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Objections to the Application by Trigall Genetics SA for permission to conduct field trials in South Africa in respect of drought tolerant and 'glufosinate tolerant' 'HB4' wheat: IND-ØØ412-7

Submitted by the
African Centre for Biodiversity

AFRICAN CENTRE FOR BIODIVERSITY
20 years of advocating for food sovereignty in Africa

The African Centre for Biodiversity (ACB) is a research and advocacy organisation that works towards food sovereignty and agroecology in Africa, with a focus on biosafety, seed systems, and agricultural biodiversity. We have a long track record of engaging with the regulation of genetically modified organisms (GMOs) in South Africa, spanning more than two decades of research, analysis, advocacy, and engagement in international, regional, and national policy and regulatory processes.

Background

In August 2022, genetically modified (GM) wheat variety HB4 was approved for importation as food, feed, and industrial processing (commodity approval) in South Africa by the Executive Council: GMO Act, on the basis that adequate scientific support exists to conclude that the GM wheat variety is safe for human and animal consumption.

The ACB is on record for applying with the Executive Council (EC) to review its decision[1] on the basis, *inter alia*, that Trigall Genetics' risk assessment lacks vital food safety evidence, including feeding studies, and that the GM wheat poses unacceptable risks to human and animal health, as well as undermining food sovereignty and nutrition security.

At the time the EC decision was made, the GM wheat variety was not grown commercially anywhere in the world. Nevertheless, to date, this GM wheat variety has been approved for commercial growing in Argentina, Brazil, and the US but nowhere else in the world.

Despite the commodity approval, no shipment of GM wheat has yet been imported into South Africa. Nevertheless, such approval will absolve the Applicant from any liability or redress that may arise from contamination of the food supply from the field trials. Where such contamination occurs in foodstuff containing GM wheat that is less than 5%, (5% being the threshold for labelling in South Africa), South Africans will not know they are consuming GM wheat and will be unable to avoid purchasing or consuming products containing the GM wheat.

1 Application to the Executive Council: GMO Act to review its decision to approve GM wheat for import into South Africa as food, feed, and processing, May 2023. https://acbio.org.za/wp-content/uploads/2023/05/call-for-review-approval-gm-wheat-acb-sumbmission.pdf

The Applicant

This GM wheat variety is the product of a 20-year Argentinian public-private partnership between the National Commission for Science and Technology (CONICET) and Bioceres. Bioceres co-owns Trigall Genetics, as part of a joint venture with Florimond Desprez, a French seed company. As far back as 2004, CONICET researchers patented the technology and subsequently it was licensed to Bioceres, which has commercial ties to Bayer, Corteva, and Syngenta, the latter now being part of the merged entity ChemChina. Bioceres has 73 institutional shareholders, including individual investors, mutual funds, hedge funds, and institutions.[2]

The Application

The Application is for permission to be granted in terms of the GMO Act for field trials to be conducted in South Africa, regarding the efficacy of the HB4 trait, the results of which are intended to be used for a future application for general release. The proposed trial release is intended to take place in four locations in South Africa – three locations in the Western Cape (near Moorreesburg, Protem, and Swellendam) and one in the Northern Cape (near Hopetown). Three of these locations are in the dryland region and one location will be under irrigation.

Eight wheat varieties will be imported from Argentina and used in the trials.

- The intention is to plant the first season of field trials in April 2025 and harvest the trials by December 2025.
- A second season of field trials is intended to be planted in April 2026 and harvested by December 2026.

According to the Application, the two seasons of trials at multiple locations will be sufficient to obtain data to support the efficacy claims. The Applicant intends thus to apply for a commercial/general release permit during 2027, when GM wheat will enter the South African food system in full force.

