Strategic Study of Biotechnology Research in CGIAR

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Independent Science and Partnership Council synthesis and commentary on the *Strategic Study on Biotechnology in CGIAR*

Background to the study

Most members of the CGIAR Consortium (Centers) have invested considerably in biotechnology over the last two decades as part of their activities in plant breeding, genetic diversity, and livestock and fish research, including policy research. Biotechnology has been seen as holding great potential for speeding up breeding and targeting complex traits, addressing previously intractable problems in plant and animal research, and in facilitating research and discovery on the more fundamental areas of genomics, cell biology and metabolism.

The need to integrate biotechnology activities across Centers for better synergy has long been recognized. The few initiatives toward this integration include the CGIAR Genomics Task Force (founded in 2002 and now practically dissolved), which comprised the genomics focal points of all Centers, and the Generation Challenge Program (GCP) that emerged from the collaborative genomics activities. The GCP has formed a partnership and research-for-development network on genomic research and molecular breeding, but the program is expected to end in 2014. In the *Summary Report on System Priorities* (Science Council, 2005), it was foreseen that CGIAR would develop a genomics platform to facilitate genetic enhancement and serve individual commodity and regional needs. In some way the GCP functioned as such a service platform, albeit with a specific research focus. The Biosciences eastern and central Africa (BecA) Hub functions as a regional platform for providing research-related services and capacity-building opportunities in biotechnology to the target region and beyond. In the first version of the *Strategy and Results Framework* (SRF) (2009), it was envisioned that a single Mega Program would focus on genomics research and breeding of the major commodities in order to combine genomics research, bioinformatics, phenotyping, intellectual property (IP) management and pre-breeding across crops, livestock and fish. In the current portfolio, the commodities are in seven different CGIAR Research Programs (CRPs).

Globally, the discourse on biotechnology has been dominated by the debate on genetic modification (GM) and acceptance of transgenic crops. CGIAR's position and strategic choices in biotechnology in general, and in GM in particular, have not been made clear or been openly discussed within the CGIAR community. This has likely resulted from the fact that a considerable segment of the CGIAR donor community does not support the use of funds for development or deployment of transgenic crop varieties. Nevertheless, research continues on biotechnology within CGIAR, and many developing countries of importance to CGIAR are approving or preparing to approve transgenic crops. Therefore, it is time for a well-informed analysis and discussion about the role of biotechnology in general and of transgenic crops in particular within the CGIAR portfolio. The Independent Science and Partnership Council (ISPC) seeks to act as an independent convener of this dialogue.

At the turn of the new millennium, when the advances in genomics were rapid but research and applications in agriculture were still quite modest and exploratory (particularly in CGIAR), there were several efforts at CGIAR system level to steer this field of research and harness its possibilities. More than a decade later, biotechnology has not been addressed strategically at the system level despite the fact that it

represents a dynamic field with huge implications for CGIAR research investments and potential impact on the system-level outcomes (SLOs).

The ISPC considered that the CGIAR system would benefit from a strategic study with three main objectives.

1. To assess the biotechnology research pipeline in CGIAR, exploring to what extent and in what time frame the research is likely to produce improved technologies and/or improved efficiencies in research with significant impact on CGIAR target beneficiaries.
2. To analyze how CRPs are positioning themselves strategically in internal partnerships and with partners outside to achieve maximum synergy and efficiency in biotechnology research.
3. To provide strategic guidance to the CGIAR system and CRPs based on an analysis of the near- and mid-term developments in biotechnology research, research application and constraints to adoption that will influence the investment choices in CGIAR. Issues of particular importance in this objective include: proprietary control of technologies, capacity and resources in CGIAR's partner and beneficiary countries, including development of regulatory frameworks and the political landscape that influences the choice of research pathways.

Conduct of the review

Biotechnology in the broad sense is a huge area for a single review to address. Therefore, the study focused first on defining the scope and setting specific strategic issues to be addressed. This step was conducted in close collaboration with the CGIAR staff who are leading CRP biotechnology research at the Centers and in consultation with focal persons nominated by the Centers and CRPs.

The first phase of the study involved an e-consultation, which took place over 10 days with 75 participants from within Centers and CRPs to assess the major issues and topics related to biotechnology (summary report provided in Appendix A). As part of this process, key individuals within CGIAR Centers were also interviewed to gain their insights. From the initial feedback from Centers and CRPs and the CGIAR Consortium, the ISPC concluded that there are two major areas of activity where strategic advice for CGIAR system- and CRP-level decisions are needed: (i) transgenic research relevant to crops and livestock, and (ii) crop genomics and bioinformatics research.

With regard to transgenics, the major issues included: application to pro-poor crops and traits (e.g. traits of relevance, IP issues) and delivery pathway (time frames, regulatory frameworks, product stewardship and capacity). The main issues for genomics research relate to rapid advances in genotyping and sequencing technologies, while bioinformatics, phenotyping and capacity still appear to be bottlenecks.

Other areas that emerged from the discussions as being important to both areas of the study included: the role of the private sector and how it develops in terms both of IP and of relevance for developing country agriculture; international and national policies and policy debates related to biotechnology and genetic resources; centralization versus decentralization; and outsourcing of research or components as technologies advance and costs change.

To assess the current status of biotechnology in the CGIAR system, several techniques were used, including a series of interviews with CGIAR stakeholders in national agricultural research systems (NARS), advanced research institutes (ARIs) and the private sector. This was followed with a survey sent to all Centers seeking information on their current biotechnology activities and future plans. The outcomes of this survey are presented in the synthesis report by the Study Panel on biotechnology research in CGIAR (Tables 2, 3 and 4). The Panel also examined a series of reports, reviews and other documents generated as part of the ongoing review and assessment processes within CGIAR. These are referred to at various points in this

report. Of particular relevance are documents supplied by the International Food Policy Research Institute (IFPRI), the Genomics Task Force and reports of several groups looking at biosafety and policy.

Synthesis of key findings and recommendations

As highlighted in this report, biotechnology plays a major role in crop and livestock improvement and has been recognized by the CRPs and Centers as an important tool that provides novel avenues for reaching CGIAR output targets and strategic goals. The key role of biotechnology in germplasm enhancement in CGIAR is to support breeding and pre-breeding activities to accelerate the delivery of advanced lines of mandate crops and animals to national programs. Some national programs need finished lines that can go directly into local evaluation, while others are looking for new germplasm that will enhance their breeding base. In addition to the delivery of improved lines, national programs look to the CGIAR system to provide techniques and resources that will accelerate the rates of genetic gain in their breeding programs; in particular, they are seeking techniques that will increase the speed and reliability of germplasm evaluation at low cost.

In a survey of Centers, all but two (Bioversity and WorldFish) listed the development and delivery of molecular marker technologies as critical for their operations. The role of genetic modification (or engineering) is relatively less developed, although several Centers are actively developing GM lines and planning for delivery with the next few years. In total, 14 different GM crop species are being developed, with the first delivery planned within the next 2 years.

This report concludes that, despite the strong support for biotechnology within CGIAR programs, there is still inadequate strategic planning and coordination across the system, with few opportunities for groups to share experiences, best practices, successes and failures. While non-GM approaches have been generally well integrated into breeding projects, GM research appears to be largely opportunistic. In particular, there is concern that many aspects of stewardship, regulatory approvals and delivery pathways have not been adequately addressed by some Centers. Previous studies (including by the former Science Council) have identified similar problems and made recommendations for change that have not been fully implemented.

The new CGIAR is seeking system-level improvements in efficiency, and there are many opportunities for organizing its biotechnology research more systematically to target efforts on key outcomes, and to work in partnership with NARS and ARIs around its core strengths in research, phenotyping, germplasm and adapted varieties for developing countries and of direct benefit for the poor. The Panel advises that Centers and CRPs need to manage the expectations of national programs carefully to encourage innovation and some level of risk-taking, while avoiding wasting resources on inappropriate and unproductive technologies. The implementation of biotechnology should build on – and not distract from – the key research strengths of Centers and CRPs. Centers and CRPs should be playing a global leadership role in developing and delivering new technologies to national programs. This report summarizes the major challenges in accomplishing this objective as follows:

- quality control systems to ensure that all outputs are of high standard and users can have full confidence in material, information and training programs;
- data management systems in place to support data capture, analysis and access;
- up-to-date technologies used to support the core capabilities: field phenotyping, genotyping and germplasm analysis (both conventional and GM);
- training and capacity building (are Centers and CRPs enabling the most appropriate people to apply biotechnologies?);

- coordination of biotechnology across CGIAR to build system-wide critical mass;
- integration of biotechnology projects into the overall objectives and delivery pipeline of CGIAR to ensure useful outcomes in a reasonable timeframe (this is particularly significant for GM outputs).

According to the Panel, many within the CGIAR system have recognized the issues and problems but appear to be struggling to address them. The experience and sophistication of the biotechnology programs at the various Centers represent a continuum. As a result, the Panel's recommendations may not be uniformly relevant to each Center, but they do seek to deliver coherence across the system to improve targeting and management of biotechnology. The Panel recognizes that CGIAR has the capability and resources to address the challenges but it needs to do more to improve quality, accountability and resource use.

The Panel recommendations presented in this report are aimed at helping CGIAR improve its internal management of biotechnology research and delivery processes. Many of the suggestions build on activities already under way within Centers and CRPs and thus should not be too onerous. However, the study highlights some significant problems in several aspects of the current biotechnology strategy, particularly with respect to the development and delivery of GM crops and livestock.

The Panel recommends the establishment of a series of coordination and advisory groups. The first should be the establishment of a CGIAR-wide biotechnology support and planning group ('Biotechnology Group') (*Recommendation 1*), which would take primary responsibility for addressing the broad strategic issues raised in this study. The group should also institute a scientific review of biotechnology capabilities and needs (*Rec. 2*). Importantly this group would also oversee the establishment of a GM advisory board (*Rec. 4*) and a CGIAR bioinformatics network (*Rec. 6*). A new biosafety network should also be established by the GM advisory board (*Rec. 7*), with the prime task of developing global GM approvals (*Rec. 8*). The Biotechnology Group should also work with the CRP on Livestock and Fish to address the needs of the animal production industries (*Rec. 5*) and ensure implementation of the training and staff development and partnership recommendations (*Recs 9 and 10*).

Under this structure, Centers and CRP representatives would be the principal actors, with support from the Consortium in the overall biotechnology strategy through their representation on the Biotechnology Group.

In conclusion, the Panel considers that learning from the study results and implementing its recommendations would help CGIAR address some of the key challenges identified and achieve the following major objectives.

- Improve coordination and collaboration across the CGIAR system for building critical mass in biotechnology research and its applications in germplasm enhancement, supporting CRPs and Centers with weak biotechnology capability, establishing quality assurance processes, and developing an effective data management capability.
- Strengthen key CGIAR capabilities for knowledge and understanding of global production constraints and environments, maintaining strong links to national programs, improving understanding and usefulness of germplasm, and strengthening field-relevant phenotyping.
- Increase scientific rigor in the biotechnology strategy and projects by developing and supporting biotechnology activities, building strong data management systems to improve data capture, analysis and access, and enhancing partnerships with ARIs and the private sector.
- Develop biotechnology delivery pathways by establishing clear and rigorous quality assurance procedures, ensuring thorough stewardship of materials generated from biotechnology projects, and developing pathways for the delivery of GM products to national programs.

Commentary from the Independent Science and Partnership Council

Overall the ISPC considers that this study has succeeded in analyzing information and identifying key issues related to biotechnology applications in CGIAR. The report is well-written and follows effectively the terms of reference set by the ISPC in a logical way, addressing issues ranging from gene discovery to the delivery of GM variety and livestock research products, phenotyping, bioinformatics, biosafety policy, IP rights, capacity and partnership issues. In addition to the study conclusions and recommendations, the Panel also offers some ideas and detailed suggestions for implementation, building on the proceedings and the report of the final study workshop (ISPC 2014).

The ISPC agrees with the Panel's conclusion that the recommendations included in this report may not be uniformly relevant to each Center. The ISPC also thinks that CGIAR has the capability and resources to address the challenges; the Consortium Office should take the lead in coordinating the efforts for improving the coherence, targeting and management of biotechnology across the system.

The Panel recommends the establishment of a series of coordination and advisory groups, including a CGIAR-wide biotechnology support and planning group ('Biotechnology Group'), a specialist management group / GM advisory board, a specialist group or advisory board to coordinate/support animal biotechnology activities across CGIAR, a CGIAR bioinformatics network, and a system-wide biosafety network. While the ISPC commends the high quality of the work done by the Panel following a very interactive methodology, it also **advises on the need to be cautious in implementing some of the recommendations and especially in endorsing all the new structures proposed in this report**. Overall the ISPC supports the need for the outcomes of such bodies and suggests that, wherever possible, existing groups could be given the responsibility for overseeing some of these functions. CGIAR must avoid the risk of providing support to new heavy command/control structures, which are generally not conducive to novel and science-based good practices.

The current CGIAR structure offers ample opportunities to strengthen coordination and enhance strategic thinking throughout the research programs on key crosscutting issues, such as investments in strategic biotechnology targets, without raising the transaction costs too much. **The ISPC concurs with the Panel conclusion that a new strategy is urgently needed for the integration of biotechnology activities across Centers and CRPs (*Rec. 1*)**, to enhance the delivery of improved germplasm and resources for their mandated crop or animal production systems. The strategy and targets should be science-based and needs-driven. **The new SRF (in development) could also provide guidance on principles for which the most value might be added with respect to the use of biotechnology within the system.** The Panel recognizes that most Centers and some CRPs have biotechnology approaches integrated into their overall research plans and breeding pipelines. However, there are advantages in having a strategy document that goes across the CGIAR system to provide transparency both internally and externally and that can be defended against the strategic objectives of CGIAR. **The ISPC agrees with the Panel conclusion that a comprehensive review of biotechnology activities across the system is urgently needed (*Rec. 2*) to inform the biotechnology strategy**.

The Panel, in many parts of this report, stresses the inadequacy of activities aimed at promoting biotechnology in the system, calling for a more strategic approach on the use of key biotechnologies in breeding activities and livestock biotechnology, and attention to poor coordination across CGIAR on the subject. In particular, **there was concern that many aspects of stewardship, regulatory approvals and delivery pathways have been inadequately addressed by some Centers. Previous studies have identified similar problems and made recommendations for change, e.g. Science Council studies on IP rights (Science Council, 2006a) and biosafety (Science Council *et al.*, 2009) that have not been fully implemented. The ISPC shares these concerns and believes that the**

development of a comprehensive biotechnology strategy and oversight should be pursued diligently as described.

Regarding CGIAR's agenda for developing GM crops and breeds, this report focused its recommendations on mechanisms aimed at improving the coordination among Centers and CRPs. The Panel expresses clear concerns on the scale and diversity of GM projects, the apparent arbitrary choice of many of the genes being used, the unrealistic timelines for delivery, and the absence of clear stewardship, regulatory protocols and expertise. These projects represent substantial investment of CGIAR resources. The ISPC concurs with the analysis and conclusions of the Panel and considers that CGIAR should demonstrate a transparent and credible justification for investment in this area that is science-based, taking into account the track record and prediction of emerging technologies. To address the GM-related concerns, the Panel proposes setting up a specialized GM advisory group in addition to the Biotechnology Group (*Rec. 1*). **The ISPC would strongly support the temporary establishment of a GM advisory board (*Rec. 4*) and biosafety network (*Rec. 7*), with the prime task of addressing the need for global GM risk assessments as long as it is required (*Rec. 8*)**.

The area of research on new breeding techniques (e.g. targeted mutagenesis and genome editing) does not appear to have been given serious consideration yet by CRPs and Centers even though it may offer tremendous benefits. The Panel believes that this indicates a broader issue that many researchers within Centers are not fully aware of some of the developments in biotechnology and molecular biology, emphasizing the need for coordination and external advice (reference to Rec. 1). A thorough analysis should be performed (using external expertise where appropriate) of the opportunities and regulatory issues around the use of targeted mutagenesis, genome editing and other new breeding techniques, and evaluation of the potential benefits relative to genetic engineering. Potential priority traits that could be tackled with the technologies, such as novel disease resistance and grain quality traits, should be identified by CRPs and Centers. Timelines and delivery costs, including regulatory and stewardship, should be compared to alternative approaches. **The ISPC suggests that such analysis could be built into the implementation of the comprehensive review of biotechnology activities across the CGIAR system (*Rec. 2*)**.

This report provided a thorough analysis of livestock biotechnology in CGIAR, and made several recommendations, including the development of a livestock genomic platform, the establishment and maintenance of a reference collection of biological materials and a database, and an investigation into the feasibility, logistics and costs associated with establishing a livestock genetic engineering platform. While the ISPC agrees with the urgent need to coordinate and prioritize livestock biotechnology activities across CRPs to identify areas where resources could be most effectively deployed, **it is not convinced that establishing a specialist group within the CRP on Livestock and Fish to coordinate animal biotechnology activities across CGIAR (*Rec. 5*) would be enough** to address all the issues related to animal biotechnology in CGIAR. The Panel suggestions in this area may also seem too ambitious for CGIAR alone, especially when CRP funding is being allocated for value chains, feeds (suggested) and health (recent bilateral). **The ISPC considers that new research investments and strategic partnerships may be needed to strengthen animal biotechnology and hence suggests that the new SRF needs to provide guidance on the priorities of livestock biotechnology research in CGIAR**.

Out of the several structures recommended by this report, **the ISPC would also retain the one for setting up a bioinformatics network (*Rec. 6*)** which, if structured lightly around experts in the domain, can be of value for most if not all biotechnology activities within the system. On the other hand, the ISPC suggests following the spirit of the recommendation and not trying to set up a permanent central bioinformatics unit. The idea is to promote and financially support a scheme through which teams can consult or collaborate. In the Panel's words, "under this network, the teams can share common tools and analysis pipelines for the

same or similar bioinformatics studies to avoid redundant efforts." The recent ISPC study on metrics (ISPC, 2014b) also provides potential guidelines on data management issues.

The comparative advantages for Centers and CRPs lie in their ability to define issues of significance to the bulk of the world's population in developing countries – issues of global significance. They also have knowledge and understanding of germplasm and the needs of end users in diverse environments. Further, Centers and CRPs have expertise in evaluating germplasm under a wide range of production systems, particularly in field and field-relevant phenotyping. These strengths can be used to help drive a global agenda. As emphasized clearly in this report, it will be important that CRPs and Centers resist the temptation to shift resources to lower priority traits or strategies in response to external pressure, particularly from ARIs or donors, unless these activities have no or minimal impact on core activities. **The ISPC supports the Panel recommendation encouraging Centers and CRPs to maintain a strong focus on building the core capability of multi-environment field phenotyping, field-relevant high-throughput trait phenotyping, and modeling and analytical support capabilities (*Rec. 3*)**.

The Integrated Breeding Platform (IBP) developed by GCP provides an example of building links between different organizations to tackle significant issues related to the delivery of molecular and germplasm tools and information to the breeding programs. GCP has formed a partnership and research for development (R4D) network on genomic research and molecular breeding, but it is closing in 2014. The IBP is an interesting model for linking genomic data directly to breeders' needs, and its current emphasis on tools to support breeders places it apart from many other data management tools being offered by ARIs. Given the experience gained in developing the IBP and progress made to date, it would be unfortunate if this were not maintained when GCP concludes. Exploring options to maintain development and delivery of the IBP should remain a priority. Although these developments were mentioned in this report, the Panel did not make any recommendations on possible scenarios for the future of the IBP/GCP, as an alternative to the establishment of several new groups and networks. As pointed out by GCP Director Jean-Marcel Ribaut in the final workshop, a clear plan of implementation is needed to move forward the CGIAR biotechnology agenda, and a crosscutting platform and coordinated support services can make a big difference in this important endeavor. **The ISPC considers that good lessons could be learned from GCP on setting up a community of practice for networking and cross-learning opportunities between CRPs**.

CRPs and Centers operate in a complex organizational environment with multiple external partners (NARS, ARIs, private- and public-sector organizations and various regulatory and donor agencies). Biotechnology advances are now emerging largely from ARIs and the private sector. It is also clear from this report that many partners in beneficiary countries are moving ahead quickly in establishing competencies in biotechnology, and CGIAR's role must surely be determined in consultation with all partners. In order to play an effective linking role between technology developers and users, CRPs and Centers need to have a clear set of priorities and targets to avoid the risk of losing control of the delivery process. CGIAR has to build on its comparative and collaborative advantages and operate in ways that are consistent with national policies, without imposing a uniform CGIAR policy. There is also a need for more strategic partnerships with the private sector and ARIs, as well as involvement of national beneficiary partners in priority setting. **Specific theories of change and impact pathways must be clearly spelled out both at CRP and system levels for the delivery of biotechnology products to end users, describing key actors and partners and changes needed along the pathways for adoption to occur, with assumptions and risks clearly articulated**.

Most countries currently struggle to maintain a strong supply of plant and animal breeders trained in new technologies and breeding methods, and most traditional breeders have only limited time and resources to apply new strategies. The skillset needed for crop and animal breeding changes with shifts in technologies. Modern breeders need expertise in biometrics, bioinformatics and molecular biology, in addition to more

traditional skills. However, breeding is not static, and further changes will inevitably demand new skills. In some cases, effective implementation of new breeding strategies will require a generational change in staff. The **ISPC would strongly support Recommendations 9 and 10 on capacity building, training and partnership**, taking into consideration that they are essential for maintaining critical mass at the Center level and in identifying key partnerships. They are especially important to help overcome the key challenges that hamper the impact of scientific achievements. Both themes are also at the heart of the ISPC's work (quality of science and strategic partnerships).

This report commented on the lack of a prompt public response from the CGIAR system to an act of vandalism in which activists destroyed a Golden Rice field trial. This also appears to reflect a general lack of coordination regarding GM projects across the CGIAR system, and the lack of clarity about responsibility in this area. In agreement with the Panel conclusions, ISPC believes it will be important to ensure that staff involved in the development and ultimate delivery of GM products are adequately protected and supported. The report states: "An early task of the GM Advisory Board should be to revise the position statement of CGIAR on GM technologies and garner support from within CGIAR and donors." **While the ISPC concurs with the need for a new position statement, it also recommends involving and garnering support from national partner governments and policy-makers**.

In conclusion, the ISPC considers that the report effectively follows the terms of reference set by the ISPC in a logical way, addressing issues ranging from gene discovery to the delivery of GM variety and livestock research products, phenotyping, bioinformatics, biosafety policy, IP rights, capacity and partnership issues. The Panel has succeeded in identifying key issues related to biotechnology applications in CGIAR and offers a set recommendations and detailed suggestions for their implementation, building on multiple interactions and consultations with various stakeholders within and outside CGIAR. The ISPC agrees that CGIAR has the capability and resources to address the challenges, and thinks that the Consortium Office should take the lead in coordinating the efforts for improving the coherence, targeting and management of biotechnology across the system. The ISPC concurs with the urgent need for a new strategy for the integration of biotechnology activities across Centers and CRPs, to be guided by the new SRF on principles for the use of biotechnology within the system. In principle, the ISPC supports most of the Panel's recommendations on GM research, bioinformatics, livestock, phenotyping, capacity building, training and partnership; and suggests following the spirit of the recommendations for delivering the desired outcomes without trying to create many additional structures.

