

# Marine Genetic Resources: from Sampling to Commercialisation

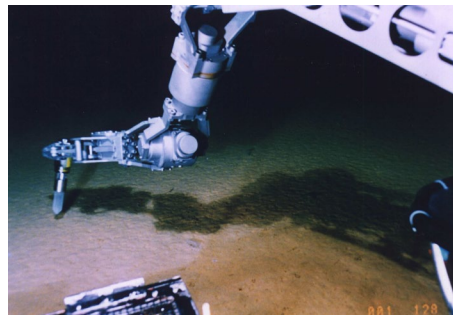
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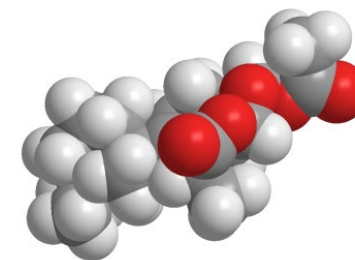
# Bioprospecting



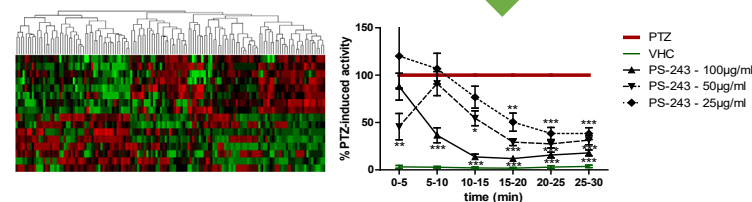
**Sampling**



**Bioresources**



**New  
Materials**



**Testing**



**Product**

**Commercialisation**

# Potential Benefits of Marine Bioprospecting

Offers advantage over comparable terrestrial resource:

Superior performance

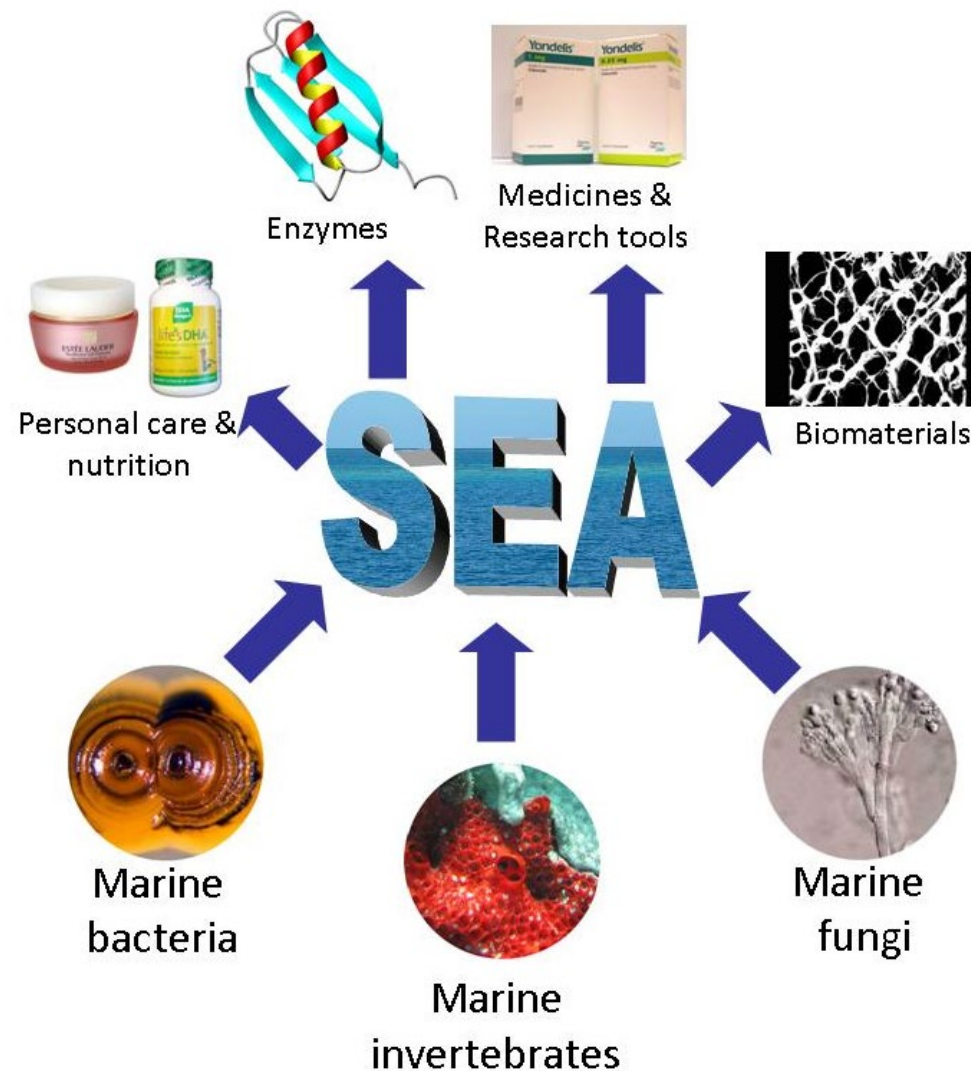
Better economics

Unprecedented activity in particular application:

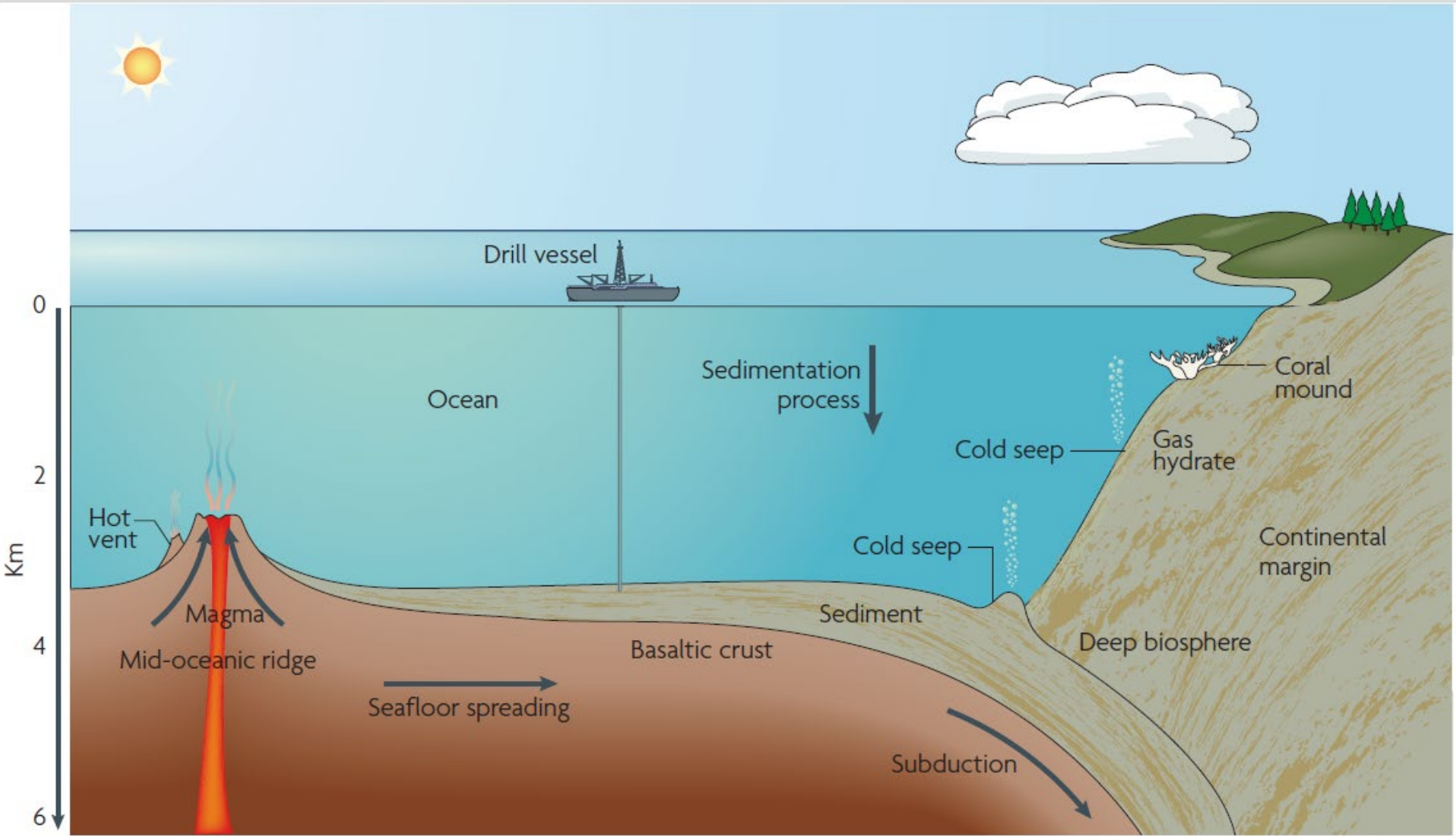
Enzymes: new reactivity/new biotransformation