2 https://fintel.io/so/us/biox

Wheat in South Africa

Wheat is South Africa's most important grain crop after maize, widely cultivated across three regions of the country, and is critical for ensuring food sovereignty and nutrition security. South Africa is both a wheat importer and an exporter. South Africa imports wheat primarily from Australia, Lithuania, Latvia, Poland, and Russia. It exports wheat to several countries in Africa, including, Botswana, Zimbabwe, Lesotho, Zambia, and Namibia. Wheat is a major source of carbohydrates for millions of South Africans in the form of starch, with its seeds also providing an important source of protein. It is used ubiquitously in everyday food (including staple foods), such as bread, noodles/pasta, couscous, cakes, muffins, biscuits, snack foods, puddings, and sauces in confectionery.

GM drought tolerant debacle in South Africa

Complex traits such as drought tolerance have yet to be widely commercialised, due to the unfulfilled, long-held promises by the biotechnology industry that drought-tolerant GMOs would be a climate change solution. A case in point is Bayer's (formerly Monsanto) MON 87460 'drought-tolerant' GM maize, which has been the subject of litigation by the ACB in the High Court of South Africa since 2017. The matter was most recently heard by the Supreme Court of Appeal sitting in Bloemfontein on 19 September 2024, before a full bench of five judges, where judgment has been reserved.

In this case, the ACB has consistently argued that there is insufficient data to demonstrate the claimed drought-tolerant benefit, based on either yield or agronomic performance advantages.

Curiously, Monsanto sought approval for the commercial growing of a triple-stacked GM maize variety that included the contested drought-tolerant trait, combined with Monsanto's ancient and failed herbicide-tolerant and insecticidal traits, respectively (MON 89034 and NK 603). ***This application was rejected by the very same South African biosafety authorities that had approved the single trait, on agronomic and biosafety grounds.***

Summary of objections

The Application submitted by the Applicant to the EC for commodity clearance for the same GM event is pertinent and must be read together with the application submitted by the Applicant for field trials. The reason is that the current application is contradicted by the commodity import application in fundamental ways, as more fully explained below.

Our objections to this application can be summarised as follows:

1. The Application for field trials is fatally flawed in that it fails to comply with the new requirements of the EC, following the decision by the South African government to regulate new genetic engineering technologies, including genome editing, in terms of the GMO Act. In this regard, the EC has updated its requirements for risk assessment, which the Applicant has flouted, raising serious concerns as to the veracity of the claims by the Applicant. These relate inter alia to the unintended introduced transgenes and the molecular characterisation information provided, which contradicts the application for commodity import.
2. The Application raises fundamental questions regarding the functioning of the so-called drought-tolerant trait, HB4, especially if the introduced transgene is not altering the expression of other genes to alter abiotic stress tolerance.
3. The GM wheat poses unacceptable risks of contamination of non-transgenic wheat in that the proposed isolation distance of five metres, and the proposed monitoring plan of a period of one year, is woefully inadequate to prevent pollen-mediated gene flow. This is particularly pertinent in light of contamination having been a feature in previous GM wheat trials in the US, where contamination events were detected up to eight to 15 years after trials.

Specific comments

Narrow risk assessment fails to address proven contamination risks of GM wheat releases

The application fails to address all the potential avenues of risk of the GM wheat event to the environment and human health, relying on outdated science and various assumptions that allow for risks to be dismissed without empirical testing.

The application also makes verifiably incorrect statements that directly contradict the previous application for import approvals, raising concerns regarding the veracity of claims in the current application.

The applicant has failed to complete the application correctly and should be required to withdraw its application because it has failed to comply with legal requirements set out by the EC. Failure to do so on the part of the EC will render the application fatally flawed as the Applicant will then be allowed to side-step its obligations regarding risk assessment (see below).

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Introduced genetic elements

Intended introduced transgenes

The wheat line has two genetic constructs introduced into it.

1. One construct expresses the *HaHB4* gene originally derived from sunflower, *Helianthus annuus*. The *HaHB4* encodes for a transcription factor called HAHB4.

Transcription factors can be described as master regulators of gene expression, one of the central molecules that *determine the levels of gene expression of numerous genes*. Its expression in sunflowers appears to be upregulated during stress conditions, altering the expression of genes in the plant to adapt to stress. As such, the introduced transgene by default, if it is functioning, should be altering numerous genes in the GM wheat.

