PLANT-BASED BIOPRODUCTS: CREATING VALUE FROM RENEWABLE BIOLOGICAL RESOURCES

A "Strategy Paper" to underpin and direct a new vision for US-EU collaboration in agricultural and industrial biotechnology

This Strategy Paper presents a vision for creating a new knowledge-based bioeconomy in which industry uses renewable raw materials for the sustainable manufacture of energy and other non-food, non-feed products needed by society.

A US-EC Task Force on Biotechnology Research has examined opportunities for developing research and technologies to underpin these "plant-based bioproducts". This Strategy Paper aims at identifying needs, processes and mechanisms to enable collaboration between the US and EU to proceed effectively. Recommendations will be made to policy-makers for new funding streams dedicated to support competitive awards for collaborative programmes involving researchers from both regions.

1. INTRODUCTION

1.1 Today's Economy is Petroleum-Based.

1.1.1 Industry and society are dependent on fossil reserves of coal and hydrocarbons for raw materials and energy. The global petrochemical industry relies on outputs from oil refineries for the manufacture of plastics and other products, based on fossil feedstocks that underpin every aspect of our society. It is recognised that the imported oil utilised by both the EU and US to support these activities create a huge external dependence on the relatively few exporting countries and contributes substantially to a trade imbalance.

1.1.2 Fossil reserves are finite, with near-exhaustion of economically viable petroleum supplies predicted within 50 years. While this conclusion is arguable to some, there is global consensus that petroleum will become far more difficult to obtain, as world population grows and standards of living improve in developing countries. Many petroleum rich countries are politically unstable, making supply stability and price problematic. Fossil fuel demand will further increase, costs will rise and the ready availability and persistent low price of petrochemical resources will cease. Renewable plant resources are one way to supplement hydrocarbon resources and meet increasing worldwide needs for consumer goods. Significantly, mankind prospered mainly under a plant-based economy for tens of thousands of years, and only became dependent on petroleum reserves within the past century.

1.2 The History of Biobased Industry:

1.2.1 Since fossil reserves are finite, plant-based renewable raw materials as a supplement to fossil reserves, and ultimately as a replacement for those reserves, are an assured certainty, not a choice. This evolution is desirable for its positive impact on the environment and to provide a sustainable basis for production. For example, petroleum-derived plastics make up a significant volume of landfills that are reaching their capacity, and they are clearly recognised as a significant detriment to our marine environment. Both EU and US scientists recognise that the consumption of fossil fuels contributes to increase of greenhouse gasses in the atmosphere.

1.2.2 Plants capture the energy of sunlight and use carbon dioxide in the atmosphere to make a complex range of functional biochemicals beyond the capabilities of synthetic chemistry. Plant-based manufacturing, carried out by “factories” within specific plant cells, is sustainable, does not involve environmentally hazardous processes and does not produce waste. Plant photosynthesis produces a wide range of bioproducts and functionalities of which thousands have been identified but far fewer utilised. Already a significant number of products, derived from plant materials, have begun to displace petroleum in limited markets. These include ethanol and organic acids produced in fermentations with glucose as chemical feedstock and a wide range of surfactants, coatings, lubricants and hydraulic oils produced from vegetable oils as well as adhesives based on starch or protein.

1.2.3 Expansion of our understanding of plant biotechnology will not only benefit and expand biobased industries, but also offers benefit to consumers and contributes to societal objectives, as well as improving the environment and creating new opportunities for farmers. As scientists probe deeper into the molecular biology of plants and their structure, properties, metabolism, and function, they may well develop technologies that can enhance the efficiency and effectiveness of plants in producing the raw materials for biobased products.

1.3 Advances in Bioscience

1.3.1 Biotechnology is not new. Humans have used it for thousands of years to produce bread, wine and cheese. Modern biotechnology employs enhanced microorganisms, such as yeast, moulds, and bacteria, along with the enzymes derived from them, to produce a wide variety of goods. Such fermentation processes, now described by some as white biotechnology, are dependent on plants as the source of fermentation substrates such as glucose. Developments in plant science, in contrast known as ‘green biotechnology’, are potentially capable of greatly extending their use in the non-food industries.

1.3.2 The rapidly increasing availability and declining cost of sequenced genomes and the enabling genomic technologies are facilitating the development of this 'green biotechnology': engineering the crop plant cell factory to improve performance and increase the diversity of products made.

