REPORT OF THE 9th EVALUATION

OF THE BIOTA-FAPESP PROGRAM

BY THE SCIENTIFIC ADVISORY COMMITTEE

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Members of the Scientific Advisory Committee

1) **Raymond Andersen**

Departments of Chemistry and Earth, Ocean & Atmospheric Sciences

University of British Columbia

Vancouver, British Columbia

Canada V6T 1Z6

2) **Koos Biesmeijer**

Naturalis Biodiversity Center

POBox 9715, 2300RA Leiden, The Netherlands

koos.biesmeijer@naturalis.nl

3) **Jérôme Chave**

Centre National de la Recherche Scientifique

Université Paul Sabatier, UMR5174

31062, Toulouse, France

jerome.chave@univ-tlse3.fr

4) **David J. Newman**

Retired from Natural Products Branch, NCI

djnewman664@verizon.net

5) **Isabel Sousa Pinto**

Department of Biology Faculty of Sciences

University of Porto

Porto, Portugal

ispinto@fc.up.pt

1. Introduction

The BIOTA Program is a core program of FAPESP. It was initiated in 1999, and renewed in 2009, for a duration of 10 years, the BIOTA+10 program, which is the object of this present evaluation (see Appendix 1).

As part of its review and quality assurance policy, the BIOTA-FAPESP Program periodically has its achievements evaluated by a Scientific Advisory Committee of independent experts. The evaluation took place in conjunction with the 9th BIOTA Program Assessment meeting in São Pedro, São Paulo, attended by both scientists and students. The meeting included short courses for attending students.

The projects were presented to the Scientific Advisory Committee in a thematic way with summaries of projects provided in each thematic group along with a summary of gaps, shortcomings, linkages and future goals. This approach was helpful in the evaluation, and it appeared to also be worthwhile in bringing related projects together to examine as a theme; shortfalls, gaps, conclusions.

2. Methodology followed by the Committee

The Scientific Advisory Committee examined the BIOTA Program, the 9th Symposium of BIOTA and the subsequent Evaluation meeting. It established its opinion through:

- Reading the report on the projects sent by the coordinators in advance

- attending oral presentations and poster sessions;
- interviews held with BIOTA Program coordinators, as well as with project leaders, students and presenters at the symposium
- presentations on the BIOTA Program
- document material, including a brief description of the current thematic projects
- previous evaluations of the BIOTA Program including the 8th Program Evaluation (2014)

The Scientific Advisory Committee focused on the program as a whole rather than on individual Projects. The aim was to (i) evaluate the achievements of the BIOTA program in view of the recommendations made by the 8th Program Evaluation Panel, and to (ii) provide a new set of recommendations keeping in mind the future agenda of the BIOTA program, which is currently funded until 2019.

The Scientific Advisory Committee endorses the reports of the previous evaluations as they represent a comprehensive and useful analysis. We do not wish to repeat much of what is stated therein. We have reiterated some points, however, that we regard as continuing to be critical to the successful continuance of the BIOTA program.

In the 8th evaluation, the BIOTA program and the BIOTA/BIOprospecTA subprogram were evaluated together, but a separate set of recommendations was provided (see Appendix 2). This strategy was justified because convergence between the two thematic activities had not yet reached completion. In the 9th evaluation, the Evaluation Panel acknowledges that

great progress has been paid in integrating these two streams of research and has thus decided to provide a single assessment for the entire BIOTA program. This clarifies, and hopefully simplifies, the present document.

3. Assessment of the BIOTA Program

Overall assessment

The Scientific Advisory Committee continues to be impressed by the BIOTA Program and by advances that continue to be made. The BIOTA Program continues to provide an example, and sets standards, that many countries should follow. Overall, the Program has excellent breadth spatially, taxonomically and thematically. The full integration of the BIOprospecTA sub-program is a good example of how much progress has been made. Importantly, this remarkable progress has been achieved in spite of an adverse global economic context. FAPESP is to be commended for its continuing support to such a flagship program.

Over the evaluated period, the objectives of the BIOTA Program have been met, within thematic projects or shorter-term projects. The issues of biodiversity characterization, sustainable use, processes of generation and maintenance of biodiversity, biodiversity loss estimation, conservation initiatives, and linkage with public and private sector initiatives for biodiversity management, were evident in the projects presented during the meeting. The strongest contribution was on the biodiversity characterization and understanding of key processes, and the extension of BIOTA to the policy-making sphere has been remarkable. During the previous evaluation, the component on marine biodiversity was

more prominent than in the current one, and this was then perceived as a great plus for the BIOTA Project, so should be reinforced in the future.

