees, and
 - b) make recommendations for consideration at the 70th meeting of the Standing Committee, including appropriate revisions to existing resolutions.

Progress to date

7. In implementing Decision 17.89, paragraph a), the Secretariat hired a consultant to conduct the study. The consultant has in-depth knowledge of techniques used for bioengineering, synthetic biology and DNA/cell culture, as well as legal and policy-related issues on the use of biotechnological methods and products, with first-hand experience in legislative and policy advice, risk assessment and risk management guidance. After the completion of the recruitment process in accordance with the United Nations rules and regulations, the consultant began his work on 1 March 2018.
8. Additionally, the Secretariat issued Notification to the Parties [No. 2018/013](#) on 29 January 2018 to begin the collection of relevant information for collating and inclusion in the study. Seven Parties and one observer responded. The result of the responses received to date is summarized in Annex 2 to the present document, which was also shared with the consultant.
9. At the time of writing (15 May 2018), the consultant has completed drafting the sections corresponding to the "first part of the study" and "third part of the study" of the terms of reference. These sections focus on the technological and scientific elements of the study, and may be of most relevance to the Animals and Plants Committees. The draft is attached as Annex 5 (English only). If a more advanced version of the draft becomes available before AC30/PC24, the document will be submitted as information document to the meeting and an oral update will be made by the Secretariat.

Summary of the study (first and third parts)

10. Decisions 17.89 to 17.91 refer to the need to review issues related to the science and legal interpretation surrounding wildlife products produced from synthetic or cultured DNA. The study points out that there are other techniques in the biological sciences, rather than synthetic DNA alone, which are used in the synthetic production or culture of cells, tissues and organs that may be considered equivalent to, or similar to "wildlife products". Furthermore, the study suggests that "cultured DNA" is not a term that is found in the biological sciences.
11. The discussion under this agenda item originates from the need to address scientific processes purportedly used by companies and researchers to develop bioengineered rhinoceros horn and rhinoceros horn powder, as well as the potential for similar processes to produce other wildlife products in the future, including elephant ivory, tiger bone, and pangolin scales. In order to address this original objective, the scope of the

study has been expanded to include the “various biological techniques used to develop organisms and their parts that allow some form of engineering at organism, organ, cellular, molecular and genetic levels”.

12. The first part of the study contains “the different ways that DNA can be synthesized, cultured or otherwise produced artificially, and how wildlife products can be produced from synthetic or cultured DNA in the context of CITES”. In light of the expanded scope, four technologies were reviewed in this section: DNA synthesis, DNA modification, cell culture, and tissue culture. The overview of the technologies, as well as an example of the kinds of wildlife products they can produce, is summarised in Annex 3 to the present document.
13. The third part of the study involves elements to be considered from a scientific or technological perspective. Information on technological developments that can be used to produce specimens of CITES-listed species within the field of synthetic biology is addressed within the first part of the study and appears in the third column of the table in Annex 3.
14. The study highlights that most synthetic products use a combination of various different technologies. The study suggests that distinguishing between wildlife products derived from wild specimens and those derived from those technologies are product level-specific, i.e. they differ depending on whether the products are chemicals, proteins, cells/tissue, and body/body parts. The ability to distinguish products from these technologies, and the potential positive or negative impacts of the use of such products on the conservation of the species in the wild are the two major contributors in considering risk management measures and best practices which can be used to help ensure that trade in wildlife products derived from synthetic and cultured DNA does not pose a threat to the survival of CITES-listed species. The summary of the product levels, relevant tools for distinguishing them, and other scientific considerations of relevance highlighted in the study are presented in Annex 4 to the present document.

Way forward

15. Between 22 July and 2 August 2018, the Secretariat and the consultant will prepare a revised draft of the study, incorporating and responding to any recommendations of AC30/PC24, and any inputs received from the intersessional working group of the Standing Committee, and submit it as part of a working document to the 70th meeting of the Standing Committee.