1.3.3 Significantly, an additional new opportunity is now available by combining microbial-based fermentation, biocatalysis and bioprocessing with the products of plant cell factories. Using renewable raw materials produced by plants as feedstocks for biorefineries, their conversion into an even wider range of useful industrial chemicals is made feasible. Biotechnology can improve both the starting material and the transformation properties.

2. PLANT-BASED BIOPRODUCTS (PBBP): OPPORTUNITIES AND CONSTRAINTS

2.1 Expanding the Opportunity: The Government’s Role

2.1.1 The development of PBBP can contribute to the enhancement of the ability of agriculture to adapt to climate change and increase the appreciation of the economic potential of biodiversity. Within the EU, such development would be entirely coherent with the ongoing "Environmental Technologies Action Plan"[1]. To encourage the successful development of PBBP, public authorities in the EU and the US should establish an overarching political strategy and integrated legislative framework that promote the long-term development of industrial crops and products.

2.1.2 There are several constraints. Irrespective of the source (genetically modified or not) biological raw materials are at present comparatively expensive as feedstocks for energy and industrial products. Industry needs flexibility and relies on international markets to enable them to obtain raw materials from the cheapest sources. Due to current price levels and administrative complexity industry will not commit themselves to source their materials exclusively or primarily from domestic agriculture. Moreover, the current subsidy system is blocking industrial crop development. Economically and logistically, it is more advantageous for multinational companies, who often own a large share of the local processing capacity, to place their non-food production in countries where incentives exist or impediments are absent.

2.1.3 These constraints can be addressed through a special framework or market introduction structure to encourage the production and utilisation of nonfood crops. Political and financial support is needed. Governments should provide suitable financing incentives for the construction of modern processing facilities, for example, domestic tax exemptions on liquid biofuels used in the transport sector.

2.1.4 When public authorities assess the true cost and benefit of plant bioproducts, they must try to attribute value to benefits such as biodegradability, ecological impacts / benefits, and sustainability, which usually escape conventional cost analysis. Viable markets for crop co- and by-products outside of the traditional low value routes (generally animal feed) have not been exploited.

2.1.5 Communication along the chain between industry, farmers, seed vendors, storage operators, research bodies, crushers, refiners and extractors, and industrial users and consumers needs significant improvement and integration. A *Communication and Education* strategy on the benefits of renewable plant products should be devised along with labeling schemes that increase consumer awareness.

2.1.6 Standards and norms are required, together with controlling legislation, to clearly distinguish between descriptions such as 'recyclable', or 'biodegradable' being applied to products of fossil origin that barely meet these criteria. Such use enables products to be placed on the market at prices significantly lower than truly sustainable products of 100% bio-origin, misleading the consumer.

2.1.7 Recent and continuing changes in EU policy (CAP reform; support reduction) have resulted in the decrease in cultivation of a number of non-food crops, particularly oilseed rape. In reality existing subsidies do not compensate for the inferior price given for non-food destinations, and the farmer has diminished economic benefit and incentive to produce. The subsidy scheme

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1) http://europa.eu.int/comm/environment/etap/developing.htm must encourage shifts towards ‘green’ targets and whole crop industrial usage, making full use of the decoupling mechanism to be applied from 2005.

2.1.8 The uncertainty concerning agricultural subsidies and the variation in taxation policies between member States in the EU acts as a disincentive to European industry. The major plant processing industries (sugar and starch) have suffered in the past where significant investment in what is the most successful biotechnical process to date (the production of high fructose syrup or iso-glucose using enzymes) was blocked by EU quotas rendering installed capacity redundant and halting further investment. In the same way some capacity installed for transesterification of rapeseed oil in biodiesel manufacture became uneconomic as oilseed prices fluctuated.

2.2 Current Markets.

2.2.1 Plant resources, mostly for paper products and chemical feedstocks, now provide about 5 percent of manufacturing inputs in the industrialised world. Plant-based chemical products include paints, adhesives, lubricants, inks, polymers, and resins. In many cases, using hydrocarbon resources is much less expensive. For some chemical products plant inputs are already cost-competitive, and they are a significant feedstock. Plant-based systems are the major sources for ethanol, sorbitol, cellulose, citric acid, natural rubber, most amino acids, and all proteins.

