Implications of access and benefit-sharing (ABS) frameworks for collection and utilisation of marine genetic resources (MGR)

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With thanks to Oonagh McMeel
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Chair of the Advisory Panel of Policy and Legal Experts – aiming to provide clear recommendations and ready-to-use solutions to address critical policy and legal barriers which impede the access and sustainable use of MGR for European biotechnological research, development and commercialisation
Work With Africa To Date

- Active collaboration
- PhD students
- Visitors
Bioprospecting is the discovery of compounds and associated ideas from genetic resources to develop novel biomedicines, biomedical research tools, antifoulants, catalysts, nutraceuticals, cosmeceuticals, etc. Unlike seabed mining, MGRs are not mined.

Why use marine genetic resources?

Offers advantage over comparable terrestrial resource:

- Superior performance
- Better economics

Unprecedented activity in particular application:

- Enzymes: new reactivity/new biotransformation
- Small molecules: novel chemical structures & new mechanism of action
- Materials: new properties
Bioprospecting in BBNJ

Sampling in ABNJ → MGR → Chemistry

Bioassay

Elements of good practice already exist at all stages of the marine biodiscovery pipeline
Marine Genetic Resources

Term has no meaning to biologists and is not defined in UNCLOS but is taken to mean the Nagoya Equivalent:

“Marine genetic material” means any material of plant, animal, microbial or other origin, found in the marine environment, containing functional units of heredity; “Marine genetic resources” means marine genetic material of actual or potential value”

Diversity of habitat is assumed to translate to biological diversity
Marine Species Diversity

Animal Diversity

Of the major divisions of animal life ~20 have no representatives on land

Microbial Diversity

There is no clear estimate of marine microbial diversity or its economic value
MGR from EEZ or ABNJ

Can we determine which legal regime an organism came from?

NO!
Non-Pharma MGR Derived Products on the Market

**Vent Polymerase**  
- **Origin:** Vent bacterium (location unknown)  
- **Production:** Recombinant  
- **Owner:** New England Biolabs

**Fuelzyme**  
- **Origin:** Deep sea bacterium (location unknown)  
- **Production:** Recombinant  
- **Owner:** Verenium (BASF)

**Cosmetic screening infra-red rays**  
- **Origin:** Vent bacterium (location unknown)  
- **Production:** Bacterial culture  
- **Owner:** Sederma (Croda)

**Anti biofilm agents**  
- **Origin:** Red seaweed  
- **Production:** Chemical Synthesis  
- **Owner:** XXXXXX
MGR Derived Pharmaceutical Products on the Market

Soft tissue carcinoma
- *Ecteinascidia turbinata*
- *Conus magus*

Breast cancer
- *Halichondria okadai*
- *Tethya crypta*

Hodgkin's Lymphoma
- *Dolabella auricularia*
- *Purified fish oil*

Chronic pain (analgesic)
- Ara-C (cytarabine) treatment of leukemia
- Ara-A (vidarabine) antiviral

Lowering very high triglyceride levels

All from EEZ apart from 1 (high seas) – All prior to CBD coming into force
None rely on harvesting natural source except fish oils
Pharmaceutical Pipeline

250+  15  10  3  7

None from ABNJ – mainly reef derived

Mainly anti-cancer with a few analgesics and antivirals

Mainly start-ups at early stage with large pharma at late stage
### Patent Claims for a Gene of Marine Origin with Source

<table>
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<th>Country</th>
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</tbody>
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- **Graph**: Patent claims associated with genes of marine origin
  - $r^2 = 0.96$
  - $P < 0.0001$

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*Science, 2011, 331, 1521*
Bioprospecting Pipeline

1. Sampling
2. Curation
3. Biomass
4. Extraction
5. Assay
6. Purification
7. Active NCE
8. Development
Notification & Reporting Requirements

Application
- Cruise plan

Award
- Feasibility
- Checks

After Cruise
- Cruise report

- Starts with marine scientific research

Where to report data?
- Nagoya Protocol clearing-house
- New clearing house linked to NP
- A new international organisation

NP already requires evidence that collection did not come from area under national jurisdiction