Contents

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Acronyms and abbreviations

AATF	African Agricultural Technology Foundation
AfricaRice	Africa Rice Center
AGERI	Agricultural Genetic Engineering Research Institute
AGI	Agricultural Genetics Institute of Vietnam
APOL1	apolipoprotein L1
ARC	Agricultural Research Council (South Africa)
ARI	advanced research institute
BecA	Biosciences eastern and central Africa (BecA)
Bt	*Bacillus thuringiensis*
CAMBIA	Centre for the Application of Molecular Biology to International Agriculture
CCAFS	Climate Change, Agriculture and Food Security (CRP)
Centers	Members of the CGIAR Consortium
CIAT	International Center for Tropical Agriculture
CIMMYT	International Maize and Wheat Improvement Center
CIP	International Potato Center
CLIPnet	CGIAR Consortium Legal and Intellectual Property Network
CRISPR	clustered regularly interspersed palindromic repeats
CRP	CGIAR Research Program
CRP-PIM	CRP on Policies, Institutions and Markets
DREB	Dehydration Response Element Binding factor
ELISA	enzyme-linked immunosorbent assay
EMBRAPA	Brazilian Agricultural Research Corporation
GALVmed	Global Alliance for Livestock Veterinary Medicines
GCP	Generation Challenge Program
GE	genetic engineering / genetically engineered
GM	genetic modification / genetically modified
GS	genomic selection
GWA	genome-wide association
IA	intellectual assets
IBP	Integrated Breeding Platform
ICAR	Indian Council of Agricultural Research
ICARDA	International Center for Agricultural Research in the Dry Areas
ICRAF	World Agroforestry Centre
ICRISAT	International Crops Research Institute for the Semi-Arid Tropics
IFPRI	International Food Policy Research Institute
IIAM	Institute of Agricultural Research of Mozambique
IITA	International Institute of Tropical Agriculture
ILRI	International Livestock Research Institute
ILVAC	ILRI Vaccine Platform
INRA	Institut national de la recherche agronomique
IP	intellectual property
IPG	international public good
IPR	intellectual property right(s)
IRRI	International Rice Research Institute
ISAAA	International Service for the Acquisition of Agri-biotech Applications
ISPC	Independent Science and Partnership Council
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JIRCAS	Japan International Research Center for Agricultural Sciences
KARI	Kenya Agricultural Research Institute
KU	Catholic University
LLP	low-level presence
MARS	marker-assisted recurrent selection
MAS	marker-assisted selection
NaCRRI	National Crops Resources Research Institute (Uganda)
NARO	National Agricultural Research Organisation (Uganda)
NARS	national agricultural research systems
NGO	nongovernmental organization
NGS	next-generation sequencing
NUE	nitrogen use efficiency
PCR	polymerase chain reaction
PhD	Doctor of Philosophy
PIPRA	Public Intellectual Property Resource for Agriculture
PPP	public–private partnership
PSC	Plant Science Center
R&D	research and development
R4D	research for development
Rec.	Recommendation
Recs	Recommendations
RNA	ribonucleic acid
RNAi	interfering RNA
RTB	Roots, Tubers and Bananas (CRP)
SLO	system-level outcome
SPVD	Sweet potato virus disease
SRF	Strategy and Results Framework
T-CAP	Triticeae Coordinated Agricultural Project
TALEN	transcription activator-like effector nuclease
USAID	United States Agency for International Development
USDA	United States Department of Agriculture

Scope of the report

The Study Panel was asked to:

1. assess the biotechnology research pipeline in CGIAR, exploring to what extent and in what time frame the research is likely to produce improved technologies and/or improved efficiencies in research that can lead to significant impact on CGIAR target beneficiaries;
2. analyze how CGIAR Research Programs (CRPs) and members of the CGIAR Consortium (Centers) are positioning themselves strategically in relation to internal and external partners to achieve maximum synergy and efficiency in biotechnology research;
3. provide scenarios for near- and mid-term developments in biotechnology research, research application and constraints to adoption that will influence the investment choices in CGIAR. Issues of particular importance include: proprietary control of technologies, capacity and resources in CGIAR's partner and beneficiary countries, including development of regulatory frameworks and the political landscape that influences the choice of research pathways.

The study focuses particularly on genomics and bioinformatics, including genetic modification (GM) and the policy and institutional aspects related to these areas. The background and objectives of the study on biotechnology are described in detail in the ISPC Concept Note (ISPC, 2013).

The potential scope of the study was very large, and the first phase involved an e-consultation over 10 days with 75 participants from within Centers and CRPs to assess the major issues and topics related to biotechnology (summary report provided in Appendix A). As part of this process, key individuals within CGIAR Centers were also interviewed to gain their insights.

Several techniques were used to assess the current status of biotechnology within the CGIAR system. The first included a series of interviews with CGIAR stakeholders in national agricultural research systems (NARS), advanced research institutes (ARIs) and the private sector (a list of those included in the interviews is presented in Appendix C). This was followed with a survey sent to all Centers seeking information on their current biotechnology activities and future plans. The outcomes of this survey are presented in Tables 2, 3 and 4.

The Panel also examined a series of reports, reviews and other documents generated as part of the ongoing review and assessment processes within CGIAR. These are referred to at various points in this report. Of particular relevance are documents supplied by the International Food Policy Research Institute (IFPRI), the Genomics Task Force and reports of several groups looking at biosafety and policy.

Throughout this report we refer to Centers and CRPs. Our understanding is that the Centers conduct research through or in CRPs. Centers have responsibility for maintaining and managing research facilities and staff, while CRPs focus on research strategies, programs and their implementation. Strengthening biotechnology in CGIAR will obviously require efficient integration and synergy among CRPs, Centers and their various partners and CGIAR stakeholders.

The initial findings of this study were discussed with CRP/Center representatives and selected partners and CGIAR stakeholders in a workshop at IFPRI in Washington, DC (ISPC, 2014). This report was revised and updated to accommodate as much as possible the conclusions and recommendations of the workshop that the Panel found relevant, focusing on guidelines for implementation of the Panel recommendations.

Executive summary

Biotechnology plays a major role in crop and livestock improvement and has been recognized by the CGIAR Research Programs (CRPs) and Centers as an important tool that provides novel avenues (discovery, enhancement, testing, dissemination and detection of products, and adoption) for reaching CGIAR's output targets and strategic goals. It must be recognized that biotechnology underpins many aspects of modern biological research and also delivers outcomes through an improved understanding of biological processes. However, the key role of biotechnology in germplasm enhancement in CGIAR is to support breeding and pre-breeding activities to accelerate the delivery of advanced lines of mandate crops and animals to national programs. Some national programs will need finished lines that can go directly into local evaluation, while others are looking for novel germplasm that will enhance their breeding base. In addition to the delivery of improved lines, national programs look to the CGIAR system to provide techniques and resources that will accelerate the rate of genetic gain in their breeding programs; in particular, they are seeking techniques that will increase the speed and reliability of germplasm evaluation at low cost.

In a survey of Centers, all but two (Bioversity and WorldFish) listed the development and delivery of molecular marker technologies as critical for their operations. The role of genetic modification (or engineering) is less developed, although several Centers are actively developing genetically modified (GM) lines and planning for delivery within the next few years. In total, 14 different GM crop species are being developed, with the first delivery planned within the next 2 years.

Despite the strong support for biotechnology within the CGIAR programs, the survey of Centers suggested that there was inadequate strategic planning or coordination across the system with little opportunity for groups to share experiences, successes and failures. While non-GM approaches have been generally well integrated into breeding projects, the same cannot be said for GM, which appeared to be largely opportunistic. In particular, there was concern that many aspects of stewardship, regulatory approvals and delivery pathways had been inadequately addressed by some Centers. Previous studies have identified similar problems and made recommendations for change that have not been fully implemented.

The new CGIAR is seeking system-level improvements in efficiency, and there are many opportunities – from organizing its biotechnology research more systematically to target efforts on key outcomes and to work in partnership with national agricultural research systems (NARS) and advanced research institutes (ARIs) around its core strengths in research, phenotyping, germplasm and adapted varieties for developing countries and directly benefit poor farmers and consumers in developing countries.

Although biotechnology offers an important and valuable set of tools, it is important to remember that these are only tools. Centers and CRPs need to manage the expectations of national programs carefully to encourage innovation and some level of risk taking, while avoiding wasting resources on inappropriate and unproductive technologies. The implementation of biotechnology should build on and not distract from the key research strengths of Centers and CRPs – namely, strong links to national programs, germplasm development and field phenotyping. Centers and CRPs should play a global leadership role in developing and delivering new technologies to national programs. The major challenges in accomplishing this objective are:

- quality control systems to ensure that all outputs are of high standard and users can have full confidence in material, information and training programs;
- data management systems in place to support data capture, analysis and access;
- up-to-date technologies used to support the core capabilities – field phenotyping, genotyping and germplasm analysis (both conventional and GM);

- training and capacity building (are Centers and CRPs enabling the most appropriate people to apply biotechnologies?);
- coordination of biotechnology across CGIAR to build system-wide critical mass;
- integration of biotechnology projects into the overall objectives and delivery pipeline of CGIAR to ensure useful outcomes in a reasonable timeframe (this is particularly significant for GM outputs).

Many within the CGIAR system have recognized the issues and problems related to biotechnology, but they appear to be struggling to address them. The experience and sophistication of the biotechnology programs at the various Centers represent a continuum. As a result, the Study Panel's recommendations may not be relevant to each Center, but they do seek to deliver coherence across the system to improve targeting and management of biotechnology. CGIAR has the capability and resources to address the challenges, but it needs to do more to improve quality, accountability and resource use. The recommendations presented in this report are aimed at helping CGIAR improve its internal management of biotechnology research and delivery processes. Many of the suggestions build on activities already under way within Centers and CRPs and should not be too onerous. However, the study highlights some significant problems in some aspects of the current biotechnology strategy, particularly with respect to the development and delivery of GM crops and livestock. These need to be addressed as soon as possible, since they are not only taking valuable resources away from higher priority areas but could also pose reputational or other risks to CGIAR.

The Panel recommends the establishment of a series of coordination and advisory groups. The first should be a CGIAR-wide biotechnology support and planning group ('Biotechnology Group') (Recommendation 1), which would take primary responsibility for addressing the broad strategic issues raised in this study. The group should also institute a scientific review of biotechnology capabilities and needs (Rec. 2). Importantly this group would also oversee the establishment of a GM advisory board (Rec. 4) and a CGIAR bioinformatics network (Rec. 6). A new biosafety network should also be established by the GM advisory board (Rec. 7), with the prime task of developing global GM approvals (Rec. 8). The Biotechnology Group should also work with the CRP on Livestock and Fish to address the needs of the animal production industries (Rec. 5) and ensure implementation of the training and staff development and partnership recommendations (Recs 9 and 10).

Under this structure, Centers and CRP representatives would be the principal actors, with support from the Consortium in the overall biotechnology strategy through their representation on the Biotechnology Group.

Recommendations

Recommendation aims

Overall, the recommendations aim to:

1. improve coordination and collaboration across the CGIAR system to:
    - build critical mass in biotechnology research and its applications in germplasm enhancement
    - support CRPs and Centers with weak biotechnology capability
    - establish quality assurance processes
    - develop an effective data management capability.

    (Recommendations 1, 2 and 5)
2. strengthen key CGIAR capabilities around:
    - knowledge and understanding of global production constraints and environments
    - strong links to national programs
    - understanding and usefulness of germplasm
    - field-relevant phenotyping.

    (Recommendations 3, 8 and 10)
3. increase scientific rigor in developing the biotechnology strategy and projects by:
    - developing and supporting biotechnology activities
    - building strong data management systems to improve data capture, analysis and access
    - enhancing partnerships with ARIs and the private sector.

    (Recommendations 4 and 6)

4. develop clear biotechnology delivery pathways by:
    - establishing clear and rigorous quality assurance procedures
    - ensuring thorough stewardship of materials generated from biotechnology projects
    - developing pathways for the delivery of GM products to national programs.

    (Recommendations 4, 7, 8 and 9).

Biotechnology

Introduction

The Convention on Biological Diversity (CBD, 1992: Article 2) defines biotechnology as: "any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use". This definition covers a very broad range of activities, including virtually all aspects of plant and animal breeding. Indeed, the case could be made that the vast majority of research activities within the CGIAR system involve some form of biotechnology. For this report we have focused on a series of new technologies that have been developed to accelerate the rates of genetic gain in crop and livestock improvement. This suite of technologies are frequently grouped under the term genomics, defined as: "a discipline in genetics that applies recombinant DNA, DNA sequencing methods, and bioinformatics to sequence, assemble, and analyze the function and structure of genomes" (National Human Genome Research Institute, 2010). The World Health Organization (WHO) makes a further distinction: "the main difference between genomics and genetics is that genetics scrutinizes the functioning and composition of the single gene whereas genomics addresses all genes and their inter relationships in order to identify their combined influence on the growth and development of the organism" (WHO, 2014).

In structuring this report, we have tried to avoid describing specific technologies and instead have placed emphasis on the processes and issues surrounding the delivery of the outcomes of genomics from or through the CGIAR system to resource-poor farmers. Consequently, we have sections devoted to the delivery of outcomes through conventional (non-GM) and genetically modified (GM) or genetically engineered (GE) organisms. Special sections of the report cover the regulatory and intellectual property (IP) issues surrounding the delivery of GM products and training and capacity building in biotechnology. In addition, there are some technologies and developments that are critical for both genomic applications and other key activities within CGIAR. These are focused on phenotyping and bioinformatics, and sections of this report are devoted to these areas. We have included a special section on the role of biotechnology and genomics in animal improvement since there are some specific issues relevant to these programs within CGIAR.

Biotechnology has already had a major impact in both animal and plant production systems. These technologies have arisen through advances in the discovery and analysis of genes, genomes and gene products, and represent the outcome of a steady progress in knowledge and understanding of genetics and breeding. As analytical techniques improve, the global impact of biotechnology can only increase. No modern crop or animal improvement program can afford to ignore these technologies.

Some biotechnologies are already widely used in Centers and CGIAR Research Programs (CRPs), including molecular genetic markers, tissue culture, wide crosses, and recombinant vaccines. These activities are largely well integrated into research programs and are not controversial. However, GM, with the exception of vaccine production, is still at early stages of development.

The 2013 concept note for a strategic study of biotechnology research in the CRPs (ISPC, 2013:1) provided a summary of previous approaches to develop a biotechnology strategy:

> "The need to integrate biotechnology activities across Centers for better synergy has long been recognized. The few initiatives toward this integration include the CGIAR Genomics Task Force (now practically dissolved), founded in 2002 and which comprised the genomics 'focal points' of all Centers, and the Generation Challenge Program (GCP) that emerged from the collaborative genomics activities. The GCP has formed a partnership and research-for-development network on genomic research and molecular breeding, but it will close in 2014. In the System Priorities (SC, 2005) it was

> foreseen that the CGIAR would develop a genomics platform to facilitate genetic enhancement and serve individual commodity and regional needs. In some way the GCP functioned as such a platform regarding services albeit with a specific research focus. The BecA (Biosciences eastern and central Africa) Hub functions as a regional platform for a broad range of biotechnology capacity building. In the first version of the Strategy and Results Framework (SRF, 2009) it was envisioned that a single Mega Program (#3) would focus on genomics research and breeding of the major commodities in order to combine genomics research, bioinformatics, phenotyping, IP management and pre-breeding across crops, animals and fish."

In 2005 the CGIAR Science Council convened a group under the chairmanship of Mike Gale to explore issues related to genomics research in CGIAR (Science Council, 2006b). The CGIAR Genomics Task Force was convened and consisted of representatives from AfricaRice, Bioversity International, CIAT, CIMMYT, CIP, Generation Challenge Program (GCP), ICARDA, ICRAF, ICRISAT, IITA, ILRI, IRRI[1] and the Science Council. The group provided a report to CGIAR which included several recommendations (actions) (Appendix D). The key recommendation was the re-establishment of a Genomics Task Force to provide support and advice on genomics technologies across the CGIAR system.

The Genomics Task Force did consider the role of GE and endorsed the recommendations of the Science Council biosafety study of 2004 (discussed further in chapter 9). The focus of the Task Force report was on non-GM delivery approaches and, although the technology has advanced considerably in the 9 years since the report, most of the recommendations remain relevant.

What is a 'biotechnology research pipeline'?

Biotechnology research can contribute to several avenues of integration, from early gene discovery and analysis through to the provision of material, methods, resources and expertise for introduction into breeding programs. While the outcomes of research feed into breeding programs, they also provide information and materials that will influence the nature and speed of germplasm progression in the breeding pipeline.

Plant and animal breeding is based on the use of variation, be it natural or induced. Breeding programs for many species have a long history of good rates of genetic gain. New technologies must show benefits over and above those achieved using existing methods. This can be done by:

- increasing the population sizes used in breeding programs through improvements in screening methods, both phenotypic and genotypic – the more lines (varieties, breeds, populations, strains, accessions) evaluated, the greater the opportunity for finding superior lines;
- increasing the speed of assessment of lines – this translates to more lines screened since unpromising material can be eliminated early;
- understanding the genetic, molecular and/or biochemical bases for key adaptive and productivity traits – this allows informed choices about the best germplasm to use and the most appropriate screening methods (molecular, physiological or other phenotype);
- prioritizing traits based on the feasibility of making substantial gains in addition to impact on production – e.g. where can greatest gain be achieved through using gene interactions and analyzing responses to multiple environmental factors?
- expanding the germplasm base – identifying new variations ideally at the molecular level as useful genes or alleles.

1. See list of abbreviations for full names.

Timelines

The timeline for the delivery of the products of new technologies to farmers' fields is lengthy. Many approaches and technologies are specifically designed to try to reduce these timelines. For example, the average time from first cross to release of a new wheat variety is about 12 years. Through the application of molecular makers, several varieties have been released in as little as 7 years after the first cross (Gupta ***et al***., 2010). The more diverse the source of variation and the more complex the trait, the longer will be the delivery timeline. For example, many important loci that have been introgressed from wild relatives have taken well over 30 years or more to work their way through to commercial varieties (Feuillet *et al*., 2008).

New technologies frequently take several decades to deliver; examples include minimum-till farming and physiological breeding for stress tolerance (e.g. carbon isotope discrimination). Molecular technologies have a better track record; for example, molecular markers linked to key agronomic traits were first developed in the late 1980s and were applied to crop improvement by the late 1990s. Similarly, GE was first achieved in the mid-1980s and the first commercial GE lines were released in 1996 (Bt-cotton and glyphosate-tolerant soybeans, also known as Roundup Ready® soybeans).

The full development of a commercial GM line from the initial genetics through gene discovery to field evaluation (Table 1) currently takes about 30 years or more. We are already far along this path for some traits, and the timelines are likely to shorten as technology and experience improve. However, there are many other practical outcomes that are produced along the pipeline, as shown in Figure 1 and Table 1.

Genome analysis and genomics are relatively new scientific approaches that arose through advances in DNA sequencing and analysis in the late 1990s. These technologies are not static but have advanced dramatically since they were first introduced, and they will continue to develop in the future.

The long lead time from the discovery a potentially useful gene or genotype to the delivery of tangible outcomes to farmers remains a major challenge. New technologies that can accelerate this process are now critical in ensuring rapid delivery of outcomes. However, the major advances in genomics technologies are coming out of the medical research community due to the massive public- and private-sector investment in human health, and the translation of these advances to crop and livestock improvement can be slow. The most significant developments in crops and farm animals are coming through national and international consortia and research programs, largely in Europe and North America, and through activities in multinational seed companies. Developing CGIAR partnerships and linkages to these programs will be increasingly critical for CGIAR over the next decade, given the expected developments in technologies for genome analysis.

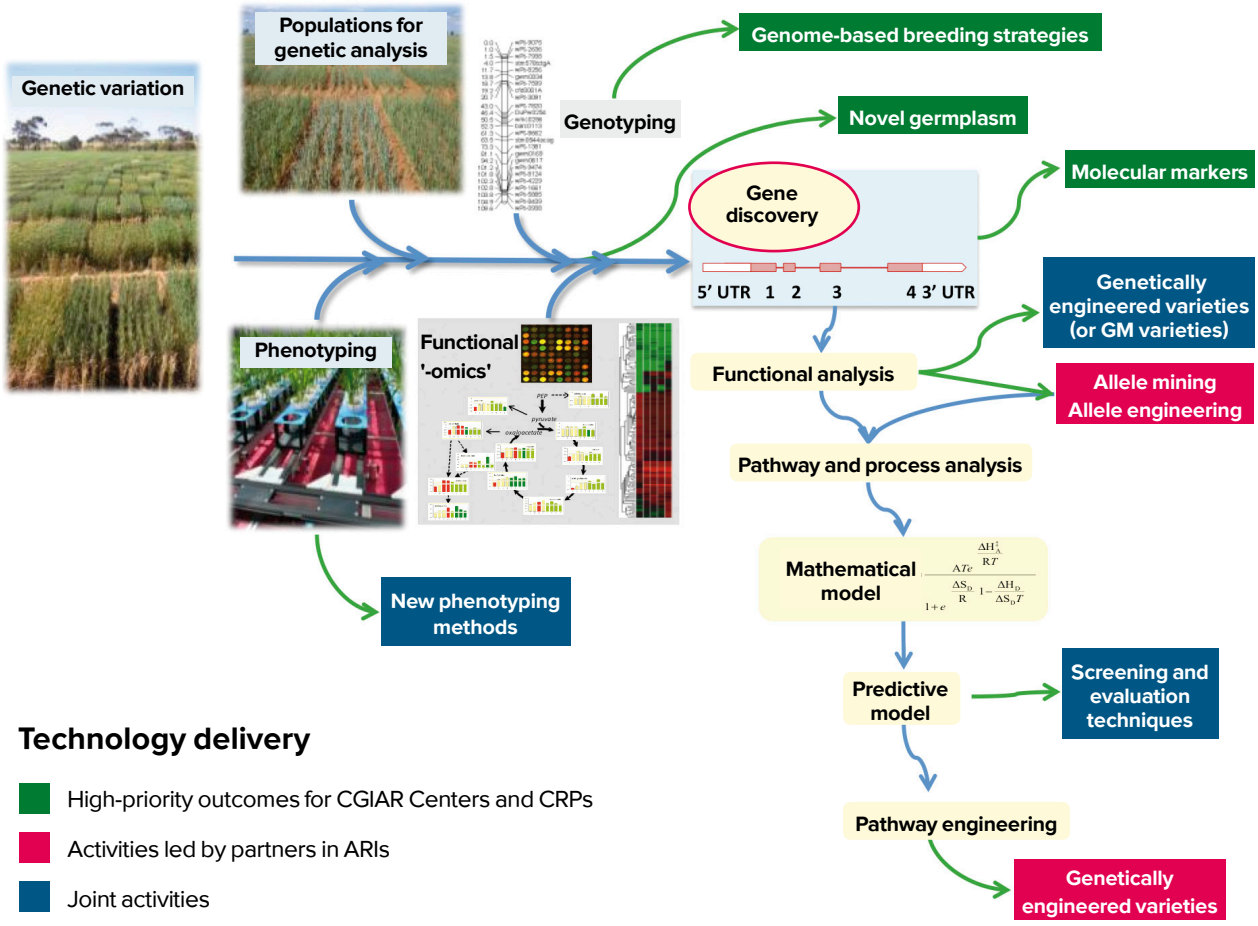
Attrition along the pipeline

A pipeline that starts at the basic or strategic end of the spectrum and moves toward delivery must maintain a steady flow of materials, ideas and outcomes through all stages. The flow passes through several bottlenecks, with limited material emerging through later stages. Early generation of information and informed decision-making are critical to maintain a steady flow and eliminate unproductive components early on. Access to a broad information base and a diverse team of researchers with skills in many aspects of genetics, bioinformatics, physiology and related fields is also key. Importantly, biotechnology now underpins many aspects of modern biological research, and a detailed knowledge of molecular science and understanding of key processes is a valuable output of research programs. Critical mass in both capacity and technology is required to maximize the chances of generating useful outcomes that survive through the full development, analysis and delivery pipeline. For example, over 5000 field trials for drought-resistant plants have been approved in the United States alone (Fernandez-Cornejo *et al*., 2014), but we have yet to see major advances in GM drought-tolerant germplasm.