Small molecules: novel chemical structures & new mechanism of action

Materials: new properties

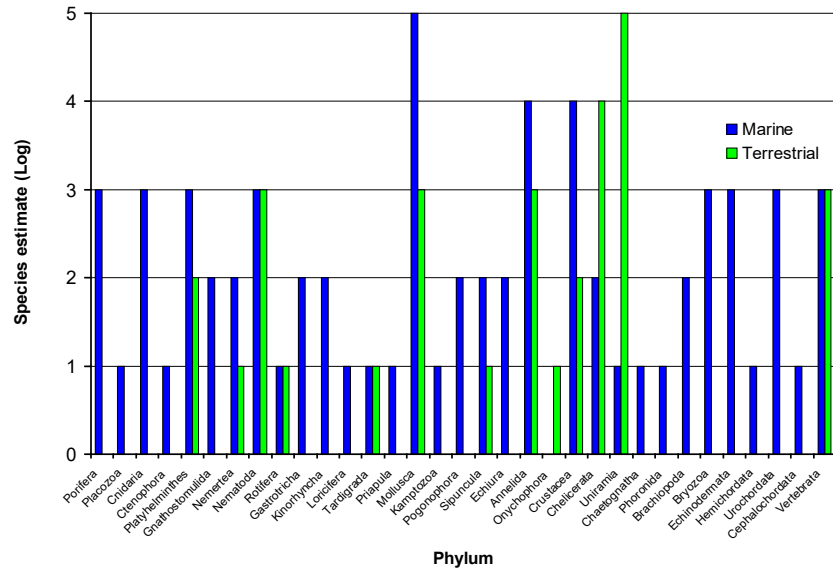


# Marine Environments



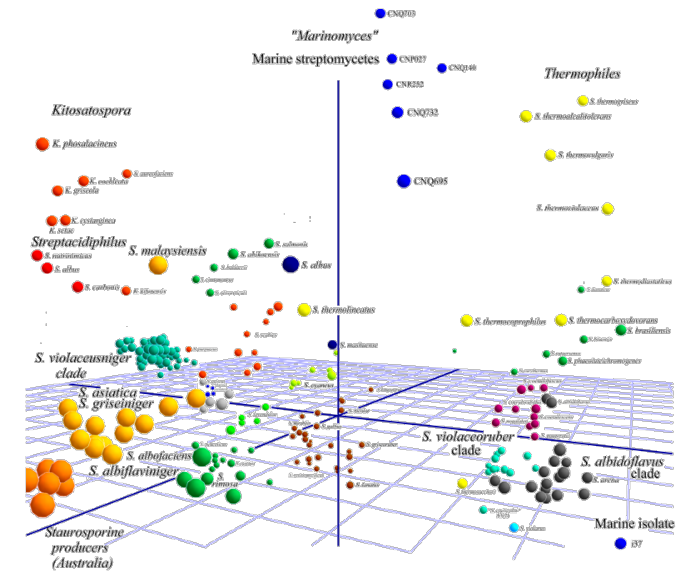
# Marine Environments are Rich in Genetic Diversity

## Animal Diversity



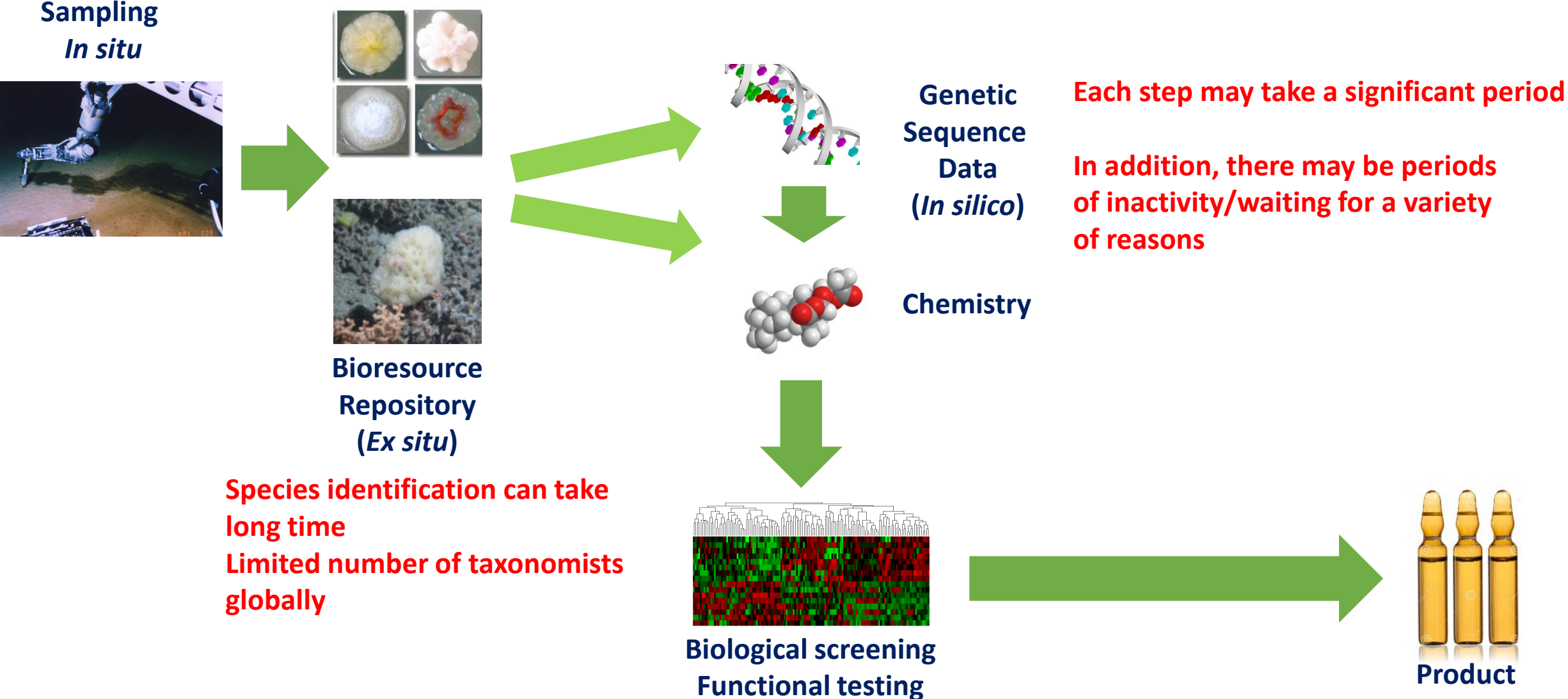
Of the major divisions of animal life ~20 have no representatives on land