2.2.2 Companies from the chemical, life sciences, forestry, and agricultural communities should be involved in establishing a renewable bioproducts industry. Their activities range from genetic engineering of new plant species to development of new technologies and processes for converting plants into useful industrial inputs.

2.2.3 Market penetration in the EU is still weak but progress has been made in the development of new products and markets, particularly in Germany. As Kyoto deadlines approach however many EU governments are for the first time making serious commitments to the development of biomass as an industrial feedstock.

2.2.4 Although biobased products have experienced modest market penetration in the U.S., policy incentives in recent years have resulted in increased production of biofuels and portend preferred government procurement of biobased products. In addition, public support to the development of technologies has played an important role in the US commercialisation of biobased products. For example, DOE and NIST supported the technological developments that led to a Cargill-DOW partnership to develop and market polylactic acid (PLA) polymers. A 2003 report by the Biomass Research and Development Initiative, funded by DOE, on PLA determines the current plastics market at approximately 100 billion pounds per year. The PLA market is expected to be greater than eight billion pounds per year of the total plastics market by 2020.[2]

2.3 Biotechnology: Regulatory Framework and Legislation

2.3.1 Certain biotechnology applications are more controversial in Europe than in the USA. Better understanding of the differences and similarities, including the regulatory context, the political and financial framework, public perception

[2)] Biomass Research and Development Initiative, “Biobased PLA Polymers Grow New Markets for American Corn Products,” January 15, 2003. http://devafdc.nrel.gov/pdfs/6980.pdf and trust, the level of knowledge and understanding, and the role of the mass media and other actors involved in the public debate, will help scientists and policy-makers to address the constraints that are placed on genetically engineered plant varieties and to address these concerns in context.

2.4 Policy and Priorities

2.4.1 Over the last 30 years the debate about biotechnology has undergone profound changes. During the whole period, developments on each side of the Atlantic influenced the situation on the other side.

2.4.2 The factors dominating the European policy on Biotechnology are: 1) Scientific Research Achievements (1973 - 1978); 2) Competitiveness, Resistance and Regulatory Responses (1978-90); 3) European Integration (1990-96) ("global competitiveness"); and 4) Renewed Opposition and Consumers' Distrust (1996-99), but these factors do not include any of an economic or business nature.

2.4.3 R&D policies have been more favorable to green biotechnology in North America than in Europe; the North American regulatory climate has had a favorable impact on the development of biotechnology and the entry of products into the market.

2.5 Public Trust and Attitudes

2.5.1 Media greatly impacts public opinion in both the USA and EU, such that it is obvious that the position of the media plays a crucial role in influencing public opinion for or against modern biotechnology. Each side however presents a different focus that must be taken into consideration:

2.5.2 In the US the priority is economy and development, whereas in Europe the priority is on ethical and social frames

2.5.3 Themes: Agrifood and Biomedical applications in the US, Regulation and Ethics in Europe

2.5.4 Actors: business and scientists in the USA, specialised journalists and politicians (as well as activists and extreme eco-groups) in Europe

2.5.5 Risk / Benefit rate: benefit orientation in the US, risk orientation in Europe

2.5.6 Researchers, as much as policy makers, must be aware of these distinctions as they address the challenges posed in the improvement crops for biobased products. In parallel to the science and technology, it will be crucial to raise public awareness and acceptability in the USA, and particularly in the EU, of the societal benefits generated by biotechnology and of the risk assessment for any particular application. Non-food applications with obvious benefits on crucial problems like “green energy” and “green products” facilitates public acceptance and makes consumers more open to future uses of biotechnology.

2.6 Intellectual Property Intellectual property will be addressed in specific agreements between institutions when appropriate and will adhere to the requirements provided under the EC-US Science and Technology Agreement.

3. EXISTING SCIENCE AND TECHNOLOGY BASE IN THE US AND EU

3.2 Context

3.2.1 There is already a considerable and rapidly expanding science and technology base in the US and EU ready to underpin the development of new plant-based bio-products.

3.2.2 As previously noted, opportunities are constrained due to the continued supplies and cheap availability of fossil hydrocarbons, the existing well established supply chains, the existing regulatory frameworks, and the lack of economic drivers for change.

