Microbial Genetic Resources (MGR's) for Food and Agriculture

Dr. G. S. Prasad

Microbial Type Culture Collection and Gene Bank
An International Depositary
Institute of Microbial Technology
Chandigarh – 160 036
INDIA

Talk Delivered Brussels, 25.01.2011

Significance of Microorganisms

- The first inhabitants of the Earth, created conditions for existence of other life forms on this planet.
- Important part of ecosystems on Earth, and are responsible for nitrogen fixation, phosphate assimilation, nutrient recycling, bioremediation of pollutants etc.
- Life of plants, animals and human beings depends on the microorganisms.
- Food chains in nature cannot be completed without microorganism.
- They possess enormous metabolic diversity, that is not probably observed in higher organisms.
- Interestingly the main studies in microbiology originated from fermentations, diseases in humans, animals and plants.

Pasteur wrote

"... we see that the yeast takes something from the sugar ..."

Between 1855 and 1875, Pasteur established, unequivocally

(a) the role of yeast in alcoholic fermentation

(b) fermentation as a physiological phenomenon

(c) differences between the aerobic and anaerobic utilization of sugar by yeasts.

First use of a microorganism for industrial application

The Value of Microbial Resources

- Worldwide, the economic value of microorganisms is estimated to be atleast tens of billions of US dollars
- Pharmaceuticals of microbial origin account for sales of approximately $35-50 billion per annum
- Microbes gave us more than 4,000 antibiotics
- Till recently, five of the pharmaceutical industry's top-selling drugs were derived from microbes ($10,000 million in annual sales)
- The total world market for industrial enzymes, all produced by microorganisms, is $3,000 million.

- The total number of fungi described till recently are about 80,000 species and 6,000 genera. Bacteria are about 8,000 species, belonging to 1200 genera.

- If we see the number of species of microbial genetic resources that are used for food or agriculture applications, it is extremely small (probably same is the case with other organisms also).

- *Saccharomyces cerevisiae* is still major player in ethanol production
- *Aspergillus niger* for citric acid producton

- Still there is lot of potential to tap the vast MGR's for benefits in food and agriculture

- The number of microorganisms that cause disease to plants is relatively low.

- Major source of the MGR's are the Microbial Culture collections

MICROBIOL CULTURE COLLECTIONS

Objectives

- Procurement of cultures and ex-situ conservation of microorganisms.
- Provide authentic microbial cultures to industries as well as academic and research institutes.
- Provide identification freeze drying and other microbiology related services.
- Act as a depository of patent cultures.
- Research on microbial diversity & taxonomy and related areas.

How MGR's reach culture collections

- Collections by researchers from the CC's personnel
- Procured or exchanged from other CC's
- General Deposits :
    1. For publication purpose
    2. Not to loose the culture, after the studies are over
    3. To make the culture available to other researchers

Confidential deposits :

1. Safe deposit
2. National Patent deposit
3. Deposit under Budapest Treaty

KINDS OF BIOLOGICAL MATERIAL ACCEPTED BY SOME INTERNATIONAL DEPOSITARY AUTHORITIES

IDA	Kinds of biological material	Cont. level
ATCC	Algae; bacteria; fungi; yeasts; embryos; human, animal and plant cell cultures; bacteriophages,animal and plant viruses; seeds; DNA; RNA; protozoa	3
BCCM	Bacteria .; fungi .; yeasts .; plasmid DNA .; animal and human cell lines	2
CBS	Bacteria; fungi; yeasts; bacteriophages; plasmid DNA	2
DSMZ	Bacteria; fungi; yeasts; bacteriophages; plasmid DNA; plant viruses; plant cell cultures; animal and human cell cultures; murine embryos	2
IMI	Fungi; bacteria	2
MTCC	Actinomycetes, Bacteria, Fungi, Yeasts, Plasmids	2
NCTC	Bacteria	3
NRRL	Bacteria, yeasts	1

Major points for discussion

1. The use of microbial genetic resources

a. Type of use and users

- What are the main activities involving the use of microbial genetic resources? To which degree does use of genetic resources and product development include genetic improvement?

