Synthetic Biology and the CBD

Five key decisions for COP 13 & COP-MOP 8

Synthetic biology threatens to undermine all three objectives of the Convention if Parties fail to act on the following 5 key issues:

1. **Operational Definition.** It's time for the CBD to adopt an operational definition of synthetic biology.
2. **Precaution: Gene drives.** Gene drives pose wide ecological and societal threats and should be placed under a moratorium.
3. **Biopiracy: Digital Sequences.** Synthetic biology allows for digital theft and use of DNA sequences – this must be addressed by both the CBD and the Nagoya Protocol.
4. **Socio-economic Impacts: Sustainable Use.** The CBD needs a process to address impacts of synthetic biology on sustainable use of biodiversity.
5. **Cartagena Protocol: Risk Assessment.** Parties to the COP-MOP 8 need to clearly move forward with elaborating risk assessment guidance on synthetic biology.

What Is Synthetic Biology?

Synthetic biology describes the next generation of biotechnologies that attempt to engineer, re-design, re-edit and synthesize biological systems, including at the genetic level.

Synthetic biology goes far beyond the first generation of 'transgenic' engineered organisms. Predicted to be almost a 40 billion dollar (US) market by 2020, industrial activity in synthetic biology is rapidly exploding as new genome editing tools and cheaper synthesis of DNA make it easier and faster to genetically re-design or alter biological organisms.

Synthetic biology-derived products already on the market include biosynthesized versions of flavors, fragrances, fuels, pharmaceuticals, textiles, industrial chemicals, cosmetic and food ingredients. A next generation of synthetically engineered (including 'genome edited') crops, insects and animals are also nearing commercialization. This includes far-reaching proposals to release gene drives – self-replicating genetic elements that aim to re-engineer or eradicate entire species at a time.

This brief has been prepared by **The International Civil Society Working Group on Synthetic Biology.** Members include: Ecoropa, EcoNexus, ETC Group, Friends of the Earth, GeneEthics, Heinrich Boell Foundation and Third World Network.

Synthetic Biology at the CBD – the story so far

Synthetic biology has been under discussion at the Convention on Biological Diversity (CBD) for six years. The CBD is the only international body addressing governance of this rapidly growing field.

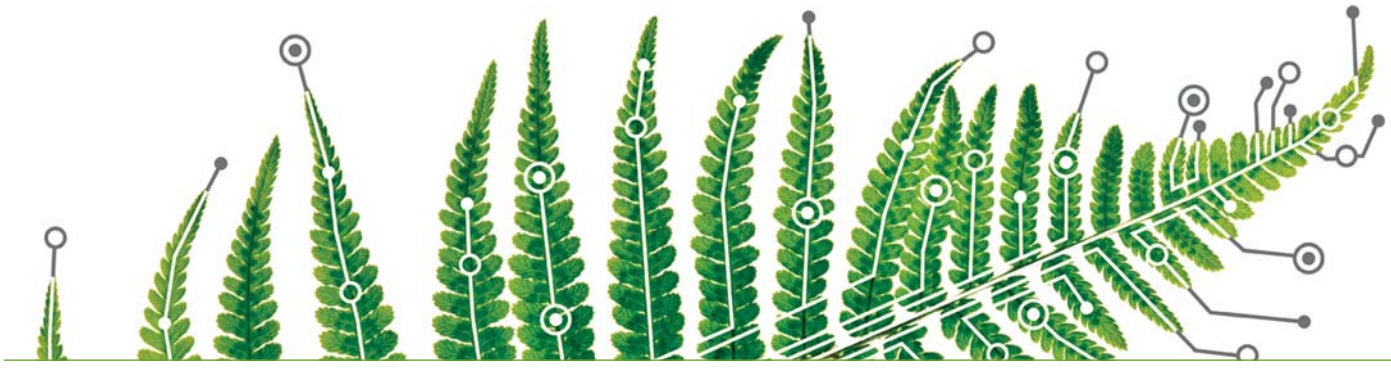
At COP 12, a landmark decision on synthetic biology (Dec XII/24) emphasized the need for precaution, regulatory systems and socio-economic and risk assessment. An online forum and AHTEG (Ad Hoc Technical Expert Group) was established to address seven questions posed by the COP and to provide an operational definition to allow further work. SBSTTA 16 then provided advice for COP. Meanwhile the AHTEG on Risk Assessment of Living Modified Organisms established under the Cartagena Protocol was also tasked to discuss this topic. The AHTEG on Risk Assessment has developed an outline of guidance on "Risk Assessment of LMOs developed through synthetic biology", and the issue will be discussed at COPMOP8 of the Cartagena Protocol. Parties to the Protocol are asked to consider establishing a process for the development of guidance on the basis of the outline developed, in coordination with relevant processes under the CBD.