The BIOprospecTA sub-program has also met its objectives to a large extent. Since 2011, the number of projects appears to have been reduced but the remaining programs are very strong – they enjoy widespread international recognition as evidenced by publications in high impact journals, or collaborations with leading researchers outside Brazil. The teams are working on challenging problems of broad interest to the natural products community – i.e. the microbial production of metabolites previously only isolated from invertebrates, chemical ecology of ants, identifying bioactive natural products from plants and marine microorganisms, and semi synthesis of new chemical diversity using abundant plant secondary metabolite scaffold starting materials.

The Scientific Advisory Committee was especially impressed by the ability of the BIOTA program to develop international programs in collaboration with the USA (with the NSF and the NIH) and the UK (with the NERC). These internationally funded collaborations testify to the quality of the overall Biota program, as the bar for such funding is very high. These projects not only dramatically increase the visibility of FAPESP program at the international scale, but also stimulate a culture of excellence and hypothesis-driven science that is already an asset for Brazilian science.

The project groups are publishing in the top journals for the field, reaching out to their colleagues all over the world. The dissemination of their work also included active

participation in a number of international meetings as invited lecturers, oral presentations and posters. Overall, the publication record was impressive, with 275 papers published in 2 ½ years (2015 to mid-2017). The Scientific Advisory Committee would advise the BIOTA coordination to provide a more direct illustration of the impact of these publications, through metrics such as mean impact factor, h-index, or number of papers in weekly scientific journals (Nature, Science …). This would help better apprehend the excellence of BIOTA at an international scale. Major impacts at society level, as e.g. inputs to new legislation or regulation or uptake by industry should also be highlighted. This practice could also be implemented for each project.

In terms of education, the students learn to work in multidisciplinary teams bridging between biology, chemistry and pharmacy, opening the way to valorisation of the national biodiversity. The training ability of the teams involved in BIOTA is remarkable, with 86 FAPESP-funded PhDs, 75 FAPESP-funded post-doctoral research associates, all associated with specific BIOTA projects.

The Scientific Advisory Committee highly values the efforts invested by the BIOTA/FAPESP program to document biodiversity in the State of São Paulo and beyond. This was one of the original motivations for the BIOTA program. This effort can only pay off if it is continued over decades. For that, continued investment into biodiversity analytics and informatics infrastructure is needed.

The individual groups have established both formal and informal networks between PIs with complementary skill sets. This is shown in areas as diverse as ecological studies at both macro and microorganism level and in the bioprospecting area where knowledge in one specific methodology is shared among PIs who need to utilize that skill set.

The Scientific Advisory Committee realizes that the new Law on Biodiversity of Brazil and its decrees of application are still placing the scientists of the BIOTA Program in a challenging situation. While the BIOTA Program coordination and scientists are very aware of the new issues raised by the changing legal landscape, this continues to be a serious challenge, especially concerning the facilitation of international collaboration.

Evaluation of the 2014 recommendations

In 2014, the Scientific Advisory Committee made a number of recommendations regarding the BIOTA Program. These recommendations are available in Appendix 2 of the present document. We have evaluated to what extent these recommendations had been taken on board by the BIOTA community.

1) Recommendation 1 that the Program is continued is still valid now.
2) Recommendation 2 regarding the modelling has been followed-up through joining the Belmont forum – Biodiversa call on Scenarios of biodiversity and ecosystem services. A total of 16 proposals were submitted with Biota partners, and are currently under evaluation. This is a good first step and after the results are known other actions may be considered to promote modelling and scenario activities under the Biota program.