- What is the degree of development, industrial establishment and professionalization of the sector using microbial genetic resources? Which ways and means are used to reward innovation and/or protect intellectual property, if at all?

- Who are the main holders and users of aquatic genetic resources? Which roles do they play at the different stages of research and product development? Under which types of ownership are genetic resources held?

b. Type of genetic diversity

- Are the genetic resources used and exchanged mainly wild or improved? Which diversity is commonly used in product development, intra- or inter-specific?
- What proportion of native vs exotic genetic material is used?
- Does genetic erosion occur in the sector? Is it perceived as a main problem/challenge for the sector by the users of genetic resources? Does the sector depend upon the effective conservation of genetic resources?

2. The global exchange of genetic resources

- What is the number and frequency of exchanges of MGR? What is the importance of cross-boarder exchanges and the direction of flows of genetic resources?

- Under which modalities are genetic resources exchanged? Which terms and conditions for use and exchange do they normally imply? How important are Intellectual Property considerations in exchange and marketing practices?

- What issues (other than ABS) are to be taken into account when exchanging MGRs?

Main activities involving MGR's in Agriculture

1. The use of microbial genetic resources

(a) Type of use and users

IN AGRICULTURE

- Microbes as plant growth promoting agents
- For Biological control
- Beneficial symbiosis in the guts of ruminant livestock
- Production of chemicals of direct benefit to agriculture
- Workhorses in agro-industrial processes.
- In the understanding and surveillance of microbial plant pathogens

IN FOOD

- Traditional Fermentation (fermented foods)
- Industrial fermentation of alcohol, wines etc.
- Cheese production
- Probiotics
- Production of chemicals of benefit to food production (vitamins, organic acids etc.)
- Understanding and surveillance of health hazardous microorganisms such as food toxins and food borne pathogens.

To which degree does use of genetic resources and product development include genetic improvement?

- Alcoholic beverages were made much before the existence and contribution of microbes in the process were known.
- Fermented foods are common in specific regions of several countries, and are based on traditional methods being followed for several years. (several generations).
- In more scientific way, the optimal microbial resources for these uses is mostly based on screening of naturally occurring microbes or of microbial resources from ex-situ holdings.
- In such cases, intellectual property is mainly taken on process and methods, and not on the microbial material as such.
- One major exception is the case of genetic improvement, which is also finding its way into microbial research, in particular in relation to synthetic biology.
- However, at the current state of affairs, this is still a marginal phenomenon, which might however grow in the future.

What is the degree of development, industrial establishment and professionalization of the sector using microbial genetic resources?

- Users of microorganisms are both from public and private sector entities and farmers.
- AMGR are used in universities and professional schools for training and education, they are the basis of the services provided by culture collections, and are an important resource for research and development in university and private industry.
- The vast majority of these collections are within the domain of the public sector: More than 80% of the more than 500 WFCC culture collections belong to public sector entities (universities or governments).
- The remaining are semi-governmental, and in some rare cases are within the domain of private non-profit or industry collections.
- All culture collections with major holdings in food and agriculture belong to the subgroup of the public sector or semi-governmental collections.
- The vast majority of materials distributed from culture collections – 77% according to a survey of 119 collections – are to public sector recipients.
- The remaining are distributed to the private sector for various uses, some of these being related to regulatory and identification purposes.

Which ways and means are used to reward innovation and/or protect intellectual property, if at all?

- For the public sector, the main incentive for innovation is the reputational benefits from publishing new findings, including the discovery of new taxonomic entities.
- Researchers working in the field of microbial diverisity will be happy to find a novel species of microorganism from a unoique ecological niche, and contributing to the field of taxonomy.
- In addition if the reported novel species has some unique capabilities to produce to some enzyme or compound of industrial use, it is considered as a bonus.
- For the private sector, IP protection (mainly process patents and methods) is well established and regulated through the Budapest Treaty.

Who are the main holders and users of MGR's? Their roles at the different stages of research and product development?