Following the outcome of those processes, COP13 is an important moment for the CBD to establish ongoing governance of the field of synthetic biology.

What is at Stake at COP 13?

For almost a quarter century, the Convention on Biological Diversity and its protocols have been the premier international body exercising oversight and carrying out international deliberation on how developments in biotechnology affect the living world. The programme of work on synthetic biology at the CBD represents the only comprehensive international process currently underway to attempt to assess the risks from these potentially disruptive new developments which may impact all 3 objectives of the Convention. As new techniques such as CRISPR gene editing, DNA synthesis and far-reaching applications such as gene drives radically transform the power and scope of biotechnology to impact biodiversity, it is urgent that international governance arrangements are kept updated and made relevant.

Worryingly, the biotechnology industry appears to be deliberately attempting to frame the new technologies as exempt from existing rules and definitions. This would leave this next generation of biotechnology less assessed and less regulated than its predecessor. Unless Parties to the CBD can agree an operational definition for synthetic biology and commit to a forward-going plan of work addressing at least the most urgent implications, the world risks hurtling blind into a very uncertain and risky future without an appropriate set of governance rules.



Five important issues for syn bio oversight

Drawing on the advice already issued by SBSTTA 20 and the AHTEG on Synthetic Biology [SBSTTA recommendation XX/8], parties preparing for COP13 should reflect on the following four priority topics:

1. Operational Definition of Synthetic Biology

Parties at COP12 requested an operational definition of synthetic biology to support ongoing work on this topic, but unless that definition is formally adopted by COP13 as an operational definition for the work within the CBD, future work will be unnecessarily obstructed.

In online comments during preparation of the AHTEG on risk assessment (under the Cartagena Protocol) some Parties used the absence of an agreed operational definition of synthetic biology as an argument against examining the risk assessment of synthetic biology.

At COP 12, parties to the CBD instructed the AHTEG on Synthetic Biology to draw on the work of the open online forum to work towards an operational definition of synthetic biology. Establishing a definition is vital to future work on this topic. After a lot of hard work and drawing on extensive definitional surveys the AHTEG provided the following definition:

> **"Synthetic biology is a further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding, design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems."**

Unfortunately, SBSTTA 16 failed to unambiguously propose adoption of this definition. Instead, the advice sent by SBSTTA to COP provides two alternative bracketed paragraphs. The first merely notes that the definition was developed, the second clearly proposes to use the definition for future work. COP 13 should clearly adopt the definition for future use. The absence of an agreed operational definition has already begun to obstruct work on this topic under the CBD and its Protocols.

In online comments during preparation of the AHTEG on risk assessment (under the Cartagena Protocol) some Parties used the absence of an agreed operational definition an synthetic biology as an argument against examining the risk assessment of synthetic biology. It would be obstructive and wasteful if Parties at COP13 deliberately fail to adopt a definition for use within the CBD and its protocols. If Parties are concerned that the definition provided is too broad, then the AHTEG could be instructed to develop a supplementary 'living list' or annex naming techniques and approaches that either are or are not commonly regarded as part of the field of synthetic biology. Such an open and non-exhaustive list of included and excluded techniques and approaches could draw on existing literature such as CBD Technical Series no. 82. The annex would also make clear that techniques for genome editing and genome synthesis are expressly covered by the definition under a positive list.

2. Precaution: Gene Drives

Gene drives, which can drive a trait through an entire population, eradicating or altering entire populations and species, have quickly emerged as an extremely high risk synthetic biology application since the last COP. Proposals for near term environmental release of gene drives into field trials are already on the table. Parties at COP should agree a moratorium on field trials or deployment of gene drives pending further work. They must also address the risk of unintended and accidental release from laboratories.

A 'gene drive' refers to a genetic engineering technology that aims to ensure that a specific trait introduced into an organism (e.g. female sterility, colour, size, behaviour) is always or mostly passed on to future generations. The effect of a successful gene drive is that a single engineered trait can be driven through an entire population until it either takes over or crashes that population.

