

Agenda Item 4

<u>For Decision</u> <u>Issued</u>: 6 July 2022

ISDC Review of Initiative Proposal "Accelerating Crop Improvement Through Genome Editing"

Purpose

This pre-read for SC16 sets out the report of the Independent Science for Development Council (ISDC) external review of the proposal for the CGIAR Initiative "Accelerating Crop Improvement Through Genome Editing". The external review of proposals is an essential part of good governance and quality assurance, delivering benefits for the researchers, leadership, and System Council. The review presented in this report provides confidence to funders that their investments in One CGIAR research are appropriately targeted with high chances for success.

Action Requested

The System Council is requested to read and reflect on the review of the proposal. The information presented is intended to support System Council in making decisions and recommendations for the One CGIAR research portfolio.

Document category: Working document of the System Council There is no restriction on the circulation of this document

Prepared by: Independent Science for Development Council



CGIAR Research Initiative Review Report Proposal: Accelerating Crop Improvement through Genome Editing

Three external subject matter experts reviewed each Research Initiative. Of the three reviewers, one served as a coordinator and worked closely with an ISDC member in the development of this report for System Council. The Quality of Research for Development in Practice for One CGIAR provided the background and guidance for reviews. Please visit the ISDC Reform Advice webpage for all external Initiative review reporting since 2021.

Review Summary and Actionable Recommendation

The proposal is very well written, has a logical flow of activities, and linkages among Work Packages are clear. It tackles a very important and advanced topic that, upon completion, will have a significant impact in the field of agricultural research and will add notable contributions. Genome editing is a recent technology that is expected to provide a state-of-the-art solution to the ever old-new plants health and/or productivity problems. Increasing capacity outside of CGIAR labs, making the technology widely understood and available, could be an explicit outcome. Sustainability of this research program will be increased with the wide-spread use of the GEd technology. The researchers have put great effort into preparing the proposal, reflected in the scientific writing skills shown. After responding to the actionable recommendations below, this Initiative has good potential to deliver the intended outcomes.

Overall Strengths of Proposal

Section 1 (the research problem) is very well addressed and is based on research findings both from within and without CGIAR. It engages all stakeholders in the project activities; however, the level of capacity building in project countries still requires more details. The timing of this proposal is excellent as the technology, while new, has been sufficiently developed to know that the products developed can fulfill important needs in the communities targeted. A question that remains is how socioeconomic analyses might facilitate deployment of GEd products.

Section 2.1 is very well written with a clear problem statement followed by a potential technical solution that leads to specific impacts and provides the rationale for the three Work Packages. The summary at the start of the proposal is excellent. The innovative problem-solving nature of the Initiative is impressive.

The diagrams in 3.2.1 Work Package Theories of Change are excellent. However, inclusion of the "priority products" that are to be generated would be a welcome addition. Priorities are hidden in the projection of benefits section—it would be good to make them explicit.

Overall Weaknesses of Proposal

Section 2.2: Measurable 3-year (end-of-initiative) outcomes would be improved if outcomes were linked to specific outputs (reports, products, crop/trait). Priorities are presented clearly elsewhere in the proposal, but reference to priority species and traits could help connect the science/policy for the reader.

Section 3.1.2: Full Initiative Theory of Change narrative is very general. Some reference to the failure of GMO crops to gain acceptance would highlight the need for Work Packages 1-2. Greater explicit attention to lessons from GMO experiences—especially around popular and political resistance and IP issues—seems essential and highlights the need for these Work Packages. IP is considered but other than discussion with Corteva it is not clear what might be done if freedom to operate (FTO) is withheld. Clarity also is required regarding the governance structures that will be put in place for the appropriate management of IP. Training for this will clearly be important. Other factors (known and unknown) need consideration and the role of farmers in adoption is not recognized.