2. The second construct carries the *bar* gene, which encodes for tolerance to glufosinate-based herbicides.

The introduction of this gene is sometimes done to assist the laboratory process only (as a marker gene for selection). In the case of this wheat line, the glufosinate expression appears to be high and is being sold explicitly by the developers as an additional trait.

As such, the wheat line can be used in conjunction with glufosinate-based herbicides, with all the attendant risks. However, on page 50, the application states that the herbicide-tolerant trait will not be used in South Africa, due to no registration for glufosinate over-the-top use on wheat. If this is the case, then the Applicant is misleading the EC and farmers that the GM event is to be sold also as herbicide tolerant.

Unintended introduced transgenes

The GJ wheat also has unintended sequences introduced. However, these have not been acknowledged in this latest application, but are raised in the import application from 2023, where it lists the unintended elements (page 33 of the Application for commodity import).[3] [4]

Unintended elements

1. pBR322 *Origin*: replication origin derived from plasmid *pBR322.* Not functional in plants.
2. *bla*: coding DNA sequence of *Escherichia coli (E. coli)* ß-lactamase enzyme. Under prokaryote promoter, not expressed in plants.
3. *prGbl1-1*: promoter of 7S wheat globulin.
4. *gus*: partial coding DNA sequence of *E. coli* ß-glucuronidase reporter enzyme.
5. *T35S CaMV*: cauliflower mosaic virus transcription terminator.

These unintended insertions are not included in the applicant's information submitted to the CBD's biosafety clearing house, where information on GMOs to be exported needs to be filed.

(N.B. These unintended insertions were detected via sequencing technologies, highlighting the rationale for those calling for such modern profiling techniques to be introduced into risk assessment requirements.)

Applicant evades new information requirements, which has resulted because of the updated requirements for risk assessment for GMOs derived from novel GMO techniques such as genome editing.

3 Application for commodity clearance of GMOs in South Africa IND-ØØ412-7 Wheat
4 ACB (2023) Unsafe GM wheat to enter South Africa's Food system https://acbio.org.za/wp-content/uploads/2023/05/unsafe-gm-wheat-sa-food-systems.pdf

1. **The molecular characterisation information provided is incorrect and contradicts the previous application for import approval.**

The application requires information on the following:

Pg 29: *Identification and location of all inserted sequences (including short indels) and genes, including the copy numbers for all inserts, both complete and partial. The organisation of the inserted genetic material at the insertion site.*

However, the applicant only lists the intended genes that have been inserted, failing to provide information on unintended insertions. Information on these unintended insertions, including antibiotic resistance genes, for example, are entirely omitted from the application and thus **it fails the basic information requirements under the updated risk assessment requirements.**

This contradicts the information provided in the import application stating that:

"the insertion contains three copies of HaHB4 (two complete and one incomplete) and eight copies of bar (seven of them complete and one incomplete). In addition, the insertion contains 19 copies of the bla gene (12 complete and seven incomplete), and four copies of gus (all incomplete). Among all these sequences, only one copy of HaHB4 and three copies of bar are functional, e.g.: have their regulatory sequences in the right position and direction to allow expression in HB4 wheat."

The only information provided in this section is the background information on the HaHB4 gene and the bar genes. The information submitted appears to not comply with the new requirements for risk assessment.

Most other information on molecular characterisation has been omitted under CBI making other aspects of the application unavailable for independent scrutiny.

2. Applicant's information raises fundamental questions regarding how the HB4 trait works

This gene's function is to control and regulate the activity of other genes (called a 'transcription factor'). Its function in sunflowers is thought to manage responses to abiotic stresses such as drought, saline exposure, mechanical damage, and herbivory. The rationale of the developer is that this gene may turn on/off genes in the event of drought, allowing the plant to cope by altering its genetic activity, including broader networks of genes. In their 2020 publication, it is acknowledged that they do not know what genes in the wheat the HB4 protein is regulating, stating that, "the way this TF is affecting such transcriptome is yet unknown" (González et al., 2019).