Table 1. The biotechnology development pathway from phenotype to genes (GM outputs are shown in pink cells)

Activities		Outputs
Phenotyping	New methods	Assays for agronomic and physiological traits
		Predictive assays for adaptive traits
	Glasshouse	High-throughput screening methods and dissection of physiological traits
	Field	Multi-location field data on adapted germplasm
		Field data on relevant traits from unadapted germplasm
Genetic analysis	Population construction and initial mapping	Populations segregating for diverse traits
		Germplasm for pre-breeding and breeding
		Novel and diverse populations suitable for trait mapping
		Highly diverse germplasm with phenotypic and genotypic data
		Statistical platforms for association mapping
		Identification of rare alleles associated with target traits
Marker–trait associations	Fine mapping	Dense genetic maps
		Marker assays for traits
Gene isolation	Positional cloning	Rare recombinant lines
		Diagnostic markers
	Biochemical screens	Gene expression and metabolite databases
		Novel genes
Genes from other crops and model systems	Genetic information and positional cloning	Novel genes and gene systems
	Biochemical or physiological information	GM lines Genes and gene systems
	Genes accessed from commercial partners	
	Genes licensed or accessed in collaboration with public sector	
Gene and allele characterization	Functional analysis	GM lines
		Targeted allele screens
	Germplasm screens for diverse alleles	Novel alleles in elite backgrounds
		Allele deployment strategies
Novel variation	Modified expression of native genes	GM lines
	Modified structural sequences	Lines modified by targeted mutagenesis

Figure 1. The biotechnology pathway and outcomes generated along the pipeline



Future scenarios

Many factors will influence the role of biotechnology in the future, and the key drivers of biotechnology application and delivery are likely to be political and societal rather than scientific. Technological advances mean that genome sequencing and genetic analysis will be routine for virtually all major agricultural species. This means that sophisticated breeding techniques such as genomic selection and marker-assisted recurrent selection will be widely deployed. The increased sophistication in analysis is also likely to drive the continued development of service providers (see Table 3), and in-house sequencing and genotyping will be rare. These developments will place pressure on CGIAR Centers and CRPs to support access of national agricultural research systems (NARS) to suitable and low-cost service providers and to facilitate the movement of samples for analysis (e.g. leaf tissues or blood samples). Management of data will become a major activity across CGIAR. This will cover not only the tracking of samples and genotypic data, but also the linking of genotypic and phenotypic data. Under these scenarios, Centers and CRPs will need to be extremely efficient in ensuring the rapid transfer of information, but also in maintaining reliable quality assurance.

The likely scenario of rapid and cheap genotypic data generation will not only pose challenges for data management and quality assurance, but will also lead to a shift in other research priorities within CGIAR Centers and CRPs. High-quality genotypic data will lead to more efficient use of germplasm, and NARS

and advanced research institutes (ARIs) will seek access to germplasm that allows them to expand the variation available within their programs. There will be an expectation that Centers and CRPs will have not only genotypic, but also phenotypic data available on relevant traits for most if not all of the lines in their collections. The phenotyping capacity of Centers and CRPs will be critical to meet this demand. NARS will be seeking advice and support in deploying new and standardized phenotyping technologies. For crops, we can expect to see expanded use of imaging and spectral analysis techniques. These will include handheld devices, as well as aerial platforms such as drones and satellites. Improvements in satellite imaging may well mean that NARS breeders can access images of their field sites and farmers' fields to assess performance of lines. However, the expertise base within CGIAR should remain firmly in field and field-relevant phenotyping.

The rise in interest and demand for novel diversity will lead to the expectation that new alleles or lines will be accompanied by detailed molecular (genotypic) and phenotypic data and will be incorporated in genetic backgrounds suited to the NARS programs. Again data and state-of-the-art data management platforms and processes will be critical if Centers and CRPs are to meet the demands of NARS.

The new genetic tools mean not only new breeding methodologies but also more efficient gene discovery options. Our knowledge of genes and molecular pathways and processes is expanding rapidly. At present this only really works well for some species, such as rice, and for simply inherited traits, such as pest and disease resistance. But this will change as techniques for genome analysis improve and gene discovery becomes routine in virtually all plant and animal species. In the future we will be able to better define gene regions that control traits such as drought and heat tolerance. This will lead to the targeted screening of germplasm collections for novel alleles. Again, the ability of Centers and CRPs to rapidly identify this useful variation in their collections and bring it into a form suitable for deployment in NARS will be important.

For CGIAR, this will mean that scientists will be able to rapidly identify genes underlying key agronomic traits. From a strictly scientific perspective, GM crops and farm animals could be widely deployed and would offer a rapid delivery pathway for newly discovered genes. However, the ease of delivery of GM technology will be largely determined by the regulatory process. There is no indication that regulation will become less rigid over the next decade. Consequently, GM delivery will likely remain a high-cost and high-risk strategy. However, if regulation was to be relaxed and science-based decision-making were able to operate, then the scene could change very rapidly. Under this scenario, the CGIAR Centers and CRPs would need to move rapidly to develop and deploy this technology.

It currently appears possible that the new genome editing technologies (such as transcription activator-like effector nuclease system [TALENs] and clustered regularly interspaced palindromic repeat associated [CRISPR] will be exempt from the strict regulatory framework surrounding GM.[2] If this is confirmed, then these technologies can be expected to rise rapidly in significance and could herald a whole new era of targeted GM. In 10–20 years this may be the preferred technique for introducing new variation into elite lines.

Role of biotechnology in the CGIAR system

The CGIAR Position Statement on Biotechnology (Appendix B) proposes: "Biotechnology must be viewed as one of the critical tools for providing food security for the poor". Biotechnology can play a role at multiple levels within crop- and animal-improvement programs. This begins with the management of specific characteristics such as defect elimination (eliminating a disease or pest susceptibility) or trait enhancement,

2. Note that while many countries have suggested that such products would not be regulated as GM products, there is no consensus on the issue internationally as the following report from New Zealand demonstrates: http://www.epa.govt.nz/search-databases/HSNO%20Application%20Register%20Documents/APP201381_EPA_Advice_Document.pdf. Without consistent policies for key exporting and importing countries, it may be difficult to bring these new products to market.

such as targeted improvement (vitamin A or high iron). Some targets will be complex, such as improved yield under stress, or may relate to overall breeding strategies, such as genomic selection. It is important to remember that biotechnology and genomics provide tools and techniques to enhance crop and livestock improvement and sit alongside many other technologies. In some cases GM can provide cheaper, more rapid and more reliable methods than the alternatives, such as molecular markers for screening and selection. In other cases biotechnology must work closely with established procedures to succeed, such as phenotyping and biometrics. However, biotechnology, including genomics, is now regarded as integral for biological research and crop and animal improvement. International effort is focusing on the opportunities presented by genomics to deliver novel outcomes for food production, human health and the environment. If Centers and CRPs are to remain relevant in the delivery of modern technologies to the resource-poor, they must remain linked to these technological advances.

Each CRP or Center will have established methods for trait prioritization and multiple options for addressing targets and specific constraints. Biotechnology application should be considered within this framework. For major traits it is likely that multiple approaches can and should be used. However, a process is needed to assess and compare progress between approaches and shift resources as appropriate. Each approach should have clear milestones and timelines. Where these are not reached, the approach should be re-evaluated and, if necessary, terminated.

CRPs and Centers operate in a complex organizational environment with multiple external partners (NARS, ARIs, private- and public-sector organizations, and various regulatory and donor agencies). Currently, biotechnology advances are coming largely from ARIs and the private sector. In order to play an effective linking role between these technology developers and NARS, technology users, CRPs and Centers need to have a clear set of priorities and targets or they will risk losing control of the delivery process. The key advantages for Centers and CRPs lie in their ability to define issues of significance to the bulk of the world's population – issues of global significance. They also have knowledge and understanding of germplasm and the needs of end users in diverse environments. Further, Centers and CRPs have expertise in evaluating germplasm under a wide range of production systems, particularly a strong capacity in field and field-relevant phenotyping. These strengths can be used to help drive a global agenda. It will be important for CRPs and Centers to resist the temptation to shift resources to lower-priority traits or strategies in response to external pressure, particularly from ARIs or donors, unless these activities have no or minimal impact on core activities.

Status of molecular breeding and genomics activities in CGIAR Centers

As noted above, genomics tools are becoming routine in many breeding programs through enhancing the effectiveness and precision of selection by predicting plant and animal phenotype from genotypic data. The survey of CRPs and Centers indicated that virtually all are either already deploying these technologies or intending to use them in the near future. AfricaRice, CIAT, CIMMYT, CIP, GCP, ICARDA, ICRAF, ICRISAT, IITA, ILRI and IRRI all rate marker-assisted selection and the development of useful marker trait associations as critical to their current work. Bioversity, ILRI and WorldFish see molecular markers of growing importance, but are currently not using them or have only limited use for them.

Not only are molecular markers now in wide use across the CGIAR system, but many Centers are using or exploring recent marker-based discovery and breeding tools. Genome-wide association mapping and genomic selection (Varshney *et al*., 2012) are still at early stages of use in most Centers, but CIMMYT, CIP, ICARDA, ICRISAT and IRRI are either using these techniques routinely or see them as critical for their future activities.

Bioinformatics and biometrics methods are clearly critical for molecular genetic methods and nearly all Centers report strong activity in these areas. Overall '-omics'[3] platforms are not widely used, although several Centers report use of transcriptomics and some have deployed metabolite analysis for some experiments; for example, researchers at IRRI have examined the entire gene transcript pool for leaves and root tissues of tolerant and intolerant lines after exposure to drought stress. Proteomics does not appear to be regarded as important for Center research programs.

A surprise in the survey of Centers is the low level of interest in targeted mutagenesis strategies and gene insertion (zinc-finger nuclease on the survey form). It is still unclear if the products of these new breeding technologies will be regarded as GM or not, though it does appear that they will not be regulated in some jurisdictions (Waltz, E., 2012). These methods have advanced rapidly, and the latest iteration of CRISPRs and TALENs, in which a synthetic guide RNA (sgRNA) directs Cas9 nuclease, are having a large impact on molecular research (Belhaj *et al*., 2013; Tan *et al*., 2013). These technologies could present an important opportunity for CGIAR Centers and should be considered more closely. However, the inability to easily detect varieties developed using these methods could lead some countries to restrict imports from countries that do not regulate such techniques. As a result, caution is warranted in adopting these techniques and even greater caution will be necessary before choosing to deploy products developed using them in the absence of consistent trade regulation or a clear understanding of the potential trade implications of deployment.

3. These include gene transcript, metabolite and protein profiling. The data provide an overview of all, or most, transcripts, metabolites or proteins in a tissue and are used to explore responses to stresses or developmental cues.

Biotechnology in conventional crop and animal improvement (non-GM)

Introduction

The rates of genetic gain achieved in breeding have been heavily dependent upon the application of new technologies. The technological advances have paved the way for the implementation of new breeding strategies. However, the level of integration of new techniques and strategies has been highly variable across different breeding programs and species. Some key examples of successful technology applications over the past few decades include the use of computers to track and manage field trials, as well as biometric methods for field trial design and assessing genotype-by-environment-by-management interactions (Baenzinger *et al*., 2006).

Techniques based around the use of molecular markers have been largely free of the political issues that have plagued GM applications. Marker-assisted selection (MAS) has been particularly powerful in cases where the target traits show low heritability, are recessive, or involve difficult and costly phenotyping (Moose and Mumm, 2008). In these cases MAS is often more convenient, cheaper and more reliable than phenotypic selection. MAS has proved important for pyramiding disease- and pest-resistance genes, where it provides the only viable method at present for grouping target genes of interest. Molecular markers have also provided valuable tools for analyzing the mode of inheritance of certain traits and assessing genetic diversity. Markers can provide knowledge of the position and behavior of genes controlling key agronomic traits, and this is frequently critical in selecting rare recombination events where desirable traits are closely linked and in repulsion.

Several strategies for deploying MAS have been applied, but the most common application has been in transferring desirable alleles by simple backcrossing into elite germplasm. Conventional breeding schemes become quite complex if multiple independent loci are being tracked, but two relatively new methods involving MAS can be deployed: marker-assisted recurrent selection (MARS) and genome-wide or genomic selection. In MARS, selected individuals are crossed at each cycle of selection. This means that desirable alleles at target loci are brought together either one at a time or by merging multiple crossing and selection streams. This approach works well if the target genes or trait loci show major effect. In contrast, genomic selection has the advantage of not requiring prior information on associations between particular markers or trait and allows selection for many loci that have only a small genetic effect. In this strategy, populations are genotyped with many markers to ensure full genome coverage and then phenotyped for the target traits. The information generated is then used to predict phenotypic performance of individual lines based on marker screens that cover the whole genome.

These new breeding and selection strategies require cheap and reliable marker assay systems. For some species, only few or poorly developed marker platforms are available. Importantly, recent advances in genome sequencing have made discovery of single nucleotide polymorphisms feasible for species where few markers were previously available. When combined with the new selection and screening strategies based on markers, there are exciting opportunities for enhanced breeding and genetics (Varshney *et al*., 2013). For example the genome sequence for pigeonpea is now available (Varshney *et al*., 2012).

Molecular markers can provide an alternative to selection based on phenotypes. However, a marker is only as useful as its success for predicting phenotype. Many key traits for breeding such as yield under environmental or disease stress are complex and highly variable. A major objective of many research

programs is to explore opportunities to dissect these traits into contributory components. It may then be possible to identify regions of the genome that control the component traits. Trait dissection and high-throughput phenotyping ('phenomics') has become a major research area (Furbank and Tester, 2011).

Breeding for both crops and animals is a slow and often labor-intensive process. Even for annual inbred crops, the time from first cross to release of a new variety can take 10–20 years. Most breeding programs in the public sector, including CGIAR Centers and NARS, have limited resources, training and capabilities (GIPB, 2008). Consequently, only a few national programs have been able to deploy molecular markers even though this technology has been available for over two decades. Most breeding programs will have allocated all of their time and resources to existing crossing and selection strategies and have little opportunity to implement new approaches. In some cases, some of the core resources (such as systems for sample collection, reliable service providers for genotyping, computing to support data analysis) are not available even though these may be crops of major regional significance (e.g. cassava, plantain). Although advances in sequencing and marker detection may help, reliable service providers are needed. Service provision must be cheap, reliable, rapid and accessible. Mechanisms are needed to support the transition to marker deployment for NARS, including staff training, arranging access to genotyping facilities, support in data analysis and additional funding.

Expanding the scope and access to marker platforms to provide efficient, cost-effective screening services to the breeders in both NARS and some CGIAR research stations is a high priority. Most countries currently struggle to maintain a strong supply of plant and animal breeders trained in new technologies and breeding methods, and most traditional breeders have only limited time and resources to apply new strategies. The skillset needed for crop and animal breeding changes with shifts in technologies. Modern breeders need expertise in biometrics and molecular biology in addition to more traditional skills. However, breeding is not static, and further changes will inevitably demand new skills. In some cases, effective implementation of new breeding strategies will require a generational change in staff. A thorough analysis, using external expertise where appropriate, should be performed of the opportunities around the use of targeted mutagenesis, genome editing and new breeding techniques to tackle the high-priority traits identified by CRPs and Centers.

This area of research on new breeding techniques does not appear to have been given serious consideration by CRPs and Centers (Table 2) even though it may offer significant benefits. The Study Panel felt that this indicated a broader issue that many researchers within Centers were not fully aware of some of the developments in biotechnology and molecular biology, emphasizing the need for coordination and external advice (see Rec. 1). The analysis should include a consideration of the regulatory issues that surround targeted mutagenesis and gene insertion, as well as an evaluation of the potential benefits relative to GE. Potential traits that could be tackled with the technology, such as novel disease resistance and some grain quality traits, should be prioritized and timelines and the delivery (including regulatory and stewardship) costs compared to alternative approaches.

Opportunities for joint activities

For all techniques listed above there would be considerable opportunity for joint activities, not only across CRPs but also between CRPs and NARS. For example, platforms (databases and statistical analysis tools) for genome-wide association mapping and genomics selection are likely to be common between different crops and between plants and animals. Similarly, high-throughput marker screening techniques will be common although the platforms themselves will be species specific. Bioinformatics and databases are also likely to have a high level of similarity across the different target species. The roles of bioinformatics and related activities are considered in more detail elsewhere in this report.

Although wide crosses, embryo rescue, and micropropagation are important technologies for many Centers, these techniques tend to be species- and circumstance-specific, and there are unlikely to be many opportunities for joint work between Centers across commodities. However, these research areas provide ample opportunity for collaborative programs among CRPs, Centers, NARS and ARIs.

As noted above, there would also be opportunities for joint development of targeted mutagenesis strategies, and the possible role of these methods should be included in the biotechnology planning for all Centers and commodity CRPs.

Table 2. Current status of non-GM biotechnology activities in CGIAR Centers (compiled from survey questionnaire, September 2013)

Center	No activity or plans	Planned	Small-scale	In common use	Critical
AfricaRice	Genome-wide association (GWA) Genomic selection (GS) Targeted mutagenesis Reverse breeding		Transcriptomics Databases	Marker development Biometrics	MAS
Bioversity	MAS GS Targeted mutagenesis Reverse breeding Biometrics	Marker development GWA Cisgenics	'-omics' Algorithm development	'-omics' Wide crossing Somatic hybrids	Databases
CIAT	Reverse breeding Proteomics	Algorithm development	GWA studies GS Metabolomics Biometrics Databases		Marker development MAS Transcriptomics
CIMMYT	Targeted mutagenesis Cisgenics Proteomics		GS Transcriptomics Metabolomics	Marker development MAS GWA studies Reverse breeding Algorithm development Wide crosses	MAS Other breeding methods Biometrics Database
CIP	Targeted mutagenesis Reverse breeding Proteomics	GS	MAS GWA Other Metabolomics Algorithm development	Marker development Biometrics Databases Tissue culture	Marker development MAS GWA GS All bioinformatics Tissue culture
GCP	New breeding Tissue culture		GWA GS		Marker development MAS Bioinformatics Biometrics Algorithm development
ICARDA	Reverse breeding Proteomics Metabolomics	GS Targeted mutagenesis Others	Transcriptomics Database Algorithm development	Bioinformatics	Marker development MAS GWA Biometrics

Table 2. Current status of non-GM biotechnology activities in CGIAR Centers (compiled from survey questionnaire, September 2013) continued

Center	No activity or plans	Planned	Small-scale	In common use	Critical
ICRAF	GS All new breeding methods	MAS GWA	Marker development		MAS
ICRISAT				Marker development MAS Transcriptomics All bioinformatics	GWA GS
IITA	'-omics'	Algorithm development	MAS GWA Metabolomics	GS	Marker development Biometrics databases
ILRI	Reverse breeding	Genomic selection '-omics'	Marker development MAS GWA	Database	Biometrics
IRRI			GS		Marker development MAS GWA Bioinformatics Biometrics Database Algorithm development
WorldFish		Marker development MAS GS '-omics' Biometrics Database			

Delivery of outcomes from molecular marker research

The level of expertise in the use of molecular tools in breeding programs varies greatly, not only between species but also between NARS in different regions. Centers and CRPs need to be positioned to provide the most appropriate support and to help catalyze the exchange of information. In some cases, the NARS will be primarily interested in access to useful marker–trait associations and sources of desirable alleles, while in other cases the breeders may have no capacity for doing marker screening themselves.

Several factors are crucial in effective implementation of marker technology.

- Access to statistical and biometric tools suited to support marker-based analysis approaches.
- Marker–trait information, for markers shown to be closely linked or diagnostic for key traits. Ideally this information should include phenotypic data to allow evaluation of trait relevance.
- Genotypic data on locally adapted germplasm and potential sources of useful traits. New sequencing platforms mean that the cost of generating single nucleotide polymorphism data is now feasible for most species and germplasm pools. Most Centers appear to be outsourcing (either partially or

completely) their sequencing needs (Table 3), and this trend is expected to continue as sequencing technology advances. The Panel agrees with and encourages this trend.

- Access to high-throughput, low-cost and reliable marker-screening services. Although some Centers have in-house capabilities, as with sequencing there is a clear trend toward greater outsourcing of genotyping services. Issues related to the transport of biological material to service laboratories present problems in some regions due to slow or unreliable transport systems, government restrictions or quarantine constraints. However, these issues can usually be resolved.
- Expertise and resources for applying molecular technologies. As noted above, there is a cost in terms of time and resources in shifting the emphasis of a breeding program from phenotypic- to genotypic-based selection. Additional resources are likely to be needed in both Centers and NARS to allow smooth transition to new methods. The Panel suggests that dedicated funding be allocated to support breeding programs in making a transition to marker-based screening systems – for example, by subsidizing access to service providers.

Building structures and facilities that support information exchange

Many of the components needed for the delivery of marker technologies are already in place but may need expansion and additional support. These include existing regional and international breeders' networks for many, but not all, mandated species. There is value in having a cross-commodity network that can help provide access to service providers by negotiating reduced prices based on increased demand, by developing common databases and/or by arranging access to data and analysis tools. The network could also help build capacity for species where molecular resources are not well developed. The network could meet via video or telephone conferencing.

Table 3. Current outsourcing of biotechnology services in CGIAR Centers (compiled from survey questionnaire, September 2013)

	Partial outsourcing	Fully outsourced
AfricaRice	Genotyping, bioinformatics	Sequencing
Bioversity	DNA isolation, transformation, regulatory	Genotyping, sequencing, biosafety
CIAT		Sequencing
CIMMYT	Bioinformatics, transformation, biosafety, regulatory	Genotyping, sequencing, antibodies
CIP	Genotyping, bioinformatics, antibodies, biosafety, IP, regulatory	Sequencing
GCP		
ICARDA	Genotyping, bioinformatics, transformation	Sequencing
ICRAF	Genotyping, sequencing, bioinformatics	
ICRISAT	Sequencing, antibodies, biosafety	
IITA	Genotyping, sequencing, bioinformatics	
ILRI	Sequencing, bioinformatics	
IRRI	Genotyping, sequencing, bioinformatics	
WorldFish		Genotyping, sequencing, bioinformatics

Centers and CRPs should also actively seek to engage with major national and international programs that aim to develop resources and tools for marker-based breeding strategies. While some of these links already exist, such as the IRRI links to rice genome analysis efforts, there are further opportunities such as the Triticeae Coordinated Agricultural Project (T-CAP) in the United States on wheat and barley. The aim should be to see a CGIAR partner in all major consortia targeting a mandated crop or animal. Even though there may be no direct cash support flowing to the CGIAR partner, there should still be a flow of information. The support and planning group could play a lead role in identifying suitable international programs and supporting integration of CGIAR groups.

The Integrated Breeding Platform (IBP) being developed by the GCP provides an example of building links between different organizations to tackle a significant issue related to the delivery of molecular information to breeding programs. The IBP has the potential to provide the database and software support capabilities. This or a similar model should be developed to ensure broad access to the biometrics and statistical support needed to drive marker-based screening strategies. A common database structure across the CGIAR system and, ideally, with other major international consortia, would be the ultimate target. This issue is considered in more detail in the section on Bioinformatics.

Identifying and addressing gaps in the CGIAR biotechnology portfolio

There is a need to assess the genomic resources that would be required for each target species to ensure that a minimal level of information is available for all species.

The level of support and molecular information across the various mandated crops and animals of the CGIAR system is highly variable. An analysis should be carried out across the CGIAR Centers and CRPs to determine what key genetic or genomic data and resources are missing for each mandated species and what it would cost to produce the resources. A minimal level of information needed to support the core CRP and Centers programs should be defined. Are the CRPs already addressing this issue for their target species, or should this be tackled in a single large program and in a systematic fashion across multiple CGIAR-mandated species? Such a cross-Center approach could be of interest to donors. The survey undertaken as part of this study represents the first step down this path, but greater detail and follow-up questions would be needed to define a clear plan.

CRPs and Centers should be encouraged to explore opportunities for outsourcing technologies (such as genotyping and sequencing) and platforms (such as database structures and packages of data analysis tools) that support biotechnology research and delivery. Many groups are already outsourcing sequencing, genotyping, bioinformatics and regulatory advice. There may be an opportunity to coordinate these activities to reduce costs and better target CRP and Center needs by increasing purchasing power.

In negotiating access to service providers, CRPs and Centers could include the options for NARS to access similar services. For many of the mandated species there may also be possibilities to link to service providers used by ARIs.

