Nissan Chemical
CORPORATION

Presentation for Agrochemicals Business Briefing

September 28, 2022

Nissan Chemical Corporation
Agricultural Chemicals Division
Biological Research Laboratories
Chemical Research Laboratories

Translation of presentation materials for
Agrochemicals Business Briefing held on September 28, 2022

1. Agrochemicals Segment's Growth Strategy

Contents

*FY2021 Actual and FY2022 Outlook thereafter are figures announced in May 2022.

Agrochemicals Segment's Business Environment

<Common Task>

➢ Rising raw material and shipping costs and stable procurement

- Higher raw material prices
- Plant environmental inspections
- Port labor force
- Container ship
- Ukraine crisis

- Price hike due to revision
- Securing multiple sources
- Advance order placement

Shanghai Lockdown

Up to double for India

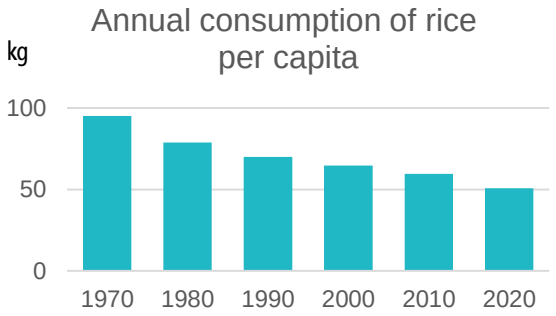
Up to triple within EU region

Agrochemicals Segment's Business Environment

<Domestic>

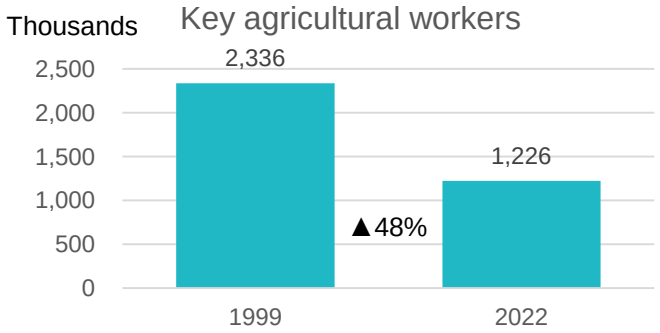
- Mature market: Continued to be worth 350 billion yen.
  Important to keep developing and launching new drugs.
  Enter to biological pesticides but limited impact for the immediate future.

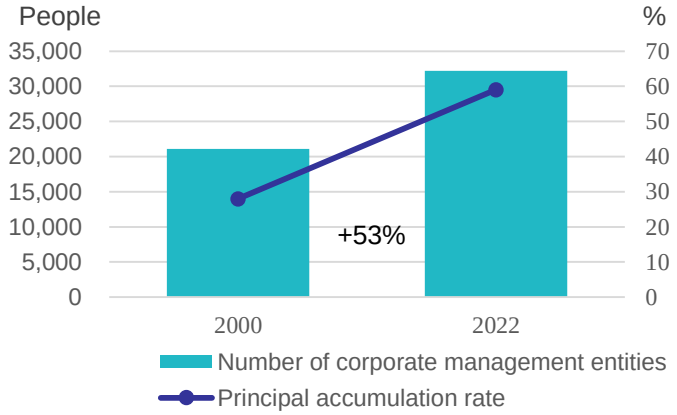
- Sluggish agricultural product prices:
  Rice consumption is declining.
  Fruits and vegetables also have few upward factors.



- Rise of production materials prices.

- Agricultural principal and consolidation: Farming population is declining and entities are becoming a large-scale.