3.2.3 It is likely that in the first instance the substitution of petrochemical-based products by bio-products will be driven by policy incentives, environmental reasons and customer preferences. In due course, the demonstration of novel functionalities, improved technical performance and comparative life-cycle analyses will undoubtedly increase the rate and breadth of uptake of bio-products relative to those derived from hydrocarbons.

3.2.4 For these demonstrations to occur, new science and technology must be directed at many targets: including improving crop varieties, designing cost-effective harvesting methods, storage and extraction technologies, and developing new bioprocessing and bio-manufacturing systems.

3.2.5 The above steps must be developed in a context of enhancing sustainability in the agriculture and forestry, developing plant based renewable resources and improving environmental performance of industry and transportation.

3.3 Post-genomic science as a foundation for realising the potential of green biotechnology

3.3.1 Genomics information and bioinformatics enable rapid advances in gene discovery. These can be applied to all aspects of plant bio-product development: crop improvement, disease resistance, quality and yield of raw materials, discovery of new functionalities and extraction and bioprocessing of plant products.

3.3.2 Through combining fast-track breeding strategies such as marker-assisted breeding, (Tilling[3] or GM) with a systems approach to identify relationships between gene expression, protein profile and metabolic status, the basis for "designer" crops can be established. This also provides an opportunity for optimising low-input, integrated farming techniques through a better understanding at the genetic level of the effects of agricultural practices on crop development and yield.

3.3.3 These designer crops can benefit from improved resistance to diseases and environmental stresses, but also ideally be optimised in their developmental pattern and metabolism for specific industrial uses.

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3) TILLING: Targeting Induced Local Lesions IN Genomes, is reliable and widely applicable. It combines chemical mutagenesis with mutation screens of pooled PCR products, resulting in the isolation of missense and nonsense mutant alleles of the targeted genes. It has two significant advantages over existing plant gene knock-out tools: first, it is applicable to any plant since it does not require transgenic or cell culture manipulations. Second, it produces an allelic series of mutations including hypomorphic alleles that are useful for genetic analysis. See <http://faculty.washington.edu/comai/tilling.htm>.

3.3.4 For example, these end-uses may require changes to the plant cell walls, (such as reduction of lignin, modification of cellulose and hemicelluloses), changes to the quantity and quality of oils and starches, replacing these storage materials with other polymers such as PHB, or improved yields of highly specific metabolites with pharmaceutical potential.

3.3.5 Green biotechnology is the enabling technology for development of designer crops, but a number of outstanding scientific challenges remain before its full potential can be realised.

3.3.6 Particular challenges revolve around the plant cell wall and the regulation of plant primary and secondary metabolism.

3.3.7 A key feature of plant biology is developmental and metabolic plasticity. The crop plant factories are continually responding to external conditions and adjusting their development and metabolism to adapt to the changes. These adaptive responses impact on the composition and organisation of the cell wall, the association and allocation of photosynthetic carbon and the flux through pathways of primary and secondary metabolism.

3.3.8 Greater understanding of these fundamentally important areas of plant development and metabolism will overcome some of the current factors that limits the means to control the quantity and quality of raw materials manufactured by crop plants, which in turn limits our ability to maximise the plant-based bio-product opportunity through green biotechnology.

3.4 Opportunities offered at the interface of green and white biotechnology

3.4.1 Biocatalysis, bioprocessing and biomanufacture, involving living cells and their components to manufacture chemical products of high utility, underpin the principle of "industrial", also termed "white" biotechnology.

3.4.2 White biotechnology makes use of native or genetically modified microorganisms and their ability to convert feedstocks such as glucose in closed containment to a wide range of organic chemicals.

3.4.3 The synthetic capacity of microorganisms can be readily improved and widened by GM. Since microbial activity is contained in fermenters, public acceptance of the technology is much greater than that of field-grown GM crops.

3.4.4 An extension of white biotechnology is the development of biorefineries, analogous to oil refineries. These use renewable feedstocks for fermentation rather than those derived from oil and gas reserves.

3.4.5 Whilst a great diversity of renewable feedstocks are compatible with liquid fermentation in biorefineries, whether starch, soluble sugars and alcohols, oils or proteins, there are outstanding technological challenges that currently constrain their uptake by the industry.