## Microbial Diversity

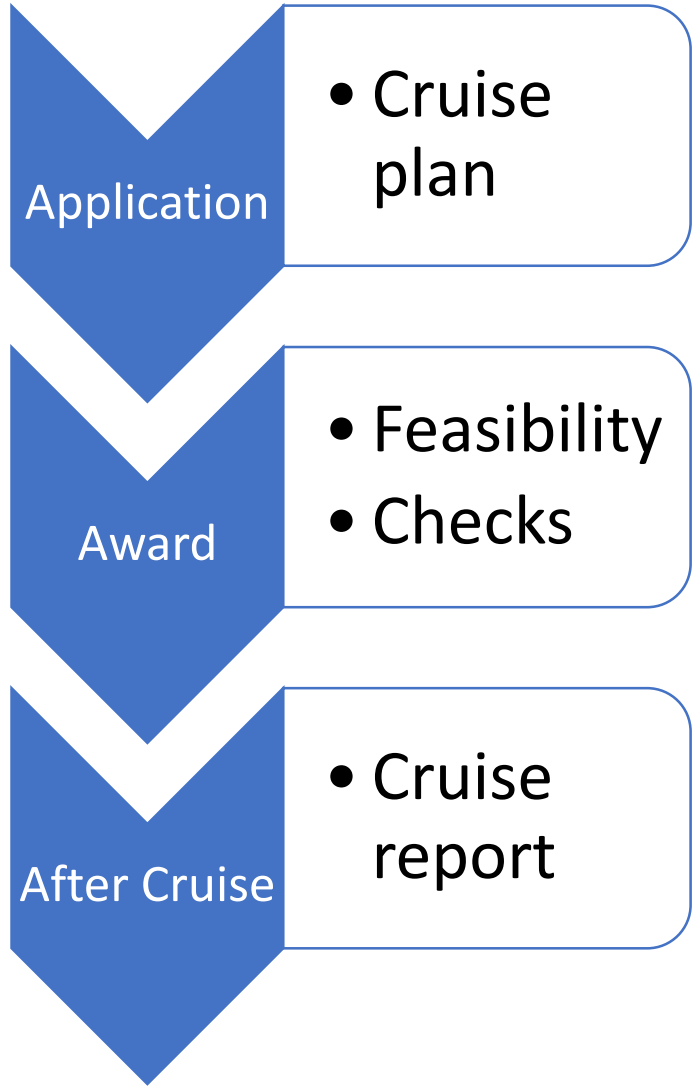


There is no clear estimate of marine microbial diversity or its economic value

# The Biodiscovery Pipeline



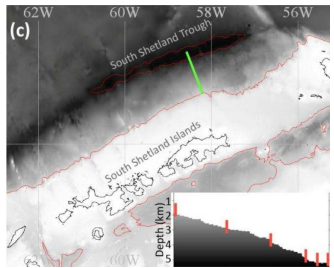
# Marine Scientific Research Planning



- Cruise plan

- Feasibility
- Checks

- Cruise report



VESSEL	CRUISE DATE	SAMPLING GEAR	DIVE #	SAMPLE NUMBER	LATITUDE	LONGITUDE	DEPTH	SAMPLE TYPE	DESTINATION
scotia	18/07/2015	Van Veen Grab	3	09155_VV_3B	57.98047N	15.548597W	1296.4	SED SubSamp	JASPARS
scotia	18/07/2015	Van Veen Grab	3	09155_VV_3B	57.98047N	15.548597W	1394.4	SED SubSamp	JASPARS
scotia	18/07/2015	Van Veen Grab	5	09155_VV_5A	57.99620N	15.539247W	1203.8	SED SubSamp	JASPARS
scotia	18/07/2015	Van Veen Grab	9	09155_VV_9B	57.99620N	15.539247W	1203.8	SED SubSamp	JASPARS
scotia	19/07/2015	Banded Lander	1	09155_M_1_E1	57.95333N	15.55079W		Amphipods	PIERTNEY
scotia	19/07/2015	Banded Lander	1	09155_M_1_E1	57.95333N	15.55079W		Amphipods	PIERTNEY
scotia	19/07/2015	Megacore	1	09155_MC_1_JA	57.95567N	15.55025W		SED SubSamp	JASPARS
scotia	19/07/2015	Megacore	1	09155_MC_1_JB	57.95567N	15.55025W		SED SubSamp	JASPARS
scotia	19/07/2015	Megacore	2	09155_MC_2_GA	57.95557N	15.55024W		Bacterial Mat	JASPARS
scotia	19/07/2015	Megacore	2	09155_MC_2_GB	57.95557N	15.55024W		Bacterial Mat	JASPARS
scotia	19/07/2015	Megacore	2	09155_MC_2_GC	57.95557N	15.55024W		Bacterial Mat	JASPARS
scotia	19/07/2015	Megacore	2	09155_MC_2_GD	57.95557N	15.55024W		Bacterial Mat	JASPARS
scotia	19/07/2015	Megacore	2	09155_MC_2_GE	57.95557N	15.55024W		Bacterial Mat	JASPARS

## MSR

- Most cruises are for basic research
- Freedom of MSR
- File cruise report to funder

## How Might Bioprospecting be Accommodated?

- Require updates on cruise report to alert to change of use
- Notify when commercialisation occurs

Opportunity – Global cruise data available in consistent format will benefit scientific community

# Collecting Materials



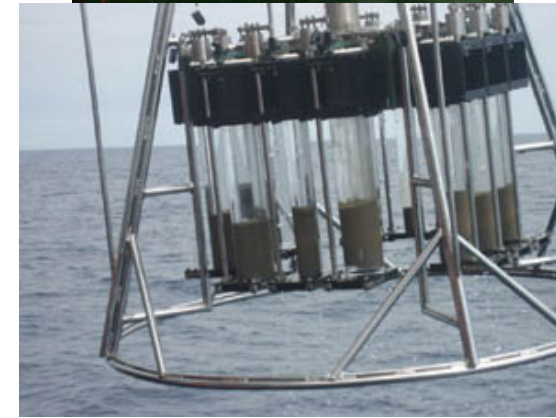
RRS Discovery (UK)



ROV Isis (UK) (6500 m)



# Sampling Devices



# Biomass – Invertebrates and Microorganisms



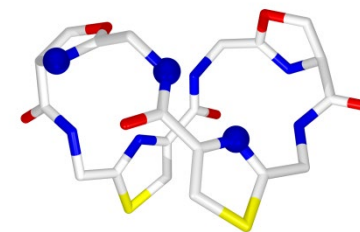
# Chemistry



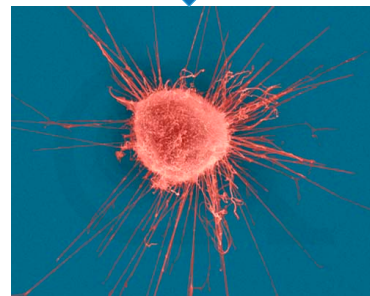
**Extraction**



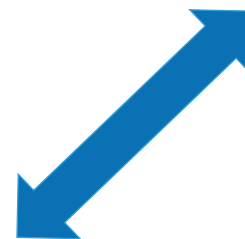
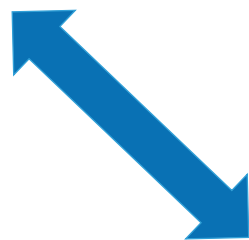
**Compound Isolation**



