



Australian Government

Department of Health

Office of the Gene Technology Regulator

Risk Assessment and Risk Management Plan

for

DIR 173

Commercial release of cotton genetically
modified for herbicide tolerance
(MON 88701)

Applicant: Monsanto Australia Pty Ltd

October 2020

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Summary of the Risk Assessment and Risk Management Plan for Licence Application DIR 173

Decision

The Gene Technology Regulator (the Regulator) has decided to issue a licence for this application for the intentional, commercial scale release of herbicide tolerant genetically modified (GM) cotton in Australia. A Risk Assessment and Risk Management Plan (RARMP) for this application was prepared by the Regulator in accordance with the requirements of the *Gene Technology Act 2000* (the Act) and corresponding state and territory legislation, and finalised following consultation with a wide range of experts, agencies and authorities, and the public. The RARMP concludes that this commercial release poses negligible risks to human health and safety and the environment and no specific risk treatment measures are imposed. However, general licence conditions have been imposed to ensure that there is ongoing oversight of the release.

The application

Application number	DIR 173
Applicant	Monsanto Australia Pty Ltd (Monsanto)
Project title	Commercial release of cotton genetically modified for herbicide tolerance (MON 88701) ¹
Parent organism	<i>Gossypium hirsutum</i> L. (cotton)
Introduced gene and modified trait	<ul style="list-style-type: none"> <i>dmo</i> gene from <i>Stenotrophomonas maltophilia</i> for dicamba tolerance <i>bar</i> gene from <i>Streptomyces hygroscopicus</i> for glufosinate tolerance
Proposed locations	Australia-wide
Primary purpose	Commercial release of the GM cotton

Risk assessment

The risk assessment concludes that risks to the health and safety of people or the environment from the proposed dealings, either in the short or long term, are negligible.

The risk assessment process considers how the genetic modification and activities conducted with the GMO might lead to harm to people or the environment. Risks are characterised in relation to both the seriousness and likelihood of harm, taking into account information in the application, relevant previous approvals, current scientific knowledge and advice received from a wide range of experts, agencies and authorities consulted on the preparation of the RARMP. Both the short and long term risks are considered.

Credible pathways to potential harm that were considered included: toxic and allergenic properties of the GM cotton; potential for increased weediness of the GM cotton relative to unmodified plants; and vertical transfer of the introduced genetic material to other sexually compatible plants.

¹ The title of the application submitted by Monsanto is “Commercial release of *Gossypium hirsutum* genetically modified for herbicide tolerance in Australia”.

The principal reasons for the conclusion of negligible risks are: the introduced proteins are not considered toxic or allergenic to people or toxic to other desirable organisms; proteins similar to the introduced proteins are widespread in the environment; the GM event has been licensed for field trials in Australia between 2013 and 2019, and for commercial release when combined with other insect resistance and/or herbicide tolerance traits since 2016 with no reported adverse or unexpected effects; and the GM cotton has limited capacity to survive in natural habitats. In addition, food made from the GM cotton has been assessed and approved by Food Standards Australia New Zealand as safe for human consumption.

Risk management

The risk management plan concludes that risks from the proposed dealings can be managed so as to protect people and the environment by imposing general conditions to ensure that there is ongoing oversight of the release.

Risk management is used to protect the health and safety of people and to protect the environment by controlling or mitigating risk. The risk management plan evaluates and treats identified risks and considers general risk management measures. The risk management plan is given effect through licence conditions.

As the level of risk is assessed as negligible, specific risk treatment is not required. However, the Regulator has imposed licence conditions regarding post-release review (PRR) to ensure that there is ongoing oversight of the release and to allow the collection of information to verify the findings of the RARMP. The licence also contains a number of general conditions relating to ongoing licence holder suitability, auditing and monitoring, and reporting requirements, which include an obligation to report any unintended effects.

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Abbreviations

APVMA	Australian Pesticides and Veterinary Medicines Authority
<i>bar</i>	Bialaphos resistance gene from <i>Streptomyces hygrosopicus</i>
bp	base pair
<i>Bt</i>	<i>Bacillus thuringiensis</i>
cm	Centimetre(s)
CaMV	Cauliflower mosaic virus
CRDC	Cotton Research and Development Corporation
DCSA	3,6-dichlorosalicylic acid
DIR	Dealing involving Intentional Release
<i>dmo</i>	Dicamba monooxygenase gene from <i>Stenotrophomonas maltophilia</i>
DMO	Dicamba monooxygenase
DNA	Deoxyribonucleic acid
dw	Dry weight
EFSA	European Food Safety Authority
FSANZ	Food Standards Australia New Zealand
g	Gram
GM	Genetically modified
GMO	Genetically modified organism
ha	Hectare
HGT	Horizontal gene transfer
HRAC	Herbicide Resistance Action Committee
ILSI	International Life Sciences Institute
ISAAA	International Service for the Acquisition of Agri-Biotech Applications
IWM	Integrated Weed Management
km	Kilometre(s)
lbs	Pound
LOD	Limit of detection
µg	Microgram
mg	Milligram(s)
MOA	Mode of action
OECD	Organisation for Economic Co-operation and Development
OGTR	Office of the Gene Technology Regulator
PAT	Phosphinothricin N-acetyl transferase
PC1SV	Peanut chlorotic streak caulimovirus
ppm	parts per million
PRR	Post release review
RAF	Risk Analysis Framework (2013)
RARMP	Risk Assessment and Risk Management Plan
Regulations	Gene Technology Regulations 2001

Regulator	Gene Technology Regulator
RNA	Ribonucleic acid
spp.	Species
T-DNA	Transfer DNA
TEV	Tobacco etch virus
the Act	The Gene Technology Act 2000
USDA-APHIS	United States Department of Agriculture - Animal and Plant Health Inspection Service
US EPA	United States Environmental Protection Agency

Chapter 1 Risk assessment context

Section 1 Background

1. An application has been made under the *Gene Technology Act 2000* (the Act) for Dealings involving the Intentional Release (DIR) of genetically modified organisms (GMOs) into the Australian environment.
2. The Act and the Gene Technology Regulations 2001 (the Regulations), together with corresponding State and Territory legislation, comprise Australia's national regulatory system for gene technology. Its objective is to protect the health and safety of people, and to protect the environment, by identifying risks posed by or as a result of gene technology, and by managing those risks through regulating certain dealings with GMOs.
3. Section 50 of the Act requires that the Gene Technology Regulator (the Regulator) must prepare a Risk Assessment and Risk Management Plan (RARMP) in response to an application for release of GMOs into the Australian environment. Sections 50, 50A and 51 of the Act and sections 9 and 10 of the Regulations outline the matters which the Regulator must take into account and who must be consulted when preparing the RARMP.
4. The *Risk Analysis Framework* (RAF) (OGTR, 2013a) explains the Regulator's approach to the preparation of RARMPs in accordance with the Act and the Regulations. The Regulator has also developed operational policies and guidelines that are relevant to DIR licences. These documents are available from the Office of the Gene Technology Regulator ([OGTR website](#)).
5. Figure 1 shows the information that is considered, within the regulatory framework above, in establishing the risk assessment context. This information is specific for each application. Risks to the health and safety of people or the environment posed by the proposed release are assessed within this context. Chapter 1 describes the risk assessment context for this application.

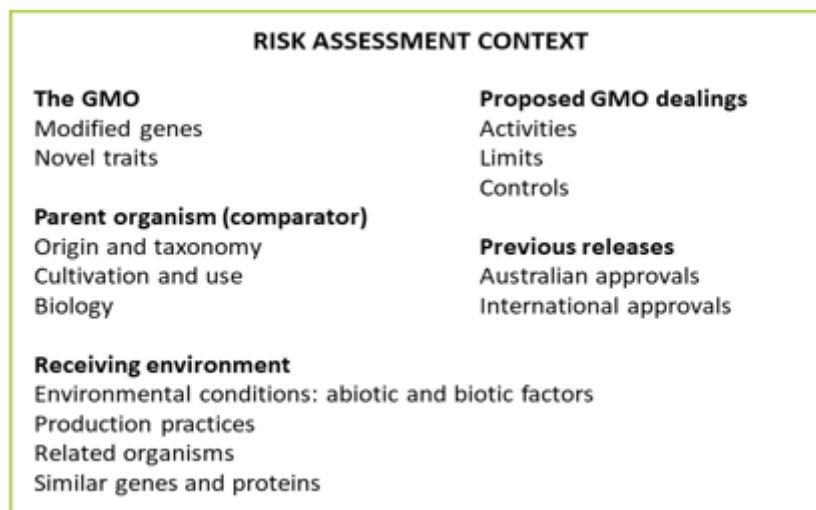


Figure 1 Summary of parameters used to establish the risk assessment context, within the legislative requirements, operational policies and guidelines of the OGTR and the RAF.

6. Since this application is not for experiments and does not propose limits and controls, it cannot be considered as a limited and controlled release application under section 50A of the Act. Therefore, under section 50(3) of the Act, the Regulator was required to seek advice from prescribed experts, agencies and

authorities on matters relevant to the preparation of the RARMP. This first round of consultation included the Gene Technology Technical Advisory Committee (GTTAC), State and Territory Governments, Australian Government authorities or agencies prescribed in the Regulations, all Australian local councils and the Minister for the Environment. A summary of issues contained in submissions received is provided in Appendix A.

7. Section 52 of the Act requires the Regulator, in a second round of consultation, to seek comment on the RARMP from the experts, agencies and authorities outlined above, as well as the public. Advice from the prescribed experts, agencies and authorities in the second round of consultation, and how it was taken into account, is summarised in Appendix B. Six public submissions were received and their consideration is summarised in Appendix C.

8. The GMOs and any proposed dealings may also be subject to regulation by other Australian government agencies that regulate GMOs or GM products, including Food Standards Australia New Zealand (FSANZ), the Australian Pesticides and Veterinary Medicines Authority (APVMA), the Therapeutic Goods Administration and the Department of Agriculture, Water and the Environment. These dealings may also be subject to the operation of State legislation recognising an area as designated for the purpose of preserving the identity of GM crops, non-GM crops, or both GM crops and non-GM crops, for marketing purposes.

Section 2 The proposed release

9. Monsanto Australia Pty Ltd (Monsanto) proposes commercial cultivation of a genetically modified (GM) cotton line (MON 88701), which contains two introduced genes that confer herbicide tolerance. This event is also known by the unique OECD identifier MON-887Ø1-3.

10. The applicant is seeking approval for the release to occur Australia-wide, subject to any moratoria imposed by States and Territories for marketing purposes. MON 88701 could be grown in all commercial cotton growing areas, and products derived from the GM plants would enter general commerce, including use in human food and animal feed.

11. The dealings involved in the proposed intentional release are to:

- (a) conduct experiments with the GMO
- (b) breed the GMO
- (c) propagate the GMO
- (d) use the GMO in the course of manufacture of a thing that is not a GMO
- (e) grow the GMO
- (f) import the GMO
- (g) transport the GMO
- (h) dispose of the GMO

and the possession, supply or use of the GMO for the purposes of, or in the course of, any of the above.

Section 3 The parent organism

12. The parent organism is upland cotton (*Gossypium hirsutum* L.), the most commonly cultivated cotton species worldwide. Cotton is exotic to Australia and is grown as an agricultural crop in New South Wales, Queensland and northern Victoria, with occasional trial or small-scale cultivation in northern Western Australia and the Northern Territory.

13. Cotton is grown as a source of textile and industrial fibre, cottonseed oil and linters for food use, and whole white (“fuzzy”) cottonseed and cottonseed meal for animal feed. A brief description of relevant biological information about the parent organism is provided in the following sections. More

detailed information can be found in *The Biology of Gossypium hirsutum L. and Gossypium barbadense L. (cotton)* (OGTR, 2016a), which was produced to inform the risk assessment process for licence applications involving GM cotton plants and is available from the OGTR [Biology documents](#) page.

14. In establishing the risk context, details of the parent organism form part of the baseline for a comparative risk assessment (OGTR, 2013a). Non-GM cotton is the standard baseline for biological comparison, while noting that 100% of the Australian commercial cotton crop is GM cotton from 2017 (ISAAA, 2017).

3.1 Cotton as a crop

15. Cotton is a domesticated crop that grows best under agricultural conditions. It prefers soils with high fertility and responds well to irrigation. Cotton has been commercially cultivated in Australia since the 1860s (OGTR 2016). It is a perennial plant that is cultivated as an annual.

16. Areas where cotton can be grown in Australia are mainly limited by water availability, the suitability of the soil, temperature and the length of the growing season. For further detail see discussion in the RARMPs for [DIR 066/2006](#) and [DIR 124](#). Commercial cultivation of cotton is also extensively reviewed in *The Biology of Gossypium hirsutum L. & Gossypium barbadense L. (cotton)* (OGTR, 2016a).

17. Based on 2017/18 commercial cropping areas in Australia, cotton was ranked as the crop with the seventh largest area of production. The cotton production area for 2017/18 was 526,000 ha but the estimated production area for 2018/19 was reduced to 343,000 ha and a further reduction to only 61,000 ha was forecasted for 2019/20 due to drought (ABARES, 2020).

3.1.1 Management of pests in cotton crops

18. The major insect pests of non-GM cotton in Australia are the heliothine moths (Lepidoptera: Heliothinae), more specifically the cotton bollworm (or corn earworm, *Helicoverpa armigera*) and native budworm (*H. punctigera*). In the 1990s, these were controlled by spraying chemical pesticides 8 – 15 times per season (Fitt, 2000). These broad-spectrum insecticides also control other pests, but disrupt beneficial insects that control secondary pests such as mites (OGTR, 2016a). The introduction of GM cotton, modified for insect resistance, in 1996 reduced the use of pesticides and is used as a tool in Integrated Pest Management (IPM) strategies in cotton (Whitehouse et al., 2005).

19. The use of IPM is promoted by the cotton industry as part of best management practices to reduce insect numbers, while reducing risks to the health of humans and the environment ([myBMP website](#), accessed May 2020). IPM involves using a range of tactics throughout the season to manage pest and beneficial insect populations in and around farms (CRDC and CottonInfo, 2017).

3.1.2 Cotton and herbicide resistance

20. Issues regarding herbicide use and resistance most appropriately fall under the *Agricultural and Veterinary Chemicals Code Act 1994*, and as such are the responsibility of the APVMA. The APVMA assesses all herbicides used in Australia and sets their conditions of use, including for resistance management.

21. A number of agricultural practices are used to control weeds in fields prepared for the planting of cotton. These practices include cultivation or the application of herbicide treatments (OGTR, 2016a). Integrated weed management (IWM) is used to avoid selection of resistant weed biotypes and reduce the likelihood of herbicide resistant weeds becoming a problem (CRDC and CottonInfo, 2017).

22. In Australia, at least 20 glyphosate-resistant weed species have been reported (Heap, 2020). To date, at least eight and three weed species from around the world are reported to have resistance to dicamba and glufosinate, respectively, but no dicamba-resistant or glufosinate-resistant weed species have been recorded in Australia (Heap, 2020).

3.2 Weed risk potential for cotton outside cultivation

23. In the context of this RARMP, characteristics of cotton are examined when present as a volunteer in relevant agricultural land uses, in intensive use areas such as roadsides and in nature conservation areas.

24. *G. hirsutum* is not recorded in the Australian government's *Weeds of National Significance* list and the *National Environmental Alert List* on the Department of Agriculture, Water and the Environment website (accessed May 2020), or the *Noxious Weed List for Australian States and Territories* (Invasive Plants and Animals Committee, 2015).

25. The Standards Australia National Post-Border Weed Risk Management Protocol rates the weed risk potential of plants according to properties that correlate with weediness for each relevant land use (Standards Australia et al., 2006). These properties relate to the plants' potential to cause economic, environmental and/or social harm (impact); to spread, establish and reproduce (invasiveness); and to its potential distribution. The weed risk potential of volunteer cotton has been assessed using methodology based on the National Post-Border Weed Risk Management Protocol (OGTR, 2016a).

3.2.1 Potential to cause harm

26. In summary, as a volunteer (rather than as a crop), non-GM cotton is considered to exhibit the following potential to cause harm:

- low potential to negatively affect the health of animals and/or people
- low potential to reduce the establishment or yield of desired plants
- low potential to reduce the quality of products or services obtained from all relevant land use areas
- low potential to restrict the physical movement of people, animals, vehicles, machinery and/or water
- some potential to act as a reservoir for a range of pests and pathogens
- low potential to adversely affect soil salinity and the water table (OGTR, 2016a).

27. With respect to the potential to negatively affect the health of people, it should be noted that workers in gins may develop byssinosis, an allergy to cotton (OGTR, 2016a).

28. Mammals, including people, can be fatally poisoned when ingesting cotton plant parts, due to the presence of natural toxins in cotton. The toxins include gossypol and the cyclopropenoid fatty acids (malvalic acid, sterculic acid and dihydrosterculic acid), all of which are found in seeds and certain other plant tissues (Bell, 1986). These compounds limit the use of cotton seed meal in human food and animal feed.

3.2.2 Invasiveness

29. With regard to invasiveness, non-GM cotton has:

- low ability to establish amongst existing plants
- low tolerance to average weed management practices in cropping and intensive land uses
- high tolerance in nature conservation areas (as they are not specifically targeted for weed management or because weed management is not applied in the area where cotton is present)
- a short time to seeding (less than one year)
- low annual seed production
- the ability to reproduce sexually, but not by vegetative means
- some ability for long distance spread by natural means (wind dispersal)
- high ability for spread long distance by people from dryland and irrigated cropping areas, as well as from intensive land uses such as road sides, but
- low ability for spread by people from or to nature conservation areas (OGTR, 2016a).