3.4.6 In theory, all of these renewable feedstocks can be available in green plant "biomass", including the outputs and by-products of agriculture, forestry and horticulture, as well as the waste of traditional harvesting and large-scale pulping or processing systems.

3.4.7 In practice, the renewable carbon in biomass as lignocellulose is not readily accessible and often requires chemical and physical pre-treatments that are expensive, hazardous to human safety and the environment and inhibit the microbial and enzyme processes subsequently needed for biorefining.

3.4.8 A major challenge is therefore the design of new, benign and effective conversion processes (including the use of multi-tasking genetically modified microorganisms or GMMs) through which the biomass is transformed into viable feedstocks for fermentation.

3.4.9 Clearly, if advances in these initial conversion technologies are combined with the development of designer crops with higher biomass utility, the full potential of biorefineries can be realised.

3.4.10 It is the integration of green and white biotechnologies that was identified as the principal opportunity by the US-EU Workshop, offering an exciting range of new collaborative research programmes in which expertise in plant genetics and biochemistry can be targeted at optimising the technical benefits of industrial crops.

4. DEFINING SCOPE/OBJECTIVES OF A NEW US-EU COLLABORATIVE PROGRAMME

4.1 Opportunities for EU-US Research Collaboration.

4.1.1 There are many opportunities for US-EU collaboration in the field of plant-based bioproducts: these were addressed at the US-EC Workshop on "Applications of Molecular Biology for the Production of Plants for Bio-based Products and Bioenergy" held in Albany, CA in April 2004.

4.1.2 The Workshop identified 3 key issues: (a) scientific challenges that must be addressed to reach the full potential of plant-based bioproducts; (b) new research tools that must be developed to underpin future progress; and (c) additional barriers, such as public distrust and existing supply chain constraints, that most be overcome to achieve success.

4.1.3 In particular, the Workshop recognised the urgent need to develop "Flagship" programmes on plant-based bioproducts that would provide frameworks within which to develop US/EC collaborative research of major significance and clear benefit.

4.2 Flagship Programmes

4.2.1 The Flagship project is one that addresses a complex technological challenge and intends to contribute to solving a major socio-economic problem. Demonstration of strong benefits, in particular for consumers and the environment, should be a major selection criterion for such a project. It should also be in line with other important policy priorities of both the EU and USA. It should build on the respective strengths, and, to some degree, complementarities, of the European and US scientific and technological knowledge base and industries.

4.2.2 Criteria for the flagship project are:

4.2.2.1 Consumer/User benefit: Projects must provide societal benefit across the entire supply chain from growers to end-user industries and consumers of the products. The benefits must be clearly demonstrable, addressing needs in the short-term, such as increased sustainability of manufacturing processes through to needs in the long-term, such as environmental and climate impacts. It will be essential to consider both the developed and developing countries in consideration of benefits provided by the projects.

4.2.2.2 Scientific challenge: The significance of the issue is the principal determinant for support of the project. The challenge must be so great and so urgent that it requires coordinated activity from both the EU and the US for its solution. For example, the project could address a scientific or technical bottleneck of such magnitude that it currently constrains progress in the economic development of plant bioproducts. The projects are likely to be large-scale, requiring complementary and multi-disciplinary input and the need for a critical mass of US-EC resources. Integration of green and white biotechnology is one area highlighted as presenting a major new opportunity and challenge.

4.2.2.3 Economic benefits and risk analysis: A risk-benefit analysis, assessment and management plan must be compiled for each project from raw material input to product output. This analysis will address both economic cost/benefit and direct environmental impact/benefit. For example, the analysis would encompass different data if the project involved non-food uses of existing food crops, compared to the development and use of dedicated non-food crops. The analysis should consider the project as a continuum: incorporating activities from pure, strategic and applied research through to demonstration of proof of concept. Given that the proposed timescale from research to demonstration is 5 years, the analysis should also address how feasible this is to achieve.

4.2.2.4 Private sector involvement: Private sector involvement will be essential to demonstrate value of the project and it is probable that industrial input will be a key feature in project planning and awareness of supply chain issues linking the grower to user and consumer. The involvement of industry will be pre-competitive, could well lead to private sector investment and must incorporate transparent IP management. Each project will end with proof of principle in a demonstration pilot and therefore will not involve marketing of specific products.