- Strategy for Sustainable Food System MeaDRI: Limited Impact

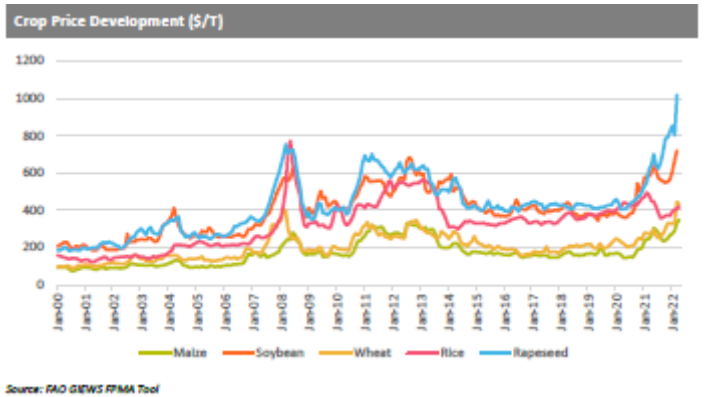
  2030: Reduce chemical pesticides' consumption (risk conversion) by 10%

  Keep and update current registration including revaluation

Agrochemicals Segment's Business Environment

<Overseas>

- Strong demand for grains and price hikes continue



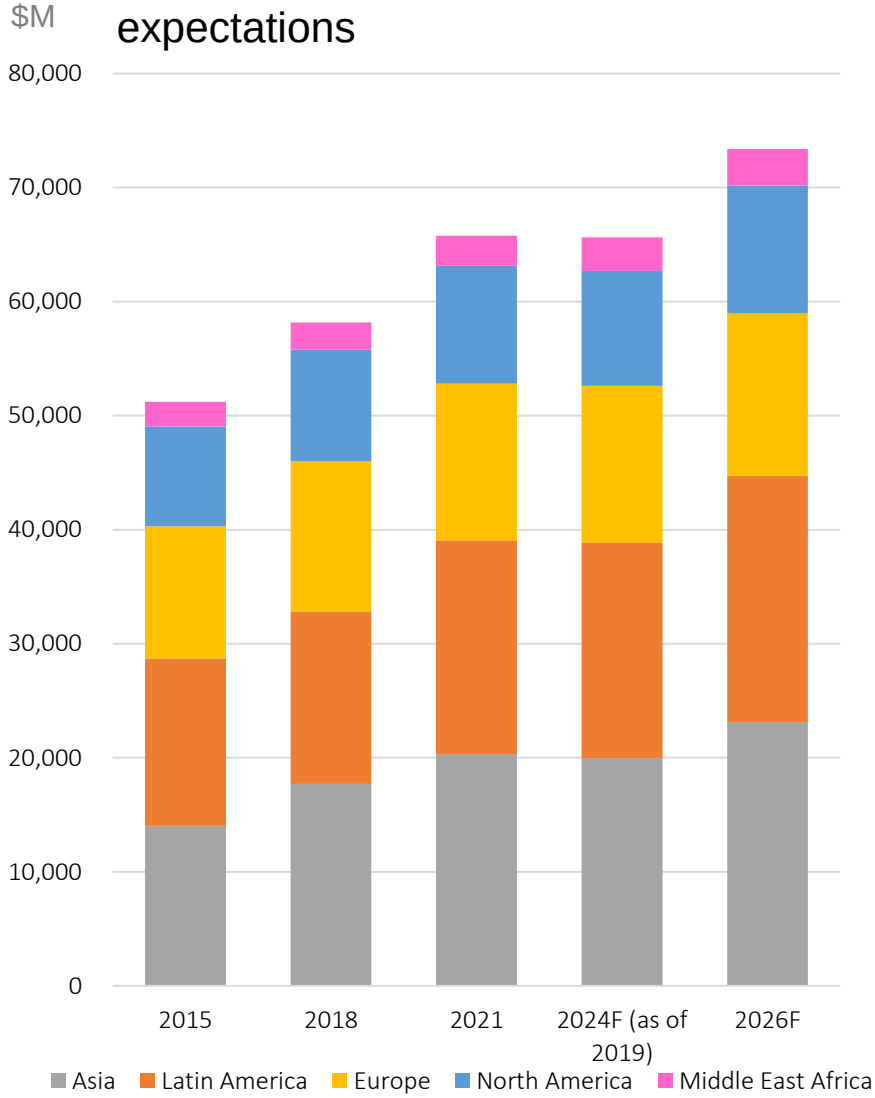
- Developed in important segments, mainly in Asia