3.2.3 *Management of volunteer cotton*

30. Seedlings are easier to kill than older plants, and volunteer seedlings that emerge over winter in southern areas of Australia are likely to be killed by frost. Seedlings that emerge later in the year are likely to establish and grow, whether in a channel, a rotation crop or elsewhere on the farm. In wet winters, much of the seed dies before spring and relatively few volunteer seedlings are likely (CRDC, 2013c). The control of cotton volunteers is usually achieved by mechanical means such as cultivation or use of a range of herbicides, preferably as part of IWM practices. Six mode of action (MOA) groups of registered herbicides, including glufosinate, are currently available for cotton volunteer control in Australia. Control of volunteer cotton by herbicides is most effective on seedling cotton and only one herbicide (fluroxypyr) is registered for control of large 15- to 30-node volunteer cotton (Holman et al., 2019).

31. Currently, dicamba is not registered for use in volunteer cotton control in Australia (Holman et al., 2019).

3.2.4 *Spread and distribution*

32. Cottonseed may be spread off-farm, primarily during transport of modules to gins. Seed is also dispersed through irrigation or stormwater runoff into common drainage channels. Ephemeral populations of cotton volunteers can be found on cotton farms, by roadsides where cottonseed is transported, or in areas where cottonseed is used as livestock feed (Addison et al., 2007). In 2012 and 2013, the Queensland Department of Agriculture, Fisheries and Forestry conducted a survey of cotton plants throughout cropping areas in Qld and northern NSW. This study showed that plants were generally localised just beyond the farm gate and very little cotton had moved into the broader agricultural landscape. Densities were highest within a 5 km radius of cotton farms and in close proximity to ginning facilities (CRDC, 2013a).

33. Volunteer cotton is present but not considered a weed in agricultural ecosystems (Groves et al., 2003). In natural Australian ecosystems, cotton is described by Groves et al. (2003) as a naturalised non-native plant with a weediness rating of 2. This rating indicates that cotton is naturalised and known to be a minor problem warranting control at three or fewer locations within a state or territory.

34. The establishment of cotton across most of Australia is limited by drought stress, cold temperatures and soil fertility. Establishment is further limited by canopy conditions of natural vegetation, as well as fire regimes and weed competition (Addison et al., 2007; Rogers et al., 2007). Thus, although there are some naturalised populations in relatively natural areas of northern Australia, there is limited potential for *G. hirsutum* populations to spread and persist in undisturbed nature conservation areas.

35. Most reports of *G. hirsutum* volunteers or naturalised populations are from tropical regions of Australia, and cotton-growing areas throughout Queensland and New South Wales ([Australia's Virtual Herbarium](#)). Persistence of feral populations is limited, as *G. hirsutum* has little ability to invade undisturbed habitats (OGTR, 2016a).

Section 4 The GM cotton – nature and effect of genetic modification

4.1 The genetic modification

36. The GM cotton line proposed for release is MON 88701. MON 88701 has been extensively evaluated in the RARMP for limited and controlled release (DIR 120), and has been approved for commercial release throughout Australia as a stack with other GM cotton lines under the licence DIR 145.

4.1.1 *Details of the introduced genetic elements*

37. The genes introduced into MON 88701 are listed in Table 1.

Table 1 Introduced genes in cotton line MON 88701

Gene	Encoded protein	Source organism	Function
<i>dmo</i>	dicamba mono-oxygenase (DMO)	<i>Stenotrophomonas maltophilia</i>	Dicamba tolerance
<i>bar</i>	phosphinothricin N-acetyl transferase (PAT)	<i>Streptomyces hygroscopicus</i>	Glufosinate tolerance

38. Short regulatory sequences that control expression of the introduced genes are also present in MON 88701. These regulatory elements are listed in Table 2. These sequences are derived from plants including cotton (*Gossypium barbadense*), thale cress (*Arabidopsis thaliana*) and petunia (*Petunia x hybrid*), plant viruses including peanut chlorotic streak caulimovirus (PC1SV), cauliflower mosaic virus (CaMV) and tobacco etch virus (TEV), and a common soil-borne bacterium (*Agrobacterium tumefaciens*).

39. Although some of these regulatory sequences are derived from a plant pathogen, by themselves they do not cause disease. The regulatory elements present in MON 88701 have been previously assessed by Australian and international regulators without identifying an increase in risk compared with endogenous regulatory elements in cotton.

Table 2 Introduced regulatory elements in MON 88701

Element	Function	Source	Reference
P-PC1SV	promoter	Constitutive promoter from full length transcript of PC1SV	(Maiti and Shepherd, 1998)
P-e35S	promoter	Constitutive promoter for the 35S RNA of CaMV containing duplicated enhancer region	(Odell et al., 1985; Kay et al., 1987)
T-E6	terminator	Terminator sequence from the E6 gene of <i>G. barbadense</i>	(John, 1996)
T-nos	terminator	Terminator sequence from the nopaline synthase gene of <i>A. tumefaciens</i>	(Bevan et al., 1983; Fraley et al., 1983)
TEV	5' untranslated leader sequence for regulating gene expression	RNA of TEV	(Niepel and Gallie, 1999)
Ctp2	Transport of the DMO protein to the chloroplast	Chloroplast transit peptide from the <i>epsps</i> gene of <i>A. thaliana</i>	(Klee et al., 1987; Herrmann, 1995)
HSP70	5' untranslated leader sequence for regulating gene expression	Heat shock protein 70 gene of petunia	(Rensing and Maier, 1994)

4.1.2 Method of genetic modification

40. MON 88701 was generated using *Agrobacterium*–mediated transformation. This method has been widely used in Australia and overseas for introducing genes into plants. More information can be found

in the document *Methods of Plant Genetic Modification* on the [Risk Assessment References](#) page on the OGTR website.

41. Genetic elements of the transformation plasmid PV-GHHT6997 were delivered into excised hypocotyls of cotton cultivar Coker 130 by *A. tumefaciens*. PV-GHHT6997 contains two expression cassettes between the right and left borders of the transfer DNA (T-DNA) for expression of the *dmo* and *bar* genes in plants. The *dmo* and *bar* genes and the regulatory elements for controlling their expression (listed in Table 1 and Table 2) were delivered as a single insert. Genetic elements outside of the left and right borders of the T-DNA (the plasmid backbone) were not transferred (Section 4.3.1). Transformed cotton cells were selected through their ability to grow in the presence of glufosinate. GM cotton plants were then regenerated from the selected cells.

4.2 The introduced genes, their encoded proteins and associated effects

4.2.1 The *dmo* gene and its encoded product

42. MON 88701 contains a *dmo* gene derived from the strain DI-6 of the gram negative bacterium *Stenotrophomonas maltophilia* (formerly known as *Pseudomonas maltophilia*) (Wang et al., 1997; Herman et al., 2005). The *dmo* gene encodes a dicamba mono-oxygenase (DMO) and confers tolerance to dicamba herbicide (2-methoxy-3,6-dichlorobenzoic acid). Dicamba is a herbicide in the synthetic auxins group, which is included in Group I in the Australian mode of action classification (CropLife Australia, 2015) and in Group O in the HRAC site of action classification (Heap, 2020). It is similar in structure and mode of action to phenoxy herbicides such as 2,4-D, that mimics plant auxin hormones and causes abnormal plant growth by affecting cell division (Cox, 1994). DMO can rapidly demethylate 2-methoxy-3,6-dichlorobenzoic acid to non-herbicidal 3,6-dichlorosalicylic acid (DCSA) and formaldehyde.

4.2.2 The *bar* gene and its encoded product

43. MON 88701 also contains the bialaphos resistance (*bar*) gene, isolated from the soil-borne bacterium *Streptomyces hygroscopicus* (Thompson et al., 1987). The *bar* gene encodes a phosphinothricin N-acetyltransferase (PAT) protein that confers tolerance to glufosinate, the active component in a number of Group N (CropLife Australia, 2015) or HRAC Group H (Heap, 2020) herbicides. Glufosinate (also known as phosphinothricin) is a synthetic analogue of the antimicrobial secondary metabolite bialaphos produced by *S. hygroscopicus*. PAT acetylates the free amino group of glufosinate and converts it to N-acetyl-L-glufosinate (NAG) and renders it inactive.

4.2.3 Toxicity and allergenicity of the proteins encoded by the introduced genes

44. FSANZ has approved food derived from MON 88701 expressing DMO and PAT proteins as safe for human consumption (FSANZ, 2013a).

DMO protein

45. The *dmo* gene and encoded DMO protein have previously been assessed in the RARMP for GM cotton field trial application DIR 120 (OGTR, 2013b) and the RARMP for GM cotton commercial release application DIR 145 (OGTR, 2016d) and the RARMP for GM canola field trial application DIR 164 (OGTR, 2018). These assessments concluded that the introduced DMO protein lacked toxicity to humans or animals, or allergenicity in humans based on the following considerations:

- the *dmo* gene was derived from the aerobic, environmentally ubiquitous gram negative bacterium *S. maltophilia*, to which people and animals are exposed naturally through their diet and the environment
- the DMO protein does not have relevant amino acid sequences similar to known toxins, allergens or other proteins that may have adverse effects on mammals
- the DMO protein is heat labile and is rapidly digested in simulated gastric and intestinal fluids
- purified DMO protein did not show observable adverse effects on mice in acute oral toxicity evaluation when administered at high doses.

46. Acute oral toxicity assessment of purified DMO proteins from different dicamba-tolerant crops including cotton, soybean and corn in mice did not identify observable adverse effect up to 1000 mg DMO kg body weight (Wang et al., 2016a). A 90-day subchronic feeding study in rats using grain from MON 87708 soybean with the *dmo* gene showed no adverse effects during the entire exposure period (Wang et al., 2016b).

47. Apart from MON 88701 cotton, FSANZ has assessed MON 87708 soybean, and MON 87419 corn containing the *dmo* gene and concluded that food derived from these GM crop varieties were as safe for human consumption as food derived from their conventional (non-GM) counterparts (FSANZ, 2012, 2013a, 2016). Food and feed derived from these GM crops were also assessed and approved by US FDA (BNF135, BNF125 and BNF148) and that from MON 87708 soybean has also been assessed and approved by EFSA (EFSA, 2013b).

PAT protein

48. The *bar* gene and its encoded PAT protein have previously been extensively assessed in the RARMPs for commercial release of GM crops including cotton (DIR 062/2005, DIR 143 and DIR 145) (OGTR, 2006, 2016c, d) and GM canola (DIR 021/2002, DIR 108 and DIR 138) (OGTR, 2003, 2011, 2016b). The PAT protein has been assessed to be lack of toxicity to humans or animals, or allergenicity in humans on the following basis:

- the *bar* gene was derived from the common soil bacterium *S. hygroscopicus*, which is not considered a pathogen of humans or other animals
- no sequence homology has been found between PAT and any known toxic or allergenic proteins
- the PAT protein does not possess any of the characteristics associated with food allergens
- the PAT protein is inactivated by heat and low pH, and is rapidly degraded in simulated gastric or intestinal fluid
- purified PAT protein was not toxic to mice and rats when administered at high doses in acute toxicity studies.

49. FSANZ has approved food derived from a number of GM crops expressing PAT protein as safe for human consumption. This includes GM cotton (FSANZ, 2005a, 2010a, b, 2013a), GM canola (ANZFA, 2001), GM corn (FSANZ, 2005b) and GM rice (FSANZ, 2008).

4.2.4 Toxicity of herbicide metabolites

50. As herbicide metabolites are produced in MON 88701 following treatment with corresponding herbicides, they are briefly discussed below. However, the potential toxicity of an herbicide and its metabolites is not in scope of this assessment as the herbicide is not part of the genetic modification. If MON 88701 cotton is to be commercially cultivated in Australia, the potential toxicity of the corresponding herbicides, dicamba and glufosinate, and their metabolites, is considered by the APVMA in its assessment of a new use pattern for registration.

Dicamba metabolites

51. As discussed in Section 4.2.1, the main metabolites produced in MON 88701 in the presence of dicamba would be DCSA and formaldehyde.

52. DCSA is not a dicamba metabolite unique to MON 88701 cotton or other GM crops expressing the DMO protein after being treated with dicamba. Conventional plants (for example wheat) and ruminants can also metabolise dicamba to produce DCSA at a low rate (EFSA, 2011).

53. Data regarding the toxicity of DCSA is limited and some uncertainty exist. DCSA generally shows low acute toxicity to mammals (EFSA, 2013a; US EPA, 2016a). From the available information, DCSA appears to be less toxic or equally toxic as parent dicamba for aquatic organisms on an acute basis, but may be substantially more toxic on a chronic basis to terrestrial organisms, specifically mammals (US

EPA, 2016b, 2018a). However, the residue amount of DCSA in the cottonseed of dicamba treated MON 88701 is very low, with a mean value of 0.08 ppm when dicamba was applied four times between the 6-leaf stage and 7-day preharvest interval at the rate of 0.5 lbs acid equivalent/acre or 0.56 kg/ha (FSANZ, 2013b).

54. Formaldehyde, as the other metabolite, is ubiquitous in the environment from plant and animal sources, and from industrial sources. In MON 88701, dicamba-derived formaldehyde is expected to be in small amounts (estimated to be 6.3 - 33 mg/kg on standard dicamba application rates) and would be rapidly degraded and incorporated into the 1-carbon pool of plants. This is well within the range of formaldehyde measured in a variety of dicot plants (up to several hundred mg/kg) and agricultural commodities (USDA-APHIS, 2014b).

Glufosinate metabolites

55. The main metabolite in non-GM plants following the metabolism of glufosinate is 3-methylphosphinico-propionic acid (sometimes referred to as 3-hydroxy-methyl phosphinoyl-propionic acid) (Müller et al., 2001; OECD, 2002). However, NAG is the main metabolite formed following application of glufosinate to GM plants expressing the PAT protein (Section 4.2.2). NAG is also referred to as 2-acetamido-4-methylphosphinico-butanoic acid.

56. NAG is less toxic than its parent glufosinate, which itself has low toxicity (FAO, 2013). NAG is generally considered non-toxic to plants (including nonvascular aquatic plants), invertebrates, rodents and mammals, including humans (EFSA, 2005; US EPA, 2014).

4.3 Characterisation of the GMO

4.3.1 Molecular characterisation

57. The applicant carried out Southern blot hybridisation analysis of the R₃ generation (R₀ is the transformed plant) to determine the copy number of the transgenes present in MON 88701 cotton. A single copy of the T-DNA containing the *dmo* and *bar* expression cassettes at a single integration site was demonstrated (Arackal et al., 2011a). DNA sequence analysis confirmed that the organisation and sequence of the genetic elements within the inserted T-DNA in MON 88701 was identical to that in the plasmid PV-GHHT6997 (Arackal et al., 2011b).

58. PCR and Southern blot analysis were used to confirm that plasmid backbone sequences of PV-BNHT2672 (ie the part of the plasmid not intended to be transferred to the plants) are not present in the MON 88701 genome (Arackal et al., 2011b). The integrity of the single insertion site in MON 88701 genome was also examined by PCR and sequence analysis using genomic DNA extracted from MON 88701 and from the parental cotton variety Coker 130 (Arackal et al., 2011b). Sequence alignment showed a deletion of 123 base pairs of genomic DNA at the insertion site in MON 88701. Such changes commonly occur during the process of *Agrobacterium*-mediated transformation, likely resulting from the plant's double-strand break repair mechanism (Salomon and Puchta, 1998).

59. Stability of the insert in MON 88701 was demonstrated by Southern blot and Western blot analyses of five MON 88701 generations (R₂ to R₆), which showed that the integrated DNA has been maintained through the generations and the DMO and PAT proteins are stably expressed in each tested generation (Arackal et al., 2011a).

4.3.2 Expression of the introduced proteins

60. In a field trial carried out in the United States in 2013 (Paul, 2015), MON 88701 cotton was planted in four replicated plots at five sites in five different states. Levels of expressed proteins from the introduced genes in MON 88701 were measured in leaves (collected at 2-3 nodes stage), roots (collected at late/peak bloom stage) and seeds (collected after harvest) determined by validated multiplexed immunoassay (Table 3). Data are shown as the arithmetic mean \pm standard deviation (SD) and the range of values recorded as microgram (μ g) of protein per gram (g) of tissue on a dry weight basis (dw). The

means, SD, and ranges (minimum and maximum values) were calculated for each tissue across all sites (n=20).

61. The mean DMO protein level in MON 88701 across all sites was highest in selected leaves at 300 µg/g dw and lowest in seed at 23 µg/g dw. However, the mean PAT protein level in MON 88701 across all sites was highest in seed at 7.5 µg/g dw and lowest in root at 2.1 µg/g dw.

62. Although the applicant did not provide data regarding the expression levels of the DMO and PAT proteins in the pollen of MON 88701 in this application, it was shown that the two proteins were expressed in the pollen of MON 88701 in a previous assessment by FSANZ (FSANZ, 2013b).

Table 3 Expression levels of introduced proteins in MON 88701 grown in the USA during 2013 (dicamba and glufosinate treated)

Protein	Tissue type		
	Leaf Mean±SD (Range) µg/g dw	Root Mean±SD (Range) µg/g dw	Seed Mean±SD (Range) µg/g dw
DMO	300 ± 110 (140 - 480)	65 ± 18 (41 - 110)	23 ± 6.4 (10 - 37)
PAT	5.1 ± 2.1 (2.2 - 9.4)	2.1 ± 0.56 (1.2 - 3.4)	7.5 ± 2.0 (3.7 - 13)

4.3.3 Compositional analysis of cottonseed

63. The applicant provided data for compositional analysis of MON 88701 cotton seed harvested from eight field trial sites within eight states in the United States in 2010, in comparison to the parental variety Coker 130 (as control) and nine reference non-GM commercial cotton varieties (Howard et al., 2012). In addition to the MON 88701 and the control, four of the nine conventional reference varieties were grown at each site.

64. MON88701, the control and reference varieties were grown under normal field conditions, including maintenance pesticides as needed for their respective geographic region. The MON88701 plots were treated at the 3-5 leaf stage with glufosinate herbicide at the label rate (0.56 kg/ha) and at the 6-10 leaf stage with dicamba herbicide at the label rate (0.56 kg/ha). Cottonseed samples were harvested and ginned from all plots. Compositional analyses were carried out on acid-delinted cottonseed.