4.3 Flagship Programmes Two examples of flagship programmes that the EU and USA are developing are:

4.3.1 *Plant cell walls: raw material quality and utility for biorefining*. Fossil reserves are finite with demand and costs likely to increase. As yet, the widespread use of biofuels derived from plant-derived renewable resources is constrained by a major bottleneck: the ability to fractionate the raw materials into easily accessible energy sources. The principal problem is the plant cell wall, with a composition and organisation preventing ready fractionation and conversion to useful industrial feedstocks. Given that these constraints represent a major barrier to realising the full potential of biorefineries, and were identified as such in the report of the Albany Workshop, "plant cell walls" is clearly a topic eminently suitable for development into a Flagship Programme.

4.3.2 A second example of a flagship programme would be a coordinated effort to *develop plant-derived oils as bio-lubricants and chemical precursor molecules*. Oilseed crops are major agricultural commodities, mostly for human and/or animal consumption. The seed oils of many other plants, however, often contain high amounts of unusual fatty acids that have potential usage in industry. These fatty acids have a variety of structural features that make them useful components in formulations of lubricants, biodiesel, drying agents, inks, dyes, and resins. The functional groups can also serve as “reactive handles” for additional chemical modification to produce compounds such as monomeric components of nylons. The plant species that produce these industrially important fatty acids, however, typically lack desirable agronomic traits and hence are not used as industrial feedstocks. Molecular approaches provide new avenues to address these constraints.

5. RECOMMENDATIONS FOR FUTURE MECHANISMS AND THEIR FUNDING TO SUPPORT A NEW PROGRAMME OF ACTIVITIES

5.1 Steering Committee

5.1.1 A Steering Committee (SC) has been established for facilitating and coordinating collaborative (EU-US) research in molecular biology to create or improve biobased products and biofuels. It is envisioned that this SC will supported by a wider advisory network of specialists and stakeholders, for example, EC Research Directorates responsible for Agriculture, Biotechnologies, Energy, Materials, other relevant EC Directorates Generals or related bodies (e.g. EFSA GMO panel, DG AGRI 'energy and non-food crops' advisory panel), USDA (ARS, NRCS and CSREES), DOE, NSF, the U.S. Biomass R&D Technical Advisory Committee, the New Uses Council/Biomass Coordinating Council, the Biotechnolgy Industry Organisation, the Association for the Advancement of Industrial Crops and the OECD. The SC will establish an integrated programme of US-EC collaboration combining research, training and dissemination. Specifically, the SC will:

5.1.1.1 Identify research needs and select priority research areas and flagship projects of common interest and benefit.

5.1.1.2 Identify and promote interdisciplinary, multinational teams to conduct research, and transfer technologies

5.1.1.3 Facilitate the identification and development of flagship projects and other joint activities of common interest, which may include scientific exchanges, training, and other opportunities for students, postdoctorals and early career scientists.

5.1.1.4 Organise and/or sponsor symposia, position papers, information delivery targeting scientific communities, stakeholders and the public

5.1.2 Stimulate interest in the application of biotechnology for the development or improvement of biobased products and biofuels among scientific and professional societies, foundations, trade organisations, governmental agencies, universities and research institutes, social scientists and environmental organisations. The relevance of biotechnology to the EC's Environmental Technologies Action Plan will be emphasised, and opportunities sought for synergy with that initiative.

5.2 Planning and Implementation of the Flagship Programmes

5.2.1 Phase 1: Throughout 2005, discussions will take place within the US and EC academic/industrial communities at grass-root level to further develop the identified Flagship Programmes that fulfil each of the essential criteria. Synergies will be exploited where appropriate with other complementary initiatives such as, on the European side, the development of technology platforms.

5.2.2 Phase 2: In 2006, the programmes could be further defined with the component projects and their integration - both scientific and geographical - identified, together with proposals for work packages encompassing research work, training programmes (for example, co-supervision of PhD students, 2+2

Fellowships, exchange of young researchers/PIs, etc) and dissemination vehicles (for example, workshops, symposia, position papers and public awareness articles).

5.2.3 Phase 3: start of Flagship Programme's work would commence in mid-2007.

5.3 **Programme Support**

5.3.1 It is envisioned that funding support will be developed through existing mechanisms on each side.

5.3.2 It is further envisioned that scientists cooperate in the Flagship Programmes initially through existing resources.