This has the potential to affect the entire species, ie. take it over or cause it to go extinct. Gene drives open up a a new field of species-wide population engineering where the introduction of just one fast-reproducing organism (e.g. insects, plants, small mammals, parasites) can deliberately alter entire ecosystems. The implications for the environment, food security and social stability are widespread and so far not assessed.

When COP last met in Korea the idea of a gene drive was still theoretical. The first working gene drive system, using the CRISPR/CAS9 gene editing system, was invented at the end of 2014 and since then has been replicated several times. Already tens of millions of dollars have been directed towards developing gene drives, with proposals advancing to field trial gene drives in Africa, USA and on islands. A consortium, Target Malaria, are proposing field trials of gene drive mosquitos in central Africa with the aim of attacking the vector for malaria. A US NGO, Island Conservation, has proposed releasing gene-drive mice onto island ecosystems by 2020 as a biological control method to attack invasive mice. A group of researchers are also investigating proposals to release gene drive mosquitos in Hawaii to counter the transmission of avian malaria. Such gene drive trials would risk going global in their impacts if, for example, a gene-drive mosquito travels beyond the initial release site.

There have been several strong warnings issued against use of gene drives.

In August 2014, an article in Nature authored by gene drive developers highlighted the risk of unintended ecological impacts as well as possible malicious use of gene drive systems.[1]

In November 2015 the AHTEG on Synthetic Biology identified gene drives as a threat to biodiversity affecting all three objectives of the convention:

> **"Applications that are aimed at altering and replacing natural populations (for example, gene drive systems) may have adverse effects at the ecosystem level, and vis-à-vis the other two objectives of the Convention" UNEP/CBD/SYNBIO/AHTEG/2015/1/3 - p9**

1 Oye, Kenneth A. et al, (2014-08-08). "Regulating gene drives". Science. 345 (6197): 626–628.

In June 2016, a 200-page report on gene drive governance released by the US National Academy of Sciences (NAS) stressed the need for precaution and ecological assessments, noting the lack of governance arrangements and that "there is insufficient evidence available at this time to support the release of gene-drive modified organisms."[2] NAS also identified the CBD as the main international regulatory instrument for addressing this topic.

> **"Because gene-drive modified organisms are intended to spread in the environment, there is a widespread sense among researchers and commentators that they may have harmful effects for other species or ecosystems. For example, using a gene drive to suppress a non-native weed population may lead to unexpected consequences, such as the loss of habitat for native species or even the establishment of a second, more resilient invasive species."**

In September 2016, a motion overwhelmingly supported by the governments and NGOs who comprise the membership of IUCN (International Union for Conservation of Nature) called on that body to adopt a de facto moratorium on any support or funding towards gene drive research or deployment pending an urgent assessment.

> **"CALLS UPON the Director General and Commissions with urgency to assess the implications of gene drives and related techniques and their potential impacts on the conservation and sustainable use of biological diversity as well as equitable sharing of benefits arising from genetic resources, in order to develop IUCN guidance on this topic, while refraining from supporting or endorsing research, including field trials, into the use of gene drives for conservation or other purposes until this assessment has been undertaken."[3]**

2 "Gene Drive Research in Non-Human Organisms: Recommendations for Responsible Conduct". National Academies of Sciences, Engineering, and Medicine. June 8, 2016.

3 https://portals.iucn.org/congress/motion/095/18902

In September 2016, a statement released by 30 leading conservation and environmental leaders (including Dr Jane Goodall, Dr David Suzuki, Dr Vandana Shiva) called for gene drives not to be promoted as a conservation tool in light of their significant risks:

> **"Given the obvious dangers of irretrievably releasing genocidal genes into the natural world, and the moral implications of taking such action, we call for a halt to all proposals for the use of gene drive technologies, but especially in conservation"[4]**

Given the urgency of this topic, Parties to the CBD should act in the spirit of precaution and in line with previous decisions to put in place a moratorium on release or field trialing of gene drive systems at this time.