The selection of countries with different regulations and policies regarding genetic technologies, linked to participants capacities (researchers, stakeholders, decision makers) could impede the success of the Initiative. Linked to this is the focus on climate change mitigation: the ways to address mitigation varies greatly across regions, as well as between and within countries. It is almost as if the drafters of this proposal were trying too hard to be compatible with the UN Sustainable Development Goals and hence "look politically correct" instead of

concentrating on what will be the most useful traits that can be reasonably expected to be successfully introduced. A sound sociopolitical analysis of the regulatory/policy environment is lacking.

The environmental component of the GxExM interactions that ultimately lead to a phenotypic response have not been highlighted. This is at odds with the focus on climate change as a driver of disease incidences and severity. For instance, plant nutrition should be more carefully considered in this context (it is well known that often the genetic potential of new varieties is not realized because of other co-limitations).

Areas of Divergence among Review Team and ISDC Resolution

During moderation, ISDC colleagues commented on a possible discrepancy between the assessment narrative and the high scores awarded by the SMEs. Hence, the ISDC recommends focusing on the actual commentary rather than just the numerical score.

Does the Initiative Align with the Cohesion of the Portfolio as Described in the Companion Document?

The Initiative has a long-term vision towards the 2030 target (Item 14 in the Companion Document) and produces a Theory of Change that identifies plausible pathways to reach the projected benefits, which includes proactively managing the major risks associated with GE (15). Priority setting is based on the criteria laid down in (19). Agrifood systems exposed to climate hazards are targeted (26). The Initiative aims to address the main challenges of the Genetic Innovation Theory of Change as it aims to increase biodiversity in the crops to be improved by GEd (32). The engagement with partners, critical to coherence and cohesion, is well covered in this proposal (51). Indeed, it recognizes that partnerships are central to the effective delivery of CGIAR's portfolio of initiatives (55). The common CGIAR policies which underpin portfolio coherence (61-65) are well addressed in the proposal. Finally, most of the measurements and reporting timeframes outlined in section 4.2 are well covered.

Scoring

The next section focuses on specific proposal scoring. Reviewers scored each of the 17 QoR4D criterion individually. The three scores were then aggregated for an overall score for each QoR4D criterion. The criterion that received a 1 or 0 are presented with a rationale.

3 2 1 0

The project addressed the criterion in an intentional, appropriate, explicit, and convincing way with supporting evidence There is good evidence that the criterion has been addressed explicitly and with good intent, but the approach is not fully persuasive or may lack some clarity There is some evidence that the criterion was considered, but is lacking completion, intention, and/or is not addressed satisfactorily There is no evidence that the criterion was addressed or that it was addressed in a way that was misguided or inappropriate

No action Significant Changes

Criteria	Proposal	QoR4D	Consensus
	Sections	Elements	Score
Clearly defined research problem that addresses Impact Areas, is a high priority in the targeted geographies, is well aligned to shared, multi-funder	Challenge statement 2.1, Learning from prior evaluations	Relevance, Effectiveness	2.5

Criteria	Proposal	QoR4D	Consensus
	Sections	Elements	Score
priorities, and is well informed by previous research findings and evaluations	and Impact Assessments 2.3, Impact statements 5		

The research problem is clearly defined and has a very high priority. In the last decade, genome editing has rapidly evolved and received considerable attention worldwide. Plant genome editing can be targeted to specific chromosomal locations and induce sequence changes to enable the precise engineering of crops with novel characteristics. It has been used sufficiently to know that it will solve some important plant health problems in targeted developing countries which might be technologically lagging. The program presents a holistic approach to sharing and building capacity, gaining technology acceptance, and delivering innovations in systems focused on smallholders. There is a good definition of impacts provided for each CGIAR impact area. On a cautionary note, a clear acknowledgment of the scientific challenges faced by GE would be helpful. This includes issues such as managing complex traits and our still rather rudimentary knowledge of individual gene actions. It would be useful to know what the Initiative's position is regarding GMO and the crops already developed with this technology. Is the team of the opinion that GE provides significant advancement by excluding the introduction of foreign DNA into the genome of target plants, which might improve their social acceptability?