Maintaining in-house capabilities can be costly and inefficient, and frequently results in groups being stuck with outdated technologies. Most ARIs use service providers for sequencing and genotyping. In several cases, advanced genotyping and sequencing platforms are only available through service providers, and the level of outsourcing is now becoming a reflection of the technical sophistication of Centers.

Our strong recommendation is that the focus and comparative advantage of CRPs and Centers should be on building core capabilities around germplasm and phenotyping, so that they can establish unique research opportunities that will attract collaborators from both NARS and ARIs. Ideally, the CGIAR groups should act as focal points for research partnerships, and this will come from a clear emphasis on their greatest strengths.

Outsourcing of bioinformatics, database management and regulatory capabilities are dealt with in later sections of this report.

Coordination of biotechnology activities

The Panel recommends creation of a forum for information exchange and collaboration among different groups within the CGIAR system. For example, many groups are developing genomics selection strategies to support their breeding work, and these groups could share skills and experiences; for example, Institut national de la recherche agronomique (INRA) in France has established a joint program between cattle and wheat groups to explore the use of genomic selection. Another example can be seen in the work on engineering drought tolerance. Many groups within CGIAR are evaluating similar transcription factors associated with drought response; could this work be done more effectively by one group and then transferred to others if it proves successful? Collaboration among these different groups could build considerable strength and minimize duplication.

The forum or group should include representation from all CRPs and Centers who wish to be engaged, and it should appoint a chair who can act as a spokesperson for CGIAR on biotechnology matters. The primary role of the forum or group would be to share experiences (successes and failures), develop collaborative projects, support links and partnerships with external groups, and ensure due diligence in determining priorities in biotechnology.

It may be appropriate to bring in outside scientists to ensure that the group is able to access latest technical advice. The chair could be someone from the Consortium Office such as the Chief Scientist.

This group should provide a forum for regular (at least twice a year) updates on biotechnology activities across the CGIAR system. They could also support the development of new biotechnology projects within the CGIAR system and explore opportunities for partnership or collaborations from both within and outside the system.

The group should, as soon as possible, develop a strategy for the integration of biotechnology activities from across Centers and CRPs to enhance the delivery of improved germplasm and resources for their mandated crop or animal production systems.

The strategy and targets should be science-based and needs-driven. Implementation of the strategy may require consideration of political and social issues, but it is important that the Centers and CRPs have a clear scientific perspective that they can articulate to donors and NARS partners. We recognize that most Centers and some CRPs have biotechnology approaches integrated into their overall research plans and breeding pipelines. However, we consider that there are advantages in having a document that goes across the CGIAR system to provide transparency both internally and externally and that can be defended against the broad objectives of CGIAR.

The key aims of this recommendation are as follows.

- Build scientific credibility within the CGIAR system and externally in the area of biotechnology so that Centers are regarded as valuable partners by ARIs, commercial organizations and NARS.
- Establish priority-setting processes that are scientifically defensible. For most target traits or conditions, multiple options will be available. Is there adequate variation in the germplasm pool? What is the likely time to delivery? Can molecular markers help, or will GE be the only or most effective solution?
- Ensure that resources for biotechnology development and delivery are used efficiently and that an appropriate balance is maintained between biotechnology research and development and other technologies. Many biotechnology approaches are expensive in terms of both cash and resources.

There is little point in initiating a biotechnology solution if there are not adequate resources to complete the task (up to deployment and delivery). Similarly, biotechnology approaches should not divert resources from other core activities of CRPs without a clear demonstration of value for money. The costs will vary depending on the point where Centers or CRP enter the delivery pipeline. However, the costs associated with technology delivery are frequently seriously underestimated.

- Enhance collaboration among CGIAR Centers and CRPs and encourage the development of joint resources and capabilities. There is an opportunity to share facilities and negotiate access to services. Many biotechnology outcomes will be applicable to multiple crops and livestock so there can be considerable benefit (economies of scale) in joint technology development across commodities and CRPs.
- Critically assess and scientifically validate activities in the biotechnology area before launching new projects. Since biotechnology outputs (such as genes for drought tolerance) are frequently developed from basic molecular studies in model species, there is frequently a tendency to extrapolate from the bench to the field too early in the development process. Molecular biologists do not usually have a good understanding of the field performance of technologies, and field-based scientists are not always in a position to effectively evaluate molecular work. As a result, biotechnology – particularly GE – has been plagued by premature and often exaggerated claims based on laboratory or contained experiments. A rigorous process is required, incorporating advice from experienced staff both within and outside CGIAR, to decide which technologies should be advanced and to establish priorities. The assessment process must involve researchers from different stages in the technology development and delivery pipeline.

Recommendation 1: Establish a CGIAR-wide biotechnology support and planning group ('Biotechnology Group'), and develop a biotechnology strategy that incorporates Center and CRP biotechnological approaches.

The strategy should be regarded as a working document and should be revised and updated on a regular basis.

Recommendation 2: An early task of the Biotechnology Group (Rec. 1) should be to review activities across the CGIAR system.

This review should:

- define minimum resource and information requirements for all mandated species and identify gaps in the existing research portfolio;
- evaluate the scope and opportunities for using targeted mutagenesis and genome editing to address target traits;
- collate existing outsource agreements and procedures and assess the opportunity for expanding outsourcing and negotiating improved contracts.

Implementation of Recommendations 1 and 2

The establishment of the Biotechnology Group will require the allocation of time and resources by biotechnology and related staff in Centers and CRPs. The early phase could be managed by the CGIAR Consortium Office, given that the current Chief Scientist has a strong biotechnology background. However, there would be significant advantages in having a person outside the CGIAR system as the chair once the Group starts operating. In particular, this would help ensure independence, international biotechnology

credibility and flexibility to provide for turnover and target-specific areas of biotechnology expertise as the technologies and priorities shift. A budget should be assigned to support the recruitment of independent member/advisors and to fund meetings. The initial phase is likely to require regular meetings (every 2–3 months).

All Centers and CRPs engaged in biotechnology research should be strongly encouraged to participate in the Biotechnology Group. This will require commitments by Centers and CRPs to allocate staff time and ensure that the person delegated to represent the Center or CRP has the ability to make decisions and is fully aware of the biotechnology activities and their relevance to the overall objectives and targets of their CRPs. Evidence that the biotechnology research strategy and projects have been assessed by the Biotechnology Group should be used as a criterion for funding and support, and these assessments should be provided to donors.

The Biotechnology Group should ensure that mechanisms are in place whereby 'bottom-up' proposals for biotechnology projects from Center staff and their collaborators are assessed for scientific credibility and utility. This process needs to be highly efficient. Some secretarial support will be needed but could be provided by the Consortium Office. The assessment process must be simple, transparent and rapid to avoid imposing unwarranted bureaucratic requirements on researchers. There also needs to be a mechanism whereby 'top-down' proposals from the Biotechnology Group can be advocated to Centers. For example, if it became clear that a single gene when overexpressed elevates photosynthesis rates by 10%, the Biotechnology Group would need to establish a plan for coordinating the activity in Centers so that this trait could be rapidly disseminated in multiple crops.

A transition phase from the current project planning system for biotechnology, which is often ***ad hoc*** and opportunistic, will require careful management. Importantly, the outcomes of the review or audit of current biotechnology activities (Rec. 2) will provide a base for determining biotechnology priorities and capabilities. Consequently, an immediate task of the Biotechnology Group will be the initiation of the review. The information provided by Centers in the survey reported in this document will provide a useful starting point for the review. For example, the review should explore the basis for some of the GM delivery timelines (see Table 4, page 23), the strategy for determining the target GM traits and leads, and the costs associated with outsourced services. It will also be useful to assess the status of implementation of recommendations from previous biotechnology related reviews (Science Council *et al*., 2009).

The Biotechnology Group should also revise the *Position Statement on Biotechnology* (Appendix B) to provide greater clarity and support for the biotechnology activities within the CGIAR system. In particular, the rather weak statement on GM technologies requires improvement (see also Rec. 4).

Phenotyping: a new role in the genomics era?

Introduction

Phenotype is defined as: "the observable physical or biochemical characteristics of an organism, as determined by both genetic makeup and environmental influences".[4]

Phenotyping is a core capability and represents a comparative advantage of CGIAR Centers due to the close association with breeding programs and the broad set of environments available for germplasm evaluation. This should remain a high priority, and Centers should use this capability to build partnerships with groups developing new imaging and analysis systems for evaluating specific traits.

Traditional multi-environment field testing for yield is essential to ensure the relevance of trait phenotyping to farmers' field conditions in the target population of environments. Trait–marker associations identified in phenotyping platforms and supported by modeling or experimentation must be tested for efficacy across target production environments. This is now possible given the extent of genotyping in breeding program material, provided the databases of multi-environment testing are continuously updated.

Plant growth and development occur in a dynamic context in which a given marker or trait has different effects on plant performance at different physiological stages, under different conditions and in different genetic backgrounds. Ecophysiological models, which are based on physiological determinants of crop growth and yield, potentially allow any trait to be linked with its effect on whole plant behavior and performance. This helps in taking new approaches to phenotyping 'beyond technique' by two methods.

1. **Trait dissection.** Using quantitative understanding of dynamics of crop growth and development to unravel complex trait variation and identify useful targets or indicators for high-throughput phenotyping. Knowledge of potential trait interactions also helps to avoid risks or errors associated with high-throughput phenotyping. The effects of major simple traits, such as flowering time, can be anticipated via modeling. Such knowledge also underpins constructing composite traits that have higher heritability than direct measures from phenotyping platforms (e.g. redefining traits per unit thermal time, sensitivity response traits, allometric ratios, growth and water use efficiencies).
2. **Phenotypic prediction.** Simulating the value of a marker or a trait in different environmental contexts can be insightful in cases where there is large variation for the target trait or phenotype The value of a simulation model is to cross this distance using physiological knowledge, thereby allowing prediction of the marker/trait value on the phenotype in a way that considers the environmental context (Hammer *et al*., 2006).

High(er)-throughput semi-controlled field phenotyping facilities or full-field phenotyping systems have been developed (e.g. Australian Plant Phenomics Facility phenomobile, ICRISAT and IRRI lysimetry facilities, and the United States mobile platform) and have direct linkages to crop improvement, especially for complex traits where model-assisted phenotyping can inform trait targets. Therefore, models can be used in a 'reverse engineering' approach to identify relevant hidden parameters. These approaches, when combined with advances in environmental sensing, offer considerable potential to increase the speed and accuracy of phenotyping.

4. http://www.thefreedictionary.com/Phenotyping

In animals, the situation is equally complex. Often the main trait of interest is simply to ensure livelihood survival at the smallholder level. However, causes of animal deaths are diverse and may include diseases, climatic pressures (e.g. drought), and/or access to food. Genetic tolerance or resistance mechanisms for these challenges have been selected for in indigenous livestock populations. However, their identification require dissection of the phenotype into its individual components – a major (although not impossible) task. In some cases (e.g. for productivity traits such as milk yield) a phenotypic platform could be immediately designed, taking the example of the private sector. In other cases, it may require innovative exploration of the opportunities offered by georeferenced environmental data and remote sensing technologies to indirectly infer livestock phenotypes (e.g. landscape genomics approaches) (Hanotte *et al*., 2010).

There are major risks in the development of high-throughput technologies, which are associated with the relevance of measures and their extrapolation to diverse environments. For complex traits, physiology-based phenotyping, supported by ecophysiological modeling, provides a means to make more effective use of genomic selection and high-throughput phenotyping.

Role of the CGIAR

There is considerable potential for the CGIAR to alleviate the phenotyping bottleneck. For simpler traits, this involves developing and applying phenotyping screens with dense genotyping for genomic selection, MAS and gene discovery. This may or may not involve high-throughput phenotyping platforms. For complex traits, Centers and CRPs are well placed to be hubs for the further development (with key collaborators) of high-throughput field phenotyping systems combined with model-assisted phenotyping. While genotyping is sensibly outsourced, in-house phenotyping, modeling and bioinformatics capability linked to breeding activity is required. Close association with breeding programs and multi-environment field testing is essential to ensure the relevance of phenotyping to impact for CGIAR target beneficiaries. While most Centers already have the necessary expertise, additional staff recruitment and expansion or upgrading of facilities will be needed in the experimental stations and NARS sites. There are also major opportunities to improve the value of phenotypic data generated by many field stations through training staff in some of the new statistical methods for designing field trials and spatially analyzing data.

The general approach to phenotyping is challenged by the emergence of whole-genome association mapping and genomic prediction/selection. The latter calculates a breeding value for a genotype from its set of genomic markers via a prediction model that was trained on individuals with both phenotypic and genotypic data. Hence, genomic selection has the potential to partly replace the costly and time-consuming phenotyping of large breeding populations by an *in silico* selection. However, a combination of both approaches should be adapted to specific target traits and populations.

What is the role of phenotyping in this new era (Furbank and Tester, 2011; White *et al*., 2012)? The efficacy of association genetics and genomic selection is constrained by the simplicity of the additive prediction models used to connect combinations of markers to complex traits. It is also restricted by the nature of the target trait and the directness of the link between performance and markers. Traits that scale more directly from gene level to plant and animal phenotypic response (qualitative/simpler traits, e.g. some pest resistances, some fertility traits such as twinning rate and micronutrient content) can be handled differently to those that do not (quantitative/complex traits such as drought adaptation or nitrogen use efficiency). Association mapping and genomic selection rely on the stability of the relationship between a phenotype and the set of genomic markers. This stability is affected by the 'phenotypic distance', i.e. the extent of the biological integration required from the causal polymorphism at genome scale to the phenotype of interest. A more physiology-based approach to phenotyping is likely in this new era to break down complex traits in order to improve:

- the ability to analyze the genetic determinism of plant and animal functions;
- the robustness of phenotypic prediction taking into account interactions with environmental conditions in marker effects on the phenotype. However, this must be at a throughput rate that is high enough to support genetic analyses.

In plants, phenotyping in the new genomics era ('phenomics') has most often dealt with this through the development of high-throughput platforms (tools and facilities), and a number of expensive automated phenotyping facilities are now available around the world. However, they have tended to focus on techniques (architecture of roots and shoots, hyperspectral imaging, etc.) rather than on the value to field crop improvement, which has yet to be well demonstrated. A trait might be measurable in high-throughput (e.g. hormone level), but its integrated effect on whole plant behavior is difficult to assess and/or its associations are not known. Phenotyping in this new era must focus on enhancing the predictive link between performance and markers. The objective must be the 'master' and the technique the 'servant'. For simple traits there may be clearly identifiable targets for high-throughput platforms (e.g. disease, micronutrient disorders). For complex traits, this will often involve model-assisted phenotyping to identify relevant component traits and provide an analytical framework cognizant of the dynamics of crop growth and development. This is essentially the same activity as that carried out for years in 'whole plant physiology' (i.e. measurement of traits and plant functions in relation to environmental conditions) but at a level of throughput that can support genetic analyses.

Recommendation 3: The Panel encourages Centers and CRPs to maintain a strong focus on building the core capability of multi-environment field phenotyping, field-relevant high-throughput trait phenotyping, and modeling and analytical support capabilities.

These priorities should be reflected in planning and investment decisions and should be high on the agenda for the planning group (Rec. 1).

Implementation of Recommendation 3

Phenotyping capability encompasses far more than just biotechnology. Consequently, the implementation of this recommendation includes – but must not be limited to – input from the Biotechnology Group. Crosscutting phenotyping platforms and coordinated support services should be strengthened. Close engagement with NARS is critical for both the development and maintenance of field phenotyping sites and capabilities, since many of the sites are owned and managed by the national partners. Building the capacity of NARS to support the application of new phenotyping techniques, and the coordination of phenotyping networks, should remain high priorities.

Selection of phenotyping sites to support biotechnology applications will not necessarily align fully with current priorities for site selection. For example, phenotyping for GM traits needs to cover environments relevant to the target trait and also to the regulatory systems and delivery options. These factors must be included in the overall biotechnology strategy (see also Rec. 4).

Genetic modification

Plant and animal breeding depends on the capacity to select new useful variation. Genetic modification (GM) methods enable additional variation to be put at the disposal of plant breeders that could not have been introduced by sexual hybridization of two parental plants or animals. Reports from ISAAA[5] attest to the rapid and widespread adoption of GM crops. Indeed, this technology has been adopted by growers at a faster rate than any other agricultural technology. The most widely-adopted traits are the herbicide resistance Roundup Ready® trait and insect-resistance traits based on the expression of various forms of the *Bacillus thuringiensis* (Bt) crystal protein. Roundup Ready® soybean has been very widely adopted in the United States and Latin America, and the Bt trait has been adopted worldwide for control of stemborers and rootworm in maize.

While GM offers many options for the delivery of novel traits, it has also become a fundamental tool for gene discovery and analysis. Molecular biology labs use transformation routinely for gene cloning and functional analysis. Functional analysis frequently involves transformation into model species such as *Arabidopsis* spp. and rice for plants, and zebra fish and mice for animals. Most gene discovery projects involving CGIAR scientists are in partnership with ARIs, where these transformation capabilities are in routine use. However, it is important to recognize that many Centers and CRPs require in-house transformation to study gene function and evaluate gene constructs prior to transformation into the target crop or animal.

Plant GM projects in the CGIAR Centers

GM research and development has been actively pursued by several CGIAR Centers over much of the past two decades. During this period many crops and genes have been evaluated in both contained and field trial facilities. However, no GM products have emerged in farmers' fields as a result of this work. Over the same period, the global area sown with GM crops has expanded at an extraordinary rate and, for the past few years, the rate of adoption in developing countries has exceeded that in developed regions (ISAAA, 2014). The CGIAR system has played almost no role in these developments, partly due to the nature of the most widely grown GM crops in the developing world, namely cotton and more recently maize and soybean. However, the well-established technologies of insect and herbicide resistance could have been applied to many of the CGIAR mandated crops; notably the use of herbicide tolerance in the control of *Striga* and Bt toxins in controlling many of the pests of grain crops, particularly pulses.

These observations suggest that the CGIAR system has focused its GM activities around research, particularly gene discovery and analysis, rather than exploring opportunities for technology delivery and, in consequence, may have missed a significant opportunity.

There are strong concerns about GM projects that are not based on a clear definition of the target trait and a sound understanding of the molecular basis for action of the transgene(s). Therefore, before any new projects are undertaken, there needs to be a compelling argument that GM is the only method by which a desired trait can be introduced into a vital crop or farm animal for resource-poor farmers. Is CGIAR the most appropriate organization to develop and deliver the GM product, or are their alternatives such as private-sector engagement? What is the target production environment or region? Are appropriate distribution and regulatory systems in place to deal with GM seeds and products?

5. International Service for the Acquisition of Agri-biotech Applications (ISAAA); www.isaaa.org;

Some traits are well established in developed countries, such as cornborer resistance in maize via Bt. The only requisite work for CGIAR in such a case might be backcrossing such traits into local varieties. For other traits of strategic importance for the rural poor in developing countries, CGIAR must take the lead, since the crop and trait may not be of sufficient interest for the private sector to bring to market; examples include insect resistance in cowpea and elevated vitamin A in rice.

Overall, there are clear examples of important projects that have real potential to address a problem that could not otherwise be tackled. Golden Rice addresses vitamin A deficiency among poor people whose diet comprises primarily rice. There are crops that are of little or no interest to advanced economies, such as cowpea, banana, cassava, but which are of great local importance to resource-poor farmers; specific GM projects address major problems in these crops, such as viruses, pests and diseases. However, there are other examples of GM work being pursued at several CGIAR Centers where the scientific challenges are higher and prospects of success are much lower – for example, nitrogen use efficiency (NUE) (McAllister *et al.*, 2012) and drought (Lawlor, 2013). For these traits, although there are some widely discussed candidate genes (such as alanine aminotransferase, DREBs and other transcription factors), even the private sector has not been able to generate commercializable events with these genes to date. It is interesting to note that there have been over 5000 field trials of GM drought-resistant plants in the United States alone (ISAA, 2014), implying that a massive effort is needed to have a reasonable chance of achieving a useful outcome. This also highlights the need for Centers and CRPs to link to activities at ARIs and the private sector if they are serious about the delivery these types of GM crops to poor farmers.

Field evaluation of GM lines

Unlike qualitative traits such as the clear plus/minus phenotype of insect resistance, phenotypes such as drought tolerance or NUE are quantitative, and it is difficult to show statistically significant effects in the field. The ability to reliably detect a yield improvement under drought stress, for example, will depend on the number, scale and environmental diversity of field trials; 10 or more field trials at different sites or over multiple years would be needed to be confident that a GM line will yield 10% more than the non-transgenic controls. It is also important to clearly demonstrate that the GM line that may give improved yield under drought stress does not lead to a yield loss under non-stressed conditions (Hervé and Serraj, 2009). Again extensive field trialing is needed. Therefore, Centers or CRPs will need access to a very large field phenotyping network to effectively validate GM events. In addition, transgenes or transgenic events must be validated in different genetic backgrounds, since transgene performance, particularly for quantitative traits like drought tolerance, will vary in efficacy.

It is also important to remember that the target level of stress tolerance will vary between species and production systems; for example, for maize a drought stress that leads to a 30% yield loss is generally regarded as severe, whereas wheat drought can reduce yields by over 80%. It is probable that varying response mechanisms will be needed to produce useful transgenic lines to match transgenics to the level of tolerance needed.

If Centers and CRP intend to seriously engage in the development and delivery of GM crops, they need:

- to access to the validated gene leads – the best available and those that have clear evidence of field performance;
- the capacity to generate and evaluate hundreds or thousands of GM events to ensure they achieve optimal and stable expression of the transgene;
- in some cases, access to multiple transgenes (e.g. several insect resistance genes in order to minimize the risk of resistance development in the target insect pest);

- field evaluation capability that covers all the likely production environments;
- capacity to ensure clear separation of their GM production pipelines from trialing systems and rigorous tracking and storage procedures;
- appropriate distribution, stewardship and regulatory systems in their target regions.

For many of the GM projects currently under way in Centers and CRPs, few of these issues have been addressed.