65. Compositional analysis was conducted in accordance with the OECD consensus document on compositional considerations for cotton (OECD, 2009). Nutrient analytes included proximates (ash, carbohydrates by calculation, moisture, protein and total fat), acid detergent fibre (ADF), neutral detergent fibre (NDF), crude fibre (CF), total dietary fibre (TDF), amino acids, fatty acids (C8-C22), minerals (calcium, copper, iron, magnesium, manganese, phosphorus, potassium, sodium and zinc) and vitamin E (tocopherol). The antinutrients included in this analysis were gossypol and cyclopropanoid fatty acids (dihydrosterculic, malvalic and sterculic acids).

66. A total of 65 analytes were measured. In order to complete the statistical analysis for any analyte in this study, it was deemed that at least 50% of the values must be greater than the assay limit of quantitation (LOQ). Statistical analyses were not conducted for the following 13 fatty acid analytes: 8:0 caprylic acid, 10:0 capric acid, 12:0 lauric acid, 14:1 myristoleic acid, 15:0 pentadecanoic acid, 15:1 pentadecenoic acid, 17:0 heptadecanoic acid, 17:1 heptadecenoic acid, 18:3 gamma-linolenic acid, 20:1 eicosenoic acid, 20:2 eicosadienoic acid, 20:3 eicosatrienoic acid and 20:4 arachidonic acid, as their values were below the LOQ. The remaining 52 analytes (47 nutrients and five anti-nutrients) were statistically assessed using a mixed-model analysis of variance method. Nine sets of statistical comparisons of MON 88701 cotton to the control were conducted. One comparison was based on

compositional data combined across all eight field sites (combined-site analysis) and eight separate comparisons were conducted on data from each individual field site. Compositional data from non-GM commercial varieties grown concurrently in the same trial with MON 88701 and the control, were combined across all sites and used to calculate a 99% tolerance interval for each component to define the natural variability in commercial varieties. Any statistically significant differences ($p < 0.05$) between MON 88701 and the control were also compared to this tolerance range, to assess whether the differences were likely to be biologically meaningful.

67. In the combined-site analysis, 28 of the 47 nutrient analytes showed no statistically significant difference between MON 88701 and the control. These are: one proximate (protein), one type of fibre (crude fibre), 15 amino acids (alanine, aspartic acid, cystine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, phenylalanine, serine, threonine, tryptophan, tyrosine and valine), seven fatty acids (16:0 palmitic acid, 16:1 palmitoleic acid, 18:0 stearic acid, 18:1 oleic acid, 18:3 linolenic acid, 20:0 arachidic acid and 22:0 behenic acid), and four minerals (copper, iron, phosphorus and sodium).

68. Statistically significant differences were identified in the other 19 nutrient analytes, with MON 88701 having statistically significant increase ($p < 0.05$) in proximate (ash, calories and total fat), amino acid (methionine), fatty acids (14:0 myristic acid and 18:2 linoleic acid), minerals (calcium, magnesium, potassium and manganese) and vitamin E, and statistically significant decrease ($p < 0.05$) in proximate (carbohydrates and moisture), fibre (ADF, NDF and TDF), amino acids (arginine and proline), and mineral (zinc). However, all these nutrient mean values were either within the 99% tolerance interval established by the non-GM reference varieties grown concurrently in the same trials or within the range of natural variability for commercial cottonseed available in the [ILSI Crop Composition Database](#).

69. Among the anti-nutrients, no statistically significant differences between MON 88701 and the control were identified in the combined-site analysis for two cyclopropenoid fatty acids (malvalic acid and sterculic acid). Statistically significant difference ($p < 0.05$) was identified for one cyclopropenoid fatty acid (dihydrosterculic acid), free gossypol and total gossypol, with increased levels of the three analytes in MON 88701 seed. However, the increases were not consistently observed across sites and their levels were within the tolerance ranges calculated for the reference non-GM cotton varieties and therefore it is unlikely to indicate any biological significance.

70. The composition of cotton can vary significantly with the site and agricultural conditions, and the identified differences most likely reflect normal biological variability. In summary, the compositional data analysis showed that the seed of MON 88701 and non-GM cotton varieties are compositionally equivalent. The component values that were statistically significant different between MON 88701 seed and non-GM seed were not considered biologically meaningful.

4.3.4 Phenotypic characterisation and environmental interaction

Phenotypic and agronomic characterisation

71. The agronomic performance of MON 88701 cotton was assessed in field trials in the USA during 2010. The applicant submitted field trial data obtained from the 2010 trials across 15 sites within cotton growing regions in the USA (Bommireddy, 2012). The field trials included MON 88701 cotton, the parental cotton variety Coker 130 as control and four commercial cotton varieties selected from a total of 11 varieties (seven conventional varieties and four glyphosate-tolerant GM varieties) as comparators at each site.

72. The phenotypic and agronomic characteristics measured represent characteristics that influence reproduction, crop survival and potential weediness. These were growth and development characteristics, including stand count at 14 days after planting (DAP) and 30 DAP, plant vigour at 14 DAP and 30 DAP, plant height at 30 DAP, nodes above white flower, final stand count, plant height at harvest and seed cotton yield; and seed characteristics, including seed index, total seed per boll, mature seed per

boll and immature seed per boll. Boll and fibre quality, including boll weight, micronaire, elongation, strength, uniformity, and length, were also measured.

73. Comparisons of MON 88701 and the control Coker 130 were conducted within each site (individual site analysis) and in a combined-site analysis, in which the data were pooled across sites for the phenotypic characteristics and environmental interactions mentioned above, except for plant vigour at 14 DAP and 30 DAP. The plant vigour data from individual sites were categorical and were not statistically analysed. MON 88701 and the control were considered different in vigour if the ranges of vigour of MON 88701 and the control did not overlap across all replications. In cases of lack of overlap, comparisons were then made to the reference range. Results of the plant vigour observation showed consistent overlap in vigour ranges between MON 88701 and the control for all sites except one. However, at this site MON 88701 plant vigour values were within that of the reference range, indicating the similarity in growth and development between MON 88701 and the control plants.

74. Data presented in Tables 4 – 6 are from combined-site analysis and numbers represent sample means with standard error (SE) in parentheses. Statistical differences were identified at a 5% level of significance ($p < 0.05$). No statistical comparisons were made between the test and reference materials. The reference range for each measured phenotypic characteristic was determined from the minimum and maximum mean values from the 11 reference cotton varieties planted among the sites.

75. As shown in Table 4, the combined-site analysis did not identify statistically significant differences between MON 88701 and the conventional control for stand count at 14 DAP, stand count at 30 DAP, stand count at harvest, nodes above white flower observation 1, or seed cotton yield. Four statistically significant differences were detected between MON 88701 and the conventional control. Plant height at 30 DAP and at harvest was lower for MON 88701 than the conventional control (18.3 vs. 19.7 and 109.8 vs. 116.4 cm, respectively). MON 88701 had more nodes above white flower than conventional control at observation 2 (6.0 vs. 5.7) and observation 3 (4.9 vs. 4.6). However, the mean values of MON 88701 were within the reference range for the above detected differences.

Table 4 Phenotypic comparison of MON 88701 to the conventional control combined across all sites in 2010 field trials

Characteristic (units)	MON 88701(SE)	Control (SE)	Reference Range
Stand count at 14 DAP ¹	146.0 (4.3)	152.4 (4.2)	96.2 - 143.5
Stand count at 30 DAP ¹	131.8 (5.5)	137.7 (5.5)	86.7 - 140.8
Final stand count at harvest ¹	125.2 (5.9)	128.9 (6.0)	88.2 - 131.4
Plant height at 30 DAP (cm)	18.3 (1.2)*	19.7 (1.2)	8.3 - 23.3
Plant height before harvest (cm)	109.8 (3.8)*	116.4 (4.2)	84.4 - 131.3
Nodes above white flower ² :			
Observation 1	6.9 (0.2)	6.7 (0.2)	5.8 - 8.6
Observation 2	6.0 (0.2)*	5.7 (0.2)	5.1 - 6.9
Observation 3	4.9 (0.3)*	4.6 (0.3)	3.7 - 5.7
Seed cotton Yield (Kg/ha)	2937.8 (153.7)	2869.9 (156.0)	2107.0 - 3636.5

* Indicates a statistically significant difference between MON 88701 and control ($p < 0.05$).

¹ Number per plot; ² Number of nodes above first white flower observed over three weeks.

76. The combined-site analysis of seed characteristics (Table 5) did not detect statistically significant differences between MON 88701 and the control for immature seed per boll, but detected statistically significant differences in the other three characteristics. Seed index was lower for MON 88701 than the conventional control (9.8 vs. 10.5 g per 100 fuzzy seed). MON 88701 had more total seed per boll (29.0 vs. 27.4) and mature seed per boll (22.6 vs. 19.7) than the conventional control. However, the mean values of MON 88701 were within the reference range for the above detected differences.

Table 5 Seed characteristics of MON 88701 and the control combined across all sites in 2010 field trials

Characteristic (units)	MON 88701 (SE)	Control (SE)	Reference Range
Seed Index ¹	9.8 (0.2)*	10.5(0.1)	8.9 - 11.8
Total Seed per Boll ²	29.0 (0.4)*	27.4(0.3)	26.4 - 30.6
Mature Seed per Boll ²	22.6 (0.7)*	19.7(0.6)	11.8 - 27.2
Immature Seed per Boll ²	6.4(0.5)	7.7(0.5)	3.4 - 16.0

* Indicates a statistically significant difference between MON 88701 and control ($p < 0.05$).

¹ Gram per 100 fuzzy seed; ² Number of seed per boll.

77. In the combined-site analysis of boll and fibre quality characteristics (Table 6), no statistically significant differences were detected between MON 88701 and the control for boll weight, fibre micronaire, fibre elongation, fibre uniformity and fibre length. One statistically significant difference was detected for fibre strength; strength was higher for MON 88701 than the control (31.8 vs. 31.0 g/tex). However, the mean value of MON 88701 was within the reference range.

Table 6 Boll and fibre quality characteristics of MON 88701 and the control across all sites in 2010 field trials

Characteristic (units)	MON 88701 (SE)	Control (SE)	Reference range
Boll weight (g)	4.8 (0.1)	4.8 (0.1)	4.2 - 6.0
Micronaire ¹	4.6 (0.1)	4.5 (0.1)	4.0 - 5.0
Elongation (%)	6.0 (0.1)	6.0 (0.1)	4.8 - 8.0
Strength (g/tex)	31.8 (0.2)*	31.0 (0.1)	30.7 - 34.5
Uniformity (%)	84.0 (0.1)	83.7 (0.1)	83.7 - 84.8
Length (cm)	2.8 (0.0)	2.9 (0.0)	2.8 - 3.1

* Indicates a statistically significant difference between MON 88701 and control ($p < 0.05$).

¹ Measure of fibre fineness and maturity (expressed in dimensionless micronaire units).

78. In summary, the differences in agronomic performance and fibre quality between MON 88701 cotton and control cotton are within the range of variation among the reference varieties tested and sites, indicating that MON 88701 has no biologically meaningful phenotypic and agronomical differences to non-GM cotton varieties.

Environmental interaction

79. Environmental interaction refers to the interaction between the crop plants and their receiving environment, which may include plant response to abiotic stress, disease and arthropods. In the same field trials in the USA during 2010, environmental interactions of MON 88701 cotton including response to abiotic stress, disease, arthropod damage and arthropod abundance were also compared to the control Coker 130 cotton and the reference varieties (Bommireddy, 2012).

80. Plant response to abiotic stress, disease damage and arthropod damage was assessed qualitatively. Observations were performed four times during the growing season at each site with the first observation made at approximately 30 DAP and the three subsequent collections at approximately 30 day intervals thereafter. If the range of injury symptoms did not overlap between MON 88701 and the control across all four replications, a difference in susceptibility or tolerance was considered to be present.

81. The abiotic stressors, diseases and pest arthropods selected for this assessment were: abiotic stressors - compaction, drought, flood, hail, heat, nutrient deficiency, wet soil and wind damage; diseases - anthracnose, Ascochyta leaf blight, bacterial blight, boll rot, cotton leaf rust, damping off, *Fusarium* wilt, leaf spots, *Pythium*, reniform nematode, *Rhizoctonia*, root-knot nematode, *Thielaviopsis* root rot and *Verticillium* wilt; and arthropods - aphids, beet armyworms, cut worms, fall

armyworms, fleahoppers, grasshoppers, heliothines, Southern corn rootworms beetles, soybean loopers, spider mites, stink bugs, tarnished plant bugs, thrips and white flies. A total of 169, 170 and 159 valid comparisons between MON 88701 and the control were carried out for abiotic stressor, disease damage and arthropod damage, respectively. No meaningful differences were observed between MON 88701 and the control for any of these comparisons among all observations at the sites.

82. The assessment of pest and beneficial arthropod abundance included aphids, cabbage loopers, fall armyworms, fleahoppers, heliothines, southern armyworms, stink bugs, tarnished plant bugs, thrips, white flies, big eyed bugs, braconids, damsel bugs, lacewings, ladybird beetles, *Orius* spp., and spiders (Araneae). No statistically significant differences were detected between MON 88701 and the control for 173 out of 178 comparisons (including 89 pest arthropod comparisons and 89 beneficial arthropod comparisons) among the collections at the five sites. The five statistical significant differences detected between MON 88701 and the control included two pest arthropod comparisons (involving stink bugs and tarnished plant bugs) and three beneficial arthropod comparisons (involving damsel bugs and *Orius* spp.). MON 88701 had lower abundance of stink bugs and tarnished plant bugs at one site and of *Orius* spp. at two sites, while had higher abundance of damsel bugs at one site. Two of these detected statistically significant differences were within the respective reference ranges (lower abundance of tarnished plant bugs and higher abundance of damsel bugs). The remaining three differences (lower abundance of stink bugs and *Orius* spp.), were outside of the reference range. However, these differences were not consistent across collections or across sites. Therefore, these differences were not indicative of a consistent plant response associated with the introduced traits.

83. Based on the assessed environmental interactions, the identified differences are unlikely to be biologically meaningful for MON 88701 due to the genetic modification compared to other commercially available cottons.

Section 5 The receiving environment

84. The receiving environment forms part of the context in which the risks associated with dealings involving the GMOs are assessed. Relevant information about the receiving environment includes abiotic and biotic interactions of the crop with the environment where the release would occur; agronomic practices for the crop; presence of plants that are sexually compatible with the GMO; and background presence of the gene(s) used in the genetic modification (OGTR, 2013a).

85. The applicant has proposed to release MON 88701 cotton in all commercial cotton growing areas, Australia-wide. Therefore, for this licence application, it is considered that the receiving environment is all of Australia, but in particular agricultural areas that are suitable to cultivate cotton. Commercial cotton production occurs mainly in New South Wales, southern and central Queensland, and northern Victoria, and on a trial basis in northern Queensland, northern Western Australia and the Northern Territory. The actual locations, number of sites and area of land used in the proposed release would depend on factors such as field conditions, grower demand and seed availability.

5.1 Relevant agronomic practices

86. It is anticipated that the agronomic practices for cultivation of the GM cotton will not differ significantly from industry best practices used in Australia. All cotton plants would be grown following standard cotton agricultural management practices and would receive applications of water, fertilisers, and herbicides similar to current commercially grown non-GM and GM cotton crops. Cultivation practices for cotton are discussed in more detail in *The Biology of Gossypium hirsutum L. and Gossypium barbadense L. (cotton)* (OGTR, 2016a).

87. The agronomic management of MON 88701 cotton would differ from the management of non-GM and other GM cotton in that dicamba and glufosinate herbicides could be applied over the top of the cotton crops to control weeds. Management of volunteer cotton following growing of MON 88701 crops would need to rely on cultivation and/or herbicide spraying using herbicides other than dicamba or glufosinate.

5.2 Relevant abiotic factors

88. The abiotic factors relevant to the growth and distribution of commercial cotton in Australia are discussed in *The Biology of Gossypium hirsutum L. and Gossypium barbadense L. (cotton)* (OGTR, 2016a). To summarise, factors restricting where cotton can be grown in Australia are water availability (through rainfall or irrigation), soil suitability and, most importantly, temperature. Cotton seedlings may be killed by frost, growth and development of cotton plants below 12°C is minimal, and a long, hot growing season is crucial for achieving good yields.

5.3 Relevant biotic factors

5.3.1 Presence of sexually compatible plants in the receiving environment

89. In the natural environment, for successful hybridisation to occur, parent plants have to occur in close proximity, flower at the same time, have pollen from one plant deposited on the stigma of the other, fertilisation must occur and progeny must survive to sexual maturity. Any progeny seed would have to be viable. Cotton is largely self-pollinating and no self-incompatibility mechanisms exist. Where cross-pollination does occur it is likely facilitated by honeybees. Cotton does not reproduce by asexual mechanisms, although root cuttings can be propagated under laboratory conditions (OGTR, 2016a).

90. There are 17 native species of *Gossypium* in Australia, most of which are found in the NT and the north of WA (OGTR, 2016a). Only three of these species are likely to occur in the regions of Australia where cotton is cultivated: *G. sturtianum*, *G. nandewarensense*, and *G. australe*. However, native *Gossypium* species prefer well-drained sandy loams and are rarely found on heavy clay soils favoured by cultivated cotton.

91. Furthermore, the likelihood that *G. hirsutum* could hybridise successfully with any of the native Australian cottons is extremely low, due to genetic incompatibility. Cultivated cottons are tetraploids of the A and D genomes (AADD, $2n=4x=52$), whereas the Australian *Gossypium* species are diploids of the C, G or K genomes. Hybrids between *G. hirsutum* and *G. sturtianum* have been produced under field conditions between plants grown in close proximity, but the hybrids were sterile, eliminating the possibility of introgression of genes from *G. hirsutum* into *G. sturtianum* populations (OGTR, 2016a).