The application requires information on whether the expression of endogenous genes is altered in the GM wheat plant compared with the conventional counterpart. However, to seemingly pass risk assessment requirements, the applicant argues that (pg31):

"*The genetic modification in HB4 wheat consists of the insertion of the HaHB4 and Bar genes and is not expected to change the expression of previously inactive genes. The only new expressed proteins because of the genetic modification in HB4 wheat are HAHB4 and PAT*.'

This begs the question as to how the trait is indeed functioning if the introduced transgene is not altering the expression of other genes. If this is not occurring then the trait itself is also not functioning to alter abiotic stress tolerance, unless it's via a yet-to-be-identified mechanism that has not been investigated.

These basic contradictions need to be addressed to ensure that the applicant is not providing arguments that support approval rather than fulfil the requirements of risk assessment.

Contamination is a feature of past GM wheat trials and should not be inaccurately dismissed

Aside from this HB4 wheat product now entering commercialisation phases, no GM wheat has been approved anywhere in the world. Despite this, genetic contamination of conventional wheat has occurred numerous times because of field trials alone. Moreover, for two of the three cases, the source of escape has not been discovered despite investigations by regulators, suggesting that it is erroneous to rely on assumptions that, for example, pollen-mediated gene flow "*might only be a concern if it occurs within fields, e.g. due to seed contamination (Rieben et al., 2011*)."

GM wheat contamination in the US led to a phasing out of US wheat by several countries, as a result. One trial that took place in Oregon, US, of a herbicide-tolerant variety, was only discovered growing in a farmer's field after the farmer noticed it wasn't dying following herbicide spraying, which was discovered only eight to 15 years after the trials took place. Despite investigations by the regulatory authorities, the source or mode of escape was not discovered, indicating that the routes of contamination are not necessarily apparent. In the case of a GM contamination event from a trial in a research centre in Montana, contamination was not discovered until 10 years after the trials were completed (USDA, 2014).

Moreover, wheat seeds can lay dormant for many years, which is also environmentally determined, with some seeds reported to lay dormant for up to five years. This raises serious concerns for national wheat production and potential economic fall damage that may occur and the potential impacts on South African wheat markets and farmers' livelihoods.

Pg. 43 of the application states that an isolation distance of five metres will be maintained between the transgenic wheat and any other non-experimental crop. Five metres is insufficient to protect against pollen-mediated gene flow, which the applicant acknowledges, may extend to a rate of 0.02 % at 40m (pg. 17). It does not, however, give estimates for five metres.

Pg. 42 states that "*No transfer of GMO´s nucleic acid sequences to other organisms is expected. There are no sexually compatible relatives of wheat in South Africa; consequently, pollen-mediated gene flow can only occur between cultivated varieties. However, such gene flow would be minimal because of the biology of wheat and the isolation distances of the trial at the release site and surrounding environment.*"

Pg. 17 of the application further states: "*Regarding gene introgression from GE wheat into non-GE wheat, research suggests that pollen-mediated gene flow might only be a concern if it occurs within fields, e.g. due to seed contamination (Rieben et al., 2011).*"

Monitoring is planned to last for one year following the trial. Given the experiences in the US with contamination events being detected eight to 15 years after trials, one year may not be sufficient for monitoring purposes.

References

González, F. G., Capella, M., Ribichich, K. F., Curín, F., Giacomelli, J. I., Ayala, F., Watson, G., Otegui, M. E., & Chan, R. L. (2019). Field-grown transgenic wheat expressing the sunflower gene HaHB4 significantly outyields the wild type. Journal of Experimental Botany, 70(5), 1669–1681. https://doi. org/10.1093/jxb/erz037

USDA APHIS 2014. USDA announces close and findings of investigation into the detection of genetically engineered wheat in Oregon in 2013. https://www.aphis.usda.gov/newsroom/2014/09/pdf/ge_wheat.pdf