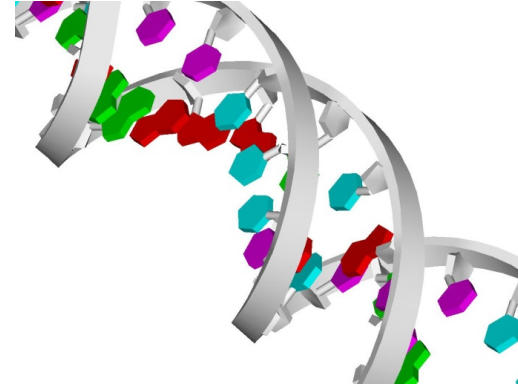
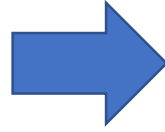
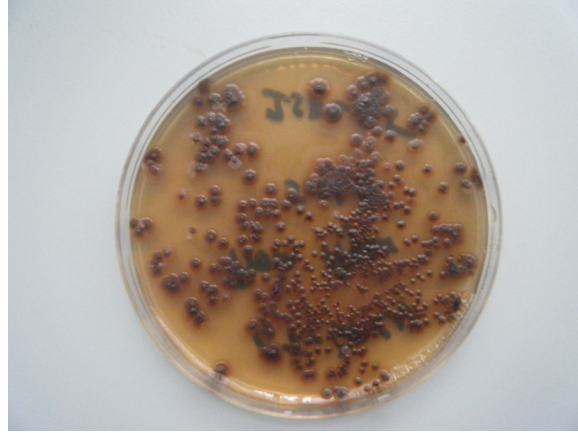
**Compound Identification**



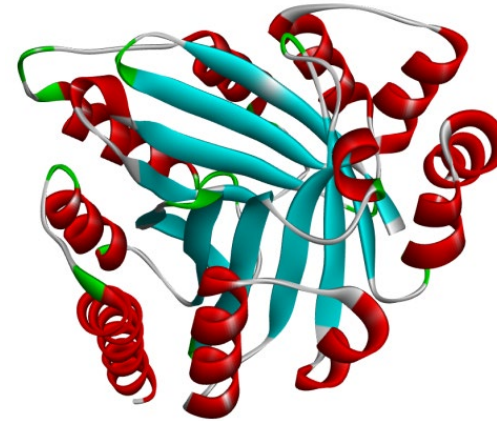
**Biological Testing**



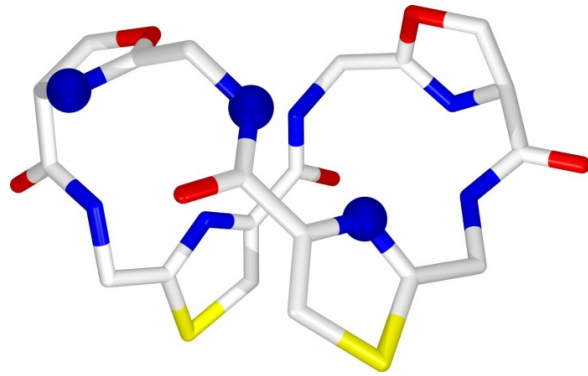
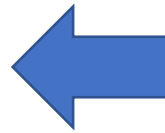
# Alternative - Using Genetic Sequence Data



DNA

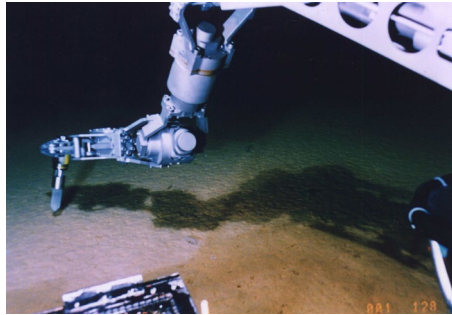


Protein

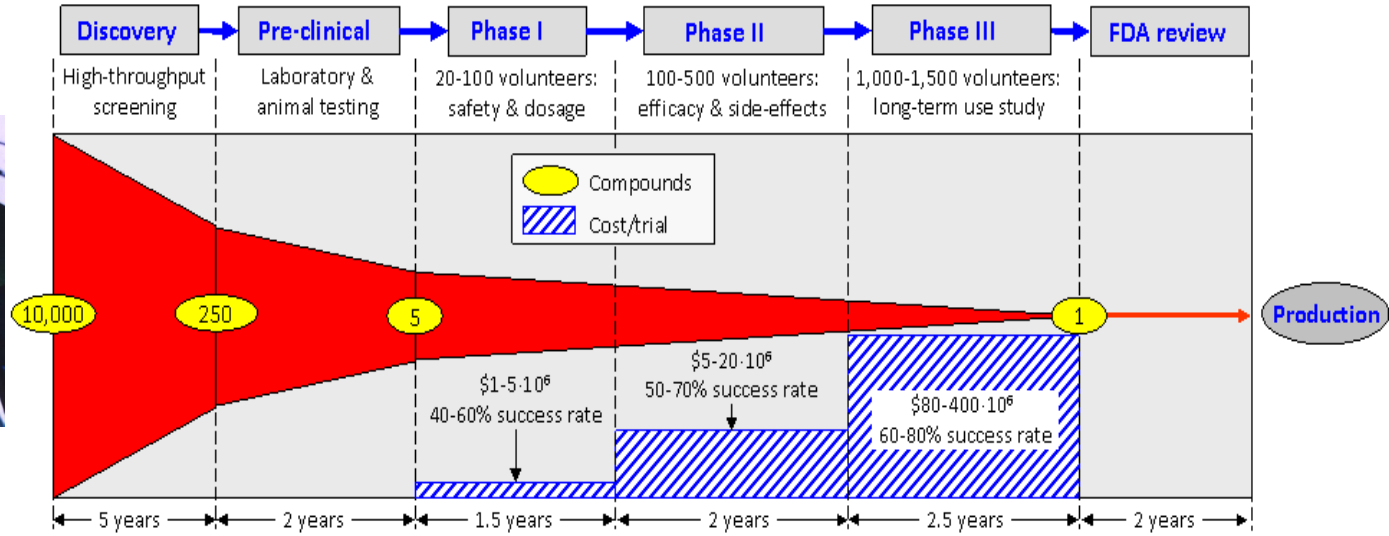


Compound

# The Biodiscovery Timeline



Sampling in ABNJ



Universities

Universities and SME's

Large companies

Scientific knowledge & data

Commercial

'Potential' value

Actual value

# The Marine Pharmaceutical Pipeline



Mainly derived from shallow reef dwelling organisms

Mainly anti-cancer with a few analgesics and antivirals

Mainly start-ups at early stage with large pharma at late stage

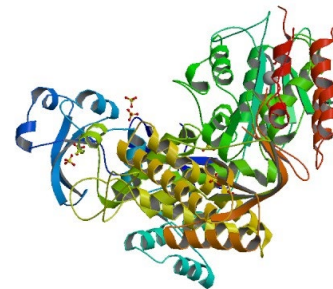




**Yondelis**  
 Cancer treatment  
 Origin: Seasquirt  
 Location: Caribbean Mangroves  
**Production: Semisynthesis**  
**Owner: PharmaMar**



**Prialt**  
 Intractable pain  
 Origin: Cone snail  
 Location: Philippines  
**Production: Recombinant**  
**Owner: Neurex/Elan**



**Vent Polymerase**  
 DNA amplification  
 Origin: Vent bacterium  
 Location: Naples, Italy  
**Production: Recombinant**  
**Owner: New England Biolabs**



**Fuelzyme**  
 Enzyme used in biodiesel production  
 Origin: Deep sea bacterium  
 Location: Unknown)  
**Production: Recombinant**  
**Owner: Verenium (BASF)**



**Venuceane**  
 Cosmetic screening infra-red rays  
 Origin: Vent bacterium  
 Location: Unknown  
**Production: Fermentation**  
**Owner: Sederma (Croda)**



**Brominated Furanones**  
 Anti biofilm agents  
 Origin: Red seaweed  
 Location: Australia  
**Production: Synthesis**  
**Owner: Unilever**



# Mare Geneticum

## **Balanced benefit sharing must consider:**

Size and timing of benefits accrued by user(s)

Cost and burden of benefit-sharing to the user

Burden of benefit-sharing to the regulator – institutional cost

Who are the beneficiaries?