2. Evidence that the Initiative is demand driven through codesign with key stakeholders and partners (Investment Advisory Groups, governments, private sector, funders) and research collaborators within and outside CGIAR

Participatory
design process
2.6,
Challenge
statement 2.1,
Work Package
ToCs 3.2

Relevance,
Effectiveness

Evidence of demand is provided for a range of countries and various commissions. Strategic use of resources investing in Work Package 2 provides evidence of acceptance. Annexes 2 and 3 show strong support from NARES, ministries, and regulatory authorities, while regional consultation meetings resulted their support as well.

3. Research questions, objectives, outputs, and outcomes are aligned to the research problem, and are measurable with defined deliverables

Work Package
ToCs 3.2,
Measurable threeyear (End of
Initiative)
outcomes 2.2,
Priority-setting
2.4, Management
plan 7.1

Work Package
Relevance,
Effectiveness
2.0

Questions and objectives are presented clearly. There is a risk that addressing too many complex climatic/abiotic stresses interventions could spread resources too thinly, but this is addressed by working with partner labs that will address these by focusing on specific crops and traits. Problems might arise if countries continue to change policies and regulation, as well as that a number of smallholder farmers may not be able to afford to implement the technology. A weak objective is the one relating to climate change (e.g., the use of fertilizers) as in some countries (e.g., for rice production) this has been inefficient. In addition, many climate change interventions will need to be multigenic and it is not clear how this will be addressed, and whether multigenic changes will obtain regulatory approval. This seems to be a weakness of most GE approaches and should be addressed.

Another problem is the timeline for scaling GEd lines, given the time it can take to incorporate changes into more than one line by crossing and subsequent evaluation. The timeline should also consider the requirement for IP issues to be resolved. GE lines may be improved in respect of the target, e.g., nutrition or disease resistance but there may be trade-offs with other traits such as decreased yields so field trials and phenotyping in collaboration with users in different agri-environments is essential.

4. Overall Theory of Change with intended outputs, outcomes, and impacts at scale clearly described.

Assumptions are documented, causal linkages are clear, especially the role of partners in driving impact

Full Initiative ToC 3.1	Effectiveness , Relevance	2.0

One of the strengths of this proposal is that partners have been selected to enhance its impact, although their roles could be made clearer. The full Theory of Change looks promising; however, some points need to be revisited in line with the objectives, the current situation and the expected results, taking into account all the challenging points in each Work Package. Work Packages 1-2 will foster environments favorable to the success of

Criteria	Proposal Sections	QoR4D Elements	Consensus Score	
this proposal, while Work Package 3 will enable GEd innovations to reach their targets. Other factors (known and				
unknown) need consideration and the role of farmers in adoption is not recognized. Again, a sound				

understanding of and ability to influence the socio-political environment seems to be key for success.

4.a Individual work package ToCs (score individually) Work package 1 Work package 2 Work package 3	Work Package ToCs 3.2	Effectiveness , Relevance	WP1: 2.5 WP2: 2.5 WP3: 2.5
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The Work Packages are well developed, with clear summary figures outlining the Theory of Change for each Work Package that clearly demonstrate their connectivity. Clarity on the following issues would, however, be helpful:

- 1. How the current situations of public awareness and acceptance of GEd technologies in individual countries will be determined. This may require training workshops using case-by-case examples.
- 2. Which WP will deal with GEd laboratory research practices and the associated risks? Will these be based on past/current research activities?
- 3. More clarity could be given on how risks in WP3 will be mitigated. Risks include the issue of GEd overpromising outcomes and under-estimating lack of the desired traits being achieved.

5. Research methodology and methods (and supporting activities) are fit-for-purpose, feasible, and assumptions and risks are clearly stated ToCs Prior 2.4, Pack	rity-setting Innovation kages and ling Readiness	2.5
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Activities are well described and are feasible with key risks for each Work Package clearly stated. Clarity is, however, needed in the methods to be used and where this lab work will be done—in CGIAR Center dedicated facilities or facilities provided by partners?