Table 4. Current GM projects in CGIAR Centers (compiled from survey questionnaire, September 2013)

Center	Target species	Trait	Genes	Partners		Expected delivery
				NARS	ARIs	
AfricaRice	None					
Bioversity	Banana	Banana weevil	Bt (Cry6a) Papaya cystatin	NARO-Uganda	FERA, UK	2017 2017
			RNAi		Vengaza Inc., USA North Carolina, USA	
		Drought			KU Leuven, Belgium	2016
CIAT	Rice	NUE		Ghana, Uganda	USAID-CRI	2020
		Drought		PSC, EMBRAPA-Brazil	JIRCAS-Riken, Japan	2018, 2020
	Cassava	Early flowering			Riken, Japan, AGI	2018
CIMMYT	Wheat	Drought	DREB1a		JIRCAS, Japan	
		Heat tolerance			Arcadia, USA	
		Disease resistance			Venganza, USA	
	Maize	NUE		KARI-Kenya; ARC South Africa	Pioneer, USA	
		Drought		AATF, KARI-Kenya, IIAM-Mozambique, ARC South Africa, Tanzania	Monsanto, USA	
		Insect resistance	Bt	AATF, KARI, IIAM, ARC South Africa, Tanzania	Monsanto, USA	
		Disease resistance			Venganza, USA	
CIP	Potato	Insect resistance	Cry1ab5		Bayer CropScience, Germany	
		Late blight	R genes	NARO-Kazardi, Kabale, Uganda, Agricultural Biotechnology Support Project II	Cornell University, USA; Wageningen University, Netherlands	2016
		Potato leaf roll virus	RNAi			
	Sweet potato	Insect resistance	Cry1ab5	NARO-NaCRRI, Namulonga, Uganda Jomo Kenyatta University, Kenya BecA-ILRI	University of Ghent, Belgium; University of Valencia, Spain	2018
		SPVD	RNAi	NARO-NaCRRI, Namulonga, Uganda	Donald Danforth Plant Science Center, USA; University Helsinki, Finland	2018

Table 4. Current GM projects in CGIAR Centers (compiled from survey questionnaire, September 2013) continued

Center	Target species	Trait	Genes	Partners		Expected delivery
				NARS	ARIs	
GCP	None					
ICARDA	Barley	Abiotic stress	HvSNAC1	AGERI, Egypt	John Innes Centre, UK	By 2018
	Chickpea	Abiotic stress	Range of genes	AGERI, Egypt	University of Hannover, Germany	By 2018
	Lentil	Herbicide tolerance	pCGP1258	AGERI, Egypt	University of Hannover, Germany	By 2018
	Wheat	Drought tolerance	HV1	INRA, Morocco		By 2018
ICRAF	None					
ICRISAT	Pigeonpea	Vitamin A		Government of India		2020
		Pod borer resistance	Cry1Ac, Cry2Aa	Government of India, ICAR		2018
	Chickpea	Pod borer resistance	Cry1Ac, Cry2Aa	Government of India, ICAR		2018
	Groundnut	Vitamin A		Government of India		2020
		Drought tolerance	DREB1A	Government of India	JIRCAS, Japan	2018
		Virus resistance		Government of India		2018
IFPRI						
IITA	Banana	Bacteria resistance		NARO Uganda, AATF		2018
	Plantain	Nematode resistance		NARO Uganda	University of Leeds, UK	
	Cassava	*Cassava brown streak virus* disease resistance		Donald Danforth Plant Science Center and KARI, Kenya	Donald Danforth Plant Science Center, USA	2020
ILRI		Virus	Vaccine antigens		Jenner Institute, UK	
		African swine fever virus			Freindrich Loeffler Institute, Germany; USDA, USA	
		Mycoplasm mycoides	Attenuated strains		J Craig Ventner Institute, USA	
	Cattle	Disease resistance			Roslin Institute, UK; University Michigan, USA	2017
	Cowpea	Drought tolerance		University of Nairobi		2017
IRRI	Rice	Nutrition	Pro-vitamin A	South Asian NARS		2015
			High iron	South Asian NARS		2018
		Drought tolerance			JIRCAS, Japan	
		Photosynthetic efficiency	C4 rice			After 2018
WorldFish	None					

Examples of major CGIAR plant GM projects

Biofortification projects (IRRI)

Micronutrient malnutrition is caused by a lack of micronutrients in the diet and can result in blindness, stunting, disease and even death. Fruits, vegetables and animal products are rich in micronutrients, but these foods are often not available to the poor, who rely on inexpensive staple foods, such as rice or cassava, which have few micronutrients. Developing crop varieties with increased micronutrient concentrations could make a valuable contribution to human health.

Vitamin A is made in the human body from β-carotene, and vitamin A deficiency is the leading cause of irreversible blindness in children. The problem is particularly severe in Southeast Asia, where rice is a staple but no existing varieties contain β-carotene in the grain. IRRI has developed locally adapted Golden Rice varieties, which produce β-carotene in their grain (resulting in the golden color). The β-carotene produced is of equivalent nutritional utility to other sources (Tang *et al*., 2012). Golden Rice has still not been authorized for cultivation, to the dismay of scientists (Potrykus, 2010).

Extension biofortification of crop varieties to iron and zinc is challenging, because metal ion concentrations in various tissues and compartments are regulated by coordinated uptake, translocation and storage. For crops like rice, removal of the outer layers of the grain during polishing removes all micronutrients, leaving only the starchy endosperm.

Micronutrients can be mobilized from the soil to the seed in rice through three different approaches: (i) enhancing iron translocation through overproduction of the metal chelator nicotianamine and phytosiderophores; (ii) enhancing iron influx into the endosperm by means of the iron–nicotianamine transporter; and (iii) enhancing expression of the iron storage protein ferritin. Combining the first two approaches has resulted in greenhouse-grown rice with levels of iron three to four times that in polished grain (Schroeder *et al*., 2013). Combining the first and third approaches has increased the iron content more than six-fold; and combining all three approaches has resulted in paddy-field-grown polished rice with iron concentrations 4.4 times higher than those found in non-transgenic seeds, with no yield penalty. Although these results bring iron levels close to those recommended by nutritionists, only a handful of studies have tested whether these enhanced levels of nutrients are available on consumption. Enhancing the nicotianamine concentration increases the levels of bioavailable iron and zinc in polished rice.

Vacuolar sequestration also enhances the amounts of iron and zinc in seeds. Metals are transported between the cytoplasm and the vacuole by transporters. Several strategies are being used to enhance iron and zinc levels in edible plant tissues, but more improvements are needed using the growing knowledge of the transporters that take up micronutrients from the soil.

Comment on the Golden Rice project

The Golden Rice project has reached its technical goals and attained useful levels of vitamin A accumulation in rice endosperm.

Many factors have contributed to the delays in delivering Golden Rice. Ensuring clearance for use of IP caused initial delays, but the complex regulatory requirements and highly organized opposition from lobby groups has been a major impediment. In interviews with some of the scientists and managers involved in the Golden Rice project, the consensus was that if they had been aware of the time and personal costs (abusive and threatening phone calls and messages), they would not have embarked on the project. These factors should be noted and staff should be appropriately trained, warned and supported to help cope with these personal attacks.

There was widespread concern in the scientific community when activists destroyed a Golden Rice field trial. The Panel was surprised at the lack of a public response from the CGIAR system to this act of

vandalism. This appears to reflect a general lack of coordination regarding GM projects across the CGIAR system, and the lack of clarity about responsibility in this area. As noted above it will be important that staff involved in the development and ultimately the delivery of GM products are adequately protected and supported.

This project is still seen by many in the scientific community as the ideal demonstration of the value of GM in tackling an important issue for poor farmers that could not be addressed by alternative techniques. It will be important for this and other GM projects that the CGIAR management stand solidly behind the researchers and their host Center or CRP to provide public support and intervention where the research or researchers are threatened.

Bt cowpea

Cowpea (black-eyed peas) is the most important indigenous African legume (especially for smallholder, low-income farmers) due to its ability to grow in drought-prone areas and improve soil fertility. However, losses to pod-boring insects can be severe, with the cowpea pod borer (*Maruca vitrata*) causing yield losses as high as 70–80%. Insecticides against cowpea pod borer exist, but they have not been widely adopted by farmers due to prohibitive costs and significant health hazards. GM Bt-resistant cowpea has been developed by an international agbiotech public–private partnership (PPP) coordinated by the African Agricultural Technology Foundation (AATF), a not-for-profit organization that facilitates and promotes PPPs for the access and delivery of appropriate agricultural technology for sustainable use by smallholder farmers in Sub-Saharan Africa. Monsanto donated the Bt gene to AATF on a humanitarian basis under a royalty-free license. The Institute for Agricultural Research in Zaria, Nigeria is responsible for the Bt *cry1Ab* gene introgression into local cowpea varieties. Field testing has been carried out in specific locations in Nigeria. Deployment is expected by 2017.

This program clearly addresses a major need and an important problem. As the time approaches for deregulation and deployment, there is a need for a comprehensive public relations strategy to communicate clearly the rationale for the work and the trait. Such a strategy should be coordinated by an advisory board (see below) responsible for the overall coordination of GM activity across the CGIAR system.

GM banana

There are four major pests and diseases of banana.

- Black sigatoka, caused by *Mycosphaerella fijiensis* is controlled by enormous fungicide application rates – usually from airplanes over plantations, with limited efficacy. Credible GM strategies for resistance are under way, but are of unproven effectiveness.
- Fusarium wilt (Panama disease) led to the abandonment of the highly susceptible variety Gros Michel and its replacement throughout much of the world by the variety Cavendish. For many local plantain and other banana varieties, fusarium is still a problem. Projects by IITA and NARO in Uganda exist to address the problem, but too little information was provided for the review group to be able to assess the plausibility of the approach(es) being taken.
- *Xanthomonas* bacterial disease causes considerable losses in bananas in Central Africa. Credible GM solutions exist; for example, from the expression of a resistance gene derived from sweet peppers (Tripathi *et al*., 2010), but they still need to be tested further. Additional genes that confer resistance are available from the public sector, such as Arabidopsis EFR, and are likely to be worth testing.
- Nematode infection of roots also suppresses yield, but new research is reported to have led to nematode-resistant bananas (Roderick *et al*., 2012).

Cassava virus disease resistance

A major challenge for cassava farmers are cassava mosaic virus and *Cassava brown streak virus*. Research funded by the Gates Foundation is exploring the use of RNAi (interfering RNA to target viral RNA for degradation) against these viruses to reduce susceptibility. In addition, *Xanthomonas* bacterial disease of cassava can also cause extensive losses (Bart *et al*., 2012) and GM disease-resistance traits being developed are likely to be available in the short-to-medium term (though not currently within the CGIAR system). This project would be extremely valuable if successful, but great care needs to be taken to ensure that traits are successful in the lab before they are field-tested, and to ensure proper networking between CGIAR and all labs that are attempting to solve the same problem.

Other current plant GM projects in the CGIAR system

The Panel was also alerted in responses to the questionnaire to GM projects on wheat, barley and legumes that aimed to increase disease and abiotic stress tolerance, but insufficient information was provided to assess the utility or likelihood of success of most of these projects. The Panel was concerned that insufficient strategic planning went into deciding whether to proceed with a GM project for a particular gene. Again, an advisory board with overarching responsibility across the CGIAR Centers and CRPs could ensure that all projects are properly considered and have reasonable prospects of delivering successful and useful outcomes.

Relevance and timing of GM projects

CGIAR should only engage in projects targeted to the development and delivery of GM products after a thorough and careful evaluation of the proposed technology, its alternatives, and the opportunities and mechanism(s) for delivery to resource-poor farmers and poor urban consumers. In many cases it may be best to wait until the private sector has defined genes with proven efficacy for complex, quantitative traits such as drought and NUE for industrialized countries, before investing scarce resources trying to achieve results in developing countries.

Many CGIAR Centers reported GM crop work (Table 4). The pro-vitamin A rice (Golden Rice, IRRI) and Bt cowpea (IITA) programs are well advanced. The Golden Rice project is part of a biofortification program that also involves projects with partners for the enhancement of zinc and iron nutrition. Other GM programs are at an earlier stage. Answers to the questionnaire brought the Panel's attention to projects on disease and pest resistance in banana and plantain (IITA with NARO-Uganda), disease- and pest-resistant potato (CIP with BecA), virus-resistant cassava (IITA and Donald Danforth Plant Science Center) and abiotic stress tolerance and NUE (CIAT). In total, projects targeting the delivery of GM products are under way at nine Centers and in 14 different crops, plus cattle. With the exception of maize, no commercial GM varieties have ever been released for any of the other targeted crops. Nevertheless, delivery timeframes of less than 5 years have been proposed by some Centers, and the first GM products are proposed for 2015 (pro-vitamin A rice) and 2016 (banana, potato). While we understand that the pro-vitamin A rice is very advanced and the targeted delivery date may be achievable, given the necessary regulatory approvals, few of the other timelines appeared realistic.

Overall, the Panel was concerned by the scale and diversity of GM projects, the apparent arbitrary choice of many of the genes being used, the unrealistic timelines for delivery, and the absence of clear stewardship, regulatory protocols and expertise. These projects represent substantial investment of CGIAR resources. Therefore, the Panel proposes setting up a coordination group across the CGIAR system (Rec. 1) and a specialized GM advisory group (Rec. 3) to help address these concerns.

GM leads and planning for delivery

The area of development and delivery of GM crops or livestock is complex and involves significant investment in resources, planning and communication. Technologies and useful gene leads are changing rapidly, and there is a danger that some leads will be followed too early – particularly if the complete research context has not been reviewed or if information is limited. It is critical that CGIAR has access to expertise and advice to ensure researchers are fully aware of opportunities and limitations related to the diverse technologies. At present, the CGIAR system does not appear well-connected to the latest GM science. While some Centers are endeavoring to compare different candidate genes for efficacy, the number and diversity is limited, and the survey (Table 4) indicated that some Centers are relying on just one or two candidate genes. For example, drought tolerance in some Centers still relies heavily on a small number of genes (the Panel noted the heavy reliance on DREB transcription factors), even when there are other candidate genes.

Some decisions about which GM traits to pursue in Centers appear to have been made on a rather *ad hoc* basis, conditioned by (for example) availability of genes from potential partners. One solution could be to invite a panel of experienced public- and private-sector scientists to comment on project proposals, and also to feed in project suggestions or to alert CGIAR staff to interesting developments. They could also advise the Centers and CRPs on the usefulness (or otherwise) of technologies that create new opportunities for crop and livestock improvement; for example, genome editing with TALENs or CRISPR/Cas9, synthetic biology for multiple genes for biosynthetic pathways (Rec. 2).

New candidate genes and technologies for crop and animal improvement appear regularly. Many very promising traits have been reported in the literature, but few have been advanced further.

Any GM project within the CGIAR system should be a major strategic decision. Given finite resources, CGIAR should not support projects that simply derive from gene discovery or early testing and which have not been properly thought through. GM projects require the same or more scrutiny and planning as any project within the CGIAR system. The project needs to be very carefully targeted, envisioned as a product all the way from the initial design of constructs through to the variety of the specific crop or animal for a particular geographical region, and should include partnerships with local organizations to get seed to farmers. Targeting should involve a thorough analysis of whether the same crop or livestock problem could be solved or addressed in the same time frame by other means, such as breeding or cost-effective agrochemicals. Due diligence should include defining the NARS with which CGIAR scientists will work to advance the trait in the germplasm that is likely to be used within a particular country.

GM trait project proposals need to have clear and quantifiable goals. Projects with insufficient evidence for efficacy within a defined time period need to be terminated efficiently. For example, a yield trait should show a clear yield increase (i.e. over 5%) compared to the best-performing lines.

It is important that, once a decision has been made to follow a GM path, the CGIAR system stands behind the project. As noted above, there has been considerable criticism of the failure of the CGIAR system to provide a clear and coordinated response to the recent vandalism of Golden Rice trials in the Philippines; the GM advisory board would be expected to provide a swift reaction to such acts.

Field evaluation of GM lines

Field phenotyping is a core CGIAR capability and comparative advantage. Nine Centers are building capability for the evaluation of GM crops or livestock. This presents an opportunity to build a global GM phenotyping network that could provide partners in both the public and private sectors with a system to evaluate GM lines in diverse production environments. It may be possible to engage some key NARS in

the evaluation of GM lines, and this could form part of the delivery processes by building regulatory and stewardship capability while also expanding the network of phenotyping sites.

The CGIAR system has a network of Centers around the world with land that could be used for phenotyping of essentially any agronomic trait. The private sector, and also public-sector ARIs, might be expected to welcome access to extra capacity to phenotype the efficacy of potentially useful GM traits and to learn more about the properties/potential utilities of specific genes. Subject to approval by the local regulatory authorities, the Centers currently involved in GM evaluation could consider opening their field sites to the evaluation of transgenic lines from both the public and private sectors. Strict assessment of potential leads should be carried out (as outlined above for CGIAR projects). The Centers could explore the possibility of building a network of GM evaluation sites around the world representing many different production environments. This could provide them with an opportunity to directly compare different GM candidate genes and also to negotiate early access to promising candidates and events. Support for the development and evaluation of GM crops varies greatly between jurisdictions; some are very supportive, while others will not even permit contained GM work. The development of a GM phenotyping network would require strong support from a well-structured and managed local regulatory system and should be in partnership with local NARS.

Recommendation 4: Establish a specialist management group to provide advice and coordinate research and development activities aimed at developing GM products.

This group could be called the 'GM Advisory Board' and could be made up key researchers within CGIAR and external advisors familiar with GM technology and issues associated with the delivery of GM products. The group would:

- provide a forum for project advice and analysis and help ensure that activities are coordinated and in line with best international practice;
- act as a public advocate of the GM strategy and for GM product development (this role could fall to the chair of the group);
- network with leading public- and private-sector scientists to ensure the CGIAR system receives the best advice about which traits are really likely be useful and successful;
- establish a communication plan for all projects aimed at GM product development, including a website through which members of the public can find an accessible account of the project, the needs that it is intended to meet, anticipated timelines and other relevant information;
- investigate the possibility of building a global GM phenotyping network;
- provide horizon-scanning for new genes and traits, and new technologies such as genome editing, as well as options for gene stacking.

Implementation of Recommendation 4

The Biotechnology Group should be established as soon as possible. Funds will be required to cover travel expenses for the members. The chair of the Biotechnology Group could act as interim chair of the GM advisory board to manage the set-up process and support consultative discussions needed to identity suitable members.

An early task of the GM advisory board should be to revise the position statement of CGIAR on GM technologies and garner support from within CGIAR and donors.

A rolling agenda should be developed to review all existing GM projects with Centers and CRPs. The review process will need to examine:

- the rationale for taking the GM pathway;
- the suitability of the transgene leads, including assessment of toxicity and allergenicity;
- the nature of any links to ARIs or commercial partners involved in the projects – including IP issues;
- the capacity of the Center or CRP to generate and assess GM events for trait validation and for production of commercial events;
- the proposed delivery pathways and the regulatory and stewardship framework (see also Recs 7 and 8);
- the communication and information access plan for the project.

The GM advisory board will also need to establish criteria for assessing GM projects. The project criteria need to clearly identify the information that will be required for launching new GM projects but also for assessing existing work.

A further task of the GM advisory board will be to develop the communication plan and to provide a high level of transparency for the decision-making processes used to follow a GM approach.

Livestock biotechnology

Introduction

The report has dealt with biotechnologies largely with respect to experimental examples in crop plant systems. The application of biotechnology to livestock improvement presents some special issues and challenges and these are the subject of this section.

Across the CGIAR, ILRI is the main Center with a livestock biotechnological research agenda, in the areas of vaccines and diagnostic developments, genomics of the host and parasites, and lately transgenesis. Its facilities include state-of-the-art molecular biology laboratories, primarily at ILRI – Nairobi (levels II and III[6]), but also to a much smaller extent at ILRI – Addis Ababa and ILRI – China); a small and a large animal research facility at ILRI – Nairobi, a livestock ranch ('Kapiti') for breeding purposes, a liquid nitrogen biobank, and high-performance computing facilities in support of the livestock research bioinformatics work.

ILRI livestock biotechnological research is of relevance to the outputs of three CRPs: CRP 3.7 – Livestock and Fish (led by ILRI), CRP 4 – Nutrition and Health (led by IFPRI) and CRP 7 – Climate Change, Agriculture and Food Security (CCAFS) (led by CIAT). More particularly, livestock biotechnology is included in CRP 3.7 within research theme 1, 'Technology development'; in CRP 4, within component 3 'Prevention and control of agricultural-associated diseases' and its subcomponent 2 'Zoonotic and emerging infectious diseases' (e.g. Rift Valley fever, cysticercosis); however, in CRP 7, the livestock biotechnological agenda remains to be articulated.

ILRI hosts and manages the BecA Hub, a shared agricultural research and biosciences platform providing capacity building and research-related services to national, regional and international agricultural research institutes, universities and private-sector organizations that conduct research on African agricultural challenges. The partnership allows both entities to benefit from the latest biotechnological equipment and technological know-how of each institution.

ILRI's biotechnological partnership is extensive, both at universities and at ARIs worldwide. ILRI is also a founding member of the Global Alliance for Livestock Veterinary Medicines (GALVmed). GALVmed aims to protect livestock and improve human lives by making livestock vaccines, medicines and diagnostics accessible and affordable to the end users (farmers), through the establishment of innovative PPPs. As a livestock health product development and adoption organization, GALVmed is a logical avenue for the delivery of ILRI diagnostic and vaccine research outputs. A good illustration is the ILRI infection and treatment method for East Coast fever, where both the production and deployment of the vaccine are now under the responsibilities of GALVmed. GALVmed also provides an entry point to address IP issues of relevance to the dissemination and use of biotechnological technologies associated with vaccines and diagnostic outputs.

ICARDA has biotechnological capacities and expertise for plant research, with several ongoing activities, but, as yet it has no articulated biotechnological livestock component. However, within its program on diversification and sustainable intensification of production systems, it has a component on small ruminant production. There is an obvious link with the ILRI-led biotechnological research framework for the improvement of animal health, nutrition and breeding practices, which includes infectious diseases of small ruminants (sheep and goat), such as the Peste des petits ruminants (ovine rinderpest). The CRP on Livestock and Fish, which involves both ILRI and ICARDA, provides opportunities for such synergies.

6. Biosafety containment facilities

The ICARDA livestock component has an extensive network of partners in Central Asia, North Africa and West Asia, providing a logical entry point for the eventual expansion of ILRI's biotechnological agenda (e.g. vaccine, diagnostic) into these geographic regions.

WorldFish Center has no in-house biotechnological capacity. However, it has identified within the CRP on Livestock and Fish the need for biobanking, including genebanking (tissues) and cryopreservation (sperm of improved aquaculture strains). Successful and sustainable aquaculture will require biotechnological research and aquatic animal health technologies, including diagnostics.

Livestock biotechnological research: vaccines

The ILRI livestock vaccines research pipeline is organized through the recently established ILRI Vaccine Platform (ILVAC). It is currently focusing on set of priority diseases: African swine fever, Contagious bovine pleuropneumonia, East Coast fever, Peste des petits ruminants and Rift Valley fever (zoonotic). The research platform has two components: basic and applied. Basic activities aim, for example, to dissect pathogen biology and diversity, study host–vector–pathogen interaction, identify vaccine (antigen molecules), characterize pathogen virulence factors and unravel immune response to infection. Applied activities include assessing candidate subunit or attenuated pathogen vaccine and different vaccination systems (e.g. adjuvant). It also includes collaborative research for the engineering of thermostable vaccine formulation and the development of Differentiating Infected from Vaccinated Animals vaccine.

ILVAC (vaccine and diagnostic) has generic technical capacities that allow it to address new disease constraints as relevant, but until now its portfolio of diseases is largely a legacy of its pre-CRP activities. Compared to non-African ARIs, ILRI also has direct access to pathogens and their different strains. The recent opportunistic set up, through an externally funded research project – the Arbovirus Incidence and Biodiversity Project – of a pathogen biobank is now an important component of ILRI biotechnological research.

Vaccine research remains a complex area, with deliveries expected at best in the medium term and final outcomes expected, more realistically, in the long term. An illustrative example is rinderpest eradication. More than 100 years separate the discovery in the 1880s of a first vaccine against rinderpest and the complete eradication of the disease, which was officially announced in 2011. The development of a thermostable vaccine was one of the key elements of this success (output of a vaccine research program). Prior to complete eradication, the disease was eradicated in several areas, through zoosanitary procedures and vaccination campaigns with major economic and development impacts (short term).

Several regulatory constraints are affecting the production and deployment of vaccines. For example, recombinant vaccine technologies use an attenuated virus or bacterium to introduce microbial DNA to animals' cells, and their development may be regulated as GM in some countries (e.g. Kenya).

Integrated within ILVAC is the diagnostics technology platform with two components: (i) an 'analyte' identification component, which aims to identify pathogen and molecules (protein or nucleic acids) for the diagnostic assay, and (ii) a diagnostic assay development component, which aims to develop diagnostic approaches to facilitate detection in the local laboratory or in the field (e.g. ELISAs, PCR, 'Pen-side' tests). Short-to medium-term deliveries of research outputs are expected for the diagnostic platform.

Livestock infectious diseases are generic issue across several CRPs (3.7, 4 and 7). Coordination and prioritization across CRPs may be beneficial to maximize impact and resource allocation. To facilitate this, the Panel recommends creating a CRP-wide livestock vaccine advisory committee to encourage disease prioritization within each CRP and help make strategic decisions on health/vaccine/diagnostic issues generic across CRPs.