How many beneficiaries are there?

Impact of benefit-sharing on the beneficiary

Timing of the transaction

## **Requirements:**

Inclusivity of developing states

Facilitated access for the scientific community

Legal certainty, predictability and stability for industry

Enforceability for the regulator

# Mare Geneticum

## **Access:**

Online notification system: OPEN

Free but conditional access

Exclusivity period

## **Benefit-Sharing:**

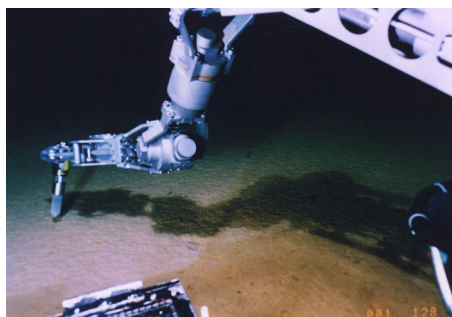
Mandatory deposit of material in biorepositories

Mandatory sharing of meta data and raw data (including GSD)

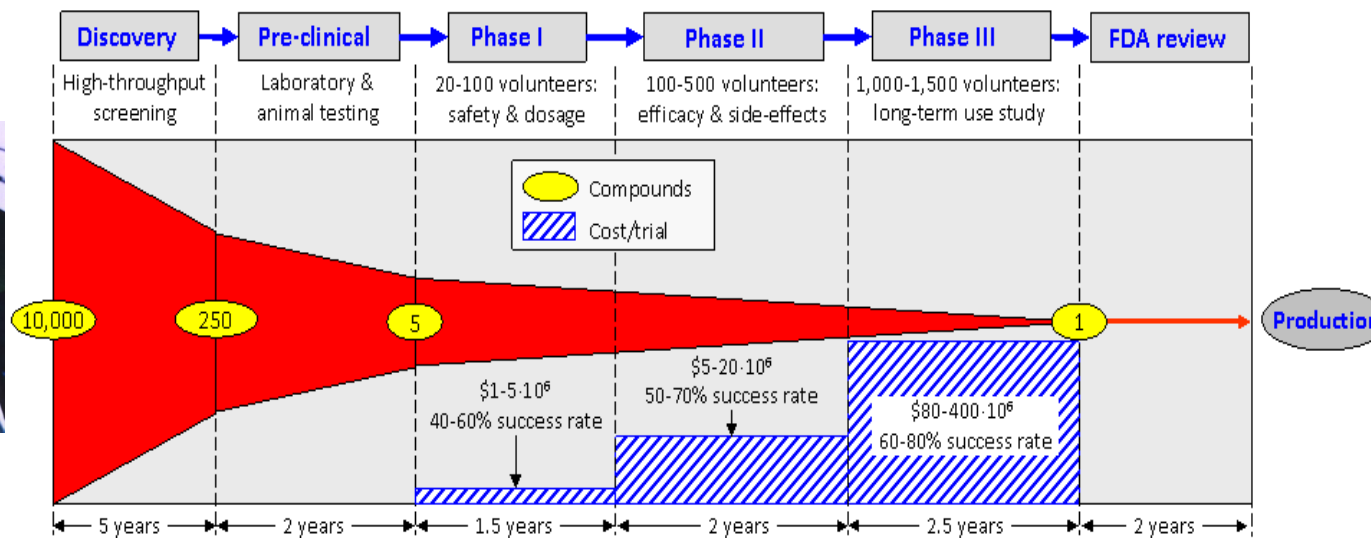
Possibility of extending exclusivity period in return for a fee

If monetary benefits are requested: at the point of commercialization, and not negotiated

# Biodiscovery Pipeline and Benefit-sharing



Sampling in ABNJ



Scientific knowledge & data

Commercial



Embargo period (fee)

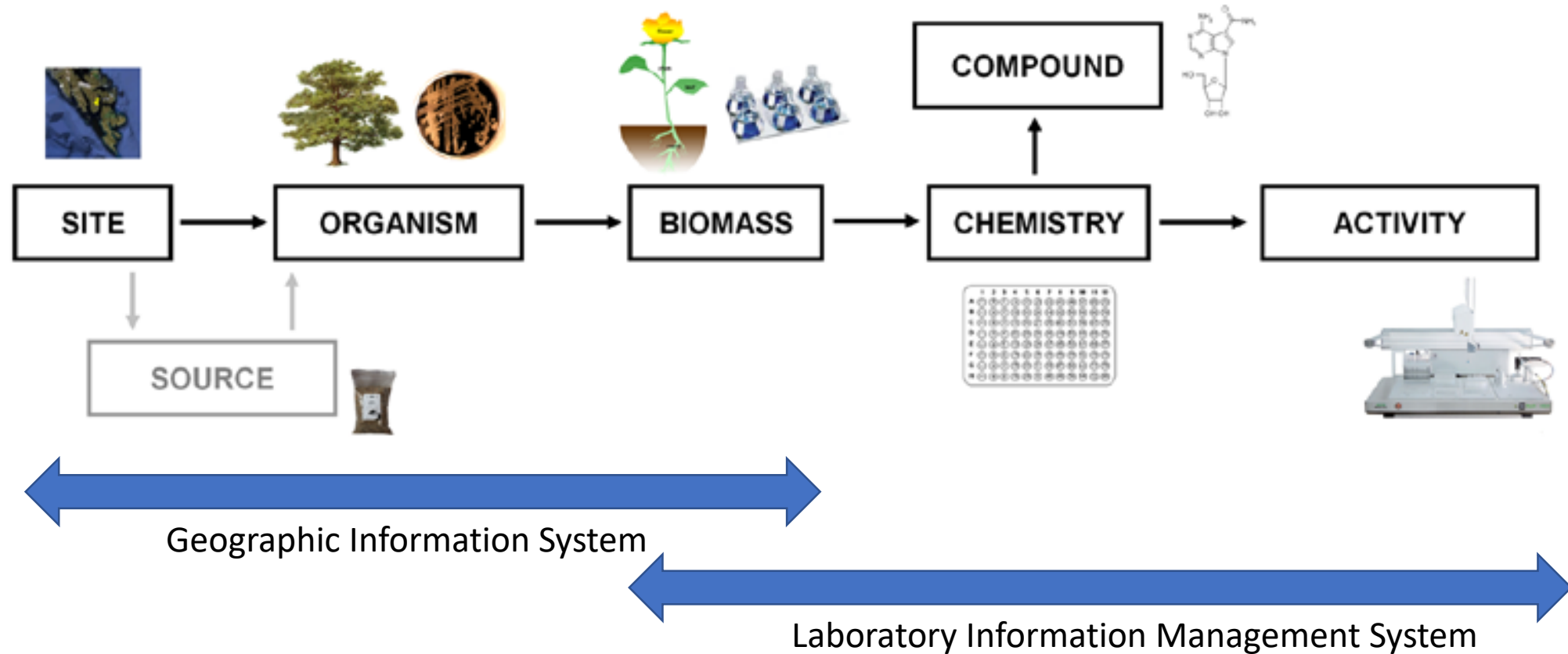


Deposit in biorepository  
Sharing of metadata

Sharing of MGR data

Monetary BS ?