Recommendations

16. The Animals and Plants Committees are invited to:
 - a) take note of this document;
 - b) provide inputs to the Secretariat on the draft study sections, included as Annex 5 (English only) to this document;
 - c) in light of the discussion on the definition and scope of the study outlined in paragraph 10 above, consider whether the title of this subject matter should be changed from “specimens produced from synthetic or cultured DNA” to “specimens produced from synthetic biology” or other terms that would encompass the wider range of techniques and technologies; and
 - d) make any other recommendations for consideration at the 70th meeting of the Standing Committee, including appropriate revisions to existing Resolutions.

Terms of reference for the study on wildlife products produced from synthetic or cultured DNA

Pursuant to Decision 17.89 and drawing upon document CoP17 Doc. 27 (paragraphs 21 to 26) and other relevant documentation submitted by Parties and observers, the study should review relevant CITES provisions, Resolutions and Decisions, including Resolution Conf. 9.6 (Rev. CoP16) on *Trade in readily recognizable parts and derivatives* and taking into consideration past discussions on specimens covered by the Convention, e.g. ambergris, etc. to examine:

- Part I – How Parties have applied the interpretation of Resolution Conf. 9.6 (Rev. CoP16) to wildlife products produced from synthetic or cultured DNA;
- Part II – Under what circumstances wildlife products produced from synthetic or cultured DNA meet the current interpretation; and
- Part III – Whether any revisions should be considered, with a view to ensuring that such trade does not pose a threat to the survival of CITES-listed species.

First part of the study

Describe in a very concise manner the different ways that DNA can be synthesized, cultured or otherwise produced artificially, and how wildlife products can be produced from synthetic or cultured DNA in the context of CITES.

Summarize cases where specimens of CITES-listed species are being produced from synthetic or cultured DNA, e.g. rhino horn, ivory, pangolin scales, medicinal plants, fragrances, etc.

The Secretariat shall issue a Notification to Parties asking for information on cases where they have issued (or not issued) CITES permits and certificates for bioengineered specimens, and the study shall collate this information and include it in the study report.

Second part of the study

Identify and analyse relevant legal/regulatory/enforcement and scientific/technological inter-related elements that should be considered by the Standing Committee and the joint meeting of the Animals and Plants Committees.

Elements that may be considered from a legal/regulatory/enforcement perspective:

- a) Resolution Conf. 9.6 (Rev. CoP16) interprets the term 'readily recognizable' but does not provide an operational definition for the term 'part or derivative'. The study shall explore the pertinence and relevance of including an operational definition of the term 'part or derivative' in Resolution Conf. 9.6 (Rev. CoP16) in this context; and
- b) The pertinence and usefulness of creating a new source code for "bioengineered" wildlife products derived from synthetic or cultured DNA as a separate category of specimens.

Third part of the study

Elements to be considered from a scientific/technological perspective:

- c) Information on existing or potential tools to distinguish between wildlife products derived from synthetic and cultured DNA;
- d) Information on technological developments that can be used to produce specimens of CITES-listed species within the field of synthetic biology; and

- e) Information on relevant risk management measures and best practices which can be used to help ensure that trade in wildlife products derived from synthetic and cultured DNA does not pose a threat to the survival of CITES-listed species.

To ensure consistency and to avoid duplication, the consultant shall – in undertaking these tasks – take into account ongoing discussions and work carried out by other relevant international organizations, including the Convention on Biological Diversity and its protocols.