- Many countries are actively involved in collecting and exchanging microorganisms in the global arena.
- The majority of big culture collections are situated in OECD countries and that is also where the majority of collection, distribution and exchange takes place.
- The microbial strains from non-OECD countries however, represent an important and growing subset in the overall network of culture collections.
- The WFCC culture collections hold more than 1,4 million strains. The largest culture collection, with approximately 25.000 strains, holds less than 2 % of the total number of strains of the WFCC members.
- Each of these collections contains an important set of unique strains (an average of 40% of unique strain.
- Intense collaboration and exchange amongst culture collections is a necessary consequence of this situation.

Who are the main holders and users of MGR's? Their roles at the different stages of research and product development?

- In the case of an in-depth study of 10 major culture collections active in the field of food and agriculture (5 OECD, 5 non-OECD), an estimated 50% or more of the strains were acquired before the Convention on Biological Diversity (CBD) came into force.
- About 80-100% of acquisitions since then (at least in 2005, 2006, 2007 in the collections analyzed here) came without any conditions.
- For the OECD collections, in most cases, the country of origin was mainly from an OECD country (that is more than 50%), even if a substantial part was non-OECD. For the analysed OECD collections, nearly all material was distributed to OECD countries (90-100%).
- Significant amount of MGR's are held in developing country culture collections. For example, Thailand and Brazil, with 57 and 46 collections each these, have a total number of 42.541 and 137.737 strains respectively.

Under which types of ownership are genetic resources held?

- Most collections consider holding the materials “in trust” for the entire humankind.
- The small percentage of private collections is an exception to this general situation.
- For example, ATCC in the US, explicitly claims full ownership rights over the resources it holds

b. Type of genetic diversity

❖Are the genetic resources used and exchanged mainly wild or improved?

Which diversity is commonly used in product development, intra- or inter- specific?

- The main benefit of use and exchange is the direct contribution to global and regional food security.
- Focused screening and study of vast amounts of microbial resources from various regions of the world is needed.
- Exchange and use of microorganisms is done by culture collectionsc that have vast amounts of in situ microbial resources as they occur in nature (so-called “wild” genetic resources instead of “domesticated”).
- The main source of diversity that is used is intra-specific.

What proportion of native vs exotic genetic material is used?

- Access to AMGR originally collected in other countries is an essential component of the process of discovering and adding value to AMGR.

- However, at present, microbial resources that are used in agriculture and food systems have been collected both from tropical and sub-tropical species-rich agro-ecosystems and from non tropical areas.

- Some are local and others are exotic

- A case in point are the microbes for bioremediation and species used in biological control of agricultural pests and in biological monitoring, which have emerged from ecosystems at a wide variety of latitudes and altitudes.

Does genetic erosion occur in the sector? Is it perceived as a main problem/challenge for the sector by the users of genetic resources? Does the sector depend upon the effective conservation of genetic resources?

•Genetic erosion occurs mainly through the disappearance of host with which the microroganisms are associated or distruction of valuable habitats where potentially interesting microbes occur in a sufficient quantity to be easily identified and purified for screening.

•For example, a well known example is a US National Cancer Institute project came to a halt because recollection of the marine species Diazona containing a new class of antitumor agents failed, until it was rediscovered on another location many years later in deep coral reef caves.

The global exchange of genetic resources

What is the number and frequency of exchanges of MGR? What is the importance of cross-boarder exchanges and the direction of flows of genetic resources?

- More than 0.5 million strains are distributed a year by the WFCC culture collections alone.
- It is difficult to say how many strains are exchanged between research collections on an informal basis in the context of laboratories, but it is fair to say that the amount of strains exchanged between laboratories is significant.
- However, the latter are materials of still unknown scientific value and only conserved for ongoing research without the quality management and certified identification of the culture collections.
- As stated above cross-boarder exchanges are ubiquitous. Flows from in-situ to ex-situ occur both from South to North as within the North and within the South.

Under which modalities are genetic resources exchanged? Which terms and conditions for use and exchange do they normally imply? How important are Intellectual Property considerations in exchange and marketing practices?