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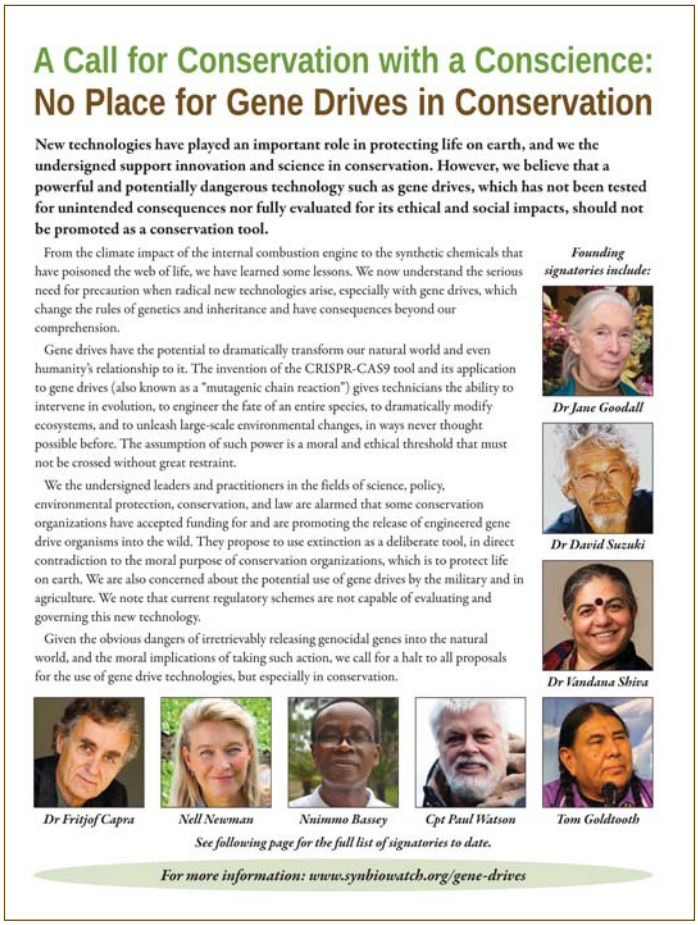

A Call for Conservation with a Conscience:
No Place for Gene Drives in Conservation

New technologies have played an important role in protecting life on earth, and we the undersigned support innovation and science in conservation. However, we believe that a powerful and potentially dangerous technology such as gene drives, which has not been tested for unintended consequences nor fully evaluated for its ethical and social impacts, should not be promoted as a conservation tool.

From the climate impact of the internal combustion engine to the synthetic chemicals that have poisoned the web of life, we have learned some lessons. We now understand the serious need for precaution when radical new technologies arise, especially with gene drives, which change the rules of genetics and inheritance and have consequences beyond our comprehension.

Gene drives have the potential to dramatically transform our natural world and even humanity's relationship to it. The invention of the CRISPR-CAS9 tool and its application to gene drives (also known as a "mutagenic chain reaction") gives technicians the ability to intervene in evolution, to engineer the fate of an entire species, to dramatically modify ecosystems, and to unleash large-scale environmental changes, in ways never thought possible before. The assumption of such power is a moral and ethical threshold that must not be crossed without great restraint.

We the undersigned leaders and practitioners in the fields of science, policy, environmental protection, conservation, and law are alarmed that some conservation organizations have accepted funding for and are promoting the release of engineered gene drive organisms into the wild. They propose to use extinction as a deliberate tool, in direct contradiction to the moral purpose of conservation organizations, which is to protect life on earth. We are also concerned about the potential use of gene drives by the military and in agriculture. We note that current regulatory schemes are not capable of evaluating and governing this new technology.

Given the obvious dangers of irretrievably releasing genocidal genes into the natural world, and the moral implications of taking such action, we call for a halt to all proposals for the use of gene drive technologies, but especially in conservation.

Founding signatories include:

Dr Jane Goodall

Dr David Suzuki

Dr Vandana Shiva

Dr Fritjof Capra *Nell Newman* *Nnimmo Bassey* *Cpt Paul Watson* *Tom Goldtooth*

See following page for the full list of signatories to date.

For more information: www.synbiowatch.org/gene-drives

"No Place for Gene Drives in Conservation," September 2016

Gene drives clearly meet the need for utmost precaution warranted when faced with "threats of significant reduction or loss of biological diversity posed by organisms, components and products resulting from synthetic biology". (Decision XI,11 Para 4). Further gene drives have yet to be fully assessed (nor is it clear at this time how they can be assessed for ecological harm), nor can they be properly regulated at this time. Decision Xii/24 paragraphs 3 (a), (b) and (c) are therefore highly relevant. Proposals by NGO Island Conservation and other promoters to use gene drives as a biological control method for invasive species within the next 5 years should be particularly discouraged.

3. Biopiracy: Digital Sequences

Rapid advances in sequencing and synthesizing DNA mean that 'digital' biopiracy is now possible, circumventing rules on access and benefit sharing. Parties at COP13 should agree to a two-step process where the issue of digital sequences can be quickly considered at a technical level by the AHTEG and then brought to the Parties to the Nagoya Protocol for a decision to address this urgent issue.