3) Recommendation 3 suggested improving accessibility of Biota information through mapping of biodiversity data and information. This would allow for future projects to benefit from previous projects and to use information in other domains, e.g. for policy or planning. While some excellent examples were presented we would suggest to pay more attention to this, developing also a map of e.g. permanent plots that Biota researchers keep, with associated information, calendar of field trips: past and planned with relevant information.
4) The Biota program has taken up recommendation 4 by putting out specific thematic calls in areas in need of additional projects. We recommend them to continue to pursue this, for example in areas such as marine biodiversity, remote sensing, urban biodiversity or socio-ecological systems.
5) Exploration of the added value of biodiversity in other societal sectors was suggested as recommendation 5. Compilation of the basic information on ecosystem services is being achieved in the national BPBES project. This could be the start of an interdisciplinary collaboration where experts from economics, anthropology and other sciences join the Biota program to address the market and non-market valuation of biodiversity and ecosystem services.
6) The previous evaluation recommended (recommendation 6) Biota to consider the challenges associated with high volume molecular data being generated in the projects. While the committee has noticed an increase in attention to bioinformatics in the various projects, the issue of data storage and analysis remains an important point.
7) The Biota program remains to be important for taxonomy and related sciences for which funding is often difficult (recommendation 7). A thematic call in this area is under evaluation at the moment.
8) The integration of microbiology and marine sciences (recommendation 8) has been achieved to a certain extent. On the topic of infectious human diseases, some projects are

being started. However, further integration into the public health domain could lead to new insights on both ecology and management of these diseases and their vectors.

9) Recommendation 9 pointed to putting more focus on the highlights of the program, e.g. high impact papers, policy impacts. This has not been done till now so we keep this as a recommendation. In addition, it would still be highly valuable to attempt synthesis and integration of the previous results of projects into meta-analyses. Consequently, this previous recommendation still holds up.

The 2014 Scientific Advisory Committee made an extra set of recommendations regarding the BIOprospecTA subprogram. These recommendations are also available in Appendix 2 of the present document. We have evaluated to what extent these recommendations had been taken on board by the BIOTA community.

1) Recommendation 1 suggested a regular external expert panel evaluation of the hits produced by the program. This was not undertaken because it was felt that there were not any lead compounds ready for this stage of evaluation.
2) Recommendation 2 concerned the opportunity of establishing a central lab facility with the capability to synthesize natural product hit compounds and active analogues on a minimum of a 10 gram scale. This has not happened. Instead several of the PIs have filled this void by either reaching out to synthetic chemistry collaborators in other parts of the world who have supplied these materials or by bringing synthetic chemistry efforts into their own labs. This is a viable alternative solution to the recommendation.
3) Recommendation 3 suggested that a common bioassay lab could be established for all of the BIOprospecTA groups. This has not been done. Establishing a facility of this sort, while desirable, is very expensive. As an alternative, the PIs have developed individual collaborations that have filled this void.

4) Recommendation 4 suggested that FAPESP should consider measures to help spin-off-up companies to be started from the BIOprospectTA projects. In response to this recommendation, BIOTA has started programs to stimulate student entrepreneurs.
5) Recommendation 5 was a reminder that a Good Practices training is indispensable for every scientist. This point has not been discussed further during this evaluation.
6) Regarding recommendation 6, the Scientific Advisory Committee continues to recommend the practice of long-term grants of 5 to 10 years.
7) The microbial sources are now considered to be part of the BIOTA/BIOprospecTA portfolio, and thus these products are being evaluated for their potential as both biotechnological and drug leads.
8) Some comparative analyses (at the genomic level) of the microbes identified in the projects where there is a component of metabolomic / genomic investigation have been performed in order to see how closely linked these microbes are. These should be extended.
9) To handle the big data sets that are and will be produced, proper storage and data analysis methods are required. The number of bioinformaticians will need to be increased.

4. Feedback from the BIOTA community

The committee organized a session with all BIOTA PIs to discuss both the benefits that the Biota project has brought them and suggestions for the future of the Biota program. Their comments are summarized here.

The BIOTA program has proven beneficial to researchers for the following reasons:

1. BIOTA is a strong brand. Membership of BIOTA brings immediate credibility and raises the profile of biodiversity research in general and of individual researchers and projects. Researchers are proud to be part of Biota
2. BIOTA allows for big, often multidisciplinary, science projects, with substantial budgets that are not possible for individual researchers.
3. BIOTA is a good environment for students, provides important community mentoring to young faculty members and facilitates experience with interdisciplinary research
4. BIOTA supports basic research such as taxonomy and biodiversity surveys. These subjects are not usually funded in other places.
5. The BIOTA community of researchers is a vibrant network where new ideas are born and new alliances are formed. In addition, the BIOTA network facilitates access to state of the art equipment
6. The high quality of BIOTA entices Brazilian scientists living abroad to come back to Brazil, raising the quality of science in Brazil
7. BIOTA is attracting people from other fields, e.g. medicine, to start integrated studies, e.g. of disease or resource management
8. BIOTA reviews are helpful networking and feedback forums
9. BIOTA gives Brazilian scientists the credibility to be invited to important international collaborations. Its international calls are hugely beneficial for collaboration and student exchange
10. BIOTA has built up 20 years of data that is not available anywhere else and an invaluable source for new projects. It also facilitates long-term ecological research