# Sample and Data Management

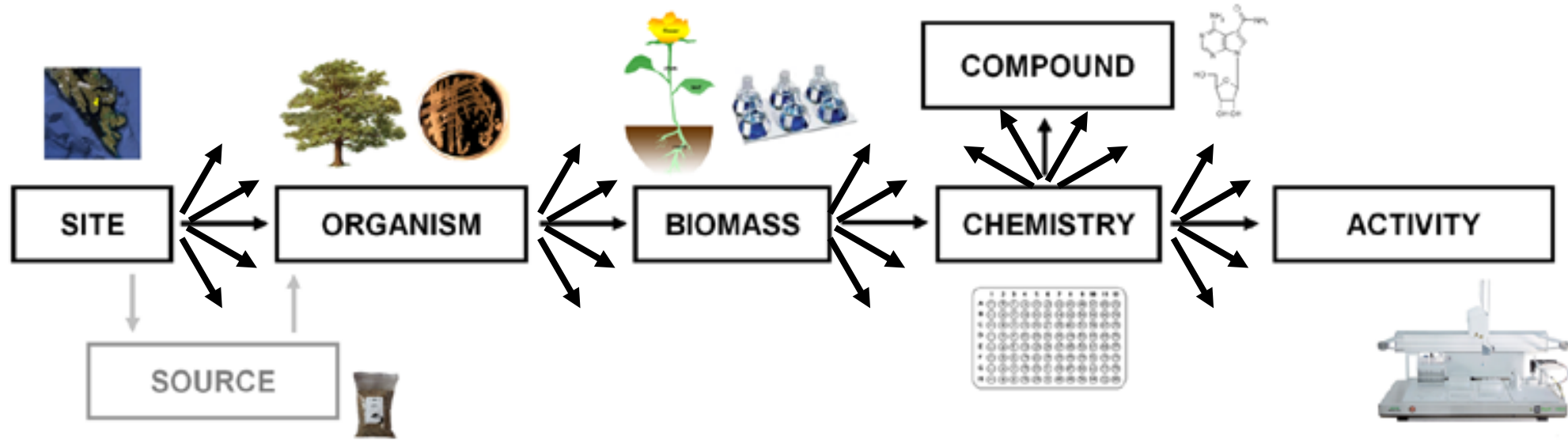


**Sample and data management from origin to exploitation is possible**

**Already part of good scientific practice but needs standards & improved data infrastructure**

# Real World Example

**25 Compounds**



Example

1 sample  
of sediment

100 new microbes  
(10 used)