Region	Market Size 2021 ($M)	Our products										
		Herbicide				Insecticide			Fungicide			
		TARGA	PERMIT	SIRIUS	ALTAIR	SANMITE	STARMITE	GRACIA	LEIMAY	PULSOR	DITHANE	QUINTEC
Asia	20,330	◎	○	○	◎	○	◎	◎	○	◎	◎	○
Latin America	18,735	◎	○	○		○	○					○
Europe	13,736	◎	◎	○		○			◎			○
North America	10,333	◎	◎			○						◎
Middle East Africa	2,641		○			○	○	○	○			○

Green shading; within 5 years after launched

◎ Sales(before discounts): more than500 million yen/year
○ Sales(before discounts): less than 500 million yen/year

- Agrochemical market grow ahead of expectations



Agrochemicals Segment's Business Environment

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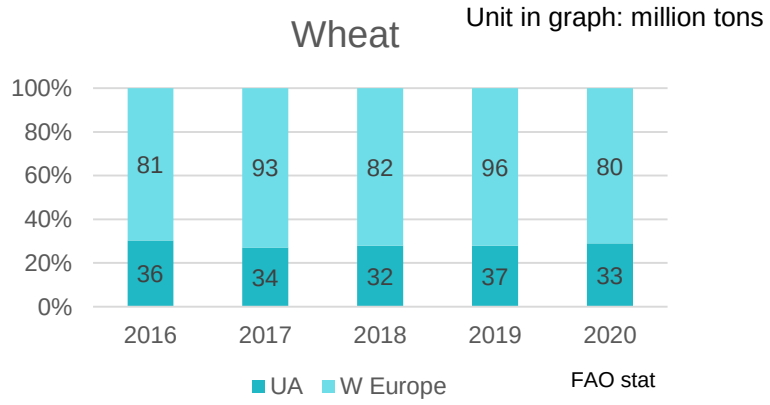
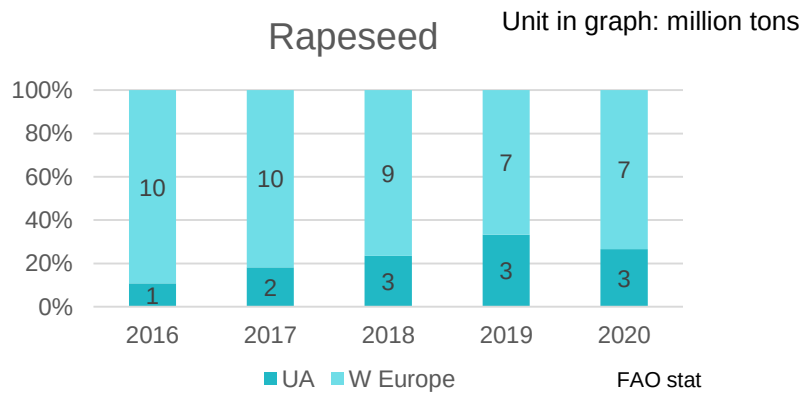
<Overseas>