92. *Gossypium hirsutum* is sexually compatible with the other species of cultivated cotton, *G. barbadense* (Pima cotton). Commercial cotton grown in Australia is predominantly *G. hirsutum*. The amount of *G. barbadense* cotton grown in Australia has declined due to low fibre yield, making up around 1% of cotton planted in 2006 (OGTR, 2016a) and no *G. barbadense* varieties are available in the 2019 cotton season (CSD, 2019). The GM *G. hirsutum* proposed for release is capable of crossing with both species of commercially grown cotton.

93. From 2017, all of the Australian cotton crops were genetically modified (ISAAA, 2017). Currently licensed GM cotton varieties are listed in Table 7. However, only Roundup Ready Flex® (RRF) and Bollgard® 3 x Roundup Ready Flex® (BG3 RRF) cottons were the GM cotton varieties available to growers in the 2019 cotton season, noting that conventional varieties were also available (CSD, 2019). To date, the dicamba-tolerant GM cotton varieties approved under DIR 145, XtendFlex™ (XF) and Bollgard® 3 XtendFlex™ (BG3 XF), have not been commercially cultivated but have been grown in smaller scale trials in Australia since 2016 (information provided by the applicant).

Table 7 GM cotton approved for commercial cultivation in Australia

DIR licence	Trade name	GM traits
062/2005	Liberty Link®	Contains the <i>bar</i> gene for herbicide tolerance
066/2006	Bollgard II® (BGII), Roundup Ready® (RR), Roundup Ready Flex® (RRF), RR/BGII, RRF/BGII (north of latitude 22° South)	Contains <i>cry1Ac</i> and <i>cry2Ab</i> for insect resistance, and <i>cp4 epsps</i> for herbicide tolerance
091	WideStrike™	Contains <i>cry1Ac</i> (<i>synpro</i>) and <i>cry1F</i> (<i>synpro</i>) for insect resistance
118	Roundup Ready Flex® <i>Gossypium barbadense</i>	Contains <i>cp4 epsps</i> for herbicide tolerance
124	Bollgard® 3, Bollgard® 3 Roundup Ready Flex®	Contains <i>cry1Ac</i> , <i>cry2Ab</i> and <i>vip3Aa19</i> for insect resistance, and <i>cp4 epsps</i> for herbicide tolerance
143	GlyTol®, GlyTol TwinLink Plus®	Contains <i>cry1Ab</i> , <i>cry2Ae</i> and <i>vip3Aa19</i> for insect resistance, and <i>2mepsps</i> and <i>bar</i> for herbicide tolerance
145	Bollgard® 3 XtendFlex™, XtendFlex™	Contains <i>cry1Ac</i> , <i>cry2Ab</i> and <i>vip3Aa19</i> for insect resistance, and <i>cp4 epsps</i> , <i>dmo</i> and <i>bar</i> for herbicide tolerance
157	VIPCOT™	Contains <i>vip3Aa19</i> for insect resistance

5.3.2 Presence of other biotic factors

94. The major insect pests of cotton are lepidopteran species. In Australia, the most damaging lepidopteran pests are cotton bollworm (*Helicoverpa armigera*) and native budworm (*H. punctigera*). Beet armyworm (*Spodoptera exigua*), cluster caterpillar (*Spodoptera litura*) and pink bollworm (*Pectinophora gossypiella*) can also affect cotton production (OGTR, 2016a). These lepidopteran pests are now managed through the widespread adoption of GM cotton varieties with *Bt* toxin genes that specifically target these insect pests.

95. Many cotton growing areas across Australia also have important non-lepidopteran insect pests. These include cotton aphids (*Aphis gossypii*), green mirids (*Creontiades dilutus*), brown mirids (*C. pacificus*), two-spotted spider mites (*Tetranychus urticae*), silverleaf whitefly (*Bemisia tabaci*), thrips (*Thrips tabaci*, *Frankliniella schultzei* and *F. occidentalis*), green vegetable bugs (*Nezara viridula*) and solenopsis mealybugs (*Phenacoccus solenopsis*) (CRDC and CottonInfo, 2017).

96. Many other arthropods are associated with cotton fields, including beneficial organisms such as spiders, ladybird beetles, earwigs, hoverflies, bugs, bees, parasitoid wasps and flies, and lacewings (Whitehouse et al., 2005).

97. Australian cotton is affected by a number of soil-borne and foliar fungal diseases, along with oomycete, bacterial and viral diseases. Fungal pathogens cause the major diseases Verticillium wilt (*Verticillium dahliae*) and Fusarium wilt (*Fusarium oxysporum* f. sp. *vasinfectum*; FOV). Common seedling diseases of cotton are black root rot (*Thielaviopsis basicola*) and damping off (caused by *Rhizoctonia solani*, *Pythium* spp. and *Phytophthora* spp.). Leaves may be affected by Alternaria leaf spot (*Alternaria* spp.) and cotton bunchy top virus spread by aphids. Boll rots are caused by different pathogens, including fungi, bacteria and oomycetes (CRDC and CottonInfo, 2017).

98. Reniform nematode (*Rotylenchulus reniformis*) emerged as a new pest in central Queensland in 2012. The soil-borne plant parasite has a wide host range and is found in a broad range of climatic conditions (CRDC and CottonInfo, 2017).

99. Cotton is susceptible to competition from weeds. Problematic weeds range from large plants such as Noogoora burr (*Xanthium occidentale*), Bathurst burr (*X. spinosum*), thornapples (*Datura* spp.) and sesbania (*Sesbania canabina*), to vines such as cowvine and bellvine (*Ipomoea* spp.), yellow vine or spineless caltrop (*Tribulus* spp.), to grasses such as nut grass (*Cyperus rotundus*) (CRDC, 2013b). Some weed species are alternate hosts for diseases of cotton, e.g. many weeds are hosts for *Verticillium dahliae* (CRDC and CottonInfo, 2017).

5.3.3 Presence of weeds resistant to dicamba or glufosinate herbicides

100. Although weeds resistant to Group I herbicide 2,4-D have been reported, no dicamba-resistant weed species have been recorded in Australia to date (Heap, 2020). Also, there has been no record of glufosinate-resistant weed species in Australia (Heap, 2020).

5.4 Presence of the introduced genes and encoded proteins in the receiving environment

101. The introduced genes were originally isolated from naturally occurring organisms that are already widespread and prevalent in the environment.

102. The *dmo* gene was isolated from the environmentally ubiquitous bacterium *S. maltophilia*, which is commonly present in aquatic environments and soil. It is also found in close association with plants (Ryan et al., 2009).

103. The *bar* gene was isolated from the common bacterium *S. hygroscopicus*, which is a saprophytic, soil-borne microbe not considered pathogens of plants, humans or other animals (OECD, 1999). Genes encoding PAT or similar enzymes are present in a wide variety of bacteria. Acetyltransferases, the class of enzymes to which PAT belongs, are common enzymes in all microorganisms, plants and animals.

Section 6 Previous authorisations

6.1 Australian authorisations of MON 88701

104. The Regulator has issued three licences for the MON 88701 event for limited and controlled, and commercial releases (Table 8). These licences have been issued for the MON 88701 event alone or GM cottons derived from MON 88701 event in combination with other herbicide tolerance and/or insect resistance traits through conventional breeding. Previous assessments of MON 88701 concluded that the event poses negligible risks to human health and safety, and the environment.

105. In 2016, DIR 145 licensed the use of the MON 88701 traits (*dmo* and *bar* genes) in combination with the insect resistance traits (*cry1Ac*, *cry2Ab* and *vip3Aa19* genes) and other herbicide tolerance trait (*cp4 epsps* gene for glyphosate tolerance) in BG3 XF and XF cottons for commercial release. However, these two GM cotton lines have not been cultivated in commercial scale in Australia since the licence was issued (see Section 5.3.1).

106. To date, the Regulator has not received any reports of adverse effects on human health, animal health or the environment caused by any releases of the MON 88701 event.

Table 8 Previous releases of MON 88701 in combination with other GM traits in Australia

DIR licence number	Licence type	Title	Additional GM agronomic traits
120	L&C	Limited and controlled release of cotton genetically modified for insect resistance and herbicide tolerance	IR: <i>cry1Ac</i> , <i>cry2Ab</i> , <i>vip3Aa19</i> ; HT: <i>cp4 epsps</i>
145	C	Commercial release of cotton genetically modified for insect resistance and herbicide tolerance [Bollgard® 3 XtendFlex™ (SYN-IR102-7 x MON 15985-7 x MON-88913-8 x MON 88701-3) and XtendFlex™ (MON-88913-8 x MON 88701-3) cotton]	IR: <i>cry1Ac</i> , <i>cry2Ab</i> , <i>vip3Aa19</i> ; HT: <i>cp4 epsps</i>
147	L&C	Limited and controlled release of cotton genetically modified for insect resistance and herbicide tolerance	IR: <i>cry1Ac</i> , <i>cry2Ab</i> , <i>mCry51Aa2</i> , <i>vip3Aa19</i> ; HT: <i>cp4 epsps</i>

^a L&C, limited and controlled release; ^b C, commercial release; ^c HT, herbicide tolerance; ^d IR, insect resistance

6.2 Approvals by other Australian agencies

107. The Regulator is responsible for assessing risks to the health and safety of people and the environment associated with the use of gene technology. However, dealings conducted under a licence issued by the Regulator may also be subject to regulation by other Australian government agencies that regulate GMOs or GM products.

108. FSANZ is responsible for human food safety assessment and food labelling, including GM food. FSANZ has approved food derived from the oil and linters of MON 88701 as safe for human consumption (FSANZ, 2013a).

109. The APVMA has regulatory responsibility for agricultural chemicals, including herbicides, in Australia. If MON 88701 cotton were to be commercially planted in Australia, the applicant is also required to register formulations of dicamba and glufosinate herbicides to be applied to the GM cotton with APVMA and obtain labels containing all information for using the products, including safety instructions.

6.3 International authorisations and experience

110. A number of countries have approved MON 88701 for commercial cultivation, as well as food and feed use (Table 9).

Table 9 International approvals of MON 88701

Country	Food - direct use or processing	Feed - direct use or processing	Cultivation - domestic or non-domestic use
Brazil	2017	2017	2017
Canada	2014	2014	
Colombia	2016		
Costa Rica			2016*
Japan	2014	2015	
Mexico	2014		
New Zealand	2014		
South Korea	2015	2015	
USA	2013	2013	2014

Source: ISAAA GM approval database; accessed March 2020; *seed production only

111. There have been no reports in the international literature of the GM cotton causing harm to human health and safety, or the environment, resulting from field trials or commercial release.

112. It should be noted that the safe use of dicamba has been the subject of some discussion in the United States, following the deregulation of dicamba-tolerant cotton (MON 88701) and soybean (MON 87708) in 2015 (USDA-APHIS, 2015a, b). The US EPA registered dicamba for OTT application on these GM crops for two years (US EPA, 2016c). During 2017 and 2018, US EPA received numerous reports of injury to crops and non-target plants in natural areas alleged to be related to off-site movement (drift) of dicamba, with a large proportion of cases attributed to drift of OTT applications of dicamba to dicamba-tolerant crops (US EPA, 2018a). This led US EPA to conduct an updated analysis and include an updated effects evaluation on threatened and endangered species; it was concluded that dicamba emission (through spray drift, volatile drift, or a combination) from the use of the registered dicamba formulations on DT-cotton and soybean fields has resulted in effects to non-target terrestrial plants offsite from the treated fields (US EPA, 2018b). As a result, US EPA included new mitigation measures (e.g. limitation on the maximum number and timing of OTT applications, introduction of omnidirectional application buffer etc.) to address the issues with the OTT use of dicamba on GM crops in its registration extension decision in 2018 (US EPA, 2018a). More recently (June 2020), the US Court of Appeals overturned this registration.

113. While these are useful examples of international approaches to management of herbicide application to herbicide tolerant GM crops, it should be emphasised that (as discussed in Chapter 1, Section 4.2.4), assessment of herbicide use in Australia, including the effects of any herbicide metabolites, is outside the remit of the OGTR. APVMA is responsible for assessing the risks of herbicide use, and registration of the formulations and use patterns of the herbicides, including any restrictions and mitigation measures suitable for conditions in Australia; the US EPA's proposed mitigation measures are mentioned only as examples. If MON 88701 cotton is to be commercially planted in Australia, the applicant will need to apply to the APVMA for an assessment and registration of OTT application of dicamba on the GM cotton crop.

Chapter 2 Risk assessment

Section 1 Introduction

114. The risk assessment identifies and characterises risks to the health and safety of people or to the environment from dealings with GMOs, posed by or as the result of gene technology (Figure 2). Risks are identified within the established risk assessment context (Chapter 1), taking into account current scientific and technical knowledge. A consideration of uncertainty, in particular knowledge gaps, occurs throughout the risk assessment process.

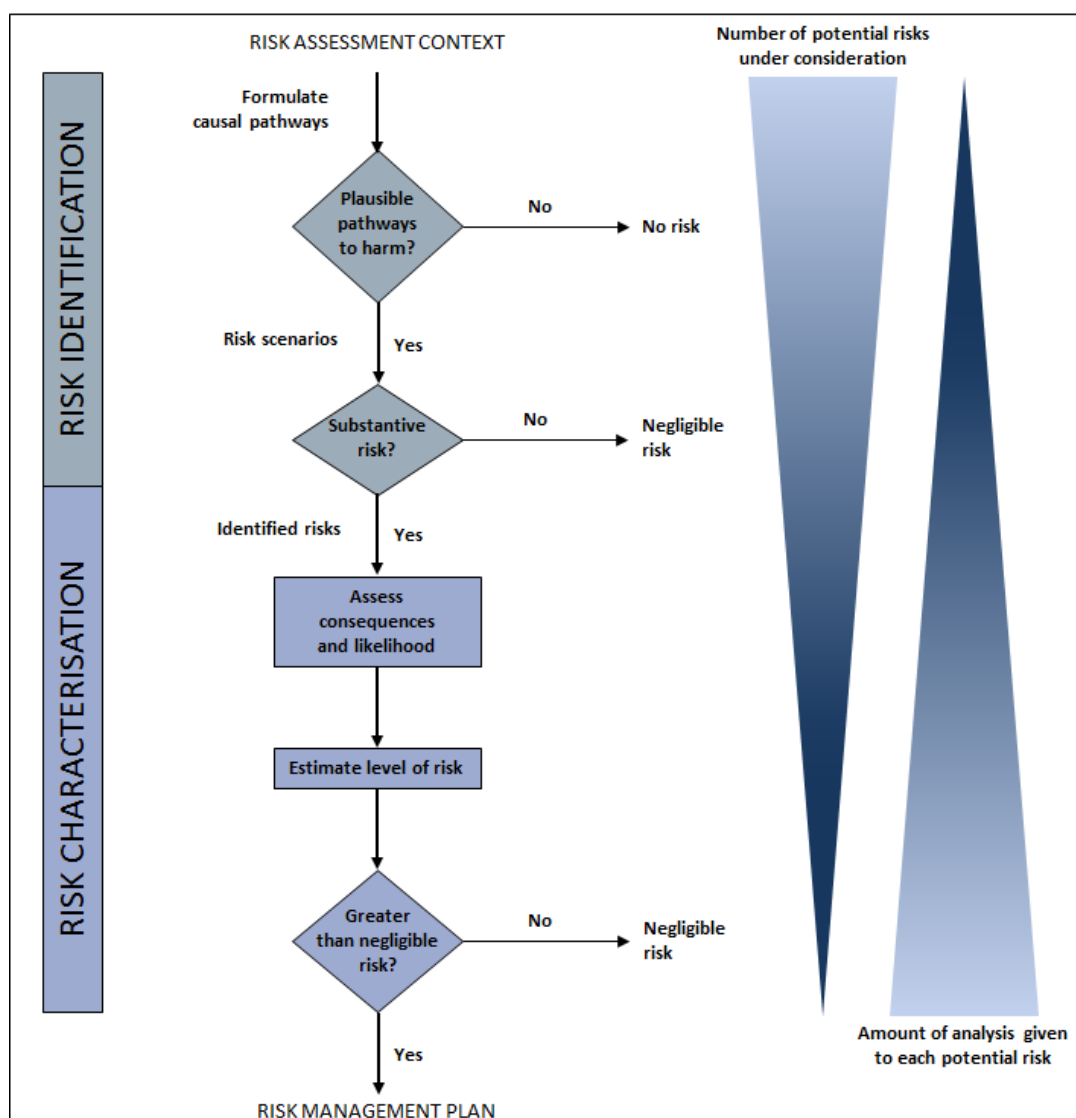


Figure 2 The risk assessment process

115. The Regulator uses a number of techniques to identify risks, including checklists, brainstorming, previous agency experience, reported international experience and consultation (OGTR, 2013a).

116. Risk identification first considers a wide range of circumstances in which the GMO, or the introduced genetic material, could come into contact with people or the environment. This leads to postulating causal pathways that may give rise to harm for people or the environment from dealings with a GMO. These are called risk scenarios.

117. Risk scenarios are screened to identify substantive risks, which are risk scenarios that are considered to have some reasonable chance of causing harm. Risk scenarios that could not plausibly

occur, or do not lead to harm in the short and long term, do not advance in the risk assessment process (Figure 2), i.e. the risk is considered no greater than negligible.

118. Risk scenarios identified as substantive risks are further characterised in terms of the potential seriousness of harm (Consequence assessment) and the likelihood of harm (Likelihood assessment). The consequence and likelihood assessments are combined to estimate the level of risk and determine whether risk treatment measures are required. The potential for interactions between risks is also considered.