Improvements could include:

- 1. Considering how variations in the climates of the regions involved will be handled
- 2. Considering how political systems in some countries my change research priorities
- 3. Preparing for differences in technology acceptance and applications in different countries, which may depend on levels of education
- 4. Improving section 4.1 on scaling and readiness
- 5. Addressing risks to climate change

Continuous monitoring and management could, however, be sufficient to deal with these problems as they arise. These problems also include the possibility that GEd may not be able to deliver the crop improvements anticipated.

6. Analysis of trade-offs and synergies across the CGIAR Impact Areas; ex-ante assessment of project benefits provides logical rationale for scaling of impacts	Projection of benefits 2.7, Result framework 6.1, Impact statements 5, Innovation Packages and Scaling Readiness Plan 4.1	Effectiveness , Credibility	3
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The innovative nature of the proposed Initiative (although a bit scattered in the proposal) and the global readiness for acceptance (although with different time responses), make it possible to achieve all the expected outcomes and other unforeseen ones. The impact statement provides the best evidence that the work will align well with CGIAR interests. The ex-ante assessments of project benefits provide logical rationales for scaling of impacts. The scaling will be planned in year 3 when the data derived from Work Packages 1-2 will inform the status of readiness for this to take place.

7.	Evidence that the Initiative will likely lead to impact at	Projection of	Effectiveness,	
	scale through integrated systems approaches that	benefits 2.7,	Credibility,	2
	drive innovation in research and partnerships,	Work Package	Relevance,	

Criteria	Proposal	QoR4D	Consensus
	Sections	Elements	Score
including linking to and leveraging of other Initiatives within and outside CGIAR	research plans and ToCs 3.2		

One of the strengths of this proposal is its partnerships, both within and outside CGIAR. These will strengthen this Initiative and open up linkages with other Initiatives that can be supportive, especially Regional Initiatives. However, any changes made through GEd must be delivered through ongoing breeding programs and existing seed/variety distribution networks if they are to be scaled up. Pushing a single GEd variety onto smallholders increases risks inherent in monoculture systems. Farmers should be recognized as partners and receivers. Improvements must be integrated into breeding programs. The proposal could be improved by clarifying the linkages with Accelerated Breeding. In addition, when new IP is generated, it will have to be managed before any GEd crops can enter the public domain. This could take a considerable amount of time. Moreover, not all GEd Initiatives might deliver the desired traits as the technology is not infallible.

How will valuable germplasm be maintained if gene-edited varieties completely replace currently existing varieties? How will the team ensure that key traits are not lost, given that many of the GxExM interactions are remain unknown but will be critically important in the ongoing race to beat pathogens? What are the expected challenges with target crops? How can GE and molecular breeding ensure success when the technology has not yet been tested in LICs or communities? The core scientific apparatus for this Initiative and associated capacity building, science communication, etc., can be adapted to different contexts most effectively if intermediated by the Regional Initiatives that steward the local and regional partnerships.

	3			
8.	Ethics, including equitable partnerships, information disclosure, biases, and potential conflicts of interest are considered; proposal defines how formal research ethics approvals will be sought/granted¹	Policy compliance and oversight 8	Legitimacy , Credibility	NA
No	t required			
9.	Research design and proposed implementation demonstrates gender and social inclusion that can be tracked in outcomes	Gender equality, youth & social inclusion 5.3, Projection of benefits 2.7	Legitimacy , Effectiveness	2

The proposal shows that attention is being taken to include gender, youth, and other potentially excluded groups. However, it could be improved by clarifying their participation in all project phases and their roles in each set objective. For instance, traits that decrease the use of on-field labor, mainly done by women and youth, are not prioritized in this proposal. It is very important that women and youth are included in the selection of traits and become co-designers of these breeding efforts.

The use of social mapping tools to enhance the benefits for these groups will be very helpful as will be training packages, including gender awareness training.