- The prolonged conflict increases the possibility of impacts becoming apparent

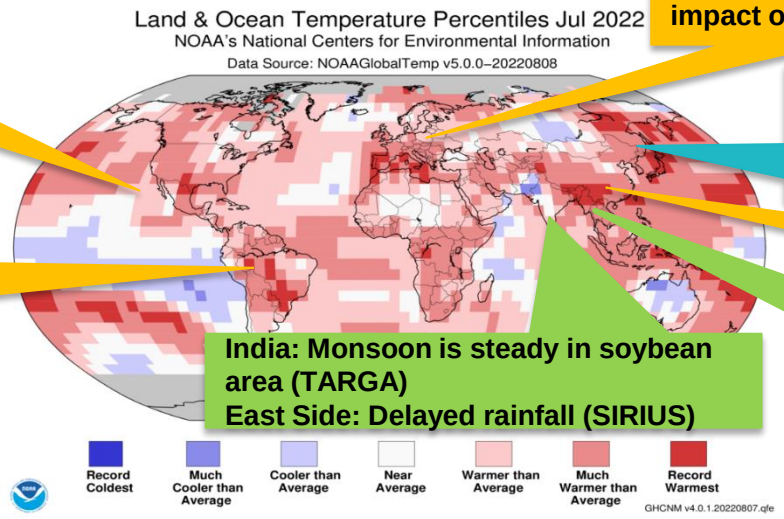




- Limited impact of climate change

United States: Severe drought reduces rice production in California (PERMIT)

Brazil: Soybean yields dramatically decreased due to severe water shortage by La Niña (TARGA)



India: Monsoon is steady in soybean area (TARGA)
East Side: Delayed rainfall (SIRIUS)

EU: Drought in about 60%, heat wave and water shortage have serious impact on crops

Korea: Flood in the Middle East. Extensive damage to farmland, but limited impact on our products

China: Drought in the Yangtze River Basin also has little impact on our products

Yue-Nan: Mekong: Rainfall timing and amounts are on par with previous years
Central China: Low rainfall, sluggish demand for fungicides

Agrochemicals Segment's Business Environment

<Overseas>

- Progress in Regulation of Chemical Synthetic Pesticides in Europe: Balancing F2F and Stable Food Production

March 10, 2022
Letter from EU Agricultural Minister to EU Chairman von der Leyen

Offer to maintain long-term sustainable food production in the EU through F2F mitigation in the face of anticipated intra-regional shortages in agricultural products due to the conflict in Ukraine, as well as soaring fertilizer prices.

- Expansion of the Microbial Pestcides Market

Plan to enter the microbial pesticides and biostimulant markets under the new mid-term plan

Expand domestic and overseas expansion through aggressive in-licensing as well as in-house development by building a foundation

External Parasite Drug Market

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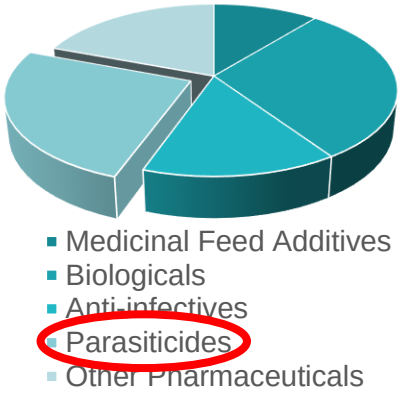
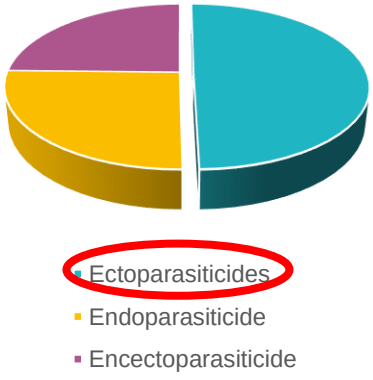
Animal Health Product Market 2020 Total: $33,848M