- Culture collections are moving in the direction of using legal instruments: acquisition agreements when acquiring materials, material transfer agreements (MTA) when distributing them.

- However, over all, collections are in a state of transition.

- There is a general understanding on the fact that responsibility in relation to prior informed consent is on the depositor. Still, in most cases, depositors of MGR are not required to provide evidence of prior informed consent, even when the materials deposited are destined for subsequent redistribution.

- Many culture collections require recipients to negotiate subsequent agreements with the depositor before commercializing products based on materials received and in accordance with specific national laws concerning benefit-sharing.

- Most culture collections distribute materials for research purposes with MTAs specifying that the materials should not be further distributed by the recipient, except if the recipient is a qualified culture collection (so called legitimate exchange).

What issues (other than ABS) are to be taken into account when exchanging MGRs?

- At present, this situation of exchange of biological materials within a global commons, which prevailed during the early days of the emergence of modern life sciences, is facing a set of important challenges, which may hamper some of the most promising new scientific opportunities.

- Exchanges of MGR have historically occurred in an informal way, without the use of written contracts.

- However, the increasing economic importance of biotechnologies and new legislation concerning the use and access to natural resources, have subjected exchanges of genetic resources to increasing controls.

- Access and distribution are submitted to many requirements and therefore, exchanges are becoming subject to more and more formal forms of control.

- As a response to financial restrictions on government spending for culture collections in some countries in the 1990s, and the growing commercial opportunities, some culture collections departed from the sharing and collaborating practices and have introduced unduly restrictive MTAs.

If these trends continue, there is a serious risk of over protection and privatization of all biological resources on the same highly restrictive conditions that are only relevant for a handful of deposits with known or likely high payoff commercial opportunities.

This would have major impacts on access and distribution of microbial research materials in the life sciences.

In particular, if the formal exchange becomes unduly restrictive, scientists might prefer to exchange strains in an informal way between research laboratories where the bulk of microbial research is done.

In an interesting development, in parallel to these restrictive trends, most public culture collections are working to maintain the tradition of global distribution and exchange.

There have been a number of initiatives to develop science-friendly MTAs that are designed under open access schemes, at least as far as the distribution for research and scientific purposes are concerned.

- For instance, both OECD and non-OECD collections include clauses of legitimate/legal exchange in their MTAs, which allow public culture collections that comply with strict quality management criteria to further distribute microbial research material that they have received from other public culture collections.

- Some majors culture collections, such as the DSMZ collection in Germany, the BIOTEC collection in Thailand feel that it would be a good step forward to facilitate the exchange of MGR by reaching agreement on a global common policy for the distribution/deposit of the material, so that material is deposited/distributed under the same conditions/restrictions all around the world.

- European Biological Resource Centres Network (EBRCN) and Asian Consortium of Microbiological Resources (ACM) are making efforts to make the cultures available within the networks without many restrictions. Expansion of these activities will eventually benefits the users.