119. A weed risk assessment approach is used to identify traits that may contribute to risks from GM plants, as this approach addresses the full range of potential adverse outcomes associated with plants. In particular, novel traits that may increase the potential of the GMO to spread and persist in the environment or increase the level of potential harm compared with the parental plant(s) are considered in postulating risk scenarios (Keese et al., 2014). Risk scenarios postulated in previous RARMPs prepared for licence applications for the same or similar GMOs are also considered.

Section 2 Risk identification

120. Postulated risk scenarios are comprised of three components (Figure 3):

- i. The source of potential harm (risk source)
- ii. A plausible causal linkage to potential harm (causal pathway), and
- iii. Potential harm to people or the environment.

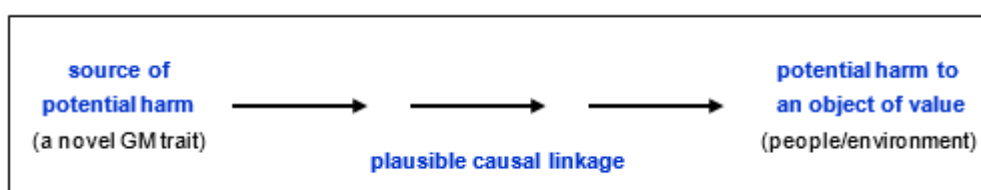


Figure 3 Components of a risk scenario

121. When postulating relevant risk scenarios, the risk context is taken into account, including the following factors detailed in Chapter 1:

- the proposed dealings
- any proposed limits including the extent and scale of the proposed dealings
- any proposed controls to limit the spread and persistence of the GMOs and
- the characteristics of the parent organism(s).

2.1 Risk source

122. The sources of potential harms can be intended novel GM traits associated with one or more introduced genetic elements, or unintended effects/traits arising from the use of gene technology.

123. As discussed in Chapter 1, Section 4.1.1, the GM cotton proposed for release has been modified by the introduction of two genes for herbicide tolerance. These introduced genes and their encoded proteins are considered further as a potential source of risk.

124. The introduced genes are controlled by introduced regulatory sequences. These regulatory sequences are derived from common plants, plant viruses and a common soil bacterium (Table 2). Regulatory sequences are naturally present in plants, and the introduced elements are expected to operate in similar ways to endogenous elements. The regulatory sequences are DNA that is not expressed as a protein, and dietary DNA has no toxicity (Society of Toxicology, 2003). As described in Chapter 1, these sequences have been widely used in other GMOs, including in GM cotton lines grown

commercially in Australia and overseas without reports of adverse effects. Hence, potential risks from the regulatory elements will not be considered further.

125. The genetic modification has the potential to cause unintended effects in several ways including altered expression of endogenous genes by random insertion of introduced DNA in the genome, increased metabolic burden due to expression of the introduced protein, novel traits arising out of interactions with non-target proteins and secondary effects arising from altered substrate or product levels in biochemical pathways. However, these types of effects also occur spontaneously in plants generated by conventional breeding. Accepted conventional breeding techniques such as hybridisation, mutagenesis and somaclonal variation can have a much larger impact on the plant genome than genetic engineering (Schnell et al., 2015). Plants generated by conventional breeding have a long history of safe use, and there are no documented cases where conventional breeding has resulted in the production of a novel toxin or allergen in a crop (Steiner et al., 2013). No biologically significant differences were found in the biochemistry, physiology or ecology of MON 88701 cotton, when compared with non-GM cotton (Chapter 1, Section 4.3), and the introduced genes are stable (Chapter 1, Section 4.3.1). Therefore, unintended effects resulting from the process of genetic modification will not be considered further.

2.2 Causal pathway

126. The following factors are taken into account when postulating plausible causal pathways to potential harm:

- routes of exposure to the GMOs, the introduced gene(s) and gene product(s)
- potential exposure to the introduced gene(s) and gene product(s) from other sources in the environment
- the environment at the site(s) of release
- agronomic management practices for the GMOs
- spread and persistence of the GM plants (e.g. reproductive characteristics, dispersal pathways and establishment potential)
- tolerance to abiotic conditions (e.g. climate, soil and rainfall patterns)
- tolerance to biotic stressors (e.g. pests, pathogens and weeds)
- tolerance to cultivation management practices
- gene transfer to sexually compatible organisms
- gene transfer by horizontal gene transfer
- unauthorised activities.

127. Although all of these factors are taken into account, some are not included in risk scenarios because they are regulated by other agencies, have been considered in previous RARMPs or are not expected to give rise to substantive risks (see Sections 2.2.1 to 2.2.4 below).

2.2.1 Tolerance to abiotic factors

128. The geographic range of non-GM cotton in Australia is limited by a number of abiotic factors including climate and soil compatibility, as well as water and nutrient availability (OGTR, 2016a). The introduced gene is unlikely to make the GM cotton plants more tolerant to abiotic stresses that are naturally encountered in the environment and is therefore unlikely to alter the potential distribution of the GM cotton plants. Also, as discussed in Chapter 1, Section 4.3.4, there was no consistent significant difference between MON 88701 and non-GM cotton varieties in response to abiotic factors. Therefore, tolerance to abiotic stresses will not be assessed further.

2.2.2 Gene transfer to sexually compatible relatives

129. As discussed in Chapter 1, Section 5.3.1, *G. hirsutum* is sexually compatible with all GM and non-GM *G. hirsutum* varieties, as well as *G. barbadense*. Therefore, some cross-hybridisation with these

plants is inevitable. Gene transfer to Australian native cotton species is not expected due to genetic incompatibility.

130. Some feral cotton does occur outside cultivation in northern Australia, including in nature reserves. However, these plants are not routinely subjected to control measures such as the use of herbicide or cultivation. Records of feral cotton presence do not indicate a marked change in the number of records or the pattern of occurrence ([Australia's Virtual Herbarium](#) accessed May 2020) since the previous comprehensive review in the RARMP for DIR 124 (OGTR, 2014). If gene transfer from the GM cottons to feral cotton were to occur, the presence of herbicide tolerance genes in these feral cottons would not be expected to provide a selective advantage in the absence of herbicide application. Therefore, only gene transfer to cultivated *G. hirsutum* and *G. barbadense* will be considered further.

2.2.3 Horizontal gene transfer

131. The potential for horizontal gene transfer (HGT) and any possible adverse outcomes has been reviewed in the literature (Keese, 2008) and assessed in previous RARMPs. No risk greater than negligible was identified, due to the rarity of HGT events and because the gene sequences (or sequences which are homologous to those in the current application) are already present in the environment and available for transfer via demonstrated natural mechanisms. Therefore, HGT will not be assessed further.

2.2.4 Unauthorised activities

132. Previous RARMPs have considered the potential for unauthorised activities to lead to an adverse outcome. The Act provides for substantial penalties for non-compliance and unauthorised dealings with GMOs. The Act also requires the Regulator to have regard to the suitability of the applicant to hold a licence prior to the issuing of a licence. These legislative provisions are considered sufficient to minimise risks from unauthorised activities, and no risk greater than negligible was identified in previous RARMPs. Therefore unauthorised activities will not be considered further.

2.3 Potential harm

133. Potential harms from GM plants include:

- harm to the health of people or desirable organisms, including toxicity/allergenicity
- reduced biodiversity for nature conservation
- reduced establishment or yield of desirable plants
- reduced products or services from the land use
- restricted movement of people, animals, vehicles, machinery and/or water
- reduced quality of the biotic environment (e.g. providing food or shelter for pests or pathogens) or abiotic environment (e.g. negative effects on fire regimes, nutrient levels, soil salinity, soil stability or soil water table).

134. These harms are based on those used to assess risk from weeds (Standards Australia et al., 2006; Keese et al., 2014). Judgements of what is considered harm depend on the management objectives of the land where the GM plant may be present. For example, a plant species may have different weed risk potential in different land uses such as dryland cropping or nature conservation.

2.3.1 Endogenous cotton toxins

135. Cotton (*G. hirsutum* and *G. barbadense*) tissue, particularly the seeds, can be toxic if ingested in excessive quantities because of the presence of endogenous anti-nutritional and toxic factors including gossypol and cyclopropenoid fatty acids (including dihydrosterculic, sterculic and malvalic acids).

136. The presence of gossypol and cyclopropenoid fatty acids in cotton seed limits its use as a protein supplement in animal feed. Ruminants are less affected by these components because they are detoxified by digestion in the rumen (Kandyliis et al., 1998). However, its use as stockfeed is limited to a relatively small proportion of the diet and it must be introduced gradually to avoid potential toxic effects (Blasi and Drouillard, 2002).

137. The presence of the introduced genes is not expected to directly affect the levels of endogenous toxins and anti-nutrients. This is supported by data provided by the applicant (Chapter 1, Section 4.3.3) showing that gossypol and anti-nutrients levels in MON 88701 cottonseed lie within the range of non-GM cottons. Furthermore, there are established management practices to control the preparation and use of cottonseed products as feed for livestock, including poultry. Therefore, endogenous cotton toxins will not be considered further.

2.4 Postulated risk scenarios

138. Four risk scenarios were postulated and screened to identify substantive risk. These scenarios are summarised in Table 10 and discussed in depth in Sections 2.4.1 to 2.4.4. Postulation of risk scenarios considers impacts of the GM cotton or its products on people undertaking the dealings, as well as impacts on people and the environment exposed to the GM cotton or its products as the result of commercial use or the spread and persistence of plant material.

139. In the context of the activities proposed by the applicant and considering both the short and long term, none of the four risk scenarios gave rise to any substantive risks that could be greater than negligible.

Table 10 Summary of risk scenarios from the proposed dealings

Risk scenario	Risk source	Causal pathway	Potential harm	Substantive risk?	Reason
1	Introduced genes for herbicide tolerance	Commercial cultivation of GM cotton expressing the herbicide tolerance genes ↓ Exposure of people and other desirable organisms by contact, ingestion or inhalation of the GM plants or products	Increased toxicity or allergenicity to people or increased toxicity to desirable organisms	No	<ul style="list-style-type: none"> The <i>dmo</i> and <i>bar</i> genes were sourced from bacteria not known to be toxic to humans and other organisms. DMO and PAT proteins have no known toxicity or allergenicity to humans or toxicity to other organisms. Genes homologous to the <i>dmo</i> and <i>bar</i> genes are widespread in the environment. FSANZ has approved products derived from the GM cotton for use in human food.
2	Introduced genes for herbicide tolerance	Commercial cultivation of GM cotton expressing the herbicide tolerance genes ↓ Establishment of volunteer GM cotton plants in agricultural areas ↓ Reduced effectiveness of weed management measures to control the volunteer GM cotton plants	Reduced establishment or yield of desirable agricultural crops OR Increased reservoir for pests or pathogens	No	<ul style="list-style-type: none"> Integrated weed management practices would effectively control GM cotton volunteers in agricultural areas. Glufosinate and dicamba are of limited usefulness in controlling cotton volunteers. Cotton volunteer with dual herbicide tolerance can be controlled using alternative

Risk scenario	Risk source	Causal pathway	Potential harm	Substantive risk?	Reason
					weed management strategies.
3	Introduced genes for herbicide tolerance	<p>Commercial cultivation of GM cotton expressing the herbicide tolerance genes</p> <p>↓</p> <p>Dispersal of GM cottonseed to intensive use areas or nature reserves</p> <p>↓</p> <p>Establishment of volunteer GM cotton plants in intensive use areas or nature reserves</p> <p>↓</p> <p>Reduced effectiveness of weed management measures to control the volunteer GM cotton plants</p>	<p>Reduced utility of intensive use areas</p> <p>OR</p> <p>Reduced establishment of desirable native vegetation</p>	No	<ul style="list-style-type: none"> Cotton is not a persistent weed in intensive use areas or a significant weed in nature reserves. The introduced herbicide tolerance genes do not increase the potential weediness of the GM cotton. Weed management strategies other than dicamba and glufosinate use can control feral GM cotton.
4	Introduced genes for herbicide tolerance	<p>Commercial cultivation of GM cotton expressing the herbicide tolerance genes</p> <p>↓</p> <p>Cross-pollination with other cotton, including cotton with other herbicide tolerant traits</p> <p>↓</p> <p>Establishment of hybrid GM cotton as volunteers</p> <p>↓</p> <p>Reduced effectiveness of weed management measures to control the hybrid plants</p>	<p>Reduced establishment or yield of desirable agricultural crops</p> <p>OR</p> <p>Increased reservoir for pathogens</p>	No	<ul style="list-style-type: none"> Hybrids between the GM cotton and other cotton would be generated at low levels. No new herbicide tolerance traits would be generated in hybrids other than those already approved. Multiple-herbicide tolerant hybrid cotton can be controlled using integrated weed management.

2.4.1 Risk scenario 1

<i>Risk source</i>	Introduced genes for herbicide tolerance
<i>Causal pathway</i>	<p>↓</p> <p>Commercial cultivation of GM cotton expressing the genes for herbicide tolerance</p> <p>↓</p> <p>Exposure of people and other desirable organisms by contact, ingestion or inhalation of the GM plants or products</p> <p>↓</p>
<i>Potential harm</i>	<p>Increased toxicity or allergenicity to people.</p> <p>OR</p> <p>Increased toxicity to desirable organisms.</p>

Risk source

140. The source of potential harm for this postulated risk scenario is the introduced herbicide tolerance genes.

Causal pathway

141. The herbicide tolerance genes *dmo* and *bar* are expressed in the vegetative parts, pollen and seed of the GM cotton plants (Chapter 1, Section 4.3.2). Therefore, people may be exposed to the GM cotton, or its products through contact or consumption of plant parts or products, or inhalation of pollen. However, the introduced genes and expressed proteins are not present in cotton products such as cottonseed oil, fibres and linters (FSANZ, 2013b). Therefore, the majority of people that would be exposed to the introduced genes and its products would be workers involved with breeding, cultivating, harvesting, transporting and processing the GM cotton. The public, who consume cottonseed oil and cottonseed linters, or have contact with cotton fabrics, would not be exposed to the introduced genes and their products.

142. Expression of the herbicide tolerance genes in cultivated GM cotton plants, or in volunteer GM cotton, may expose other organisms, including livestock, to the GM proteins through contact or ingestion. Apart from presence in all parts of the GM cotton plants, the DMO and PAT proteins may also occur at low levels in the soil from plant material left after harvesting and exudates from roots.

143. Livestock are exposed to cotton in the form of fuzzy white cottonseed and cottonseed meal in feed rations, or through limited grazing of stubble. However, the amount of cotton plant material (both GM and non-GM) that is consumed by livestock is, by necessity, limited due to the presence of endogenous toxins such as gossypol. Other organisms, including wild mammals, birds, soil microbes and invertebrates would also be exposed to GM cotton material in agricultural areas under cotton cultivation. These organisms may be exposed to the introduced proteins through contact, ingestion or indirectly by feeding on herbivores that have ingested the GM cotton.

144. Cotton volunteers outside cultivation areas may provide a pathway for exposure. However, cotton has limited potential to spread and establish persistent populations in undisturbed nature conservation areas (Chapter 1, Section 3.2.4), so extended exposure to the GM cotton will occur mostly in the agricultural context.

Potential harm

145. Toxicity is the adverse effect(s) of exposure to a dose of a substance as a result of direct cellular or tissue injury, or through the inhibition of normal physiological processes (Felsot, 2000). Allergenicity is the potential of a substance to elicit an immunological reaction following its ingestion, dermal contact or inhalation, which may lead to tissue inflammation and organ dysfunction (Arts et al., 2006).

146. The introduced *dmo* and *bar* genes were isolated from the bacteria *S. maltophilia* and *S. hygroscopicus*, which are widespread and prevalent in the environment and are not known for human or animal pathogenicity. Their encoded proteins DMO and PAT are well characterised. Based on all available information, these proteins are not known to be toxic or allergenic and do not share relevant sequence homology with known toxins or allergens (Chapter 1, Section 4.2.3). People or other mammals exposed to these proteins are therefore not expected to suffer toxic effects or allergic reactions.

147. Analysis of the compositional data for cottonseed of MON 88701 did not identify meaningful differences in the levels of compounds, including natural toxicants, when compared to non-GM cotton from the same background and to other commercial cotton varieties (Chapter 1, Section 4.3.3). FSANZ has approved the use of food derived from MON 88701 for human consumption in Australia. Food and feed use of MON 88701 have also been approved in a number of other countries (Chapter 1, Section 6.3).

148. The environmental safety of the PAT protein present in GM crops, including cotton, sugarbeet, canola, chicory, soybean, corn and rice, has been extensively assessed by regulatory authorities worldwide (CERA, 2011). From these risk assessments, no adverse impacts on other organisms by the PAT protein expressed in any GM plants in the receiving environment were identified. The DMO protein in GM soybean, cotton and corn have been assessed by USDA-APHIS (USDA-APHIS, 2014a, b,

2016), and no potential environmental safety concerns were identified. As discussed in Chapter 1, Section 4.3.4, no significant differences were identified in the abundance of a representative selection of beneficial arthropods between MON 88701 and its parent control Coker 130. This indicates that MON 88701 is unlikely to cause any significant adverse effects on other organisms compared to other commercial cotton varieties.

Conclusion

149. Risk scenario 1 is not identified as a substantive risk because the DMO and PAT proteins are not considered toxic or allergenic to humans or toxicity to other desirable organisms. The GM cottonseed is compositionally equivalent to non-GM cottonseed so the risk to workers is not expected to be greater than exposure to conventional cotton varieties, and proteins the same or similar to DMO and PAT are widespread in the environment. Therefore, this risk could not be greater than negligible and does not warrant further detailed assessment.