Livestock characterization genomic platform[7]

There has been a revolution in livestock genomics. It has been embraced by the commercial sector, where major productivity and economic gains are expected. Reference genomes are now available for nearly all livestock species (including several aquaculture species). Genome characterization (sequencing and genotyping) of indigenous livestock and their crossbreeds at relatively low cost and large scale (large populations) is a short-term reality. It is already leading to the widespread application of genome-wide selection methodologies in the developed world (for example, for milk yield and meat quality). In the developing world, the requirement for large-scale phenotyping and the diversity of productivity systems and environments mean that the successful application of genomic selection approaches in indigenous livestock is not expected in the short term. Nevertheless, the characterization and understanding of livestock genomes is a promising new research avenue, with deliverables expected in the short and medium terms for improvement of productivity within breeds or through crossbreeding. For example, the adaptations of indigenous livestock and their wild relatives to the local production environment are undisputed. Disease resistance, heat and drought tolerance, and altitude adaptation are major traits with genetic components that may be identified through genome-wide analysis. Also, the genetic host remains an important element in the application and success of vaccine development, and animal-specific traceability along value chains is essential for health and safety purposes.

Given the genetic uniqueness of the livestock breeds and populations from the developing world, their importance to the poor farmers, and the relative lack of national genomic expertise in countries where the livestock are found, it is recommended that a special 'livestock genomics platform' be developed within the CGIAR livestock biotechnological research program.

The livestock genomics platform should have the expertise to analyze at large scale full-genome livestock genotyping sequencing data for the identification of the genomic control of environmental adaptation and productivity traits, and the design of a within-breed or crossbreed 'genomic selection' program. The platform should be closely linked with other phenotyping activities in CGIAR to address gaps in genome resources (Rec. 2), as well as with the already established ILVAC. Genome characterization of livestock will also provide information for the development of new animal genetic resources conservation strategies. Although the phenotyping platform is likely to represent a long-term goal, there is clearly a need for information on adaptive and productivity traits for livestock in their home environments and production systems.

There are now several next-generation sequencing and genotyping technologies that have been commercialized (e.g. Illumina HiSeq, ABI Solid, PAC BIO RSII), with new sequencing technologies becoming available or in the pipeline (e. g. 'electronic sequencing', Oxford Nanopore Technologies). There is little justification for the livestock biotechnology component to lead *de novo* sequencing projects of eukaryote genomes, which remains a complex task, including on the bioinformatic side. However, re-sequencing of livestock, vector and parasite genomes, high-throughput genome-wide genotyping, targeted sequencing, sequencing of small genome pathogens are – or will be soon – relatively well-established routine technologies. There is a need therefore for continuous investment in relevant technologies, taking into account that the private sector may represent in some case a cheaper alternative (Rec. 2). Also, there is a need to recruit and train staff particularly in bioinformatics skills to handle such data.

7. Following the model of ILVAC (http://cgspace.cgiar.org/handle/10568/29063), a platform represents a consortium for research, product and capacity development within a specific theme. The aim is here to facilitate achievement of research objectives and impact in the discovery-to-delivery pathway. In livestock biotechnology the platform will include typically and non-exclusively the following partners, BecA-ILRI Hub, CGIAR Research Programs, as well as national and regional academic, public, private and development sectors.

Reference collections

The need for reference samples, reference biological materials of known origins, and easy access to database information are increasingly underpinning the success of collaborative biotechnological research projects. Biobanking and database management are key elements.

ILRI is ideally placed to play a leadership role, with its close association with BecA being an advantage. The development of such an entity will require addressing IP (ownership) and biosafety issues in relation to national legislation (storage and distribution of samples). It is recommended that the ILRI biobanking, biological materials and database management platform be expanded and developed in partnership with relevant ILRI stakeholders. Importantly, this should remain a research platform storing tissues and semen DNA for research purposes – not a substitute for national biobanking facilities (e.g. for animal genetic resources).

Livestock biotechnological research: genetic modification

Until recently, there was no transgenic or livestock cloning project within the ILRI biotechnology program. The situation has now changed, with an ongoing project aiming to produce, through cloning, transgenic bulls of African cattle (Kenyan Boran) carrying a baboon *Papio* sp. gene (*APOL1*). *APOL1* gene is a trypanosome lytic factor acting against both cattle- and human-infective trypanosomes. The gene is not present in cattle. Human and baboon versions of the gene share 95% similarity. The research partnership involves ARIs in the USA (New York University and Michigan State University, on the construction of recombinant vectors and validation in transgenic mice), in the UK (the Roslin Institute, on the preparation of the bovine embryonic fibroblast transgenic cells) and ILRI (nuclear transfer, cloning and phenotyping of transgenic calves). Progress suggests that the project will be ultimately successful. Importantly, by focusing on indigenous livestock and bulls (expected to produce transgenic semen), an impact at farmer level may be anticipated in the medium term, at least in East Africa. Although farsighted, the project is an example of ILRI's comparative advantage. None of the cloning technologies were developed at ILRI, but ILRI state-of-the-art technological capacity meant that they were successfully implemented, as relevant, within the CGIAR institute in a short time period.

Over the past years, several examples of transgenic livestock animals have emerged, including transgenic salmon, pigs with greater milk production potential, mastitis-resistant cows and even chickens that do not propagate influenza. Project activities such as vaccine development and livestock cloning should be built up to form a livestock genetic engineering platform to ensure the delivery of new livestock genotypes for poor farmers.

Centers and CRPs should not be expected to take a leadership role in technological development, but they should ensure that once the technology is established it is quickly adopted and used within CGIAR. The commercial sector is the expected beneficiary of these projects, but so far there are no real applications in the developing world.

Also, the regulatory bodies have been in some cases reluctant to approve the commercialization of products from genetically engineered livestock following adverse opinions from the general public. Nevertheless, in the meantime the technology is advancing. An important example is the recent demonstration that genetic variants can be directly and efficiently introgressed into livestock genomes using a modified TALEN system, as shown in research performed under the leadership of a biotechnology company (Recombinetics, Inc.) through funding from the National Institutes of Health (Tan *et al.*, 2013). The technology is of direct interest to the livestock sector of the developing world, as it is not only of general applicability for interspecific introgression but also provides opportunities for intraspecific introgression

of alleles in livestock. In other words, the technology demonstrates that livestock genotypes that could have arisen from natural mating, albeit after several generations of backcrossing, can now be produced efficiently in one generation. Combined with the increasing knowledge of the functional diversity of livestock genotypes from the developing world, the technology may represent a major new avenue to improve the productivity of developing country livestock production systems. However, it remains to be seen how the new technology will be treated by national regulatory agencies.

It is therefore recommended that ongoing project activities involving recombinant DNA technologies (e.g. *APOL1* transgenic cow project) and livestock cloning (*APOL1* transgenic cow project) be built up to articulate a livestock genetic engineering platform within the livestock biotechnology program.

Recommendation 5: Establish a specialist group or advisory board within the CRP on Livestock and Fish to coordinate and support animal biotechnology activities across CGIAR.

Implementation of Recommendation 5

This group should work closely with the Biotechnology Group (Rec. 1) and would support:

- the development of a livestock genomic platform;
- the establishment of a reference collection of biological materials (biobank for livestock and pathogens) and database, which it would maintain;
- the coordination and prioritization of activities across CRPs to identify areas where resources could be most effectively deployed;
- the investigation of the feasibility, logistics and costs associated with establishing a livestock genetic engineering platform.

Bioinformatics

Introduction

Bioinformatics covers diverse topics – from the design and planning of field trials through to the analysis of images generated from high-throughput phenotyping systems (or even satellite images), through to the analysis of genome sequence datasets. The Centers and CRPs have only some of these capabilities in house; some are routine and generic tasks (such as field designs), but many bioinformatics tasks need to be outsourced or accessed through key partnerships. Across the CGIAR system there are strong and diverse capabilities in biometrics and biostatistics. However, within individual Centers and CRPs the capacity is limited and often specialized in specific aspects of bioinformatics. It does not appear that any Centers have the full spectrum of capabilities necessary for modern biotechnology programs.

Recent advancements of biotechnology have produced a large amount of data to support crop and livestock improvement, including MAS, genome-wide association studies, genomic selection, high-throughput phenotyping. Many of these advanced technologies are already in wide use, resulting in the need for Centers to process large data sets rapidly. These studies cannot be handled with PC-based small-scale computing. Consequently, Centers and CRPs need access, either in-house or through partnerships, to well-trained bioinformaticians with a strong foundation of high-performance computing. The issues to be solved include:

- biostatistics or biometric to support analysis of phenotypic data;
- large-scale data analysis, e.g. next-generation DNA sequencing, image data sets produced through high-throughput phenotyping;
- database to allow data analysis and retrieval by Center and CRP staff and partners in national programs or ARIs.

Large-scale data analysis

Bioinformatics analysis of next-generation sequencing (NGS) data will play a pivotal role in modern and near-future breeding. For example, millions of markers can be designed from a single line by genome sequencing and genotyping by sequencing is being deployed for many crops and livestock (Institute of Biotechnology, 2014). In addition to genome sequences, CGIAR should be prepared to cope with transcriptome, methylome and other '-omics' data. The survey of Centers (Table 2) indicated that nine Centers intended to develop either transcriptome or metabolome data sets, albeit at a small scale. To make such data useful, CGIAR bioinformatics teams will need an efficient analysis capability to develop data processing pipelines – or they will need to partner with groups which have this expertise.

Likewise, high-throughput phenotypic data are being produced for both crops (Araus and Cairns, 2014) and livestock, so that an efficient data processing platform is essential. Phenotyping, particularly field phenotyping, represents a major strength of Centers, and they have good capacity in field trial design, data collection, and special analysis. Their capability to manage the resulting data and present them in an easily accessible and usable form for national programs and other partners is less well developed. Over the next few years it is probable that the scale and complexity of phenotypic data will increase as new tools come online. These include large image files generated by a range camera systems covering visible, infrared, near-infrared, fluorescence and spectral reflectance, tomographic or X-ray images and even nuclear magnetic resonance devices. These types of images are being generated from systems ranging from microscope

cameras through to satellites covering leaf sections, roots or whole landscapes. As noted earlier in the section on phenotyping, Centers and CRPs will need to carefully evaluate the different techniques and focus on the methods that support their field-based or field-relevant phenotyping strengths.

In many cases the phenotypic information can be reduced to a set of numbers (plant biomass, greenness, temperature, etc.). However, the supporting images will require a suitable storage and retrieval system. A significant challenge will be linking such phenotyping information with genotype data, including sequence information and various other '-omics' datasets, such as transcript and metabolite profiles.

Many of the new breeding and selection techniques, such as MAS, genome-wide association studies and genomic selection, are dependent upon the efficient use of both genotypic and phenotypic data sets. The various problems involved in managing these large and complex data sets – ensuring the information can be analyzed and displayed in a suitable format and providing access to the appropriate information to research scientists within the CGIAR system, and in national programs and ARIs – are a major challenge but they not unique to the CGIAR system. This is a challenge being faced by many research groups and programs.

Developing international linkages

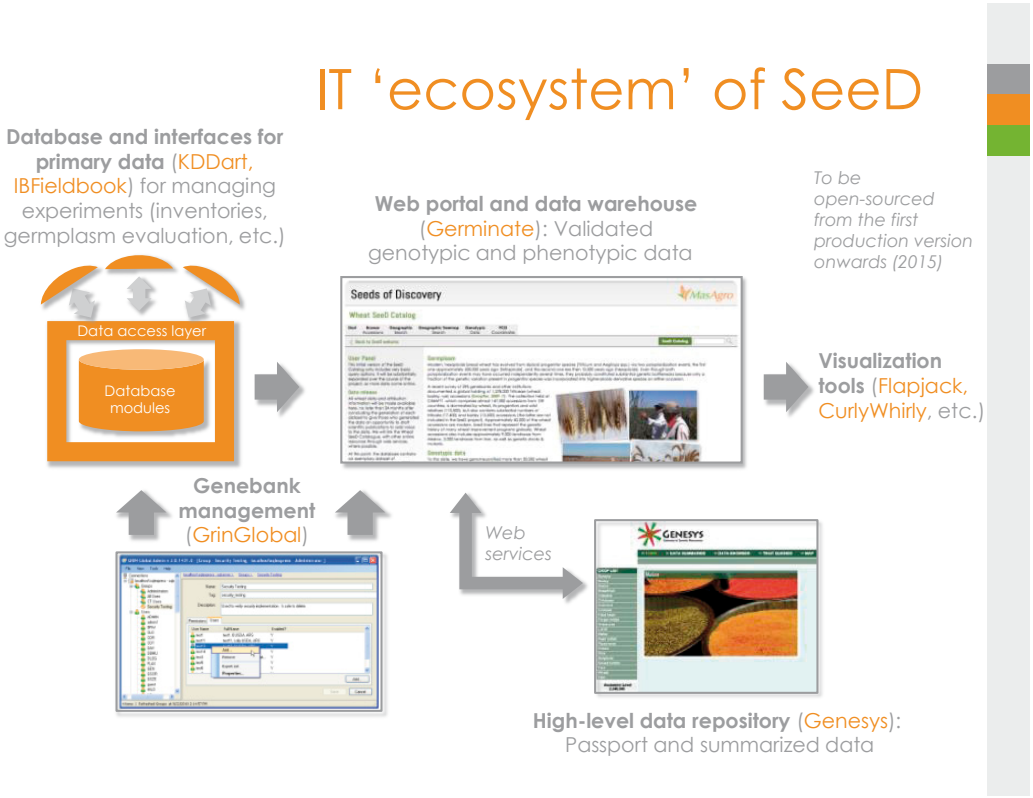
Today's demands on bioinformatics are increasing dramatically with the exponential growth of biological data. While the Centers have bioinformatics teams, the current capacity is not sufficient to support the demands of the non-bioinformatics users (i.e. the scientists). Hence, in addition to enhancement of the bioinformatics capacity, collaborative networks need to be developed inside and outside the CGIAR to strengthen the capability to effectively cope with bioinformatics problems. Several systems are under development both within Centers (such as the International Rice Informatics Consortium launched by IRRI in 2013 and the Saga system being developed by CIMMYT to support the Seeds of Discovery program) and through major national and international programs, such as the T3 database that supports the United States Department of Agriculture (USDA) T-CAP, Germinate[8] and iPlant[9] programs. The use of different data management and analysis tools is nicely illustrated by the approach used in the Seeds of Discovery program at CIMMYT (Figure 2).

A key objective in developing international partnerships will be to gain access to bioinformatics tools and resources and to ensure that data being generated by public-sector programs, particularly in Europe and North America, are accessible to CGIAR partners. For example, extensive genotypic and phenotypic data sets for wheat and barley are available through the T3 database. Similar programs are in place for maize, soybean, sorghum, sheep and cattle. A dispersed model framework for linking information derived from Center and CRP activities with these international databases will be important.

Since many of the CGIAR bioinformatics teams do not have sufficient resources for massive data analysis, one or two teams could possibly develop model bioinformatic systems for data entry, analysis and display, and retrieval. The bioinformatics network would allow bioinformaticians based in Centers or CRPs to link to the larger development teams. A common database format should be possible given the similarities in the objectives of Centers and CRPs – despite the differences in their targeted commodities or environments. Common formats and tools within the data management systems would also reduce user confusion and assist in the smooth retrieval of data. For this approach to succeed, the bioinformatics team network will need to play a coordination role that cuts across the Centers and CRPs. Holding one or two meetings or workshops a year for the bioinformatics teams may provide a useful way to more efficiently develop this network.

8. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1255981/
9. http://www.iplantcollaborative.org/about-iplant/powered-iplant

Figure 2. The bioinformatics platforms being developed by the Seeds of Discovery program



Source: Peter Wenzl, CIMMYT.

Coordination of bioinformatics activities

A network of the CGIAR bioinformatics teams should be developed so that teams can consult or collaborate. Under this network, the teams can share common tools and analysis pipelines for the same or similar bioinformatics studies to avoid redundant efforts. For example, the Integrated Breeding Platform (IBP)[10] being developed by GCP is developing tools to support field trial design and phenotypic data analysis. This forms a pipeline of data analysis that is relevant to most crops.

In addition to the network construction among the bioinformaticians at Centers and CRPs, each Center should establish national or regional collaborations with other institutions that have the capacity to conduct large-scale bioinformatics. Since CGIAR is unlikely to develop state-of-the-art software tools, the bioinformatics teams should maintain up-to-date information about such software and adapt it for their own purposes, with support from collaborating institutes.

While outsourcing should be actively explored, it should be noted that this may lead to the loss of expertise in bioinformatics within Centers and CRPs. Appropriate training of bioinformaticians should be carried out in the course of collaborations with external partners or within research networks.

Meeting end-user needs for data access

In general, breeders are not familiar with bioinformatics data, so bioinformaticians should be aware that even though large amounts of data are passed to users, they are not necessarily satisfied with the information they receive or the ease of access to information.

10. https://www.integratedbreeding.net/

Users' requests are, in many cases, relatively simple; breeders who need markers may only need to map DNA sequence data to a reference genome and design appropriate markers and primers. Bioinformaticians should remain in close contact with potential users and discuss proposals for developing new data management, display and retrieval tools with the users.

Supplying information in a format and system that meshes directly with breeder needs would provide an ideal opportunity for Centers and CRPs to deliver outcomes to their own breeding programs and to NARS. The IBP has moved well down the path of developing such a system. The IBP is an interesting model for linking genomic data directly to breeders' needs, and its current emphasis on tools to support breeders places it apart from many other data management tools being developed in ARIs. Given the experience gained in developing the IBP and the progress made to date, it would be unfortunate if this were not maintained when the GCP concludes. Exploring options to maintain development and delivery of the IBP should remain a high priority.

Database development

Many of the databases used within CGIAR Centers have been developed independently and as a result they are dispersed. Intensive reorganization of the databases is recommended within and between Centers. Related data should be linked and common analysis packages developed.

Similar data can be collected and integrated in a single database. However, physical centralization of such data may not be realistic in many cases due to the size of some of the data sets and the need for rapid data transmission between sites. If so, a distributed database system that integrates different databases virtually is likely to be the best option. Many of the major international programs are following the dispersed database models, and it may be most appropriate for the databases developed within CGIAR to link into or even become a component of these dispersed databases.

Open access, storage and security

The data produced and processed should be shared within a Center, CRP or across CGIAR, and should eventually be open to the public (G-8, 2013). CGIAR has committed to an open-access policy for data and information (CGIAR, 2013a). However, data still being processed in preparation for publication or analysis may need to be kept closed for some period, and access to the data will need to be controlled appropriately. CGIAR is still developing the implementation framework for open access, and future developments in database design and access will need to pay close attention to these developments (CGIAR, 2013b). Recent studies have shown that open access does lead to increased data use and higher citations; both would be good outcomes for CGIAR and researchers (Piwowar and Vision, 2013).

Although petabyte class storage is urgently needed, Centers are unlikely to have access to such a capability in the near future. Therefore, large data, such as NGS, can be hosted on a cloud-style storage system provided by the private sector or a collaborator at a public institute. The following two critical issues should be considered: (i) for confidential data, secure data transfer should be guaranteed and the data should be safely stored, and (ii) all data should be backed up and preserved appropriately so that accidental data losses will be avoided. Data storage is decreasing in cost and backup storage is now offered by several service provides. The cost and feasibility for effective data protection should no longer be a major concern.

Recommendation 6: Establish a CGIAR bioinformatics network.

Data management is an area of critical importance across the CGIAR system, and effective data acquisition, analysis and access systems will be needed if Centers and CRPs are to take on a leadership role in

biotechnology development and delivery. There is good capability both within Centers and CRPs and with partners to develop a strong system.

Bioinformatics activities within the CGIAR system present special issues. Importantly, bioinformatics is critical not only for genomics research but for many other activities across Centers and CRPs. Therefore, the Panel recommends establishing a dedicated coordination group made up of bioinformaticians from across the CGIAR system and carefully selected external advisors. The role of the bioinformatics group will be to:

- liaise closely with the Biotechnology Group;
- establish a bioinformatics network that links together all bioinformatics groups with the CGIAR system;
- build international partnerships to access and develop databases, analysis tools and data storage capacity;
- establish data quality assurance protocols for all data types entered into CGIAR databases;
- ensure data management systems meet user needs (covering data acquisition, analysis and access);
- develop procedures to improve data capture from Center and CRP projects and staff (e.g. by supporting the development of electronic data capture devices and developing common data standards);
- reorganize existing databases to improve access and develop a common database system for use across CGIAR;
- establish a common policy for data sharing and storage that is consistent with the open-access policy of CGIAR.

Implementation of Recommendation 6

The development of an open-access data policy within the CGIAR system provides an ideal opportunity for reviewing all aspects of data acquisition, analysis and access. It must be recognized that the CGIAR will not be the world leader in developing the specific components of an open-access data management system. However, CGIAR can be leader in the integration and use of data across the spectrum from research to breeding and information delivery to NARS. This should be the focus of bioinformaticians and biometricians in the Centers and CRPs.

The development of a CGIAR bioinformatics network will need to be managed by bioinformaticians within the CGIAR system. Resources should be provided for an initial meeting of groups involved in bioinformatics, data management and analysis in Centers or CRPs. The meeting should focus on the most appropriate structure and objectives of the network and also develop a budget outline for maintaining an active network. Funding will be required to support a part-time manager for the network, to fund a communication strategy and to support meetings (most meetings could be conducted via video links).

An important early task of the network will be the allocation of specialist roles to the different groups within CGIAR and a consideration of the benefits of physical consolidation of bioinformatics capabilities.

The feasibility of bringing groups from outside the CGIAR system into the network should also be considered, and any budget implications for expanding the network or bringing in external experts should be flagged early.

Data management and access are a high priority across the CGIAR system, and these activities are also seen by donors and funding agencies as essential for effective development and delivery of research outcomes. Therefore, there are likely to be opportunities for dedicated funding to support the establishment of the bioinformatics network and for high-priority bioinformatics projects. The network should look to both external agencies and internal funding mechanisms to support its activities.

Biosafety policies

Introduction

A biosafety regulatory framework (or biosafety system) is the sum total of the policies, laws and practices that regulate the research, development, commercialization and post-market monitoring of GM organisms. The biosafety regulatory system is comprised of the written policies; domestic laws, regulations and institutions; and international agreements that regulate the development and approval of GM products.

Four key elements in the development and implementation of biosafety policies and practices are:

- written guidelines to define the structure of the biosafety system, the roles and responsibilities of those involved, and the development and review process;
- regulatory authorities that consist of trained individuals in the host country, with clearly defined responsibilities within the biosafety framework;
- an information system that ensures the biosafety evaluation process is based on up-to-date and relevant scientific information, that takes into account the concerns of the community, and that includes appropriate data management;
- a feedback mechanism to incorporate new information and revise the regulatory system as needed (Science Council, 2007).

The written guidelines may include the terms of reference of biosafety committees, or documents related to safety regulations in laboratories, in the field and in transit. Regulatory authorities may include both national and institutional committees or bodies involved in approving research. Information systems include public and institutional awareness materials as well as records and databases. The feedback mechanism should include the establishment of a responsible body and procedures to report on, monitor and adjust current research, events or regulatory systems.

The environmental release of a GM product should follow the biosafety process outlined in each country's biosafety regulatory framework, which should include a food safety and environmental risk assessment. A socioeconomic risk assessment may be required by some countries.[11] In order to ensure confidence in the research of Centers and CRPs, it is essential that institutions comply fully with the relevant biosafety requirements of each country where they operate or intend to release products (Horna *et al*., 2013).

A number of international conventions, agreements and guidelines govern the use of genetic resources and the related issues of biotechnology and IP rights. The Centers have developed and agreed on various policy instruments, guidelines and position statements to guide and validate their decisions regarding biosafety, genetic resources, biotechnology and IP rights.

Historical context

The Science Council has considered the issue of biosafety in the past. In particular, the 2007 *Report of the Biosafety Panel to the CGIAR Science Council on Biosafety Policy Practices of the CGIAR Centers* made 12 specific recommendations (Science Council, 2007):

1. Enhance CGIAR Center biosafety policies.

11. Article 26.1 of the Cartagena Protocol on Biosafety notes that inclusion of socioeconomic considerations is not a mandatory element of a functioning biosafety framework. However, many developing countries have, or are considering, requiring such an assessment.