**Responses to Notification to the Parties No. 2018/013
(as at 24 April 2018)**

Party	Issued permits or assessed permit applications?	Any other information
Australia	NO	According to the national law, the Management Authority expects that it would require CITES permits in the event that a bioengineered CITES specimen was to enter/exit Australia.
China	YES Issued 5 permits deemed to be related to bioengineering, including paclitaxel (582.9kg) and docetaxel (4kg) from <i>Taxus chinensis</i> and cultured cells of <i>Chlorocebus aethiops</i>	2 projects of synthetic biology, using plant-derived compounds in microbial cell cultures (taxol and ginseng) ^{1,2} Few projects launched recently on plant synthetic biology and mammalian cell synthetic biology ³
European Union	NO	Germany would like to flag that the CITES community may consider creating rules for specimens produced from synthetic or cultured DNA because the demand for those specimens could lead to an increase in the demand for (illegal) real specimens (e.g. rhino horn) and because these specimens could be mixed with (illegal) real specimens. It could be detrimental to the aims of CITES (to protect species in the wild) if those specimens (continue to?) simply fall out of the scope of CITES. This new field reminds us of challenges with look-alike species in the case of listing proposals.
Switzerland	NOT SURE Switzerland exports regularly medicinal products or research material derived from research on primates. However, to determine whether these products are based on bio-engineered or synthetic or cultured DNA has not been required or possible to date.	Database where examples of synthetic bioengineered products are listed: http://www.synbioproject.org/cpi/ Website created by the Swiss Natural Science Foundation specifically devoted to the topic of synthetic biology: https://naturwissenschaften.ch/topics/synbio FAO CGRFA study “Digital sequence information” on genetic resources for food and agriculture (CGRFA-17 Bureau 2/18/4) ⁴ A Fact-Finding and Scoping Study on Digital Sequence Information on Genetic Resources in the Context of the Convention on Biological Diversity and the Nagoya Protocol (CBD/DSI/AHTEG/2018/1/3)

¹ Liu, W.C., T. Gong and P. Zhu, 2016. Advances in exploring alternative Taxol sources. RSC Adv. 2016, 6-48800-48809.

² Zhuang, Y. et al. 2017. Biosynthesis of plant-derived ginsenoside Rh2 in yeast via repurposing a keypromiscuous microbial enzyme. Metabolic Engineering, 42:25-32.

³ Chen, G. and Y. Wang, 2015. Progress in synthetic biology of “973 Funding Program” in China. Chinese Journal of Biotechnology 31 (6): 995-1008.

⁴ This document is not yet available on the FAO Website.

Thailand	NO	No other relevant information
United Kingdom	NO	Not aware of any records of applications for trade in CITES specimens derived from synthetic biology or from 'cultured DNA'
United States of America	NO	<p>Response from the U.S. Fish and Wildlife Forensics Laboratory: "it is important to consider the differences between the protein products that arise from recombinant DNA and cultured cells and the products that are now being proposed by the biosynthetic tissue industry. One major difference is that proteins and antibodies produced from cultured cells are targeted products translated <i>in vitro</i> that do not require the presence of viable DNA molecules from the source organism for production or validation. Therefore, it appears that the biosynthetic tissues (for example, rhino horn) themselves would not require DNA for construction or translation, but that the value of the final product would likely be dependent upon the presence of rhino DNA to create the illusion that it is a real product.</p> <p>From a law enforcement perspective, there needs to be a method by which enforcement is able to discriminate between natural tissue and biosynthetic tissue, regardless of whether it's presented as a 3-D object (horn or tusk or carving) or a medicinal (powder or liquid). Without this detection ability, it is not possible to distinguish between genuine and fabricated items.</p> <p>The Laboratory was informed by an industry representative working with biosynthetic rhino horn that such a detection system would need to be proprietary in the event that a competitor wanted to exploit the fact that a product was synthetic, or to maintain the illusion that that biosynthetic product shares the same traditional characteristics of the natural product.</p> <p>Unfortunately, proprietary detection systems will not stand up in a court of law if we have to demonstrate that a product is real or biosynthetic as we would not be able to exclude a natural source. There are ways to "label" a biosynthetic product to prevent identification challenges for enforcement – a known DNA barcode could be incorporated into the DNA sample included in the synthesis of the final product, or an inert rare earth element could be added to the product that could be easily detected but not interfere with the commercial value of the product.</p> <p>For example, "biosynthetic" caviar can be distinguished from genuine fish eggs. These "eggs" are beads of a gelatinous substance made with flavor and color additives to resemble the properties of sturgeon roe. They do not contain DNA and the Laboratory has a method by which they can distinguish this product from real fish eggs, so there is no question that they are synthetic and are not real eggs.</p> <p>Synthetic DNA is a related topic, which is different from "biosynthetic products. " The Laboratory considers primers and polymerase chain reaction (pCR) product to be "synthetic DNA" because it's an artificial copy of a DNA sequence, which is easily detected by the lack of methylated groups on the molecule.</p> <p>References for recombinant DNA can be found at: https://www.genome.gov/25520302/</p>