2.4.2 Risk scenario 2

<i>Risk source</i>	Introduced genes for herbicide tolerance
<i>Causal pathway</i>	<p style="text-align: center;">↓</p> <p style="text-align: center;">Commercial cultivation of GM cotton expressing the herbicide tolerance genes</p> <p style="text-align: center;">↓</p> <p style="text-align: center;">Establishment of volunteer GM cotton plants in agricultural areas</p> <p style="text-align: center;">↓</p> <p style="text-align: center;">Reduced effectiveness of weed management measures to control the volunteer GM cotton plants</p>
<i>Potential harm</i>	<p style="text-align: center;">Reduced establishment or yield of desirable agricultural crops</p> <p style="text-align: center;">OR</p> <p style="text-align: center;">Increased reservoir for pests or pathogens</p>

Risk source

150. The source of potential harm for this postulated risk scenario is the introduced genes for herbicide tolerance.

Causal pathway

151. If volunteer GM cotton plants establish in cotton fields after cultivation of a cotton crop, the presence of the genes for herbicide tolerance could reduce the ability to control volunteer cotton plants.

152. Volunteers are likely to occur in the fields following a cotton crop and also where bales or modules are placed. In addition, volunteers may be found along roads between farms and processing facilities as well as in irrigation channels and drains where cotton trash may accumulate (Chapter 1, Section 3.2.4). In southern Australia, most volunteer seedlings that emerge over winter are likely to be killed by frosts. However, seedlings that emerge later can establish and grow at all these locations.

153. Volunteer cotton plants are also likely to occur following dispersal of GM cottonseed within agricultural areas. Short-range dispersal of cottonseed into field margins or adjacent fields could occur due to extreme weather such as strong wind or flooding. Short to medium-range dispersal of cottonseed within agricultural areas could be mediated by human activities such as movement of agricultural machinery. For example, cotton pickers can transfer cottonseed between fields if they are not cleaned prior to transport (CRDC and CottonInfo, 2017).

154. MON 88701 cotton only has a survival advantage in the presence of glufosinate and/or dicamba. If these herbicides were the primary means of weed control, expression of the herbicide resistance genes in volunteer cotton plants would reduce the effectiveness of weed management measures to control the volunteer cotton. However, as noted in Chapter 1, Section 3.2.3, dicamba is not currently

registered for control of volunteer cotton. Although glufosinate is registered for controlling young cotton volunteer, it is not the only herbicide for cotton volunteer control. MON 88701 volunteers have the same susceptibility to other herbicides registered for cotton volunteer control (e.g. MOA groups B, C, G, I, L and Q) (Holman et al., 2019) as non-GM cotton plants. Thus these herbicides could be used as part of weed management practices to control MON 88701 volunteer plants. Bromoxynil, carfentrazone and a combination of paraquat and diquat have been shown to be very effective (CRDC, 2013b). Mechanical removal is the preferred option for older plants but the herbicide fluroxypyr can also be used (Holman et al., 2019).

155. The GM cotton volunteers could therefore be effectively controlled using IWM practices, which include using the herbicides in the MOA groups mentioned above as well as non-chemical management methods such as cultivation and mechanical removal.

Potential harm

156. Volunteer cotton is a weed of agricultural production systems. If left uncontrolled, volunteer cotton plants could establish and compete with other crops and reduce establishment/yield of other crops (CRDC, 2013c). However, GM cotton volunteers that are effectively controlled would not be expected to cause greater harm to other crops than that of non-GM cotton volunteers.

157. Volunteer cotton could also act as a reservoir for pests and pathogens. For example, volunteer glyphosate-tolerant (GT) cotton in GT soybean production field could provide oviposition sites for boll weevils and allow the insects to build up undetected (York et al., 2004). This could lead to infestation of subsequent crops and result in yield loss. However, comparing to its parent control Coker 130 and other commercial cotton varieties, MON 88701 cotton does not display significant differences in the seed germination characteristics (USDA-APHIS, 2014c), or in other weedy traits such as plant vigour and seed yield, or in pest and disease responses and arthropod abundance (Chapter 1, Section 4.3.4). Therefore, it is unlikely that MON 88701 volunteers would behave significantly differently from volunteers of other commercial cotton varieties. Effective control of cotton volunteers (both GM and non-GM) will reduce the potential for those volunteers to act as pest or disease reservoirs.

Conclusion

158. Risk scenario 2 is not identified as a substantive risk because the genetic modification would only give an advantage to the GM cotton plants in managed environments, where dicamba and/or glufosinate herbicide is applied and because integrated weed management practices would control GM cotton volunteers in agricultural areas. Therefore, this risk could not be considered greater than negligible and does not warrant further detailed assessment.

2.4.3 Risk scenario 3

<i>Risk source</i>	Introduced genes for herbicide tolerance
<i>Causal pathway</i>	<p style="text-align: center;">↓</p> <p style="text-align: center;">Commercial cultivation of GM cotton expressing the herbicide tolerance genes</p> <p style="text-align: center;">↓</p> <p style="text-align: center;">Dispersal of GM cottonseed to intensive use areas or nature reserves</p> <p style="text-align: center;">↓</p> <p style="text-align: center;">Establishment of volunteer GM cotton plants in intensive use areas or nature reserves</p> <p style="text-align: center;">↓</p> <p style="text-align: center;">Reduced effectiveness of weed management measures to control the volunteer GM cotton plants</p>
<i>Potential harm</i>	<p style="text-align: center;">Reduced utility of intensive use areas</p> <p style="text-align: center;">OR</p> <p style="text-align: center;">Reduced establishment of desirable native vegetation</p>

Risk source

159. The source of potential harm for this postulated risk scenario is the introduced genes for herbicide tolerance.

Causal pathway

160. GM cottonseed may be transported from farms into intensive use areas or nature reserves by humans, water or extreme weather. After harvest, modules of seed cotton would usually be transported to gins for processing and storage. Seed spillages could lead to establishment of feral cotton populations along transport routes or near processing or storage sites. However, such feral cotton may be subject to weed management practices (e.g. slashing/mowing or appropriate herbicide treatment), thereby limiting their potential to reproduce (Eastick, 2002). For example, a survey of about 1400 km cottonseed transport routes between Emerald and Atherton Tablelands in QLD found only 22 cotton plants over three years and no secondary spread was detected (Addison et al., 2007).

161. Cottonseed may also be dispersed during extreme weather events, i.e. via wind during wind storms and water during flooding, to natural environments (OGTR, 2016a). However, cottonseed is not likely to be spread by wind over long distances, so unless nature reserves are close to production areas spread into these areas by wind is unlikely. Good Management Practice of the cotton industry includes retaining irrigation water runoff and some stormwater runoff, so this would reduce the dispersal of cottonseed by water. Viability of cottonseed would also reduce after water-borne transport (OGTR, 2016a).

162. GM cotton volunteers may also be introduced into regions that do not grow the crop through the use of whole cottonseed for supplementation feeding of cattle and sheep, particularly during drought when large piles of cottonseed are dumped into a paddock for stock to feed on over the course of several days ([QDAF website](#) and [Business Qld website](#), accessed May 2020). However, grazing and trampling by livestock would minimise the establishment of these volunteers in these areas (Eastick, 2002; Eastick and Hearnden, 2006).

163. MON 88701 is similar to non-GM cotton with respect to the intrinsic characteristics contributing to spread and persistence, such as seed production, plant competitiveness and environmental interaction (Chapter 1, Section 4.3.4). As such, the genetic modification is unlikely to alter the tolerance of the GM plants to biotic or abiotic stresses that normally restrict the geographic range and persistence of cotton (Chapter 1, Sections 5.2 and 5.3.2). Therefore, MON 88701 cotton volunteers would not be expected to show higher potential than non-GM cotton to naturalise and compete with native plant species in nature reserves where weeds are not actively managed.

Potential harm

164. If the GM cottonseed expressing the introduced genes for dual herbicide tolerance were dispersed into intensive use areas or nature reserves and GM plants became established, this could reduce the utility of intensive use areas or reduce the establishment of desirable native vegetation. Feral cotton on roadsides could potentially reduce services from the land use by obstructing lines of sight around corners and signs, as *G. hirsutum* is a perennial shrub that can grow to a height of 2 m in nature (OGTR, 2016a). It could also give rise to lower abundance of desirable species, reduced species richness, or undesirable changes in species biodiversity in nature reserves.

165. None of these potential harms are increased in MON 88701 cotton proposed for release compared to non-GM cotton, as MON 88701 is no more likely to establish weedy populations than other existing cotton varieties, and such populations can be controlled using current weed control practices.

Conclusion

166. Risk scenario 3 is not identified as a substantive risk because cotton is not a persistent weed in intensive use areas or a significant weed in nature reserves, and the introduced herbicide tolerance

genes do not increase the potential weediness of the GM cotton. Therefore, this risk could not be greater than negligible and does not warrant further detailed assessment.

2.4.4 Risk scenario 4

<i>Risk source</i>	Introduced genes for herbicide tolerance
<i>Causal pathway</i>	<p style="text-align: center;">↓</p> <p style="text-align: center;">Commercial cultivation of GM cotton expressing the herbicide tolerance genes</p> <p style="text-align: center;">↓</p> <p style="text-align: center;">Cross-pollination with other cotton, including cotton with other herbicide tolerant traits</p> <p style="text-align: center;">↓</p> <p style="text-align: center;">Establishment of hybrid GM cotton as volunteers</p> <p style="text-align: center;">↓</p> <p style="text-align: center;">Reduced effectiveness of weed management measures to control the hybrid plants</p>
<i>Potential harm</i>	<p style="text-align: center;">Reduced establishment or yield of desirable agricultural crops</p> <p style="text-align: center;">OR</p> <p style="text-align: center;">Increased reservoir for pathogens</p>

Risk source

167. The source of potential harm for this postulated risk scenario is the introduced genes for herbicide tolerance.

Causal pathway

168. The GM *G. hirsutum* cottons proposed for release are sexually compatible with other *G. hirsutum* cultivars and with *G. barbadense*, including both GM and non-GM lines of both species, but not native Australian cotton species (Chapter 1, Section 5.3.1 and this Chapter, Section 2.2.2). Therefore, the introduced herbicide tolerance genes could be transferred to other GM herbicide tolerant cotton plants by pollen flow.

169. The applicant proposes the MON 88701 cotton would be cultivated on a commercial scale in all Australian cotton-producing areas. Outcrossing could occur when the GM cotton proposed for release and other cotton crops are grown in close proximity, with synchronous flowering times. Cotton is primarily self-pollinating and low level of cross-pollination (1 to 2%) between plants in adjacent rows can occur through the activity of pollinating insects but wind dispersal of pollen is negligible (OGTR, 2016a). Out-crossing rate also decreases rapidly with distance from the pollen source and correspondingly very low levels of hybridisation are expected between the GM cotton and the neighbouring commercial cotton fields.

170. The commercial *G. hirsutum* seed available for grown in Australia in the 2019/20 season are RRF cotton approved under DIR 066/2006 and BG3 RRF cotton approved under DIR 124 (CSD, 2019). Limited areas of Liberty Link® (glufosinate tolerant) cotton approved under DIR 062/2005 were grown previously. Insect resistant *G. hirsutum* Widestrike™ and VIPCOT™ have been approved for commercial release, but none has been planted commercially. Small amount of non-GM *G. barbadense* has also been grown commercially in Australia. Although RRF *G. barbadense* has been approved for commercial release under DIR 118, no planting has yet occurred.

171. Gene transfer to non-GM cotton or to non-herbicide tolerant GM cotton could occur. However the resulting progeny would be highly similar to the GMO proposed for release. Therefore, any adverse outcomes expected for those progeny would be comparable to MON 88701 cotton.

172. MON 88701 cotton is a parent for XF and BG3 XF cottons approved under DIR 145. If these cottons were to cross with MON 88701, the resulting progeny would not have an increased range of herbicide tolerance as the genes in both parents are the same. Thus there is no increased risk to spread and persistence for progeny of this cross than is present for the parental cottons.

173. Liberty Link® cotton contains the same *bar* gene as that in MON 88701 cotton. Therefore, in the event of hybrids being produced, no new herbicide tolerance traits will be generated. However, as this is a different event, there could be two copies of the *bar* gene so there may be an additive effect, such that the hybrids could tolerate higher rates of herbicide application for glufosinate.

174. GlyTol® and GlyTol TwinLink Plus® have been approved for commercial release under DIR 143. These cottons have either glyphosate tolerance (GlyTol®) or glyphosate and glufosinate tolerance, in combination with three insect resistance genes (GlyTol TwinLink Plus®). Both contain the maize *2mepsps* gene for glyphosate tolerance and GlyTol TwinLink Plus® cotton also contains the *bar* gene for glufosinate tolerance. MON 88701 cotton could cross with them and result in progeny with a stack of three herbicide tolerance genes conferring tolerance to glyphosate, glufosinate and dicamba herbicides. As glyphosate is not commonly used for cotton volunteer control (Holman et al., 2019), it therefore would not affect the current weed management practices. Therefore, the same IWM practices discussed in Risk Scenario 2 would still be effective for controlling these hybrids with multiple herbicide tolerance.

Potential harm

175. If left uncontrolled, volunteer cotton plants could establish and compete with other crops. If hybrid progeny with multiple herbicide tolerance were to establish in agricultural areas, the effectiveness of existing weed management measures to control volunteer cotton could be compromised. As a result, the establishment and yield of desirable agricultural crops might be reduced. In addition, surviving volunteer cotton could act as a reservoir for pests and pathogens, as described in Risk Scenario 2.

176. However, hybrid cotton volunteers are expected to be present at very low densities. Small numbers of volunteers would have limited capacity to cause the above adverse effects and would also be controlled by the IWM similar to the parent MON 88701.

Conclusion

177. Risk scenario 4 is not identified as a substantive risk because hybrids between the MON 88701 and other cotton would be generated at low levels, and multiple-herbicide tolerant hybrids can be controlled by IWM. Therefore, this risk could not be considered greater than negligible and does not warrant further detailed assessment.

Section 3 Uncertainty

178. Uncertainty is an intrinsic property of risk and is present in all aspects of risk analysis². There are several types of uncertainty in risk analysis (Bammer & Smithson 2008; Clark & Brinkley 2001; Hayes 2004). These include:

- uncertainty about facts:
 - knowledge – data gaps, errors, small sample size, use of surrogate data
 - variability – inherent fluctuations or differences over time, space or group, associated with diversity and heterogeneity
- uncertainty about ideas:

² A more detailed discussion of uncertainty is contained in the Regulator's *Risk Analysis Framework* available from the [OGTR website](#) or via Free call 1800 181 030.

- description – expression of ideas with symbols, language or models can be subject to vagueness, ambiguity, context dependence, indeterminacy or under-specificity
- perception – processing and interpreting risk is shaped by our mental processes and social/cultural circumstances, which vary between individuals and over time.

179. Uncertainty is addressed by approaches including balance of evidence, conservative assumptions, and applying risk management measures that reduce the potential for risk scenarios involving uncertainty to lead to harm. If there is residual uncertainty that is important to estimating the level of risk, the Regulator will take this uncertainty into account in making decisions.

180. MON 88701 cotton has been approved by the Regulator for limited and controlled release (field trial) under licence DIR 120. The RARMP for DIR 120 identified additional information that may be required for a large scale or commercial release of MON 88701 cotton. This includes the uncertainty associated with the potential for any unintended effects as a result of changes in biochemistry, physiology or ecology of the GM cotton plants. Information provided by the applicant addressing these areas of uncertainty is presented in Chapter 1, Section 4.3 and discussed in relevant sections in Chapter 1 and in risk scenarios.

181. Uncertainty can arise from a lack of experience with the GMO. Although BG3 XF and XF cottons containing the *dmo* gene have been approved under DIR 145 since 2016, they have not been cultivated in commercial scale in Australia. Therefore, there is uncertainty with respect to commercially growing cotton with the *dmo* gene conferring dicamba tolerance.

182. Overall, the level of uncertainty in this risk assessment, which considers risks of the GMO, is considered low and does not impact on the overall estimate of risk.

183. Post release review (PRR) will be used to address uncertainty regarding future changes to knowledge about the GMO or the receiving environment (Chapter 3, Section 4). PRR is typically required for commercial releases of GMOs, which generally do not have limited duration.

Section 4 Risk evaluation

184. Risk is evaluated against the objective of protecting the health and safety of people and the environment to determine the level of concern and, subsequently, the need for controls to mitigate or reduce risk. Risk evaluation may also aid consideration of whether the proposed dealings should be authorised, need further assessment, or require collection of additional information.

185. Factors used to determine which risks need treatment may include:

- risk criteria
- level of risk
- uncertainty associated with risk characterisation
- interactions between substantive risks.

186. Four risk scenarios were postulated whereby the proposed dealings might give rise to harm to people or the environment. The level of risk for each scenario was considered negligible in relation to both the seriousness and likelihood of harm, and by considering both the short and long term. The principal reasons for these conclusions are summarised in Table 10.

187. The *Risk Analysis Framework* (OGTR, 2013a), which guides the risk assessment and risk management process, defines negligible risks as risks of no discernible concern with no present need to invoke actions for mitigation. Therefore, no controls are required to treat these negligible risks. The Regulator considers that the dealings involved in this proposed release do not pose a significant risk to either people or the environment.

Chapter 3 Risk management plan

Section 1 Background

188. Risk management is used to protect the health and safety of people and to protect the environment by controlling or mitigating risk. The risk management plan addresses risks evaluated as requiring treatment and considers limits and controls proposed by the applicant, as well as general risk management measures. The risk management plan informs the Regulator's decision-making process and is given effect through proposed licence conditions.

189. Under section 56 of the Act, the Regulator must not issue a licence unless satisfied that any risks posed by the dealings proposed to be authorised by the licence are able to be managed in a way that protects the health and safety of people and the environment.

190. All licences are subject to three conditions prescribed in the Act. Section 63 of the Act requires that each licence holder inform relevant people of their obligations under the licence. The other statutory conditions allow the Regulator to maintain oversight of licensed dealings: section 64 requires the licence holder to provide access to premises to OGTR inspectors and section 65 requires the licence holder to report any information about risks or unintended effects of the dealing to the Regulator on becoming aware of them. Matters related to the ongoing suitability of the licence holder are also required to be reported to the Regulator.