2. Enhance capacity building in national biosafety policies and practices.
3. Strengthen Center capacity in biosafety practice and research through proactive approaches to biosafety.
4. Develop an integrated approach to the practice of biosafety in the Centers.
5. Establish a CGIAR system biosafety network.
6. Increase biosafety-related research by the Centers.
7. Publish and communicate results of biosafety research.
8. Prepare for forestry and fisheries biosafety issues.
9. Undertake more risk–benefit analysis.
10. Develop plans for preparing risk assessment dossiers for product approval.
11. Better address bioethical issues.
12. Initiate a CGIAR system-wide biosafety workshop to plan implementation of the biosafety panel's recommendations.

In 2006, the Science Council issued the final report on research ethics in CGIAR (Adair *et al*., 2006), which had been recommended by the aforementioned Biosafety Panel (even though the final Biosafety Panel report was issued after the report on research ethics). The Ethics Panel issued the following advice relevant to biosafety within the CGIAR: "Biosafety issues should always be handled through dialogue with the relevant stakeholders …, in order to choose means where the risk of harm to others or to the environment is acceptably low for all affected parties. National regulation of risks should of course always be respected" (Adair *et al*., 2006: 18–19).

In February 2009, the Science Council issued the report *Biotechnology, Biosafety and the CGIAR: Promoting Best Practice in Science and Policy*, which summarized the outcomes of a workshop held in response to the 2007 Biosafety Panel (Science Council *et al*., 2009).

Biosafety policies and practices

Many of the recommendations of the 2007 Biosafety Panel remain relevant today and, while progress has been made in strengthening the biosafety policies and institutions of the Centers, the findings from surveys and interviews demonstrate that the work of implementing these recommendations is far from complete. As a result, the Study Panel repeats in full three recommendations from the previous biosafety study and includes two additional recommendations that would further strengthen the biosafety capabilities of the Centers.

The 2007 Biosafety Panel recommended the establishment of a biosafety network that would allow the CGIAR Centers to share experience and expertise across the Centers. The Science Council endorsed this approach in the commentary to the 2007 Biosafety Panel report, noting: "[T]here may be a need for the Network to adopt the role of a 'central supplier of information'. Because of the increased scrutiny of transgenic breeding, preparation to meet regulatory standards will be a major part of the business" (Science Council, 2007: vii).

IFPRI's Program for Biosafety Systems has been the primary repository for biosafety policy and regulatory information within the CGIAR system. However, its work is conducted primarily as a service to other Centers or to international aid programs rather than as a central supplier of information or repository within the CGIAR system itself. As a result, the policies and procedures at each Center may vary in their quality of design and implementation.

Some Centers have partnered or contracted with organizations outside the CGIAR system for biosafety regulatory support. While there are undoubtedly good reasons for going outside the CGIAR system for such support, a 'central supplier of information' within the CGIAR system with the overall responsibility for biosafety programs across the Centers would ensure that GM research and commercialization are undertaken according to appropriate and consistent standards.

A number of centers of excellence for biosafety exist, providing support to development agencies, foundations and governments, in addition to the IFPRI Program for Biosafety Systems. These include the South Asia Biosafety Program implemented by the Center for Environmental Risk Assessment, which was established in 2007 by the International Life Sciences Institute Research Foundation, as well as the Donald Danforth Plant Science Center's Biosafety Resource Network. These organizations already collaborate on many biosafety projects and even share some personnel on a project-by-project basis.

In the 2009 workshop on biosafety, participants suggested that CGIAR could assist other public-sector institutions in providing regulatory services. Participants commented: "An agreed set of regulatory requirements, endorsed by multiple countries, might be necessary to avoid over-regulation and a corresponding rise in regulatory costs" (Science Council *et al*., 2009: 10).

Findings on biosafety policies and practices at and across the Centers

The current Panel reviewed the Center responses to the questionnaire, survey and interviews to arrive at summary findings and recommendations regarding biosafety practices in terms of biosafety science, research and capacity building at the Centers, as well as coordination across the Centers.

The main findings and recommendations are as follows.

- All Centers meet or exceed the capacity and requirements of their host country to govern the biosafety of GM products. Some host countries are still developing their biosafety governance frameworks.
- Most of the Centers are actively helping their host country to develop its biosafety governance frameworks.
- The Centers are currently focused on containing and confining GM products within projects under way in labs, glass/screen houses and confined field trials.
- Prior recommendations to establish biosafety policies across the Centers appear to be limited in their implementation.
- Centers use a range of partners to conduct biosafety support, including expertise inside and outside the Centers.

Trade considerations and global risk assessments

The development of new plant varieties, whether through the application of GM technology, conventional breeding or other molecular techniques, includes the risk that the research will not result in a viable commercial product. However, the application of genetic engineering techniques includes additional risks associated with regulatory approval, consumer acceptance and economic impact. While not all GM research is undertaken with the expectation that the final product will be made commercially available, given limited financial and human resources CGIAR Centers should focus their research on applications with commercial potential. There is a potential distinction between research undertaken to characterize genes or gene systems without the intention of developing a commercial GM product and research targeted to producing a GM product. However, these distinctions can become blurred over time and it may be more efficient to operate on the assumption that all GM research will lead to a commercial product.

Ideally, product development should focus on countries (i) where there is a clear **need** for the GM product, (ii) that have biosafety regulatory **capacity** in place, and (iii) that have expressed the political **will** or desire to adopt such technologies.

In the 2007 Biosafety Panel report, the Science Council endorsed the need for Centers to consider the regulatory requirements of some GM products (i.e. those intended for eventual release) at an earlier stage of research. The focus should be on the development of a full business plan outlining all aspects of regulation and pathways for outcomes, including the roles and responsibilities of the Centers and their partners involved in the release of the product (Science Council, 2007).

Business plans should consider the following factors:

- likelihood of success compared to alternative approaches
- timeline for development, including regulatory approval
- development cost, including regulatory approval
- likelihood of consumer/market acceptance
- potential for market or trade impacts or disruptions.

GM products currently under development by the Centers are being developed to meet the local needs of smallholder farmers or those with nutritional deficiencies and are not intended to enter into the global trading system. However, whether or not the GM products are intended to enter into international trade, the possibility exists that such products will appear accidentally in trade as a result of normal business practices. The unintended presence of GM material in a shipment or food product where it should not exist is sometimes referred to as 'adventitious presence'.

In November 2007, the Codex Alimentarius Commision (2007) *Ad Hoc* Intergovernmental Task Force on Foods Derived from Biotechnology reached consensus and produced an annex to the Codex Plant Guideline that addresses safety assessments in situations of low-level presence (LLP) of recombinant DNA plant material. Unlike adventitious presence, LLP situations relate to GM products that have completed a food safety review in at least one country.

As GM products developed by the Centers approach the market, it is essential that steps are taken to reduce the likelihood that such products will inadvertently enter international trade. While it is not possible to completely eliminate such possibilities, efforts should be taken to minimize LLP incidents, which may cause trade disruptions and undermine public confidence in the work of the Centers and partner organizations and governments. It could also lead to economic liability for partners along the value chain. By taking steps to reduce or eliminate trade disruptions, CGIAR Centers and their commercialization partners can enhance public confidence in the work of the Centers and partner organizations and governments.

In March 2012, representatives of 15 countries met to consider the problem of LLP of unapproved GM plant materials in trade. The Government of Canada proposed the creation of an expert group to conduct risk assessments of new GM products in LLP situations (Tranberg, 2013).

Such approvals by an independent expert group might provide greater confidence to trading partners regarding food safety, should products appear in trade. However, an expert group that conducts full safety assessments for GM products developed by public-sector research institutions for smallholder farmers in developing countries would be even more useful to the Centers. A full safety assessment would have two advantages over a limited LLP review. First, a full review would provide greater confidence to regulators in importing countries should the products inadvertently appear in trade. Second, the assessments would be

available to countries that are considering adoption of the GM product for cultivation, which might reduce the regulatory burden for approvals. A special funding mechanism would probably be needed to support this activity, but it could attract interest from donors in both the public and private sectors since it might reduce the need to seek approvals in each country individually.

Findings on trade considerations for GM products

The Panel reviewed the Center responses to the questionnaire, survey and interviews to arrive at summary findings regarding trade implications for GM research and commercialization in partner countries. The main findings are:

1. Centers recognize that the unintended release of research products or the comingling of approved GM products in trade could have negative economic and policy consequences for the Centers as well as their partner organizations and governments.
2. All Centers are implementing biosafety containment measures in labs, glass/screen houses and confined field trails to ensure that research materials do not inadvertently enter the conventional breeding and germplasm development programs.
3. A few Centers are in discussion with regulatory authorities in countries where regulated events might appear at low levels due to adventitious presence in grains or processed products but where these products have not been authorized for commercial release.
4. None of the Centers have the capacity to seek regulatory approvals in major export markets where the low-level presence of unapproved GM products might occur.

Intellectual property rights, liability and licensing

Introduction

Seeds and plant materials protected by IP can raise the cost of accessing new plant varieties, but they can also spur investment in the seed sector. IP, such as patents and plant breeders' rights, protects the rights of an inventor and plant breeder, but those rights should also be balanced with those of the farmer in order to benefit society as a whole.

The IP challenge for the development community is how to stimulate the development of new agricultural technologies, including GM, while ensuring smallholder farmer access to these technologies. Partnerships between CGIAR Centers and the private sector raise questions about farmers' right to save and share seed, as well as possible costs for products developed by the public sector.

CGIAR has made significant strides in the management and control of IP over the last 10 years. Particular progress has been made in just the last few years.

The 2010 report *Product Stewardship and Liability in the Context of IPR: Report of a Study* (ISPC, 2010) noted the challenges linked to the sustainable use and distribution of Center research products, with particular attention to regulatory and liability issues, including IP. The report highlighted previous reports, such as *CGIAR Research Strategies for International Public Goods (IPG) in a Context of Intellectual Property Rights (IPR)* (Science Council, 2006), *Liability of CGIAR Centers and NARS partners under intellectual property and biosafety laws arising from the supply of biological resources* (ISPC, 2010) and *Recommended Stewardship Framework for the CGIAR*. The recommendations from the Liability Study remain germane to our discussion and have been included under Appendix E.

More recently, CGIAR has undertaken efforts to put some of the prior recommendations into practice. For example, the *CGIAR Principles on the Management of Intellectual Assets* ('CGIAR IA Principles') (CGIAR, 2012a) were approved and adopted by the CGIAR Consortium in February 2012. The management of intellectual property or assets requires a careful balance between maximizing global accessibility and minimizing the risk of misappropriation and misuse, while maintaining commitment to international public goods versus leveraging the strengths of private-sector partners. These challenges are tackled by the CGIAR Consortium Legal and Intellectual Property Network (CLIPnet), a multidisciplinary group from the members of the CGIAR Consortium comprised of lawyers, grant managers and senior managers from genetic resources, communications and corporate services.

Related documents include:

- *CGIAR Principles on the Management of Intellectual Assets* (CGIAR, 2012a)
- CGIAR Consortium *Policy on the Management of Intellectual Assets*
- *Examples of Restrictions to Global Access to Maximize Impact* (CGIAR, 2012b)
- *IP Management to Facilitate Sustained Impact of CRP Research* (CGIAR, 2010)
- *The Intersection of Public Goods, Intellectual Property Rights and Partnerships Maximizing Impact for the Poor* (CGIAR, 2011).

The 2009 workshop on Biosafety highlighted the cost implications of accessing proprietary technology from the private sector as well as of the regulatory approval process, as an issue of central concern to

stakeholders. In some cases Centers have been able to negotiate royalty-free agreements for the use of private-sector technology, but concerns remain that there may still be costs. These concerns were reflected in the findings of the current Panel as well and are covered in the recommendations on planning and evaluation of GM projects.

Liability

In addition to costs related to IP, Centers are also aware of potential liability associated with the development of GM products and are taking steps to mitigate these risks through licensing agreements. Liability issues can arise due to damage caused by the use of agricultural technologies to persons, property or the environment; for example, damage that may result from the contamination of conventional seed and organic crop purity. Centers can protect technology donors from liability through indemnification provisions and warranty disclaimers in agreements. The Liability Study goes into some detail regarding mechanisms such as insurance and compensation funds to mitigate the risk of liability.

Organizations working to ensure such access to GM technologies include the following.

- The African Agricultural Technology Foundation (AATF), a Kenya-based initiative focused specifically on negotiating access to proprietary technologies and facilitating the delivery of the technologies to smallholder farmers in Sub-Saharan Africa.[12]
- The Public Intellectual Property Resource for Agriculture (PIPRA), a United States initiative with global reach that seeks to pool publicly owned and patented technologies for use by research institutions in developing countries.[13]
- The Centre for the Application of Molecular Biology to International Agriculture (CAMBIA), an Australian initiative that aims to provide technical solutions that empower local innovators to develop new agricultural innovations (Boadi and Bokanga, 2007).

Findings on intellectual property rights and licensing

The Panel reviewed the Center responses to the questionnaire, survey and interviews to arrive at summary findings and recommendations regarding IP rights, licensing and liability and the impact on GM product development.

The main findings and recommendations are as follows.

1. IP rights, liability and regulatory cost are seen as barriers to the delivery of GM products and may limit the establishment or expansion of partnering opportunities.
2. Centers are aware of the need to ensure royalty-free access to IP.
3. Centers have generally been successful in negotiating royalty-free access to materials but may need to accept liability associated with the release of the materials through indemnification clauses in licensing agreements.
4. Centers have sometimes looked to outside consultants for help in negotiating IP licenses and regulatory compliance.
5. Centers recognize the negative impact that strict liability would have on GM product deployment but have yet to include these considerations in their planning and priority setting for GM.

12. http://www.aatf-africa.org
13. http://www.pipra.org/

Partnerships and public outreach

Findings on partnerships and public outreach

The Panel reviewed the Center responses to the questionnaire, survey and interviews to arrive at summary findings and recommendations regarding partnerships and outreach. This is in terms of the types of partnerships and variety of partners, as well as interaction with stakeholders and outside organizations as factors contributing to or detracting from the success of GM product development.

The main findings and recommendations are as follows.

- Centers are currently engaged in a wide range of partnerships with NARS, nongovernmental organizations (NGOs) and private-sector partners.
- Centers generally agreed that a close partnership between CGIAR Centers and NARS was vital.
- Centers have provided significant capacity building and knowledge transfer to partner organizations.
- Consultations identified the importance of maintaining transparency and dialogue with partner organizations and interest groups in order to lay the groundwork for the Centers to be able to maintain their good reputation and exercise a positive role.
- Opposition to genetically engineered crops from some NGOs has had negative impacts on partnership activities.
- IP rights, liability and regulatory costs are seen as barriers to the delivery of GM products and limit the establishment or expansion of partnering opportunities.

The Centers engage in a wide variety of partnerships, both within CGIAR and with partners outside the Centers, to enhance crop development and dissemination. This occurs with respect to development of conventional varieties as well as those that have been genetically engineered.

Over the last 10 years, there has been an expansion of partnerships among the Centers and with outside partners in GM crop development, particularly on work related to environmental and food safety evaluations. (Spielman *et al*., 2010, examined 75 PPPs in a 2010 study on the extent to which PPPs can overcome market and institutional failures that limit technology development and adoption.)

The 2007 Science Council Biosafety Study recommended that its findings: "be discussed at a workshop involving members of the CGIAR Science Council, the Biosafety Panel, representatives of the CGIAR Centers, their R&D partners and other stakeholders, including national regulators, policy-makers, civil society, farmers and consumers."

As a result, a report from the workshop, *Biotechnology, Biosafety and the CGIAR: Promoting Best Practice in Science and Policy*, was issued in February 2009 (Science Council *et al*., 2009).

The workshop examined partnerships with various stakeholders, including NARS, private-sector organizations and other organizations. Participants noted that one of the most critical issues in GM product development for Centers and other public-sector institutions is the cost for meeting regulatory requirements, and how the public sector will be able to meet them. GM crops are also expensive because of the transaction costs and the human time invested in helping to establish regulatory procedures with partner governments. Over-regulation, experienced in some instances, quickly increases the regulatory costs in meeting requirements.

In comparison with many GM crops being developed by CGIAR Centers, IRRI has a much higher visibility as a partner institute for the Golden Rice project. Private-sector partners have taken a relatively low profile in the development of Golden Rice.

Partnerships with the private sector raise important questions about how CGIAR research outputs are disseminated to the public. In addition, when the public sector takes the lead on projects, it also has the responsibility to increase public and consumer awareness of the involvement of public-sector research institutions in GM product development. Consumer-friendly versions of technical reports (that are already available internally) or summaries should be made public.

Regarding GM research, it is difficult to find the right balance between increasing visibility for the public and being sensitive to the media reaction. A proactive approach is necessary to respond quickly to public questions about GM research, including anticipating media reaction to the achievement of research or regulatory milestones.

Recommendation 7: Establish a system-wide biosafety network to share experiences, expertise, and scientific and financial resources for biosafety across the CGIAR system.

The network should take responsibility for addressing the issues listed below. Many of these reflect recommendations made by the 2007 Biosafety Panel, but they remain highly relevant and should receive further consideration.

- Centers should continue to develop biosafety policies governing research, technical analysis and transparent, participatory deliberations on the biosafety of their research and proposed releases of GM products, aimed at achieving scientifically reliable and publicly trusted decisions about whether a given GM product developed or tested by the Centers is sufficiently safe and beneficial to release (see also Rec. 2).
- Develop a comprehensive approach to biosafety that integrates biosafety research, risk analysis, post-release monitoring, and feedback to inform future decisions about the use of GM in different situations.
- Serve as a clearinghouse for biosafety policies, best practices, training and support that would be available to the Centers as well as to partner countries and organizations. Such a clearinghouse could lay the foundation for a global alliance on biosafety that would make such information available to all developing countries and public-sector researchers and partnerships.
- Continue to support their partner countries in developing scientifically sound and publicly credible biosafety policies, in building national capacity for framing regulations, and in implementing and monitoring them.
- Foster the skills required for the preparation of dossiers of information on individual GM crops, which will form the basis for decisions by regulatory authorities. The Centers' activities in capacity building should be better coordinated with other bilateral and international programs.
- Enhance media and public outreach to promote transparency and public understanding of new agricultural technologies, including genetic engineering, in addressing global challenges related to food security, poverty and climate change through early consultations with farmer organizations, local and regional officials where field trials may occur, and public meetings (see also Rec. 2).

Implementation of Recommendation 7

This recommendation aligns closely with the recommendations from the 2007 Biosafety Panel report (Science Council, 2007). An analysis is needed to understand why the 2007 recommendations were not fully

implemented. This could be accomplished as part of the overall audit of biotechnology across the CGIAR system (Rec. 2), since several Centers have made significant advances in developing biosafety strategies while others have not.

The potential role of the CRP on Policies, Institutions and Markets (CRP-PIM) in leading and managing the biosafety network should be evaluated and the resource requirements documented. The primary aim should be to establish a base level of support that Centers and CRPs can build upon and to avoid further polarizing the biotechnology debate, both within the CGIAR system and with donors and NARS. For some Centers, little support will actually be needed but others clearly require assistance. There is currently considerable sensitivity in several Centers and CRPs to the assignment of biosafety issues to alternative groups including CRP-PIM. Therefore, the review process and network establishment must be handled carefully and with full consultation across all the groups engaged in biotechnology, particularly in GM research.

Many of the sites where GM crops or animals will be evaluated are managed by national partners. The biosafety network must address the needs of NARS partners in addition to supporting activities within the CGIAR system. Several agencies both within and outside the CGIAR system already offer training and support programs on various aspects of biosafety policy, regulation and stewardship. These programs are not all of a consistently high standard and the biosafety network will need to provide advice on those programs that are most appropriate to the needs of Centers, CRPs and NARS.

Recommendation 8: Address the need for global risk assessments of GM products from CGIAR Centers.

The CGIAR should consider the trade implications of commercialization of GM technologies whether the GM crops are intended for trade or not. To reduce the risks of trade disruptions, CGIAR should promote the development of an international expert group to conduct food safety risk assessments consistent with international standards for GM products, developed specifically for developing countries and not intended to enter into international trade.

This would provide countries with a consistent science-based risk analysis on which to base risk-management decisions. Centers have neither the funds nor personnel to seek regulatory approvals in major export markets for the developing countries where their GM technologies are likely to be commercialized. As a result, liability for trade disruptions will be an important consideration in the commercialization of these products. An expert group could be modeled after the Joint FAO/WHO Expert Committee on Food Additives (JECFA) using the Codex Alimentarius Plant Guidelines to provide consistent, transparent and predictable assessments.

Implementation of Recommendation 8

The biosafety network should take the lead in determining if a global approval strategy is feasible and desirable. This evaluation could be conducted through the CRP-PIM.

Training and capacity building

Training

Training and capacity building are key activities of Centers and CRPs. In the area of biotechnology there is high demand from national programs to ensure their staff are trained in the new techniques for crop and livestock improvement. Expectations of new technologies are often higher than actual results, and training must ensure that trainees leave with a clear understanding of the opportunities, limitations and practicalities of using the new technologies. Given the rapid changes that are occurring in nearly all aspects of biotechnology, it is becoming increasing difficult for organizations to offer comprehensive up-to-date training programs. An outcome of outdated or poorly structured training can be that trainees return to their home organization with misdirected prioritization of the relative merits of biotechnological compared with alternative approaches.

The Panel noted that some Centers offer training in aspects of biotechnology for which they have little or no experience themselves or do not have the appropriate facilities to ensure high standards of training are met.

In many cases Centers and CRPs may be able to link to an established training program or a skilled external partner who can work with them in developing the training activity or share in the actually training. If formal links can be established to universities, it may be possible to provide formal qualifications (such as graduate certificates).

The wide availability of internet access offers the opportunity to deliver training programs remotely and also to target training to specific environments. Where appropriate, Centers and CRPs should include remote learning techniques as a component of their strategy for technology delivery.

Many universities and other organizations now develop and offer modules for training in many aspects of plant and animal breeding and biotechnology. There are also several coordinated programs that link together multiple universities to share materials. For example, the Plant Breeding Training Network brings together the resources of seven universities to develop and deliver training modules.[14] In some cases Centers already have links to these types of programs, but this could be greatly expanded and possibly linked to an accreditation system so that students receive a formal award after successful completion of a series of training activities. Importantly, in both North America and Europe training is regarded as an important component of large genomic and genetic programs; for example, T-CAP has established a highly successful web-based training program that is accessed by many breeders and researcher in NARS.[15] This provides an opportunity Centers and CRPs to link into well-developed capacity-building systems.

Recommendation 9: Establish an accreditation system for training courses targeted to biotechnology.

Each biotechnology-related course or workshop should be subject to independent scrutiny by external advisors to ensure that it is taught by appropriately skilled staff, contains reliable and balanced information, and addresses the needs of the target audience.

The accreditation process would provide an opportunity for the identification of gaps or weaknesses in training programs.

14. https://www.integratedbreeding.net/plant-breeding-training-network
15. http://passel.unl.edu/communities/pbtn

Implementation of Recommendation 9

The simplest method for implementing this recommendation and ensuring accreditation is to link the Centers' or CRPs' training courses to reputable academic institutions that are able to offer an academic qualification, such as a graduate certificate, diploma or similar. However, in the long term there should be coordination across Centers and CRPs so that they can support each other in providing high-quality biotechnology training and, at the same time, build an international partnership in biotechnology training that involves ARIs, universities and the private sector (see also comments under Recs 1 and 2). These linkages would also provide an opportunity for placement of trainees in ARIs as part of the capacity-building program. Providing trainees with recognized academic qualifications would again be highly beneficial in attracting students and ensuring a high standard of training.

The monitoring of developments in biotechnology training and the establishment of an internationally recognized accreditation system should be undertaken by the Biotechnology Group. This recommendation could also be integrated in the implementation of the new CGIAR strategy and the systems approach to capacity development being proposed for the new Strategy and Results Framework (SRF). Centers and CRPs may wish to opt out of the accreditation system, but such programs should be given a low priority for funding, as they are likely to decline in relevance as students and donors transfer support to the internationally recognized system.