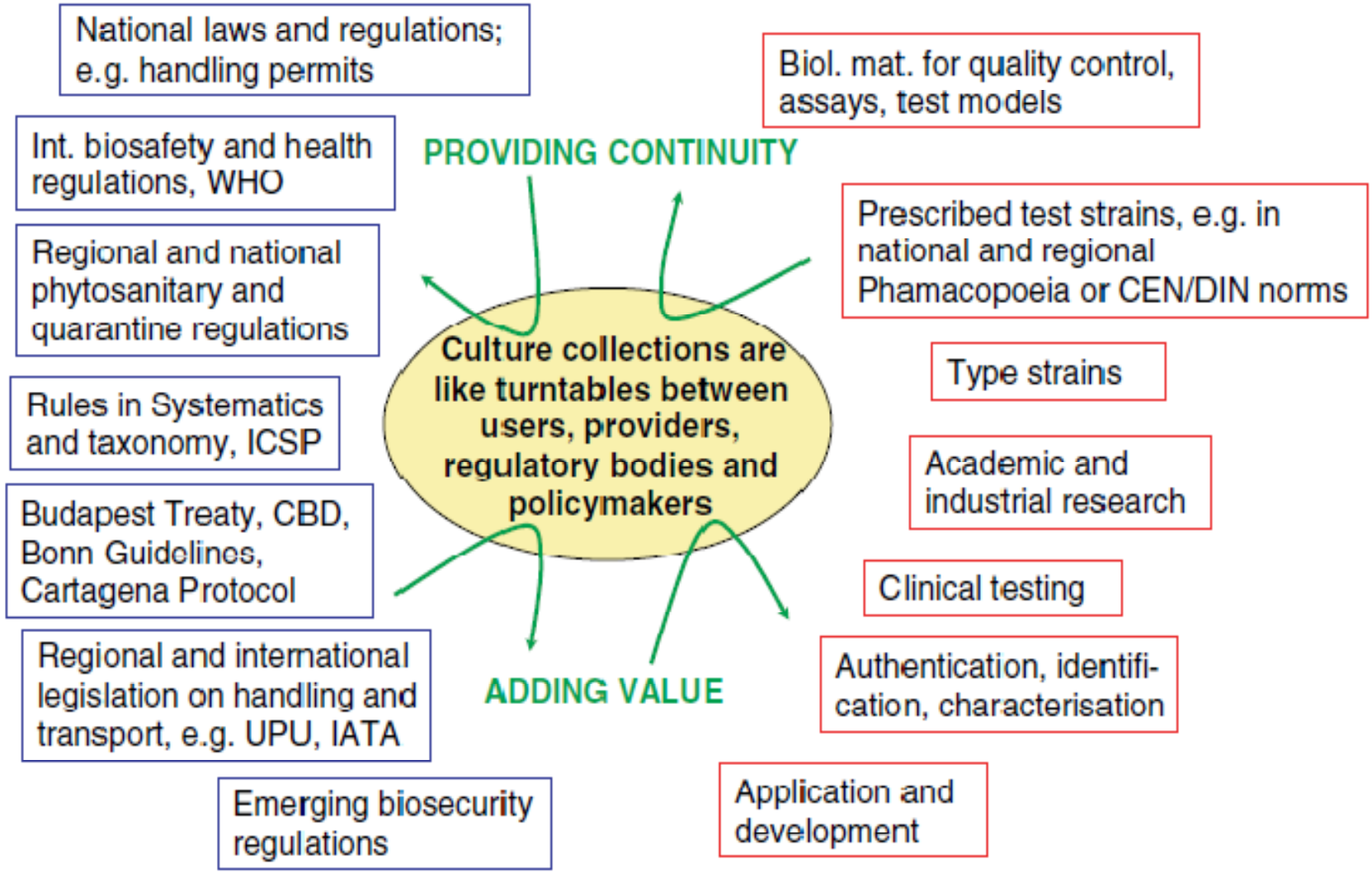
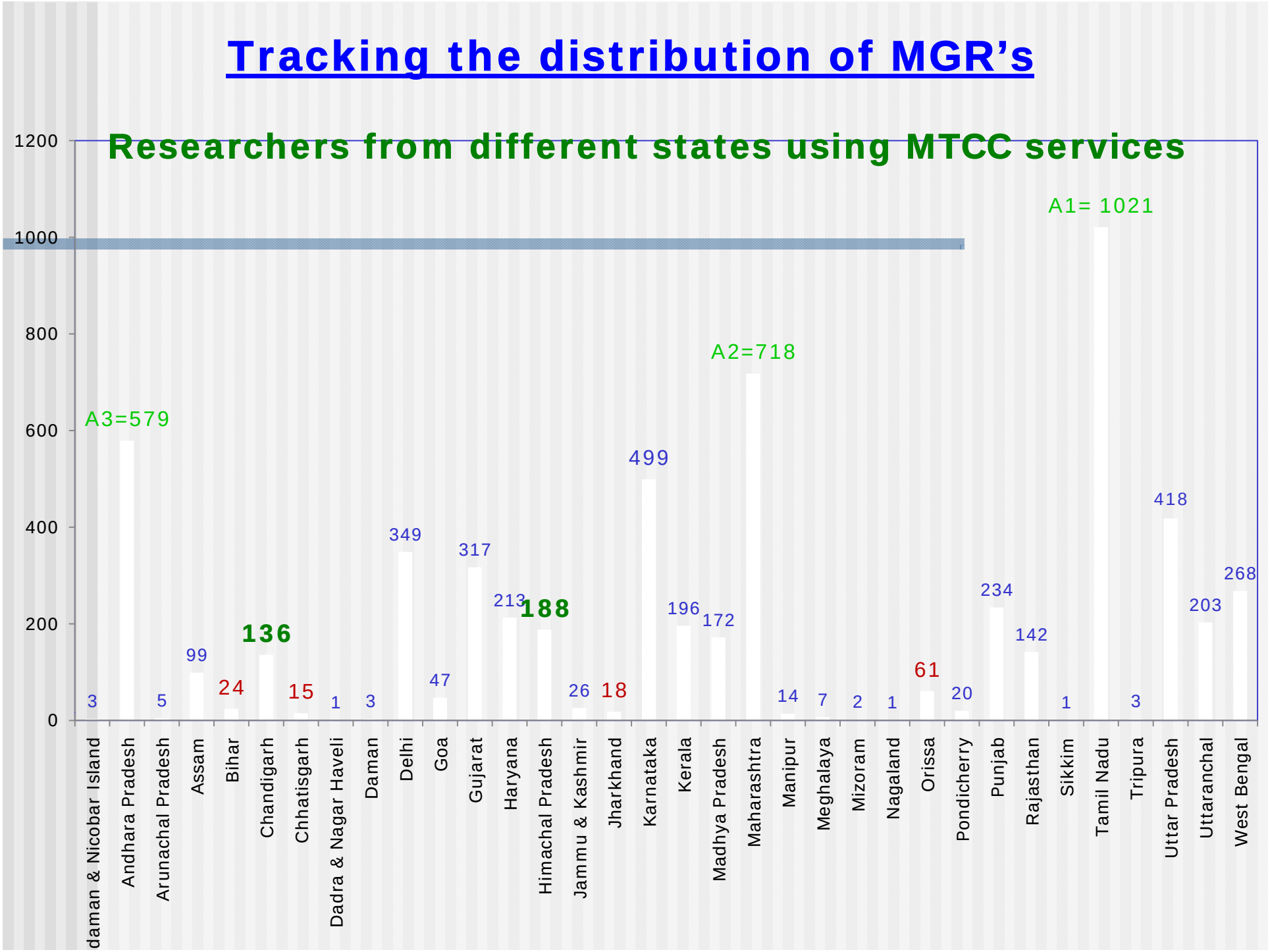