 A risk framework that details main project risks and mitigation actions across areas of science, funding, 	Risk assessment	Credibility , Legitimacy,	2
operations, partnerships, ethics, and environment	7.3	Relevance	

GEd is a fairly new technology and risks need to be taken very seriously. While this is clearly done in the proposal the following could be included:

- 1. State more explicitly how the risk of social acceptance will be addressed in, for instance, sections 3.2.2, Work Packages and Theory of Change. Is there a risk that groups who may not accept GE plants become suspicious, which may inhibit uptake?
- 2. Consider the Initiative to be more proactive in engagement with communities and policymakers in promoting GEd technologies rather than approaching it through a risk minimization lens.
- 3. Consider that obstacles to release and adoption of GEd crops could be expected at different rates in different countries. Thus, constant monitoring is essential.
- 4. Explicitly address the issue of IP management to ensure transparency and equity.

¹ Proposal will not include individual Initiative ethic statements but robust all-CGIAR policies and mechanisms. Initiatives will confirm alignment with CGIAR's Research Ethics Policy. This was a CGIAR decision during proposal development.

Criteria	Proposal	QoR4D	Consensus
	Sections	Elements	Score
11. CGIAR capacity and its comparative advantage and appropriateness to lead the work is justified. This includes the skills, diversity and multi-/trans-disciplinarity of the research team and approaches to meeting gender and diversity targets	Comparative advantage 2.5, Initiative team 9.1, Gender, diversity and inclusion in the workplace 9.2	Relevance, Legitimacy, Effectiveness	3

A clear indication of CGIAR's capacity and comparative advantage is the extent to which partners will be, and wish to be, involved. This becomes evident in the enthusiasm shown in their support letters (Annex 2). To our knowledge, there is no potential alternative provider other than CGIAR for the work proposed here. While CGIAR might not be the most technically advanced group when it comes to GE, they have many capable staff with adequate experience to lead.

The inclusion of women and youth is also emphasized and needs to be monitored throughout. The Initiative bears the hallmarks of an enabling platform, more so than a hard-nosed research program. This seems appropriate, given the CGIAR's mission and focus on the generation of public goods. Here, CGIAR will be able to fill a knowledge and capability void that will be essential for the achievement of the desired outcomes.

The current proposal relies heavily on the Capacity Development Coordinator who is to be appointed. Perhaps consider tasking this Coordinator with developing capacity outside partner organizations? Also consider the following:

- 1. Adding to Work Package 2 the multiplier effect that can be derived from training specialists in startup labs and university labs using structured workshops and exchanges with other partner labs for training in techniques
- 2. Adding to Work Package 1 a metric for increasing the number of labs that are regenerating GEd lines
- 3. Including comprehensive training programs in some countries, even before the start. Some countries may even need to recruit more researchers (e.g., Kenya). Different countries might need different levels of training—basic, intermediate, and advanced

13. Project management mechanisms and (if applicable) additional scientific oversight and governance measures effectively and efficiently support the Initiative objectives ²	Management plan and Risk assessment 7, Research governance 8.1	Legitimacy , Credibility	3
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The pathway to the Initiative's objectives is well described. The timeline and Gantt chart look reasonable, and it is good to see deliverables associated with timelines. Consider the following for clarification purposes:

- 1. Increasing the number of labs producing GEd lines to ensure that methods and data are readily available outside the CGIAR. The LMT and REO Units could be tasked with this.
- 2. Ensuring that a process is in place to ensure the entire process is placed in the public domain and all IP managed accordingly.

No budget justification is provided, especially for the allocation for each country. Although there is a good distribution across regions, the allocated budget is not balanced with the activities proposed to be carried out in the various countries (compare Kenya with Colombia and India). The largest share of budget going to Work Package 3 is well supported, although this might need to be revised depending on work finally assigned to the different Work Packages.

² Each proposal will have standard text on CGIAR research governance arrangements already agreed for section 8.1. This was a CGIAR decision during proposal development.