Inputs from observers		
Lewis & Clark Law School and the Center for Biological Diversity	NA	Legal analysis regarding whether "products produced from synthetic or cultured DNA" are covered by CITES ⁵

⁵ Revised version of CoP17 Inf. Doc. 22 submitted by the United States. The legal analysis has also been endorsed by WildAid and Natural Resources Defense Council

Summary of Part 1. Overview of different technologies and their potential of the consultant’s study on *Wildlife products produced from synthetic or cultured DNA*

Technology	Brief description	Example of CITES-related specimens that can be produced from the technology	Status and forecast of scientific advancement
DNA modification	Modify the DNA (and its expression) of both eukaryotic and prokaryotic organisms using a variety of techniques		Causes genetic variation in a given organism. Could result in significant changes in lifecycle, expression of proteins and other chemicals produced by the organism. Possible in most organisms already, and continuously being refined and precise
DNA synthesis	creating genetic elements from scratch		This constitutes ‘synthetic biology’ and is primarily a research tool. Will become more and more important as the techniques are refined. (see “Minimal’ cell raises stakes in race to harness synthetic life” in https://www.nature.com/news/minimal-cell-raises-stakes-in-race-to-harness-synthetic-life-1.19633)
Cell culture	the removal of cells from an animal or plant and their subsequent growth in a favourable artificial environment New genetic materials can be introduced into a cell before they are grown	Cells of rhino horn may be isolated, immortalized and grown in cell culture to produce a “rhino horn powder”	<ul style="list-style-type: none"> • Unicellular organisms (e.g. bacteria): can be generated and grown over many ‘generations’. Is already a major tool in research and for commercial production of microorganisms or their metabolites in industrial plants • Plants: many whole plants can be generated from a single cell. This is heavily used to produce plants through vegetative propagation (e.g. bananas) • Animals: possible to isolate animal cells and culture them, but cell immortalization, not as simple as for other organisms, can be achieved for most cell types. Remains primarily a research tool, but cloning of animals involves this as a first sept.
Tissue (organ) culture	A number of different cell types are grown, often in some form of matrix (a layer of cells on gel or suspension of the cells in liquid culture) in order to develop the characteristic structures in three dimensions (to aid self-assembly of cells)	Muscle (meat) of CITES-listed animal, elephant tusks and rhino horns (the actual organ), can potentially be created	Can synthesise organ/tissue from any organism using the techniques of modern biotechnology, including modifying the DNA in the tissue and/or using cell culture technology. However, each tissue/organ generated cannot be propagated further, the reproducibility is low it remains difficult/expensive. The technology is constantly changing, and with 3d printing it is likely to be a major technology in the near future

Summary of Part 2. Identification and distinction of products, and other scientific issues of the consultant’s study on *Wildlife products produced from synthetic or cultured DNA*

Product type	Examples of plant-based products	Examples of animal-based products	Ways in which the products can be distinguished from wild-sourced ones	Other scientific issues to consider
Chemicals	Plant oils for fragrance (agarwood, sandalwood, etc.), active ingredient of medicinal plants	Shark oil, civet/deer musk	Difficult or impossible to distinguish, as the chemicals are purified and markers cannot be used. Impurities in the chemical extracts of natural-sourced products may distinguish them from synthetic ones, which may only contain the active (target) chemical compound.	Synthetic products could replace the natural-sourced materials
Proteins	Aloe gel, orchid root powder	Rhino horn powder, coral accessories, bear bile, caviar essence	Minor changes can deliberately be made to the protein sequence of the synthetically produced protein as a positive identification tool (“label”)	
Cells, tissue, organisms	Plant tissue, wood products, timber, whole plants and trees	Horns, bones, skin, fur, whole animals	Genetic markers could be inserted into the genome of the cultured products as a positive identification tool (“label”) For some complex multi cellular products, the regularity of the cell structure may allow the distinction between synthetic and wild-based products	Epigenetic differences could theoretically be used to distinguish synthetic from natural, or even identify the source of the material