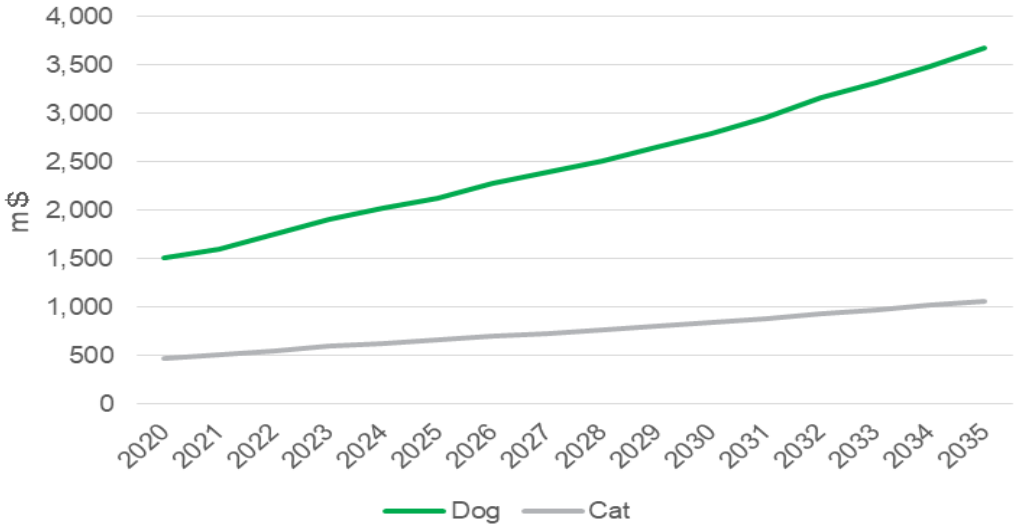


Pesticide Drug Market 2020 $8,592M

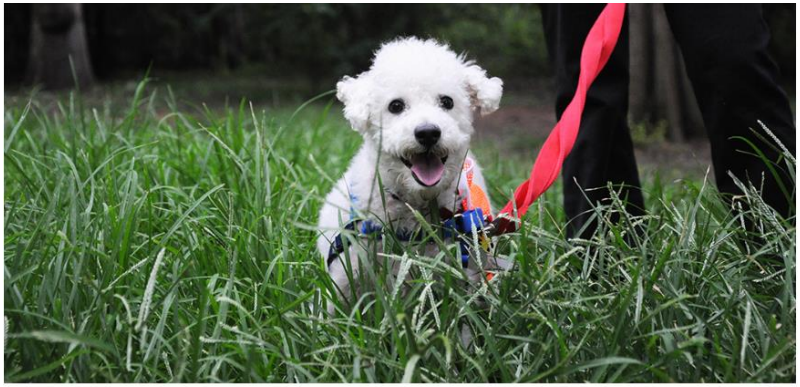


Ref. Vetnosis review 2020

Flea, Tick control： USA, EU, China, Japan, Australia



Ref. IHS Markit Animal health market analysis 2022



Fleas and ticks are two of the most frequent pet care concerns in America. While prevention is the best defense against these parasites, it's important to be able to recognize the signs and symptoms of fleas and ticks so you can help your pets if necessary. Read on for more information.

Ref. American Society for the Prevention of Cruelty to Animals.

Ectoparasticides is 13% of whole Animal Health Product Market. Estimate products for companion animal to grow more until 2035.

Major Issues for Business Divisions and Related Divisions

Domestic	Securing stable revenue and launching new products in the market
ROUNDUP	Diversification of sales channels
Overseas	Expansion of existing products and launch of new products
Animal health product	Measures against patent expiration and development of new drugs
R&D	New chemical pesticides exploratory research (safety), commercialization of biological pesticides
Manufacturing	Cost reduction through domestic and overseas production system by strengthening self-manufacturing system by NBR

Numerical Targets

<Business scale in 2027>

(Billions of yen)

		2021 (Actual)	2022 (Outlook)	2024 (Plan)	2027 (Plan)	2024 vs. 2021	2027 vs. 2021
		(1)	(2)	(3)	(4)	(3) - (1)	(4) - (1)
Agrochemicals	Net Sales	65.8	72.9	77.8	82.3	+12.0	+16.5
	Operating Profit	18.3	19.5	21.7	21.0	+3.4	+2.7

New Products (pipeline)

Launch	Products	Application	Product development type	Notes	Peak sales target
2024	NC-653 (Dimesulfazet)	Herbicide	In-house	Effective against resistant weeds, having excellent safety to rice	¥3.5 billion
2025	NC-520	Insecticide	Joint development	Insecticide for paddy rice co-developed with other companies. Highly effective against planthoppers	¥2.5 billion
2027	NC-656	Herbicide	In-house	Our first foliar application rice herbicide with excellent efficacy against resistant grass weeds	¥10 billion