Cruises are expensive! $40,000+ per day
Good Practice for Cruise Data and Samples

**Metadata may include**
- Location
- Depth
- Temperature
- Salinity
- pH
- Oxygen content
- Seafloor conditions

**Sample storage**
- Ambient temperature
- Cooler (4°C)
- Freezer (-20°C)
- -80°C Freezer
- Liquid nitrogen (-196°C)
- Formaldehyde
- Ethanol
- DNA/RNA preservation liquids

*Needs standardisation*
Flag State Problem

Funders: EU

Vessel Owners: Spain

Port of Departure: Argentina

Cruise Participants: Global
(samples will go to many countries)

Where will data be deposited?
Who maintains data?
Who monitors requirement?

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Benefit Sharing

• Must be multilateral compared to bilateral for Nagoya Protocol
• In many cases most important benefits from use of MGR are non-monetary.
• Non-monetary benefits may include:
  • Scientific exchanges/training
  • Technology transfer
  • Capacity building (infrastructure)
  • Enhanced reputation
  • Increased number/quality of scientific publications
  • Biodiversity conservation
  • Valuable regional resources developed (knowledge, samples, data)
• Non-monetary benefits still cost money – however they are upfront compared to royalties
Real Benefit Scenario

- Cost in 2014 to bring drug to market US$2,558 M* - >70%
  - Clinical trials
- Typical industry royalties on natural products developed into drugs is 1-3%
- Halaven (Eisai), derived from a Japanese sponge makes US$200 M per year – in principle yielding US$ 2-6 M pa.
- Currently 7 approved marine drugs – total royalties would be US$ 10-50 M.
- Blockbuster drug (> US$ 1 Bn pa income) would yield US$10-30 M pa
- Currently 7 approved marine drugs come from ~28,000 discovered marine compounds (1 in 4000 chance) – none are ‘blockbusters’
- All examples were discovered pre-CBD – not clear if actual royalties are being paid
- Other markets – nutraceuticals/cosmeceuticals, lower risk, quicker to market, lower investment and lower returns.

Benefit Sharing

• Multilateral NOT Bilateral
• Most important benefits are non-monetary.

Public domain approach

• Low cost
• Benefits will accrue locally
• All should be able to benefit from discoveries
• Requires capacity building to ensure fairness
• This approach will lead to greater innovation, transparency and openness
Capacity Building with Ghana

Results
Built biology and chemistry labs
University support for big equipment
Trained 3 PG students
7 publications
Where is the transition from basic research to research with commercial intent? (when does actual value become apparent?)

- When research is initiated?
- When organism is found to be active?
- When active pure compound is identified?
- On patent filing?
- When NDA is filed?
- When industry gets involved?
- When NDA is filed?

Note: Some industries don’t patent.
Monitoring Sample and Data Flows

Possible to track sample from origin to exploitation (but better databases are needed)

Modifications to DNA or compound may make it hard to trace MGR origin
An UNCLOS implementing agreement developed over the next few years would need to be flexible enough to deal with rapid scientific progress.
Nightmare (But Realistic) Scenario

Gene 1

Gene 2

Gene 3

Gene 4
(ABNJ)

Vector

Host

Vector and host may have associated IP rights

Originally found in Australian EEZ Marine organism

Known bioactive compound
Overly restrictive regime can damage progress of products (Australian example)
Questions for Discussion

• How can we make sure MSR on MGR is not impeded?
• How will the process be monitored/policed and by whom?
• Who will collect monetary benefits and who will distribute funds and how?
• Traceability becomes an issue as benefits may take a long time to be realised. Who will trace this?
• How can we manage expectations for financial returns?
• Can we make an IA flexible enough to cope with scientific progress?
• Is a public domain model acceptable to the parties?
  • At what scale does the collection of BBNJ occur?
  • Will adapting current good practice be sufficient as monitoring tool?
  • Is it possible/desirable to control the flow of data, much of which is open access?
  • How can we be sure that all can utilise and benefit from MGR from ABNJ?
  • How can we ensure capacity building so all can truly benefit?
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