Staff development

The CGIAR system is built around highly skilled and dedicated staff. Ensuring that Centers and CRPs are seen as preferred employers for young scientists is critical in continuing to attract the very best scientists into CRPs. Scientists tend to be highly mobile, often spending periods during their careers in different countries and different organizations. Young scientists require tangible outcomes from their research in order to be able to advance their careers, either within the CGIAR system or if they choose to move to research or academic positions in their own countries or elsewhere. Publications in high-profile journals are still regarded as a key criterion for advancement in science (*Nature*, 2010). Therefore, building collaborations that support career development are of considerable importance.

Many aspects of modern biotechnology require access to expensive facilities, resources and large research teams. These are not always available within the CGIAR system, nor are they appropriate for the core activities of Centers and CRPs. As outlined elsewhere in this report, it is important that Center and CRP programs build on their areas of core expertise to leverage research collaborations and partnerships in some of the cutting-edge areas of biotechnology.

Recommendation 10: Use external linkages and research partnership to support staff development.

Collaborations with ARIs should be structured so that Center and CRP staff are able to gain training and actively participate in cutting-edge research to help expand their career options.

There are a number of ways to achieve this outcome. Opportunities for active engagement by Center and CRP staff with ARIs in particular should be exploited. Examples include:

- Identifying key ARI partners and actively engaging them in project development
- Joint appointments of staff
- Co-supervision of PhD students
- Joint development and delivery of training programs (see Rec. 8)

- Secondments or sabbaticals of Center and CRP staff at ARIs, and vice versa
- Co-authorship of publications arising from collaborative projects to ensure that Center and CRP staff provide intellectual rather than just technical input into joint projects
- Actively seeking participation in major national and international research projects.

Implementation of Recommendation 10

The Panel acknowledges that this recommendation is largely a reflection of activities and support systems already in place in most Centers and CRPs. However, there is considerable opportunity to expand the programs that link CGIAR scientists to groups in ARIs and to improve the engagement of researchers in joint research and training activities. Dedicated funding from the Consortium Office to support these exchanges or new programs with donor countries could provide an opportunity to build on the current activities. In recent years, there has been increasing interest by the private sector in building research collaborations with Centers and CRPs. These interactions could provide an opportunity for the secondment of CGIAR scientists to the private sector and vice versa.

Implementation plan

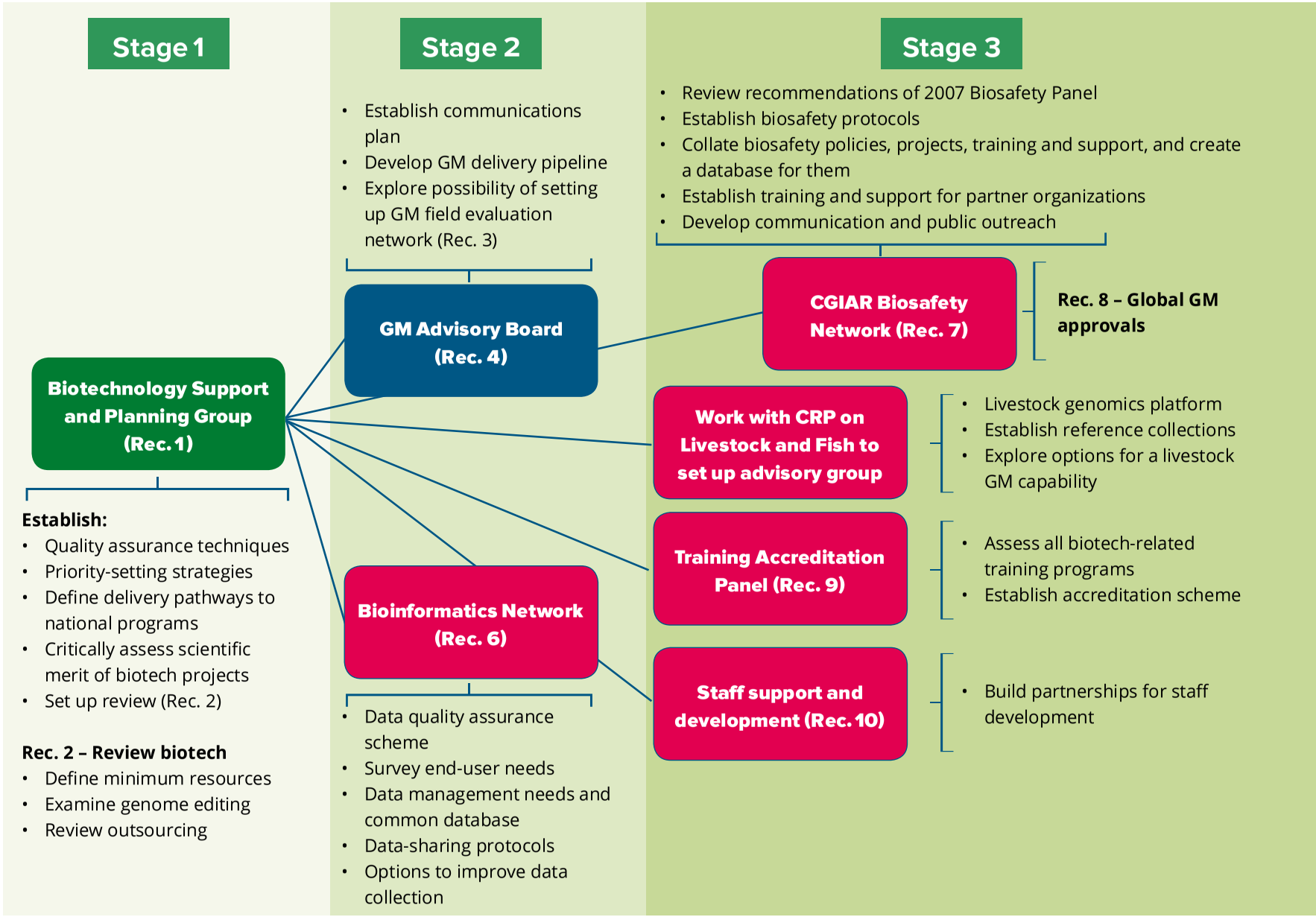
The recommendations presented in this study report are aimed at helping CGIAR improve its internal management of biotechnology research and delivery processes. Many of the suggestions build on activities already under way within Centers and CRPs and should not be too onerous. However, the study did identify some significant problems in some aspects of the current biotechnology strategy, particularly with respect to the development and delivery of GM crops and livestock. These need to be addressed as soon as possible since they are not only taking valuable resources away from higher-priority areas, but also because they could pose reputational or other risks to CGIAR. The Panel also noted that several of its recommendations mirror those of previous studies, indicating a reluctance within the CGIAR system to address some of these problems.

An implementation plan has been proposed for all recommendations, and it is summarized in Figure 3.

The Panel has recommended the establishment of a series of coordination and advisory groups. The first (Stage 1, Fig. 3) should be the establishment of a CGIAR-wide biotechnology support and planning group ('Biotechnology Group') (Rec. 1). This group would require a small budget to be able to arrange meetings and to bring in one or two external advisors, and it could then take primary responsibility for addressing the broad strategic issues raised in this report. The group should also institute a scientific review of biotechnology capabilities and needs (Rec. 2). Importantly this group would oversee the establishment of a GM advisory board (Rec. 4) (Stage 2, Fig. 3), and provide input into phenotyping developments (Rec. 3) and the CGIAR bioinformatics network (Rec. 6). In Stage 3 (Fig. 3), a CGIAR system-wide biosafety network (Rec. 7) should be established by the GM advisory board. A prime task of this group will be promotion of global GM risk assessments (Rec. 8). The Biotechnology Group should also work with the CRP on Livestock and Fish to address the needs of animal production industries (Rec. 4). The final establishment tasks of the Biotechnology Group will be implementation of the training and staff development recommendations (Recs 9 and 10).

Under this structure, Centers and CRPs would remain in control of the overall biotechnology strategy through their representation on the Biotechnology Group. The Group would also act as a channel to feed information and decisions made by the other groups back into their organizations.

Figure 3. Implementation plan for recommendations contained in this report



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Appendices

Appendix A

Summary of CGIAR biotechnology e-consultation, 7–17 June 2013

The e-consultation ran for 10 days and the discussion was divided into four topics: (i) the objectives of the study; the two broad areas of focus – (ii) genomics/bioinformatics and (iii) GM – and (iv) approaches to conducting the study. A kick-off message initiated discussion on each topic.

There were 75 participants. Twenty messages were posted, not including messages from the organizers of the consultation. There were no specific suggestions for changing the objectives of the study or the two main focus areas; however, there was support for examining the integration of biotechnology activities across CRPs for synergy. The discussion centered around generic issues regarding biotechnology in general and GM in particular. Several participants suggested additional areas that, in their view, required attention. The Study Panel will take the suggestions into account. However, the study must remain sufficiently focused to be feasible and useful.

Ideas from the contributions are grouped by main topics.

Genomics/bioinformatics

- The comparative advantage of CGIAR is mainly to ensure the use of genomics technologies as an integral part of breeding, rather than for basic science.
- NARS capacity is an essential question and requires that CGIAR be well equipped. Enhancement of modern genomics and breeding approaches is CGIAR's role and requires human and infrastructure capacity enhancement (several comments) in the continuum of genomic data analysis, decision support, databases and modern breeding.
- The power of bioinformatics for gene/marker discovery is likely to reshape plant breeding.
- Support for genomic selection to be included in the scope of the study, as well as other '-omics' tools that complement genomic selection. CGIAR's experience and role in association studies should be analyzed.
- Many participants noted that all of the genomics methods described for crops are also available for livestock and fish.
- While the choice of technologies should be driven by the problems to be solved, CGIAR needs to capitalize on new discoveries and appreciate serendipity.
- Issues regarding outsourcing generated some comments, including that occasional needs could be met using outside services and some level of consolidation of services may be needed. Consolidation may apply to any advanced technologies and should be discussed.
- Tools derived from genomics and bioinformatics are essential to modern biotechnology. CGIAR cannot be competitive in developing them, but outsourcing runs the risk of loss of expertise, capacity and opportunity.
- Genotyping for routine breeding is best done in a decentralized way at breeding institutes, as there is no delay and no difficulties in sending germplasm/DNA.
- CGIAR needs a strong analytical pipeline (analysis of NGS data and use in molecular breeding) for meeting the demands of breeders in NARS.

- Bottlenecks related to data will need to be looked at, as well as how to link current data. With the ongoing activities in commodity CRPs on genomics analyses, the issues of data storage, database management and bioinformatics analysis should be included, drawing from successful examples in setting up and running genomics and bioinformatics platforms.
  - Attention should be given to high-throughput genotyping, converting genomics data into useful knowledge for breeding and making use of CGIAR's access to unique genetic diversity.
  - The application of biotechnology in tree species has not progressed as with food crops and was not much discussed, despite its potential.
  - Crop protection and plant health improvement should also be included in considering the use of biotechnological tools.
  - Understanding pests/pathogens and mechanisms of resistance, and diagnostics related to plant protection are largely unexploited areas and are urgent for maintaining resilience.

Genetic modification

- The GM component should include everything that contributes to responsible development of GM technologies all the way to use (IP rights, risk assessment, advocacy and stewardship). Also, coexistence (cultivation) and segregation (supply chain) issues should be considered, especially how they can be implemented in smallholder settings.
- Regulatory and IP issues and negative public perception (i.e. the general public in the European Union and activist groups around the world), and export market issues are as important as scientific and technical challenges. Acceptance among groups other than farmers is lacking (i.e. groups outside CGIAR's stakeholders). The international dimensions of GM should be considered.
- It was suggested that the study should discuss in some detail: IP issues, both for the inventor and the user; CGIAR's role in science-based regulatory assessments and an overview of the situations regarding GM acceptance, particularly in Africa; and the social and ecological impacts of GM across adopting countries. There is ongoing work in CGIAR on public-sector proof of concepts in transgenics and commercialization through partnerships with the private and public sectors, including developing models for product stewardship. International regulatory requirements also affect CGIAR's mandate.
- Enhancing dissemination of GM (and other) technologies requires an understanding of political economy and institutional issues around R&D – science, evidence and facts are not sufficient. There was some pessimism as to whether CGIAR will be able to influence the 'battle' about GM, with the debate becoming more negative.
- Contrary to its earlier positioning on the science-based application of GM, CGIAR has become silent in responding to misconceptions and ill-guided reporting on GM. This has had a negative impact on CGIAR's R&D. Several comments noted that CGIAR should demonstrate the utility of GM for public goods and that its passive stance should change.
- What drives the passive stance in CGIAR regarding GM technology, particularly since economic evaluations are in support of the technology as a tool for breeding purposes? The study should address the public perceptions within CGIAR's stakeholder context and from its strong scientific and public goods position. CGIAR is an example of focusing on pro-poor traits and the humanitarian mandate.
- Studies will be made available by IFPRI on the state of biotechnology in Africa, GM technologies and status of capacity in selected African countries.

- The study should look at the role of NGOs, donors and other agents in shaping public opinion, on the one hand, and affecting regulatory issues on the other hand.
- Non-crop GM deserves some attention – e.g. environmental remediation and livestock health/vaccine vehicles. For livestock research, issues of food safety and public health concerns are important.
- There was agreement that the study ought to include GM technologies such as gene discovery and evaluation of transgenics.
- The study should consider CGIAR's position in an area where the private sector is active in developing and using new technologies.
- Non-GM genome technologies with potentially no regulatory hurdles should be studied with respect to the extent that they work for CGIAR crops. They should definitely be included in the analysis, including scenarios for regulatory frameworks for which decisions are not yet made. Next-generation sequencing will change the dynamics of this research and metagenomics (also GM).

Phenotyping and other areas

- Phenotyping is a large area and may require a study of its own. In this study some coverage will be needed.
- Field-based phenotyping is in the interest of CGIAR and NARS, and cost-effective phenotyping should be included. Choice of sites (representativeness) and partners are key in field phenotyping. Can CGIAR access private-sector locations?
- Field phenotyping is not sufficient; other approaches/technologies for environmental cues are needed. How to secure accuracy and superior capacity? Centers of Excellence in phenotyping?
- There was a suggestion to consider high-throughput phenotyping, including different potential technologies.
- In phenotyping, technology must serve the needs.
- Does CGIAR have capacity and does it need to have capacity on the more upstream technologies, for instance in phenotyping (capacity issues also apply to bioinformatics)? How far the should CGIAR go in equipping itself with sensing gadgets in the upstream, where pipelines for the applications are very long.
- *In vitro* technologies for vegetatively propagated crops in the CGIAR context is important in Sub-Saharan Africa.
- In the future, microbiomes will be important regarding e.g. epigenetics and symbiotic relationships among organisms. The issues include: coverage of CGIAR breeds and crops and their wild relatives, links with global initiatives, the critical role of public databases and metadata, and overcoming the challenges of phenotyping – particularly with livestock and trees, which require long generation times.

Partnerships and capacity

- Capacity building and awareness creation about the benefits of technology is extremely important to improve adoption rate, otherwise benefits will not be forthcoming.
- Capacity building should not be restricted to genomics and bioinformatics, but should cover a higher level of biosciences, responding to demand.
- CGIAR needs to be a strong interface between ARIs and NARS.

- It is important to consider the mechanisms for partnerships, given that technology advances very rapidly.
- In livestock health, more interaction is needed between the veterinary and medical communities. Private-sector involvement is essential, but challenged by IP issues.

Appendix B

Centers' Position Statement on Biotechnology (1998)

Given the immensity of the long-term food security and environmental conservation challenges confronting countries of the South, the Centers firmly believe in the following propositions.

- Biotechnology must be viewed as one of the critical tools for providing food security for the poor.
- The Centers advocate the prudent application of the full range of biotechnology tools to achieve substantial and sustainable growth in agricultural productivity in poor countries. These tools include, but are not limited to, molecular markers, genetic engineering and recombinant vaccines.
- The Centers view biotechnology as an important means for ensuring environmental protection over the long term.
- The Centers have a clear comparative advantage in ensuring access by the countries of the South to the advanced tools of biotechnology. This advantage accrues by virtue of its present credible mass in biotechnology, its global network of partnerships within and among countries of the South, and its increasingly close linkages to advanced research institutions of the North, both public and private.
- Given the extremely rapid pace of new developments in biotechnology, the Centers are committed to increasing their partnerships with ARIs, both public and private, North and South, to ensure ready access of Center scientists and our partners in the South to advanced technologies.
- The Centers make adequate investments in the arena of biotechnology in order to: (1) maintain their own credible scientific mass, (2) be proactive in assisting countries of the South to establish effective biosafety regulations, and (3) contribute substantially to developing the human capital needed to ensure the judicious application of appropriate biotechnology tools to important food security and environmental problems.
- The Centers are firmly committed to the application of genomics (molecular genetics, molecular markers) for immediate use in better understanding and manipulating the genomes of plants, animals and their pathogens and pests.
- The development and deployment of transgenics (via genetic engineering) is seen by the Centers to provide important options for meeting the food security and environmental challenges of the future.
- The Centers will carry out all of their activities in the arena of biotechnology under high standards of appropriate and approved biosafety regulatory frameworks, within both individual countries and institutions. The Centers will seek partnerships with institutes that have such frameworks in place (thus our commitment to policy and capacity building in this area).

Source: SGRP. 2003. *Booklet of CGIAR centre policy instruments, guidelines and statements on genetic resources, biotechnology and intellectual property rights*, volume II. Rome, System-wide Genetic Resources Programme with the CGIAR Genetic Resources Policy Committee (SGRP) (available at http://library.cgiar.org/bitstream/handle/10947/203/sgrp_policy_booklet_2003.pdf).

Appendix C

List of discussants

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Appendix D

Recommendation of the CGIAR Science Council workshop on Genomics Research in CGIAR: effective means of establishing platforms for genetic research

Different genomics technologies will follow different paths for delivery to breeding programs. Several technologies, such as genotyping, sequencing, proteomics and metabolomics will be most appropriately delivered through service providers. Several options exist for ensuring the effective and timely development of such providers where they do not already exist. Centers should collaborate in the establishment of such service providers and help set an example to NARS and related organizations for outsourcing.

1. The CGIAR Genomics Task Force (TF) should be reestablished and a chair, and possibly an Executive, appointed. The roles and responsibilities of the TF are outlined below.
2. The first objective of the TF is to articulate the broad strategy for the delivery of genomics technologies by the CGIAR Centers over the next 10 years. To this end the TF will work closely with NARS genomics researchers and NARS and CGIAR breeders and genetic resources researchers. This document should establish a series of key objectives that demonstrate the value of molecular technologies for addressing simple and complex traits and germplasm characterization. These would be developed as models for technology delivery. They could be, for example, a set of key traits for a small number of commodities that could be developed as technology application 'flagship' objectives.
3. The involvement of breeders and other scientists from the Centers and NARS should be consolidated through the reestablishment or enhancement of breeder networks. During the initial phases, it would be useful to define a set of priority traits that could be integrated through pre-breeding programs and delivered to NARS as well defined packages. This is likely to involve only a few traits initially.
4. The TF will identify and collaborate with potential service providers to explore options for outsourcing specific technologies. It may be possible to embed Center or NARS staff within a service provider to access critical mass and capabilities. It could be a role of the Hubs to form a close association with specific service providers and provide regular reviews and assessment of breeders' needs to the service providers and regular reports on the effectiveness and capacity of the providers to breeders. The Hubs could also investigate and help organize transfer of materials to ensure timely delivery of results. The TF should develop a database summarizing resources and service providers that will act as a corporate memory as experience is gathered. The TF would help lead and coordinate development and maintenance of the information in an easily accessible format.

Source: CGIAR Genomics Task Force. 2006. *Genomics research in the CGIAR: effective means of establishing joint platforms and cooperative systems for enhanced genetic research* (available at http://ispc.cgiar.org/sites/default/files/ISPC_Genomics_Taskforce_Report%20.pdf).

Appendix E

Recommendations from the 2010 Stewardship and Liability report

Recommendation 1. CGIAR Centers implement the Guiding Principles for the development of CGIAR Centers' policies to address the possibility of unintentional presence of transgenes in *ex situ* collections, and "take proactive steps to determine the risk of the unintentional presence of exotic genes, including transgenes, in their *ex situ* collections."

Recommendation 2. As part of their risk analysis, when collecting or acquiring new accessions Centers should consider the following regarding testing:

a. whether transgenic events (commercial and research) in the relevant taxa are likely to be present in the area of collecting or acquisition;

b. the distance between the collecting site and areas where transgenic events (commercial and research) are situated; or

c. whether germplasm providers can provide adequate documentation of their germplasm management practices with respect to the material in question.

Recommendation 3. With respect to existing accessions, Centers' testing procedures should be guided by the following criteria.

a. No testing would be required when:

   (i) there are no transgenic events (commercial or research) in the relevant taxa at the present time;

   (ii) there were no transgenic events (commercial or research) in the relevant taxa at the time of acquisition (e.g. maize prior to 1996);

   (iii) it is determined that, unless there are other factors, there is no presence of transgenic events within a distance that would allow for introgression; or

   (iv) there are transgenic events (commercial or research) present; however, proper management practices have been followed and documented in the management of the accession.

b. Tests should be undertaken when there are transgenic events (commercial or research) present and good management practices cannot be demonstrated.

c. Once an accession has been determined to either not require testing or has tested negative, the Center will follow best practice regeneration and maintenance procedures to maintain the genetic integrity, as for all accessions.

Recommendation 4. If and when transgenes are detected in an accession, Centers will take appropriate steps to prevent introgression of those transgenes to other accessions.

Recommendation 5. To facilitate risk analysis, Centers should establish and maintain a database on the global status of GM research and development for the crops within their collections and the database should be posted on a publicly accessible website.

Recommendation 6. Upon request by the recipients of materials, Centers should provide information describing procedures and tests that they have followed for the accession concerned and all data resulting from any testing should be properly documented and made publicly available as soon as it is considered scientifically reliable (e.g. by posting on the Center's website).

Recommendation 7. CGIAR Centers will inform the relevant authority of the country of collecting or acquisition of the material in question when transgenes are found and the Center will also inform the relevant authority of the country in which the Center is located.

Recommendation 8. CGIAR Centers should establish:

a. Written guidelines – to clearly define the structure of the biosafety system, the roles and responsibilities of those involved and the review process.

b. Regulatory authorities – comprising well trained individuals in the host country, who are confident about their decision-making ability and to ensure the support of their institutions.

c. An information system – enabling the biosafety evaluation process to be based on up-to-date and relevant scientific information and the concerns of the community; and to ensure that biosafety data and procedures are recorded and archived.

d. A feedback mechanism – for incorporating new information and revising the regulatory system.

Recommendation 9. In all situations where a CGIAR Center provides products or materials under a [Material Transfer Agreement] or a contract a provision should be inserted excluding the Center from any IP or biosafety liability which may arise from the use of that material.

Recommendation 10. CGIAR Centers to conduct biosafety management reviews, with a view to verifying the establishment of effective biosafety management procedures and structures at Centers.

Recommendation 11. CGIAR Centers should establish a biosafety coordination office, responsible for coordinating both biosafety and IP administration and procedures within Centers and would be responsible for external biosafety and IP liaison.

Recommendation 12. CGIAR Center staff should be provided with access to the biosafety policies of Centers in a handbook.

Recommendation 13. Service contracts with staff should notify their obligation to comply with Center biosafety policies and should identify the responsibility and authority of the Biosafety Coordination Office and refer to the Biosafety Handbook as the primary source of information about Center biosafety policies and procedures.

Recommendation 14. All visitors to CGIAR Centers should be obliged to execute a biosafety agreement, similar to that executed by Center staff.

Source: ISPC. 2010. *Product stewardship and liability in the context of IPR: report of a study*. Rome, CGIAR Independent Science and Partnership Council (ISPC) Secretariat (available at http://www.fao.org/docrep/013/i1627e/i1627e00.pdf).

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