The combination of faster genome sequencing with rapid DNA synthesis and powerful gene editing techniques such as CRISPR is creating new avenues for biopiracy that must be addressed. The combination of these synthetic biology techniques could undermine implementation of the Convention's access and benefit sharing obligations, including the Nagoya Protocol. Genetic resources –whether DNA sequence of specific interest or even entire microorganisms and other small genomes – may now be transferred digitally and synthesized into living matter without physical exchange of biological material.

4 www.etcgroup.org/files/files/final_gene_drive_letter.pdf

This emerging reality poses major challenges to the many access and benefit sharing systems that assume and utilize material transfer agreements. As an ever-greater proportion of genetic resources are sequenced, transferred, and stored digitally, it is urgent for the Convention to carefully study the implications in order to facilitate policy action to defend the Convention's objective of fair and equitable benefit sharing.

Developed by SBSTTA 20, the Draft Decision on Synthetic Biology (UNEP/CBD/COP/13/2, pages 122-125) contains two bracketed recommendations on digital sequence information. Paragraph (o) of the decision invites the COP-MOP of the Nagoya Protocol to take up the issue, while paragraph 1(e) of the Terms of Reference for the Synthetic Biology AHTEG instructs it to propose elements to the Nagoya COP-MOP to "facilitate the clarification" of how digital sequence information relates to access and benefit sharing.

Tomorrow's biopirate will have no need to sneak a biological sample across borders. Instead, the loot can be stored on a memory card.

Both sets of brackets should be removed and both items retained in COP's final decision. They together reflect a "two-step process" to address digital sequence information that was discussed by the Synthetic Biology Contact Group at SBSTTA 20. In the process, the Synthetic Biology AHTEG will first perform a technical analysis of the implications of the combination of gene sequencing and gene editing. In the second step, the Nagoya COP-MOP will take up the AHTEG's findings at its meeting in 2018 or 2020, and then develop a decision.

Both items can and should be improved to more clearly reflect the central importance of this issue to the future of access and benefit sharing for all biodiversity.

Digital sequence information is an emerging issue not only at the Convention. It is also strongly surfacing at the World Health Organization (WHO), whose Pandemic Influenza Preparedness Framework is developing procedures for exchange of virus sequence data, and at the International Treaty on Plant Genetic Resources for Food and Agriculture (ITPGRFA), where "big data" sequencing projects such as DivSeek have prompted strong concerns from developing countries, farmers' organizations, and civil society.

As the overarching international treaty on biodiversity, it is important for the CBD to take a leading role in determining how to ensure that digital sequence information and gene editing are not used to amplify biopiracy and undermine access and benefit sharing regimes. The approach taken by the CBD may serve as an important reference point for WHO, ITPGRFA, and other processes where the topic arises, and a clear and strong position from the CBD may provide guidance to other entities.

Additionally, prompt action, particularly starting quickly at the Synthetic Biology AHTEG, would serve the interest of the CBD and particularly its developing country Parties in many ways.

For example, many of the crops and wild relatives targeted for mass genome sequencing by DivSeek and similar projects are not part of the ITPGRFA multilateral system and thereby fall under CBD and Nagoya ABS rules. The big data generated by these projects can be accessed and analyzed by companies and others, and key genetic diversity from developing countries can be identified and recreated using gene editing – all without ever signing an access and benefit sharing agreement.

In the realm of health, it is already possible to generate many viruses, including potentially extremely valuable vaccine viruses, entirely from digital sequence data. In fact, it is now faster to synthesize an influenza virus from data available in internet databases that it is to send the virus by courier from Asia to Europe or North America.

It is also true that transfer and synthesis of digital sequences enables LMOs to cross boundaries "virtually" and evade biosafety rules predicated on physical transfer of materials or whole organisms, as well as blurring the line on 'intended use'. This challenge to the advanced informed agreement and other provisions of the Cartagena Protocol, as well as national laws implementing the Protocol, needs to be quickly addressed.

What holds true today for many pathogens, and in agriculture, will soon be reality for practically all other biodiversity. As sequencing improves and technological strategies like "sequence in place" become a reality – allowing small or even handheld devices to quickly sequence samples and distribute the result – tomorrow's biopirate will have no need to sneak a biological sample across borders. Instead, the loot can be stored on a memory card, or uploaded to the cloud.