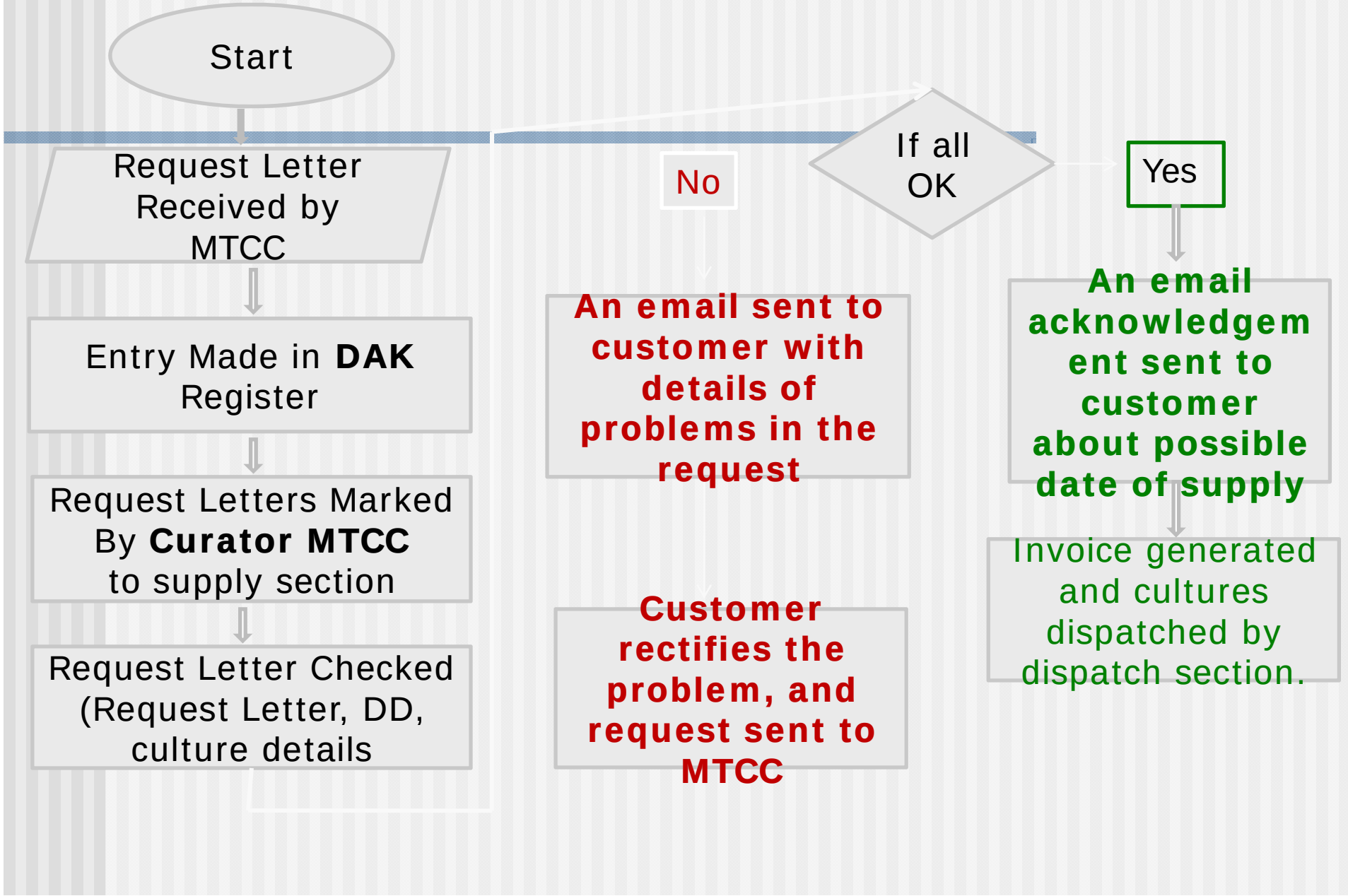