The following suggestions came up that may be relevant for the future Biota program:

1. BIOTA should continue!
2. Promote the use of the BIOTA brand more. This will improve the visibility of biodiversity research in general and its credibility for policy development
3. Provide funding for knowledge transfer and outreach to the wider society
4. Improve the links between BIOTA and other areas of science, e.g. agriculture, bio-energy, planning, medicine, to facilitate integrated solutions to complex issues. In addition, areas such as history and the arts may be interested as a partner in future projects.
5. Think of ways in which students can be more involved in the BIOTA meetings. One way could be to include student oral presentations into review meetings
6. Think of ways that Brazilian scientists can use the biodiversity of Brazil as a living laboratory to ask big picture questions with general application to all parts of the world
7. Increase information on current projects to advertise for future field trips that can be used by other teams to get samples and information on (sometimes) hard to get field sites

5. Recommendations for the future

1)	A long-term funding horizon is a very important component of the stability and visibility of the BIOTA/FAPESP program. The Scientific Advisory Committee firmly

states that the BIOTA program is a tremendous success, and fully supports continued funding beyond 2020. There is every reason to believe that it is an excellent investment for FAPESP and, beyond, for Brazilian science. BIOTA has been built into a strong internationally-recognized Brazilian brand.

2) We suggest for BIOTA/FAPESP to create a synthesis and analysis centre following the model of the US National Center for Ecological Analysis and Synthesis, so as to generate integrative science and gather among projects and with international scientists. The requirement would be to publish syntheses or meta-analysis papers. This would reinforce the synergies across BIOTA projects and also with the international research community.

3) BIOTA's impact on society could be increased by linking to research programs in areas such as climate, water, bio-energy, agriculture and green economy. The latter domains would benefit from BIOTA science to come up with better, more integrated solutions, and BIOTA could focus on more priority areas e.g. those addressed by the UN Sustainable Developmental Goals.

4) The BIOTA Program should explore how to contribute to the implementation of Sustainable Development Goals as one of the frameworks for the program (Aichi targets will be done by 2020).

5) The Scientific Advisory Committee recommends that dissemination and knowledge transfer should be an integral part of all BIOTA projects. One option would be to dedicate a fixed small percentage of the project budget to this. Dissemination could for example target school children, professionals, managers,

retired people or even all citizens. This type of outreach action is now mandatory in many national scientific funding agencies.

6) Given that BIOTA is a respected and trusted source of knowledge for policy makers, we recommend an increased effort in producing science for and with policy, planning, conservation and natural resource management, including specific products targeted for policy makers and managers.

7) BIOTA is increasingly connecting with the wider society and citizens. However, citizens can play a more important role in the future, for example by recording and studying biodiversity in citizen science projects. This will not only increase biodiversity data and information for science, it will also increase societal awareness and people's connection with nature.

8) The individual projects are of high standard, but the committee would recommend even further integration of projects in the future, and more collaboration in permanent experimental setup (such as forest plots). One idea would be to make information on ongoing projects (plots, locations, field trips planned, target organisms) more readily available on a single Geoportal platform to allow for sharing of these resources.

9) High-throughput sequencing technologies and bioinformatics are crucial tools for the BIOTA Program, and are fundamental in biodiversity discovery, phylogenomics, and microbiology. Adoption of these technologies is a significant challenge. BIOTA scientists should continue to invest resources in high-level training, and encourage early-career scientists to acquire expertise in

bioinformatics. Bioinformatics and sequencing facilities/resources funded by FAPESP should be made more easily available to scientists of the BIOTA Program.

10) The strategy of launching targeted calls for proposals has created the opportunity to truly develop areas of research heretofore missing in the BIOTA program. This strategy has permitted to accelerate the integration of these sub-disciplines. In that spirit, the Scientific Advisory Committee recommends to create a call to respond to policy needs. It is also important to maintain the opportunity for scientists to submit BIOTA/FAPESP projects, even if they do not fall within the scope of a specific call.