191. The licence is also subject to any conditions imposed by the Regulator. Examples of the matters to which conditions may relate are listed in section 62 of the Act. Licence conditions can be imposed to limit and control the scope of the dealings and to manage risk to people or the environment. In addition, the Regulator has extensive powers to monitor compliance with licence conditions under section 152 of the Act.

Section 2 Risk treatment measures for substantive risks

192. The risk assessment of risk scenarios listed in Chapter 2 concluded that there are negligible risks to people and the environment from the proposed release of MON 88701 cotton. These risk scenarios were considered in the context of the large scale of the proposed release and the receiving environment. The risk evaluation concluded that no containment measures are required to treat these negligible risks.

Section 3 General risk management

193. All DIR licences issued by the Regulator contain a number of conditions that relate to general risk management. These include conditions relating to:

- applicant suitability
- testing methodology
- identification of the persons or classes of persons covered by the licence
- reporting structures
- access for the purpose of monitoring for compliance.

3.1 Applicant suitability

194. In making a decision whether or not to issue a licence, the Regulator must have regard to the suitability of the applicant to hold a licence. Under section 58 of the Act, matters that the Regulator must take into account include:

- any relevant convictions of the applicant

- any revocation or suspension of a relevant licence or permit held by the applicant under a law of the Commonwealth, a State or a foreign country
- the capacity of the applicant to meet the conditions of the licence.

195. On the basis of information submitted by the applicant and records held by the OGTR, the Regulator considers Monsanto Australia Pty Ltd (Monsanto) suitable to hold a licence. The licence includes a requirement for the licence holder to inform the Regulator of any circumstances that would affect their suitability.

196. In addition, any applicant organisation must have access to a properly constituted Institutional Biosafety Committee and be an accredited organisation under the Act.

3.2 Testing methodology

197. Monsanto is required to provide a method to the Regulator for the reliable detection of the GMO, and the presence of the introduced genetic materials in a recipient organism. This instrument is required prior to conducting any dealings with the GMO.

3.3 Identification of the persons or classes of persons covered by the licence

198. Any person, including the licence holder, could conduct any permitted dealing with the GMO.

3.4 Reporting requirements

199. The licence obliges the licence holder to immediately report any of the following to the Regulator:

- any additional information regarding risks to the health and safety of people or the environment associated with the dealings
- any contraventions of the licence by persons covered by the licence
- any unintended effects of the release.

200. The licence holder is also obliged to submit an Annual Report containing any information required by the licence.

201. There are also provisions that enable the Regulator to obtain information from the licence holder relating to the progress of the commercial release (see Section 4, below).

3.5 Monitoring for compliance

202. The Act stipulates, as a condition of every licence, that a person who is authorised by the licence to deal with a GMO, and who is required to comply with a condition of the licence, must allow the Regulator, or a person authorised by the Regulator, to enter premises where a dealing is being undertaken for the purpose of monitoring or auditing the dealing.

203. In cases of non-compliance with licence conditions, the Regulator may instigate an investigation to determine the nature and extent of non-compliance. The Act provides for criminal sanctions of large fines and/or imprisonment for failing to abide by the legislation, conditions of the licence or directions from the Regulator, especially where significant damage to the health and safety of people or the environment could result.

Section 4 Post release review

204. Regulation 10 requires the Regulator to consider the short and the long term when assessing risks. The Regulator takes account of the likelihood and impact of an adverse outcome over the foreseeable future, and does not disregard a risk on the basis that an adverse outcome might only occur in the longer term. However, as with any predictive process, accuracy is often greater in the shorter rather than longer term.

205. The Regulator has incorporated a requirement in the licence for ongoing oversight to provide feedback on the findings of the RARMP and ensure the outcomes remain valid for future findings or changes in circumstances. This ongoing oversight will be achieved through PRR activities. The three components of PRR are:

- adverse effects reporting system (Section 4.1)
- requirement to monitor specific indicators of harm (Section 4.2)
- review of the RARMP (Section 4.3).

The outcomes of these PRR activities may result in no change to the licence or could result in the variation, cancellation or suspension of the licence.

4.1 Adverse effects reporting system

206. Any member of the public can report adverse experiences/effects resulting from an intentional release of a GMO to the OGTR through the Free-call number (1800 181 030), mail (MDP 54 – GPO Box 9848, Canberra ACT 2601) or via email to the OGTR inbox (ogtr@health.gov.au). Reports can be made at any time on any DIR licence. Credible information would form the basis of further investigation and may be used to inform a review of a RARMP (see Section 4.3 below) as well as the risk assessment of future applications involving similar GMOs.

4.2 Requirement to monitor specific indicators of harm

207. Collection of additional specific information on an intentional release provides a mechanism for ‘closing the loop’ in the risk analysis process and for verifying findings of the RARMP, by monitoring the specific indicators of harm that have been identified in the risk assessment.

208. The term ‘specific indicators of harm’ does not mean that it is expected that harm would necessarily occur if a licence was issued. Instead, it refers to measurement endpoints which are expected to change should the authorised dealings result in harm. The licence holder is required to monitor these specific indicators of harm as mandated by the licence.

209. The triggers for this component of PRR may include risk estimates greater than negligible or significant uncertainty in the risk assessment.

210. The characterisation of the risk scenarios discussed in Chapter 2 did not identify any risks greater than negligible. Therefore, they were not considered substantive risks that warranted further detailed assessment. Uncertainty is considered to be low. No specific indicators of harm have been identified in this RARMP for application DIR 173. However, specific indicators of harm may also be identified during later stages, e.g. through either of the other components of PRR.

211. Conditions have been included in the licence to allow the Regulator to request further information from the licence holder about any matter to do with the progress of the release, including research to verify predictions of the risk assessment.

4.3 Review of the RARMP

212. The third component of PRR is the review of RARMPs after a commercial/general release licence is issued. Such a review would take into account any relevant new information, including any changes in the context of the release, to determine if the findings of the RARMP remained current. The timing of the review would be determined on a case-by-case basis and may be triggered by findings from either of the other components of PRR or be undertaken after the authorised dealings have been conducted for some time. If the review findings justified either an increase or decrease in the initial risk estimate(s), or identified new risks to people or to the environment that require management, this could lead to changes to the risk management plan and licence conditions.

Section 5 Conclusions of the RARMP

213. The risk assessment concludes that the proposed commercial release of GM cotton (MON 88701) poses negligible risks to the health and safety of people or the environment as a result of gene technology.

214. The risk management plan concludes that these negligible risks do not require specific risk treatment measures. However, general conditions have been imposed to ensure that there is ongoing oversight of the release.

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Appendix A: Summary of submissions from prescribed experts, agencies and authorities

The Regulator received a number of submissions from prescribed experts, agencies and authorities³ on matters relevant to preparation of the RARMP. All issues raised in submissions relating to risks to the health and safety of people and the environment were considered. These issues, and where they are addressed in the consultation RARMP, are summarised below.

Submission	Summary of issues raised	Comment
1	Council does not have specialist scientific advice available and therefore will not be able to provide comment.	Noted.
2	No comment/advice outside of local government public health expertise.	Noted.
3	<p>Shire lies within an area which supports about 8,000 taxa of vascular plants, representing two thirds of the estimated plant taxa in WA and over 80% of the plant taxa are unique.</p> <p>Council previously considered the issue of GM crops and foods, and passed a motion in 2009 with the following key points:</p> <ol style="list-style-type: none"> 1. Shire does not have jurisdiction over the growth, transport or sale of either GM crops or GM food; 2. Council lacks sufficient scientific knowledge to reach an overall conclusion on whether genetic modification of crops is harmful or not to human health and the environment; 3. Negative perceptions of GM crops and GM food exist in the residents and some market destinations have the potential to harm the marketing of organics and other local produce, if the region was to become associated with GM crops; 4. Council therefore does not support the use of GM crops in the shire. <p>Community concerned that there could be a potential contamination of local biodiversity with insect-borne GM pollen or organisms. This could have negative environmental impacts on the shire, with a risk of spread throughout the environment, resulting in the modification in the indigenous flora.</p>	<p>Noted.</p> <p>When deciding whether or not to issue a licence, matters that relate to marketing and trade, including coexistence of GM and non-GM crops, are outside the legislative responsibility of the Regulator. These are matters for State and Territory governments, who may designate GM free zones for marketing purposes that are unrelated to human health and safety and the environment.</p> <p>Pollen transfer from the GM plants to other organisms is considered in the RARMP (Chapter 1, Section 5.3.1) and Chapter 2, Section 2.2.2, and it was concluded that there is negligible risk.</p>

³ Prescribed experts, agencies and authorities include GTTAC, State and Territory Governments, relevant local governments, Australian government agencies and the Minister for the Environment.

Submission	Summary of issues raised	Comment
4	<p>Advises caution in the use of GM crops within Australia and the shire from a precautionary principle perspective.</p> <p>Availability of GM crops enables increased herbicide and pesticide use. These chemicals enter the environment with detrimental effects including:</p> <ul style="list-style-type: none"> overspray or runoff into uncropped areas or waterways, and affecting the soil where the mycorrhiza fungi and other micro biome capabilities of the soil are depleted. <p>Would rather see sustainable farming supported by governments rather than genetic modification that allows the use of greater amounts of potentially harmful chemicals within our shire and nationally.</p> <p>Cites news article demonstrates the widespread use and contamination of land with Roundup.</p>	<p>Issues relating to herbicide use are outside the scope of the Regulator's assessments. The APVMA has regulatory responsibility for the registration of agricultural chemicals, including herbicides, in Australia. A range of issues, including effects on human health, resistance management and environmental impacts are considered by the APVMA in assessing agricultural chemicals for registration.</p> <p>Choice of different farming systems is the responsibility of the States, Territories and industry, not the Regulator.</p> <p>The GM cotton included in this licence application is not tolerant to Roundup (glyphosate) herbicides. Therefore, Roundup cannot be used on this cotton crop.</p>
5	As the Council does not have a specialist scientific expert to make an assessment, no comment will be provided.	Noted.
6	No comment.	Noted.
7	Shire is not a cotton growing area so there would be no impact from a farming or environmental view.	Noted.
8	No comment.	Noted
9	<p>Council has concern with this application as the region is reliant on its agricultural production. Aware that some GM cotton is already approved for commercial release in Australia and that trials are currently undertaken in the shire. The main concerns include:</p> <ol style="list-style-type: none"> Herbicide resistance of a variety of weed species is likely to increase/develop (as it has done elsewhere) and this may make them more difficult to control on farms and in natural areas. Believes there are better and more sustainable crops, better suited to the region. Notes that GM cotton is likely to be disruptive to the existing agricultural sector, lead to unemployment of other agricultural industries and negatively impact on local economic development. The quality of any existing cotton and its current markets may be compromised similar to what occurred in Burkina Faso in 2008/09. Past corporate behaviour in other countries indicates GM cotton may have 	<p>Noted.</p> <p>Note that over 99% of Australian cotton crops are GM cotton since 2017.</p> <p>Issues with herbicide resistance in weeds come under the regulatory oversight of the APVMA. Relevant discussion is included in Chapter 1, Section 3.1.2.</p> <p>Choices of farming systems and crops, quality of agricultural products and any associated socio-economic impacts are outside the scope of the Regulator's assessment required by the Act. These issues are the responsibility of the States and Territories, and industry.</p> <p>As required by the Act, the Regulator considers whether the applicant is suitable to hold a licence.</p>

[illegible]

Submission	Summary of issues raised	Comment
	target organisms from dicamba use in GM cotton fields and the potential toxicity of DSCA to non-target organisms related to this use.	
	2. The RARMP should include a discussion on outcomes from previous releases (DIR 120, DIR 145).	This information is included in Chapter 1, Section 5.3.1 and Chapter 2, Section 3 (Uncertainty).
	a. The RARMP for DIR 145 refers to the relative uncertainty and lack of experience with this trait both in Australia and globally. Information or reporting of outcomes from this release should be included. If there was no information submitted, or the crop was not commercially cultivated, then this should be made clear in the RARMP for DIR 173. The information or lack of information for critical natural habitats or threatened species in Australia that may be exposed and adversely impacted should also be set out in the current RARMP.	
	3. Potential for the introduced trait to increase the GM cotton's weediness and ability to spread and persist in the environment should be considered in the RARMP. The discussion of risks of increased weediness as set out in DIR120 and DIR145 should be included. In particular noting the following:	Relevant discussion of these issues [a. to d.] can be found in Chapter 1, Sections 3.2 and 5.3, as well as Chapter 2, Sections 2.4.2 (Risk Scenario 2) and 2.4.3 (Risk Scenario 3). Additional background information is referenced from the OGTR Cotton Biology document.
	a. Cotton is not considered a weed.	
	b. The possible risk that the volunteers from a cotton plant with multiple herbicide tolerances could be more difficult to control than those with a single herbicide tolerance (glyphosate).	
	c. The risks of growing cotton in northern Australia has been discussed in previous RARMPs but should be revisited in this RARMP.	
	d. There are indigenous wild <i>Gossypium</i> species in Australia. The potential for gene transfer into wild cotton species, while unlikely, should be discussed.	

Appendix B: Summary of submissions from prescribed experts, agencies and authorities on the consultation RARMP

The Regulator received a number of submissions from prescribed experts, agencies and authorities on the consultation RARMP. All issues raised in submissions that related to risks to the health and safety of people and the environment were considered in the context of the currently available scientific evidence and were used in finalising the RARMP that formed the basis of the Regulator's decision to issue the licence. Advice received is summarised below.

Submission	Summary of issues raised	Comment
1	Notes that FSANZ had assessed and approved food derived from this GM cotton as being as safe for human consumption as food derived from conventional cotton cultivars.	Noted.
2	Council does not have the expertise to make any meaningful comment on this matter.	Noted.
3	The GM cotton is unlikely to have any direct implications for the Council, as there is no commercial cotton growing areas within or adjoining the LGA. In terms of more broad and indirect environmental impacts from its release, notes the RARMP concludes that there is a low risk of the strain causing harm. Its ability to spread in the environment seems to be fairly localised around cotton growing areas so it is highly unlikely that the LGA would experience any intrusion of the strain into the local environment. Council does [not] have any specialist knowledge in the field of GMO regulation and defers to the conclusions of the RARMP.	Noted.
4	No comment as Council does not have a scientific expert to make an assessment.	Noted.
5	<p>Council previously considered the issue of GM crops and foods, and passed a motion in 2009 with the following key points:</p> <ol style="list-style-type: none"> 1. Shire does not have jurisdiction over the growth, transport or sale of either GM crops or GM food; 2. Council lacks sufficient scientific knowledge to reach an overall conclusion on whether genetic modification of crops is harmful or not to human health and the environment; 3. Negative perceptions of GM crops and GM food exist in the residents and some market destinations have the potential to harm the marketing of organics and other local produce, if the region was to become associated with GM crops; 4. Council therefore does not support the use of GM crops in the shire. 	<p>Noted.</p> <p>When deciding whether or not to issue a licence, matters that relate to marketing and trade, including coexistence of GM and non-GM crops, are outside the legislative responsibility of the Regulator. These are matters for State and Territory governments, who may designate GM free zones for marketing purposes that are unrelated to human health and safety and the environment.</p>

Submission	Summary of issues raised	Comment
	Community concerned that there could be a potential contamination of local biodiversity with insect-borne GM pollen or organisms. This could have negative environmental impacts on the shire, with a risk of spread throughout the environment, resulting in the modification in the indigenous flora.	Pollen transfer from the GM plants to other organisms is considered in the RARMP (Chapter 1, Section 5.3.1) and Chapter 2, Section 2.2.2, and it was concluded that there is negligible risk.
6	No comment.	Noted.
7	<p>The release appears to be of low risk to human health and the environment.</p> <p>Provides the opinion that plant compositional analysis and environmental interaction studies should be undertaken in Australia, rather than relying on data generated in the USA.</p> <p>Has no objection to the issue of a licence for DIR 173.</p>	<p>As the compositional analysis and environmental interaction studies are for comparison of the GM cotton with its parent control under the same environmental conditions, it is expected that the data generated from the trials in the USA would be comparable to that from Australia.</p> <p>Also, the licence contains a range of conditions to ensure ongoing oversight of the release, achieved through post release review activities. If any adverse effects of the release in Australia are identified, the licence can be varied, suspended or cancelled.</p>
8	No specific comment on the risks to the health and safety of people and the environment in the consultation RARMP or the management of those risks.	Noted.
9	Notes that there is a history of the genetic modifications covered by this application having a proven track record of safety and several relevant authorities have approved these genetic modifications in human food products. On this basis, no objections or concerns about this application.	Noted.
10	<p>Concurs with a number of issues raised in submissions at Appendix A of the consultation RARMP, and noted that none of these relate to the focussed remit of risks to the health and safety of people and the environment.</p> <p>Supports the OGTR's conclusion that DIR 173 poses negligible risk of harm to human health and safety and the environment.</p>	Noted.
11	<p>Agrees with the overall conclusions of the RARMP that the direct risks to the environment from the genetic modification are negligible. However, inclusion of further details on indirect risks will support a full understanding of the issues associated with the GMO and support transparency and coherence between regulatory schemes.</p> <p>Provides the following advice for consideration in finalising the RARMP:</p>	<p>Noted</p> <p>It is the responsibility of the APVMA to carry out a thorough risk assessment on the herbicides and their metabolites and make decisions on</p>

Submission	Summary of issues raised	Comment
	<p>1. <i>The RARMP should include additional relevant information from the US EPA in the discussion of toxicity of dicamba and its metabolites to non-target organisms:</i></p> <p>While the indirect risk of toxicity to non-target organisms (NTOs) from herbicides and their metabolites is outside the scope of the RARMP, there is some useful discussion on this topic (par 53) because as stated in the RARMP (par 50) herbicide metabolites are produced in the GM plant following application of dicamba. Considers that this information is relevant when considering the overall risk of this GMO.</p> <p>Recommends incorporating information about toxicity to NTOs from US EPA reports (US EPA 2016a, US EPA 2016b, US EPA 2018a, US EPA 2018b) in par 53.</p>	<p>whether or not to register the herbicides to be used on the GM cotton if such an application is received in the future.</p> <p>Nonetheless, a brief discussion about the toxicity of dicamba metabolite DCSA was included in the RARMP because DCSA is produced in the GM cotton following dicamba application.</p>
	<p>2. <i>Relevant information on adverse effects and mitigation measures from the US EPA should be added to the discussion of uncertainty:</i></p> <p>Recommends including additional information from US EPA reports on the effects on NTOs and proposed mitigation measures to reduce uncertainty and assist in explaining issues around dicamba use in GM cotton.</p> <p>Recommends including relevant evaluation results, e.g. adverse effects on non-target terrestrial plants (both crop and natural species) from US EPA report. Suggests that it is unknown whether, and if so, which NTOs will be exposed in Australian GM cotton fields and this should be included as an area of uncertainty in this section.</p> <p>States that the application of dicamba and the generation of herbicide metabolites will increase due to cultivation of this GMO and suggests the RARMP could list some of the US EPA's proposed mitigation.</p> <p>Recommends that the Regulator work closely with APVMA to ensure any risks from use of dicamba were considered and do not fall through any regulatory gaps.</p>	<p>As noted above, APVMA is responsible for assessing the risks of herbicide use, and registration of the formulations and use patterns of the herbicides, including any restrictions and mitigation measures suitable for the situations in Australia. The US EPA's proposed mitigation measures are mentioned only briefly as examples.</p> <p>The Gene Technology Regulator is obliged to seek advice from APVMA and to take relevant advice into consideration before deciding whether to issue a licence.</p>
12	Agrees with the overall conclusion of the RARMP.	Noted.