Figure 3: Collections of living biological material: Hubs of interest.
Examples for legislation and regulations affecting collection work (left, blue) and examples for potential and prescribed uses of the biological material (right, red).

Tracking the distribution of MGR's



Flow Chart for Supply



Dear Dr. P. Gomathi (pgoms@yahoo.com),

We have received your request for along with a demand draft numbered **990750** for Rs. **4412**/- on **31-08-2010**. Your request is in process, with reference number **33772**.

The expected date of completion would be **16-11-2010**.

Please feel free to contact **Dr. G. S. Prasad (prasad@imtech.res.in),** for any query/information.

Thank you for your interest in MTCC.

MTCC Customer Support

- Depositors send the cultures to CC's in good faith to ensure that they are available for other researchers for future research.
- They also understand that depositing the MGR's in CC's gives authenticity to their work.
- Users normally donot want regulations, for them procuring the culture from reliable source is important.
- Eg. A graduate student doing a 3-6 months project will be interested in getting the culture than going through lengthy formalities.
- It is difficult to make him understand the regulations of MTA and its implications.

Who is the owner of the culture ? Who should share the benefits ?

- Person isolating the culture
- Person who deposits the culture in CC
- Organization of the depositor
- Country ? Who in the country ?
- Culture collection
- Person who bought the MGR’s from CC
- How to share the benefits

Thank you for your kind attention