11) The adoption of a "Proof of Principle" funding mechanism would further the development of a very small number of compounds that look like genuine drug candidates. This would support costs of scale up production, pharmacokinetic studies, oral bioavailability, toxicity and efficacy studies in animal models. This could be supplemental funding only given out on special cases after the PI has made a convincing case that they had a compound worthy of this funding. This would facilitate the further evaluation and development of some of the promising lead compounds for drugs to treat neglected diseases that we saw in the presentations. FAPESP could use this example to expand Proof of Principle funding mechanism beyond BIOTA.

12) The Scientific Advisory Committee was made aware that the projects submitted through the BIOTA Program have a surprisingly slow turnover time. A process with faster response and flexibility of management would be desirable.

6. Conclusions

The Scientific Advisory Committee strongly emphasizes that conserving biodiversity is the best bet-hedging or insurance strategy for maximizing our chances of finding new benefits, including new uses and products, from nature. Biodiversity assures benefits for future generations. Research is pivotal to underpin the best possible sustainable use of the abundant Brazilian biological resources while also helping to conserve and restore its ecosystems.

In that respect, the Scientific Advisory Committee recognizes that the BIOTA/FAPESP program has turned itself into an internationally recognized brand. It can now count on several international collaborations with prestigious institutions. In addition, the BIOTA/FAPESP program has permitted to make significant progress in education and training on biodiversity.

Overall, the members of the BIOTA/FAPESP program see membership in the program as a very prestigious and productive transdisciplinary association. This demonstrates that the program is working extremely well. The Scientific Advisory Committee emphasizes the success that has resulted from integrating, conceptually and practically, BIOTA and BIOprospecTA.

The Scientific Advisory Committee made a number of critical recommendations on the BIOTA Program. The intention is to provide a constructive feedback and some guidance to the BIOTA research community.

Appendix 1 – Objectives of the BIOTA+10 program

In the 2010 strategic document (Joly et al. Science 2010), the BIOTA+10 program established the following five objectives

- To inventory and characterize the biodiversity of the State of São Paulo, by defining the mechanisms for its conservation and sustainable use;
- To understand the processes that generate and maintain biodiversity, as well as those that can result in its deleterious reduction;
- To produce estimates about biodiversity loss in different spatial and time scales.
- To evaluate the effectiveness of conservation initiatives within the State of São Paulo, identifying priority areas and components for conservation.
- To increase the ability of the State of São Paulo and public and private organizations in managing, monitoring and using biodiversity in a sustainable way

In addition, the following priorities were discussed for the 2010-2019 period (i) including native biodiversity restoration as one main objective of the BIOTA/FAPESP Program; (ii) development and implementation of a new information system for the BIOTA/FAPESP Program; (iii) Biodiversity Inventories & DNA Barcoding; (iv) Marine biodiversity; (v) Phylogeography; (vi) Invasive species & GMOs; (vii) Landscape Ecology & Ecosystem functioning and services; (viii) Applied ecology and human dimensions in biological conservation; (ix) Modelling & Climate Change; (x) Short, medium and long term plans for the BIOprospecTA sub-program; (xi) Education & Public Outreach; (xii) BIOTA NEOTROPICA; (xii) National & International Partnerships

The BIOprospecTA sub-program of BIOTA is a more recent initiative that organizes a network of researchers and laboratories with the following objectives:

1) Standardized collection of biological samples and pre-processing of raw materials for the subsequent preparation of extracts;
2) Establishment of a bank of extracts and pure compounds from plants, microorganisms, marine organisms and other natural sources, with the required automation and data management facilities;
3) Establish a flow between complementary research groups from standardized extracts, fractionation and purification; screening of extracts; identification and characterization (NMR, Crystallography, LC/GC-MS, ect …) of promising extracts/compounds; pharmacology and toxicology of promising bioactive extracts/compounds; synthesis of bioactive natural products and their derivatives; medicinal chemistry and drug design applied to the development of promising compounds, whenever possible with private sector partners.
4) Development of new in-vitro and in-vivo bioassays;

Appendix 2 – Recommendations from the BIOTA 8th Evaluation Report (2014).

Recommendations regarding the BIOTA Program

1) International BIOTA projects have created a unique opportunity for conducting frontier research within BIOTA. The Scientific Advisory Committee recommends that this approach be pursued, and continue collaborations with other countries.