Each microbe  
grown in 4  
different media

Each one  
gives 8 fractions

Each fraction  
tested in 10  
assays

**1**

**10**

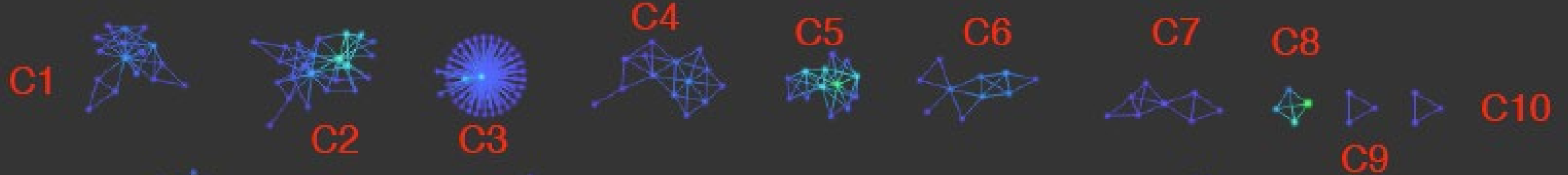
**40**

**320**

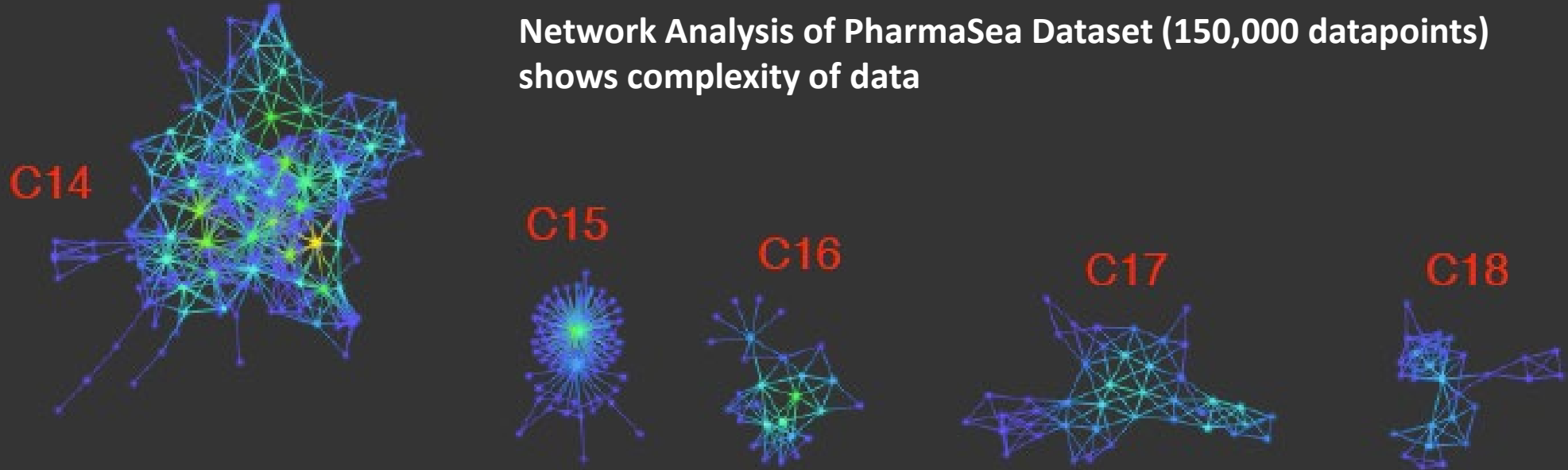
**3200**

**Total 3596 datapoints – for 1 sample  
& Genetic Sequence Data**

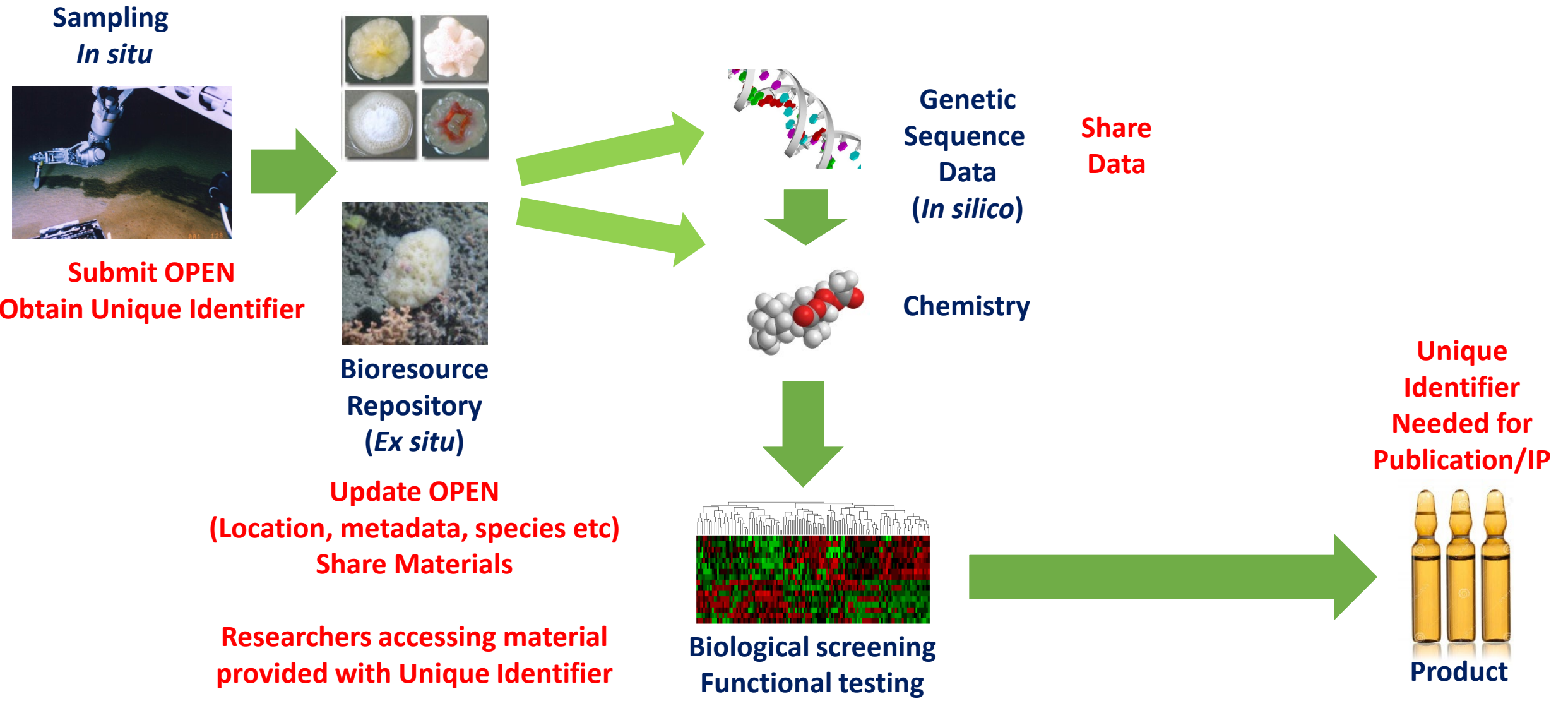
C19  C20 



**Network Analysis of PharmaSea Dataset (150,000 datapoints)  
shows complexity of data**



# Obligatory Prior Electronic Notification (OPEN)



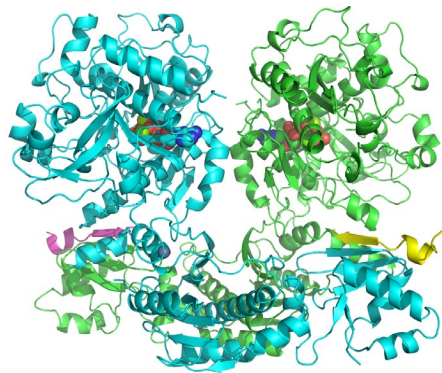
# Online Prior Electronic Notification

- Use of cruise plans and cruise reports builds on existing practice.
- Agree on minimal dataset to accompany each sample collected.
- Share materials, but have processes to ensure maximum value is obtained from rare samples.
- Develop unique identifier to work with existing ex situ collection data infrastructure and digital sequence information databases
- Fee-free access to materials and raw data – scope to be clarified but initially intended to mean nucleotide sequence data (DNA/RNA sequences).
- Possibility for exclusivity period on samples/data to enable scientific research to be completed, or for commercial research to be protected. Exclusivity period can be granted without fee for defined period, after which payment to central fund must be made.



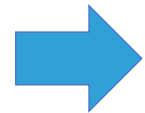
# Exclusivity Periods in Scientific Practice

- Protein Data Bank entries are placed on hold for one year from the date of deposition. They may be released earlier on a date specified by the Contact Author. When the corresponding electronic or paper publication occurs, the entry must be released if the journal policy requires release upon publication.



Solve protein crystal  
structure

<http://www.rcsb.org/pdb/home/home.do>



RCSB **PDB**  
PROTEIN DATA BANK

Deposit data  
Get PDB ID



ARTICLE  
PUBLISHED ONLINE: 22 JUNE 2015 | DOI: 10.1038/NCHEM810.1841

nature  
chemical biology

**Structural analysis of leader peptide binding  
enables leader-free cyanobactin processing**

Jesko Koehnke<sup>1,6</sup>, Greg Mann<sup>1,6</sup>, Andrew F Bent<sup>1,4</sup>, Hannes Ludewig<sup>1</sup>, Sally Shirran<sup>1</sup>, Catherine Botting<sup>1</sup>,  
Tomas Lebl<sup>1</sup>, Wael E Houssen<sup>2-4</sup>, Marcel Jaspars<sup>2</sup> & James H Naismith<sup>1,5\*</sup>