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Criteria	Proposal	QoR4D	Consensus
	Sections	Elements	Score
15. Anticipated research outputs (knowledge, technical, or institutional advances, specific technologies or products, policy analyses) are described and knowledge/gaps they will fill are evident. Protocols for open-data and open-access compliance are evident in plan (including budget)	Work Package research plans and ToCs 3.2, Open and FAIR data assets 8.2	Credibility , Effectiveness	3

The anticipated outputs are well explained and justified. However, as the project progresses the outputs may need to be refined depending on changing circumstances in different regions/countries. Protocols will be shared with all partners. The outputs described in 6-1 results framework could be summarized for the Theory of Change section. More clarification is needed regarding the IPRs and patent regulations which will differ within the project phases and between activities.

16. Monitoring, evaluation & learning (MEL) plan for the Initiative is clearly defined, with flexibility to adapt. MEL plan supports effective management and learning, including baseline data collection, and evaluative and review processes corresponding to stage-gates and course-correction decisions. MEL occurs during the life of Initiative and is used proactively to reflect on and adapt the Theory of Change, where appropriate	MELIA plan 6.2, Planned MELIA studies and activities 6.3, Measurable three- year (End of Initiative) outcomes 2.2	Credibility , Effectiveness, Legitimacy
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The MEL plan provides clear targets for reporting and is explicit about flexibility. During the first quarter of every year and following the product life cycle, WP outputs will be evaluated and, if necessary, course corrections applied. Other regular reports will cover gender impacts and any relevant local policy changes—essential in the changing world of GEd introduction. The three specific foci of the impact assessment plan are sound. 2.2 could use more quantifiable objectives or SMART objectives.

MELIA plan 6.2,

17. Well-defined plan for Initiative-level evaluation and impact assessment based on expected end-of-Initiative outcomes and impact. Links between the impact assessment plan and indicators in the Theory of Change are clear	studies and activities 6.3, Full Initiative ToC 3.1, Work Package ToCs 3.2, Projection of benefits 2.7	Effectiveness , Relevance	2
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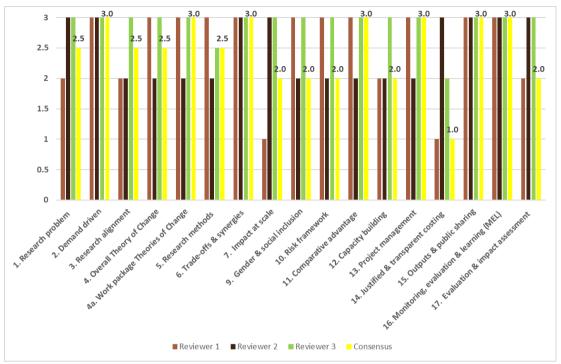
Impact assessments are covered in many places in this proposal, showing the importance of considering the Theory of Change and MEL in achieving the desired outcomes. The plan is sound with clear timelines provided. However, while the impact assessment plan is clear, the linkages to the other initiatives such as 'accelerated breeding' and 'market intelligence' are unclear. The revisions to the Theory of Change should help.

Additional Comments Not Presented Above

It is not clear how this Initiative will get from the five target crops (bananas, cassava, potatoes, wheat, rice) to a broader product range that reflects the CGIAR mandate, including some of the orphan crops and, e.g., vegetables, which have now been identified as a priority for CGIAR. The proposal seems to jump from the very general to the very specific without providing the pathways between them.

The Figure below represents original scoring from each reviewer and consensus scoring for each criterion. *The consensus score across reviewers may not reflect the mathematical average.* For purposes of the Figure, the QoR4D criteria have been shortened. Please note that criterion 8 on ethics was not scored.

Review continued on next page.



*Three consensus scores were greater than 0.5 variance from the mathematical average. Please refer to criteria 9 and 10 (both with a variance of 0.7 from the mathematical average) and criterion 14 (variance of 1.0) above for rationale of these consensus scores.