Appendix C: Summary of submissions from the public on the consultation RARMP

The Regulator received six submissions from the public on the consultation RARMP. The issues raised in these submissions are summarised in the table below. All issues that related to risks to the health and safety of people and the environment were considered in the context of currently available scientific evidence in finalising the RARMP that formed the basis of the Regulator's decision to issue the licence.

Submission	Summary of issues raised	Comment
1	Wants to remind the OGTR of the introduced species that turned to pests, such as cane toad and rabbit/hare, as well as the drug thalidomide. Strongly opposes the commercial release of GM cotton. Long-term consequences of this release are unknown, but believes this will not be good judging by the previous examples.	<p>The RARMP concludes that the commercial release of this GM cotton poses negligible risks to the health and safety of people and the environment.</p> <p>Cotton is an agricultural crop that has been grown widely in Australia for many decades. It is not identified as a weedy species and the genetic modification in DIR 173 is not expected to change its characteristics in this regard. Other GM cottons have been grown since 1996 and they now comprise over 99% of the commercial cotton crop. No adverse effects from these GM cottons have been reported.</p>
2	<p>Cannot believe OGTR is even considering an application from multinational Monsanto for the commercial cultivation of GM cotton because they do not care about our health or the environment, only money.</p> <p>Asks what 'negligible risk to human health and safety or to the environment' actually means and suggests it is a non-committal statement which means nothing. Asks what tests and trials have been done to absolutely prove that this proposal will cause no side effects to humans and the environment.</p>	<p>The commercial motives of biotechnology companies are outside the scope of responsibility of the Regulator.</p> <p>The Regulator's approach to risk analysis can be found in the Risk Analysis Framework on the OGTR website, and includes definitions of the various terminology used. The Regulator is required to assess GMO applications in accordance with the Act and prepare a risk assessment and risk management plan (RARMP). The RARMP includes a thorough and critical assessment of data supplied by the applicant, together with a review of other relevant national and international scientific literature. It is finalised following an extensive consultation process involving prescribed experts, Australian Government authorities and agencies, experts, State and Territory Governments, relevant Australian local councils, the Minister for the Environment and the public. The Regulator cannot issue the licence</p>

Submission	Summary of issues raised	Comment
	Strongly opposes this licence application and any approval for commercially planting MON 88701 cotton in all cotton growing areas of Australia.	<p>unless satisfied that any risks posed by the dealings proposed to be authorised by the licence are able to be managed in such a way as to protect the health and safety of people and the environment.</p> <p>The RARMP concludes that the commercial release of this GM cotton poses negligible risks to the health and safety of people and the environment.</p>
3	<p>Strong objection to release of herbicide tolerant GM cotton being used in human food and animal feed.</p> <p>Particularly concerned about the amount of herbicide retained by the crop, and accumulates and moves down the food chain, which may affect the health of future generations.</p> <p>Asks that the GM crops not be used in food for humans or animals.</p>	<p>The APVMA is responsible for registering agricultural and veterinary chemicals. The registration process involves scientifically evaluating the safety of using herbicides on GM crops in order to protect the health and safety of people, animals, plants and the environment.</p> <p>FSANZ has regulatory responsibility for food safety assessments in Australia. FSANZ has approved food from the GM cotton. More information about their assessments is available from the FSANZ website.</p>
4	<p>Supports the granting of a licence to Monsanto allowing it to commercialise this trait in cotton in Australia on the following basis:</p> <ul style="list-style-type: none"> Endorses the rigorous scientific review and approval process applied by OGTR to independently assess to the trait for cultivation in Australia. MON 88701 has been approved for cultivation in other jurisdictions and by other comparable regulatory agencies. The opportunity for Australian growers to cultivate cotton containing this trait does not pose an unacceptable risk to public health or the environment. The technology will provide Australian cotton growers an opportunity to apply the herbicides glufosinate and dicamba in crop to more effectively manage weeds, should appropriate herbicides be approved for such purposes. Further, we note that these herbicides are currently approved for certain uses in Australia by the APVMA. Access to biotechnology traits is important to our customers as it greatly assists their ability to sustainably manage their cotton production practices. 	<p>Noted.</p> <p>As indicated in the RARMP, if MON 88701 cotton is to be commercially cultivated in Australia, the formulations and new use patterns of the herbicides dicamba and glufosinate for use on the GM cotton must be approved by APVMA.</p>

Submission	Summary of issues raised	Comment
	Australia cotton growers have demonstrated their ability to responsibly manage cotton varieties containing both insect protection and herbicide tolerance traits since 1996. The technology has supported the continual improvement in environmental sustainability for the cotton industry since introduction.	
5	<p>Opposes the patenting of life forms, including genetically modified cultivars –supports the principle of non-patentability of gene sequences.</p> <p>Advocates alternatives to the use of herbicide resistant plants created by genetic modification.</p> <p>Argues that genetically modified cotton should not be used in Australia.</p> <p>Should the licence be granted, there are a number of requirements that should be included. We need strong, transparent, precautionary, regulatory compliance and monitoring systems, to prevent GM contamination events.</p> <p>Aware that a consultation RARMP has been prepared, which concludes that the proposed release would pose negligible risk to human health and safety or to the environment. Claims that this conclusion is based on limited evidence and does not adequately support ongoing oversight of the use of the organism.</p>	<p>Patenting is outside the remit of the OGTR; any patenting issues should be addressed to IP Australia.</p> <p>Matters relating to choice of different farming systems is outside the scope of the Regulator's assessment required by the Act.</p> <p>The licence includes a number of conditions to ensure ongoing oversight of the release. This oversight will be achieved through post release review (PRR) activities that, depending on the outcome, may result in no change to the licence or could result in the variation, cancellation or suspension of the licence.</p> <p>The RARMP concludes that the commercial release of this GM cotton poses negligible risks to the health and safety of people. The RARMP was prepared using a combination of critical assessment of data provided by the applicant, review of published scientific literature, information on relevant previous approvals and any adverse effects of these releases, and advice received from a range of Australian government authorities, agencies, experts and the public. It was supported by a previous assessment by FSANZ who found that food derived from the GM cotton is safe for human consumption. In the context of the activities proposed by the applicant and considering both the short and long term, none of the risk scenarios postulated in the RARMP gave rise to any substantive risks associated with the GMO that could be greater than negligible. As mentioned above, ongoing oversight will be achieved through PRR activities.</p>
	Suggests that the OGTR should require the applicant to provide the complete genome sequences of the parent and the GM cottons before any licence is granted. Claims that these genome sequences are necessary for assessing the	The full genome sequence of the parent organism <i>Gossypium hirsutum</i> is already publicly available, and the applicant has provided data to show that the introduced genes are inserted into the

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	likely risks including those posed by genetic drift, making sure that the backbone sequences of plasmids used to transfer the genes into the cotton have not been transferred, and ongoing monitoring to identify any outcrossing or inter- or intra-species transfer of the (herbicide) tolerance genes.	genome as a single copy of the T-DNA containing the gene expression cassettes; no plasmid backbone sequences are present (see Chapter 1, Section 4.3.1 of the RARMP). The potential for harm to result from transfer of herbicide tolerance genes to other cotton or closely-related species (gene flow) have been considered in Chapter 2, Sections 2.2.2 and 2.4.4 of the RARMP and the associated risk was considered to be negligible.
	Suggests that as part of the post [release] review, there should be a requirement to monitor the GMO progeny population at different sites over time to identify if genetic drift has occurred and to precisely reveal the basis of any changes by genome sequencing. These sequencing steps would inform a better risk assessment of the organism and provide rigorous objective benchmarks, and enable standards and quality assurance systems to be effective. These steps would help to ensure that any license requirements are met and provide information that could alert regulators if unexpected genetic changes occur over time that could be problematic and require adaptive management, including cessation of use. Ideally, this research should be carried out independently and peer reviewed by an independent scientific panel.	<p>The applicant has provided data showing that the introduced herbicide tolerance genes are stably inherited through many generations in MON 88701 cotton without change (see Chapter 1, Section 4.3.1 of the RARMP). Genetic changes occurring by natural means, such as mutations and random genetic drift unrelated to the genetic modification, are outside the scope of the Regulator's assessment required by the Act.</p> <p>The licence holder is required to report any adverse or unintended effects of dealing with the GMO. The Regulator has the ability to vary, cancel or suspend a licence if a risk to human health and safety or to the environment is identified.</p>

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Requests rejection of the licence application DIR 173 for reasons summarised below.

1. **Applicant unsuitable to hold a DIR licence:** challenges the suitability of the applicant to hold a licence because of litigation and overseas regulatory actions relating to the applicant and related companies.
 - Claims that overwhelming evidence shows that Monsanto/Bayer's actions have been frequently and intentionally egregious, without regard for the environment and public health, making the applicant unsuitable to hold a DIR licence.
 - Cites a list of court cases against Monsanto/Bayer in the USA as evidence to show that Monsanto/Bayer's products including herbicides, medical devices and medicines, have caused damages to the environment and public health, and have been punished by the US courts.

The RARMP prepared in relation to the proposed dealings considers the risks to human health and safety and to the environment posed by genetic modification being assessed in the application. The Regulator's decision regarding the suitability of the applicant to hold the licence involves a separate and additional consideration in accordance with sections 57 and 58 of the Act. The majority of the matters raised in this submission relate to the suitability of the applicant rather than the matters of the RARMP.

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	<ul style="list-style-type: none"> Claims that DIR 173 application is in breach of legal requirements in Sections 57 and 58 of the Act. Sections 57(2) and 58(2) of the Gene Technology Act 2000 require the OGTR to be satisfied of the applicants' suitability to hold licences. Claims that licence holders are required to meet contemporary community standards of probity, good standing and ethical behaviour. Requests that if the GTR's discretion under Section 54 (2) (b) of the Act was exercised in Monsanto's favour, the public needs to be advised of the basis on which this decision was reached and the evidence should be published, so the process and the decision are transparent and open to public scrutiny. 	<p>The actions of related corporates internationally do not necessarily reflect on the Australian registered company (the applicant for DIR 173).</p> <p>No such discretion exists with respect to providing documents to a person under Section 54 (2) (b). The subsection is clear that documents provided pursuant to that section must not include information about relevant convictions.</p>
2.	<p>Environment: The Gene Technology Act 2000 requires the OGTR to apply the precautionary principle and exercise a duty of care to dealings that may adversely affect the environment and public health. So the OGTR should only make a decision on DIR 173, when and if the APVMA and the Department of Agriculture, Water and the Environment have comprehensively assessed and cleared both dicamba and glufosinate for over-the-top spraying onto the cotton with GM traits.</p> <ul style="list-style-type: none"> Claims that the OGTR is duty bound to consider not only the genetics of MON 88701 cotton but also the direct and indirect collateral environmental damage that licensing a crop with dicamba and glufosinate tolerance traits would cause by enabling the repeated spraying of dicamba and glufosinate over cotton, anywhere in Australia. States that can only effectively occur through an open, transparent and public process between the OGTR, the product regulators and the Department of Environment. Chemical and GMO residues left in the environment, that may affect human food and animal feed supplies, also require such precautionary assessment. Asserts that dicamba and glufosinate tolerance traits would enable the unchecked and repeated spraying of the herbicides over cotton plantations growing anywhere in Australia, including near 	<p>The Regulator is required to seek advice from both the APVMA and the Department of Agriculture, Water and the Environment on the RARMP before making a decision.</p> <p>Many of the concerns raised in this submission relate to application of herbicides to the GM cotton and persistence of residues. The APVMA has regulatory responsibility for agricultural chemicals, including herbicides, in Australia. The APVMA considers risks to human health, animals and the environment in assessing agricultural chemicals for registration and in setting maximum application rates, use patterns and maximum residue levels. The Regulator is also obliged to consult with the Department of Agriculture, Water and the Environment (formerly Department of Environment and Energy) on environmental aspects of the proposed release.</p>

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	<p>major waterways and in water catchments that drain to the sea.</p> <ul style="list-style-type: none"> Comments that the Department of Environment has a key role to play in decisions about DIR 173 but its engagement is opaque and any advice it may have tendered is unpublished. Believes that all notes, transcripts, advice and correspondence between the OGTR, APVMA and the Department related to DIR 173 should be published and available for review as part of this public consultation. Speculates that although no dicamba-resistant or glufosinate-resistant weed species have been recorded in Australia as described in the RARMP, it can be reasonably certain that dicamba and glufosinate resistant weeds will be generated before long if the herbicides are widely and repeatedly sprayed on cotton here. Claims that widespread glyphosate-tolerance in a variety of weeds in cotton crops appears to be driving the push for new herbicide tolerant GM cotton varieties like those proposed in DIR 173. States that the APVMA PubCRIS database shows three registrations of glufosinate and glufosinate ammonium, but the applicants for DIR 173 approval are not the registrants. Believes that the OGTR must know and assess exactly what formulations of dicamba and glufosinate the APVMA will approve for spraying on the GM cotton, before reaching any conclusions on application DIR 173. 	<p>Summaries of advice received for DIR 173 application and how they were considered are included in the Appendix A and Appendix B of the final RARMP. This includes any advice from the Department of Agriculture, Water and the Environment (formally Department of Environment and Energy).</p> <p>Managing the development of herbicide resistance comes under the regulatory oversight of the APVMA.</p> <p>The APVMA has approved registrations of glufosinate and dicamba herbicides for various weed control applications in Australia. Monsanto would need to apply to the APVMA for registration of over-the-top (OTT) use of these herbicides on the GM cotton.</p> <p>Issues relating to herbicide use are outside the matters to which the Regulator may have regard when deciding whether or not to issue a licence.</p>
3. Public Health		
	<ul style="list-style-type: none"> Links the approval of MON 88701 cotton with intensive spraying of glufosinate and dicamba herbicides. Claims that the OGTR has a clear responsibility to consult other personnel within the Health Department about possible increased public exposure to the herbicides to be sprayed over the GM cotton. Cites several journal articles about the adverse effects of glufosinate and dicamba to human health including some symptoms. States that resolution of public health hazards and risks is required prior to any OGTR decision on MON 88701 cotton. If it is to be commercially cultivated in 	<p>The Act requires the Regulator to identify and manage risks to human health and safety and the environment posed by or as a result of gene technology. The RARMP concluded that the commercial release of this GM cotton poses negligible risks to the health and safety of people and the environment.</p> <p>Issues relating to herbicide use are outside the scope of the Regulator's assessments. The APVMA has regulatory responsibility for agricultural chemicals, including herbicides, in Australia. The APVMA considers risks to human health, animals and the environment in</p>

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	<p>Australia, the APVMA must first consider and resolve issues around the toxicity of dicamba and glufosinate and their metabolites.</p> <ul style="list-style-type: none"> Claims that it is unacceptable that the RARMP states “Data regarding the toxicity of DCSA is limited and some uncertainty exists.” But then it asserts that, “From the available information, DCSA appears to be less toxic or equally toxic as parent dicamba for aquatic organisms on an acute basis, but may be substantially more toxic on a chronic basis to terrestrial organisms, specifically mammals.” Claims there are big data and evidence gaps, which the OGTR would fill with best guesses under the Regulatory Science Regime that Australian regulators use. Approval of MON 88701 cotton would facilitate the exposure of terrestrial organisms, specifically mammals (including humans), to harmful dicamba and glufosinate herbicides and their metabolites. 	<p>assessing agricultural chemicals for registration and in setting maximum application rates and use patterns. Although the Regulator has approved dealings with MON 88701 cotton, APVMA approval would be needed before OTT herbicides can be applied to the GM cotton.</p> <p>A brief discussion about the toxicity of dicamba metabolite DCSA is included in the RARMP (Chapter 1, Section 4.2.4) because DCSA is produced in the GM cotton following dicamba application. It is the responsibility of the APVMA to carry out a thorough risk assessment on the herbicides and their metabolites and make decision on whether or not to register the herbicides to be used on the GM cotton if such an application is received in the future.</p>
	<p>4. Conclusion</p> <p>The OGTR must reject application DIR 173 as it would enable the selling, sowing and spraying of commercial MON 88701 dicamba and glufosinate tolerant cotton seed. The known hazards, risks and impacts of the crop itself, and the chemicals sprayed over-the-top of vast tracts of the crop, make this application absolutely unacceptable.</p>	Noted