**1 Year**

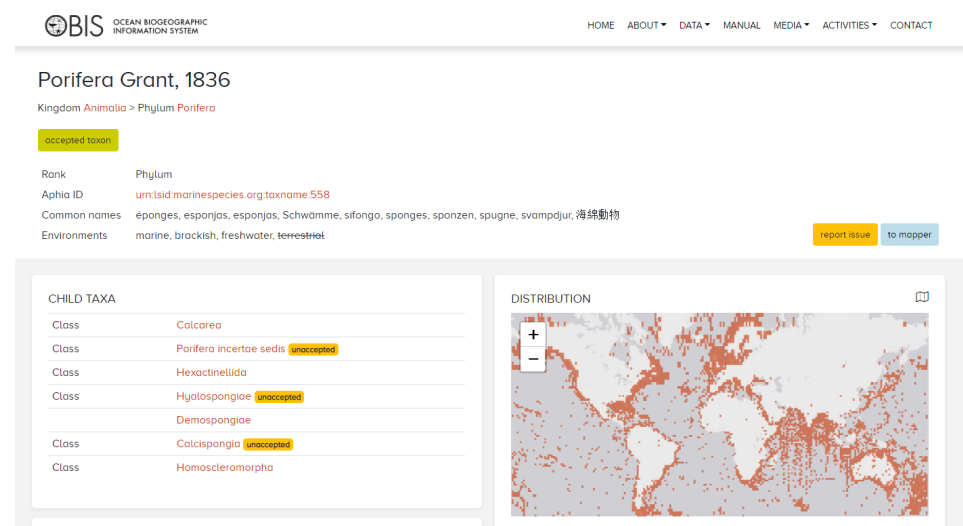
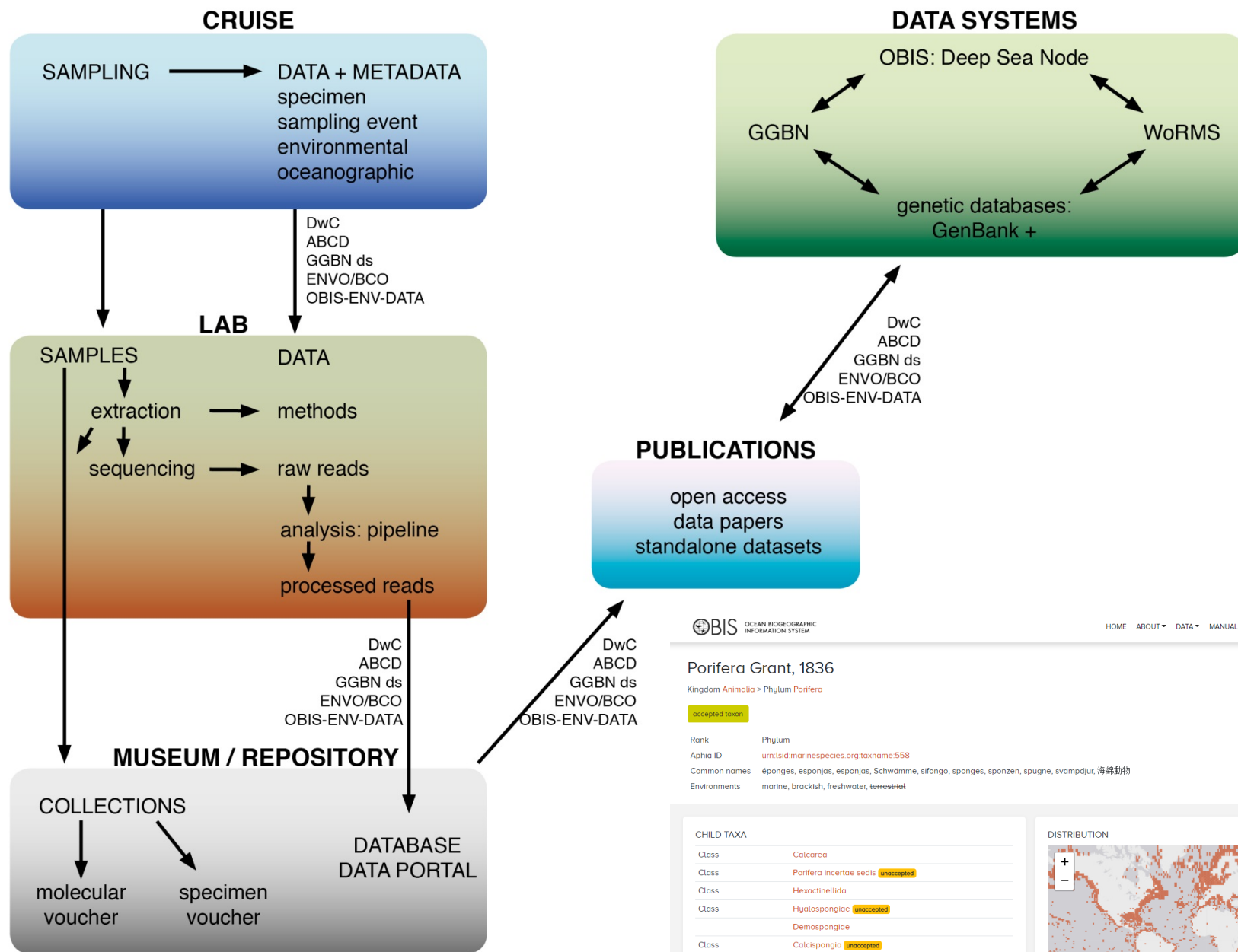
Data Released

# Current Thinking on Exclusivity Periods for DSI

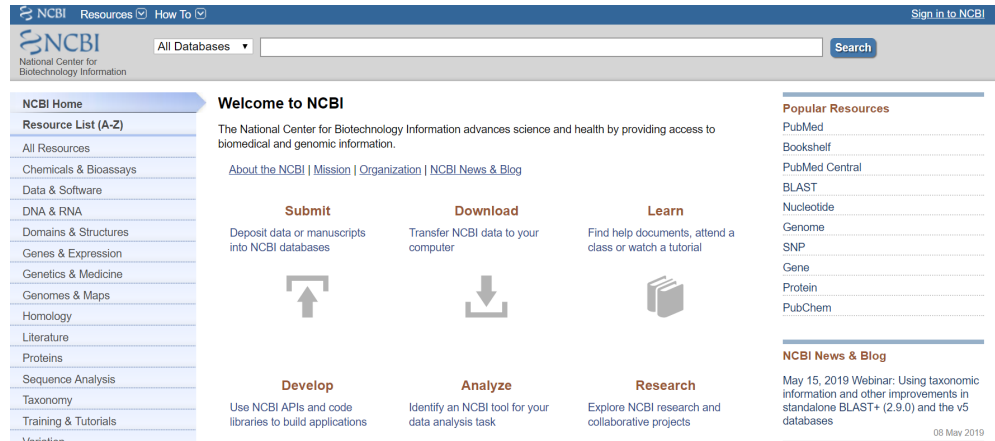
- Importance of free and unconditional use of these data vs. the “right” of the data producers to the first publication.
- Argues that the publicly available data should be treated as open data, a shared resource with unrestricted use for analysis, interpretation, and publication.
- Some projects have already eliminated exclusivity period (e.g. ENCODE).
- Availability of large complex datasets are best analysed by as many researchers as possible without restriction.
- Data producers credited in publications or via online tools such as DOIs. Journals and data repositories must lead the way in this.
- Wider data sharing is likely to allow more participation in the research enterprise of the many scientists who work in resource-poor settings and may be less able to compete in generating expensive new data.

# Build on Science Good Practice

**Data Must Be:**  
**F**indable  
**A**ccessible  
**I**nteroperable  
**R**eusable



# IT Solutions (e.g. Blockchain)



**Build on existing data infrastructure**  
**(Data Curation Essential)**

**But: Human Compliance main issue**

**Feasibility Study?**

Marine Science

Collections/Curation

Marine Bioprospecting

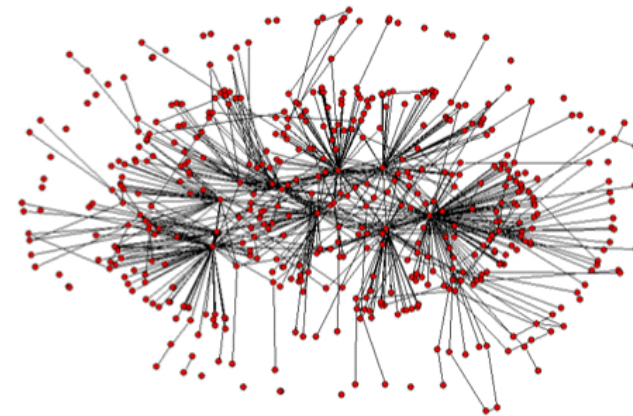
Computing Science

Behavioural Science

Law/Policy



**Blockchain adapters**



**Decentralised/Minimal traceability requirement**

Prof. Pete Edwards, Computing, Aberdeen University

# Acknowledgements

## PharmaSea & MarPipe

Arianna Broggiato, Thomas Vanagt,  
Laura E. Lallier, Geoff Burton, Dominic  
Muyldermans, Jane Collins, Torsten  
Thiele, Isabelle Huys

& the rest of both consortia

## Deep Ocean Stewardship Initiative

Muriel Rabone, Tammy Horton, Maria  
Baker, Harriet Harden-Davies & many  
others

## University of Aberdeen

**Law:** Abbe Brown, Anne-Michelle Slater

**Chemistry:** Rainer Ebel (& the Marine  
Biodiscovery Centre)

**Biological Sciences:** Frithjof Kuepper,  
Ursula Witte

**Computing:** Pete Edwards

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