2) Discussions highlighted the need for predictive models of biodiversity. The need for modelling across different projects suggests an opportunity for integrative work towards a common toolbox. The Scientific Advisory Committee recommends that specific effort should be paid to developing such predictive models of biodiversity within the BIOTA/FAPESP program. These models will extend beyond conventional models for single species to allow inferences to be made about overall biodiversity patterns. Such models can better serve the objectives related to estimates about biodiversity loss and evaluation of the effectiveness of conservation initiatives. This action could be stimulated through a thematic call for proposals.
3) Conservation planning critically depends on the availability of maps that facilitate the work of prioritization. The Scientific Advisory Committee recommends that methods to create biodiversity maps be implemented at the state scale, perhaps in relation with the SinBIOTA plateform.
4) The State of São Paulo remains understudied. The Scientific Advisory Committee recommends that spatial gaps for surveying be prioritized (e.g. based on "Survey gaps analysis"). This could include biome gaps, such as the deep sea, or habitat gaps such as the microbiome of non-model organisms. We note that such mapping will be expected to integrate with mapped information on ecosystem services and opportunity costs of conservation.
5) The Scientific Advisory Committee recommends that steps be taken to enhance the awareness of BIOTA as playing an essential role in any initiative that FAPESP may take towards a green economy. The essential role of BIOTA in this context is the provision of a framework for biodiversity assessment and conservation. This

provides the foundation for ensuring the well being of future generations, and so will be an essential ingredient of a green economy.

6) High-throughput DNA sequencing is both an opportunity and a concern within the existing organization of BIOTA. Such data are orders of magnitude larger in size than before, yielding novel challenges. Also, analysing these data requires new techniques (bioinformatics). The Scientific Advisory Committee recommends attracting expertise in bioinformatics within the BIOTA program.
7) Taxonomy and field surveys have been a major drive for the BIOTA program and much of its success is associated with this vision. The Scientific Advisory Committee recommends developing a specific line of funding dedicated to conducting taxonomic research, with a thematic call for proposals.
8) The integration of both microbiology and marine science within the BIOTA program are perceived as a clear success. These subprograms should continue to be supported by FAPESP within the BIOTA program; (8b) BIOTA should also examine the pertinence of collaborating with the health sciences through a subprogram in epidemiology. The mapping of the spread of diseases particularly those "mediated" by insect vectors such as malaria and leishmaniasis may well provide an early-warning system of changes in the environment that are permitting the invasion by insects into areas where the diseases were not previously reported; conversely, the absence of such reports in previously "infected areas" may also indicate changes.
9) An increased focus could be placed on significant publications in international journals. The Scientific Advisory Committee suggests for BIOTA/FAPESP to create a synthesis and analysis centres (see e.g. the NSF-funded National Center for

Ecological Analysis and Synthesis), so as to generate integrative science and gather among projects and with international scientists. The requirement would be to publish syntheses or meta-analysis papers. This would reinforce the synergies across BIOTA projects and also with the international research community.

Recommendations regarding the BIOprospecTA sub-program

1) A regular evaluation of the hits produced by the program by experienced drug developers in the form of a workshop with the PIs is recommended to select the priority compounds and make a roadmap for further development to the level of a lead.
2) BIOTA/ BIOprospecTA should consider establishing a central lab facility that has the capability to synthesize natural product hit compounds and active analogues on a minimum of a 10 gram scale. This facility would be funded directly by FAPESP and it would serve the needs of all of the natural product groups in BIOprospecTA (or even in all of Brazil).
3) The central production lab might include a common bioassay lab for all of the BIOprospecTA groups, and as compounds moved forward, it might also make sense to add an animal facility and some analytical chemistry resources to support PK, toxicology, and efficacy studies.
4) FAPESP should consider measures to help spin-off-up companies to be started from the BIOprospectTA projects. This might include also educational programs for biobased business.

5) Good Practices training will be indispensable for every scientist that intend to work in partnership with pharmaceutical industry in the process of drug development
6) The practice of long-term grants of 5 to 10 years should be continued as it creates a proper environment for high-risk innovative projects.
7) The microbial sources should be considered as part of the BIOTA/BIOprospecTA portfolio, and thus the products evaluated for their potential as both biotechnological and drug leads.
8) It may be worth performing comparison analyses (at the genomic level) of the microbes identified in the projects where there is a component of metabolomic / genomic investigation in order to see how closely linked these microbes are.
9) A market survey for industrial enzymes including food, washing, fine chemical production and research tools should be made, setting the standards for the discovery proteins of interest.
10) For handling the big data sets that are and will be produced, proper storage and data analysis methods are required. Bioinformaticians should be included in the program.