4. Socio-economic Impacts: Address Sustainable Use Challenges

While the Cartagena and Nagoya Protocols may ultimately be able to address the impact of synthetic biology on conservation and equitable sharing of benefits (Goal 1 and 3 of the CBD), the Convention requires an ongoing process to address the impacts of synthetic biology on sustainable use of biodiversity – especially the socioeconomic impacts.

While clear procedures exist within the CBD to evaluate direct biosafety impacts of engineered organisms on biological diversity (through the Cartagena Protocol) and to establish access and benefit-sharing arrangements (through the Nagoya Protocol) there is no clear forum for Parties to raise and assess the impact of synthetic biology developments on sustainable use of biodiversity – particularly the indirect impacts of products created through synthetic biology which may be significant.

Examples of such indirect impacts would include large scale changes in land management and loss of sustainable livelihoods as a result of natural products being produced for market by synthetic biology techniques or as a result of changes in feedstock patterns.

Such indirect effects and sustainable use implications are often socio economic impacts in the first instance, but later reveal serious biodiversity implications. The importance of socio-economic impacts was consistently flagged in the intersessional period.

"Some members of the AHTEG noted the following needs with regard to international regimes:(a) provisions to address the socioeconomic impacts of the components and products of synthetic biology;" (p6 para 41)

"With regard to the socioeconomic considerations of the impacts of synthetic biology on the three objectives of the Convention, some members of the Group noted that the issues are not sufficiently addressed by existing frameworks." (p11 para 61)

"Another aspect of the relationship between synthetic biology and biological diversity that was noted was its potential positive and negative indirect effects, which also have to be taken into account in the adoption and use of organisms, products and components of synthetic biology in order to ensure that the sustainable use of biodiversity is maintained." (p5 para 30)

As COP moves forward with addressing synthetic biology within the CBD, the Parties should make a priority of assessing socio economic and indirect impacts of synthetic biology with particular attention to issues of sustainable use.

As COP moves forward with addressing synthetic biology within the CBD, the Parties should make a priority of assessing socio economic and indirect impacts of synthetic biology with particular attention to issues of sustainable use. By way of example, if a country (e.g. Madagascar) believes that the novel biosynthesis of a natural commodity in one location threatens sustainable use within its own border (e.g. biosynthesis of vanillin elsewhere threatens vanilla growing in the rainforest) then there needs to be a body, process or mechanism for a country to raise concerns and seek redress. Such a process can be pursued through making synthetic biology a standing item in the CBD or raising the item under sustainable use.

5. Biosafety Protocol and Risk Assessment

In addition, coordinated efforts to address synthetic biology under the Cartagena Protocol on Biosafety are needed, particularly in relation to the risk assessment of LMOs that are developed through synthetic biology. Some CBD Parties have acknowledged that there could be specific challenges and limitations with regard to risk assessment principles and methodologies that are currently applied to evaluate LMOs, given that synthetic biology is likely to lead to the development of organisms that will differ fundamentally from naturally occurring ones. SBSTTA 20 noted that risk assessment methodologies may need to be updated and adapted for synthetic biology. This is to ensure that the risks are adequately assessed. The AHTEG on Risk Assessment under the Cartagena Protocol has developed an outline of guidance on "Risk Assessment of LMOs developed through synthetic biology". It is therefore crucial that Parties establish a process for the development of guidance on the basis of the outline developed, at COPMOP8.

Further information

The **International Civil Society Working Group on Synthetic Biology** (ICSWGSB) is a collaboration between the following organisations:

EcoNexus, Ecoropa, ETC Group, Friends of the Earth, GeneEthics, Heinrich Boell Foundation and **Third World Network.**

For Civil Society online resources on Synthetic Biology see Synbiowatch: www.synbiowatch.org

ICSWGSB contacts attending COP 13 / COP-MOP 8:

Lim Li Ching – ching@twnetwork.org
Neth Dano – Neth@etcgroup.org (mobile +63 917 532 9369)
Lili Fuhr – Fuhr@boell.de (mobile +49 (0)151 40201775)
Ed Hammond – eh@pricklyresearch.com
Helena Paul – H.Paul@econexus.info
Dana Perls – dperls@foe.org (mobile +1 925 705-1074)
Dr Ricarda Steinbrecher – r.steinbrecher@econexus.info
Silvia Ribeiro – silvia@etcgroup.org (mobile +52 1 55 2653 3330)
Jim Thomas – jim@etcgroup.org (mobile +1 514 5165759)