- Peak sales target is 31.0 billion yen, including the above 3 pipeline products and 3 new products (GRACIA, QUINTEC and DITHANE)

2. Domestic Sales Strategy

Contents

Domestic Agrochemical Market and Nissan Chemical's Position

Market Size of Agrochemicals by Country (CY2021)

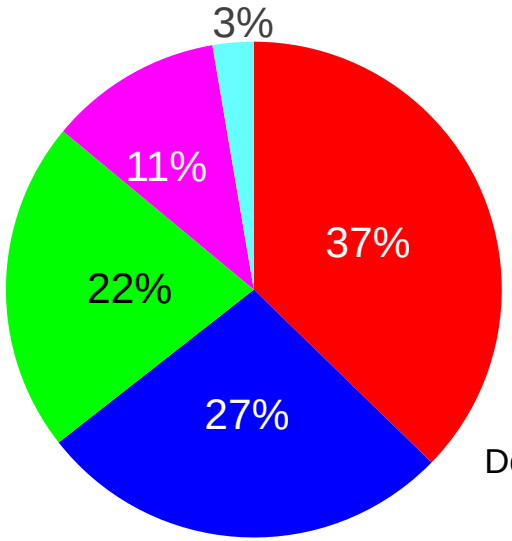
Rank	Country	Sales($M)
1	Brazil	11,327
2	USA	8,753
3	China	7,521
4	Japan	3,572
5	India	3,104
6	Argentina	3,010
7	France	2,206
8	Australia	1,883
9	Russia	1,726
10	Canada	1,580
11	Germany	1,561
12	Italy	1,310
13	Spain	1,237
14	Mexico	984
15	Vietnam	791
16	UK	779
17	South Korea	748
18	Ukraine	674
19	Chile	614
20	Romania	599
	World	65,775

Domestic Agrochemical Sales Ranking (October 1, 2019~ September 30, 2020)

Rank	Company	Market Share
1	Nissan Chemical Corporation	17%
2	Sumitomo Chemical Company	13%
3	Syngenta Japan	12%
4	Bayer CropScience	10%
5	Kumiai Chemical Industry	10%
6	Hokko Chemical Industry	9%
7	Mitsui Chemicals Agro	9%
8	Nihon Nohyaku	7%
9	BASF Japan	7%
10	Nippon Soda	6%
Top10 Total		100%

Source: AgbioInvestor

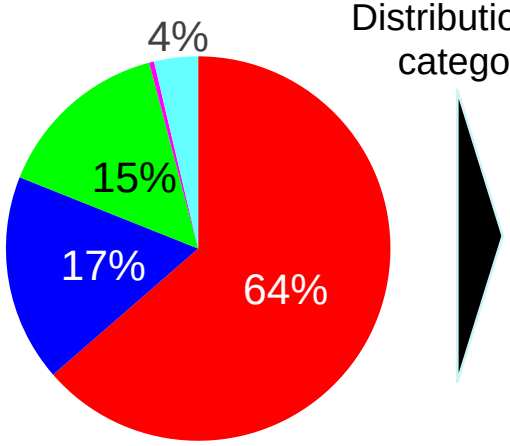
Nissan Chemical's Domestic Agrochemicals Portfolio and Its Growth



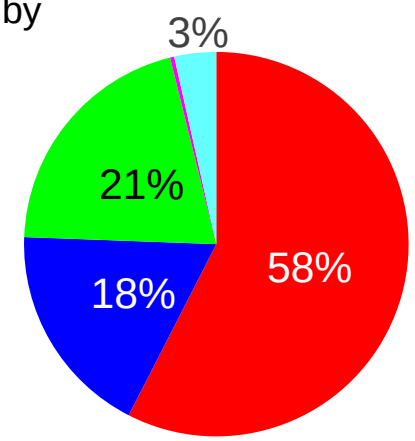
- Herbicide
- Insecticide
- Fungicide
- Insectticide and Fungicide
- Others

Domestic Agrochemical Market
2021 Agrochemical Year

Distribution by category



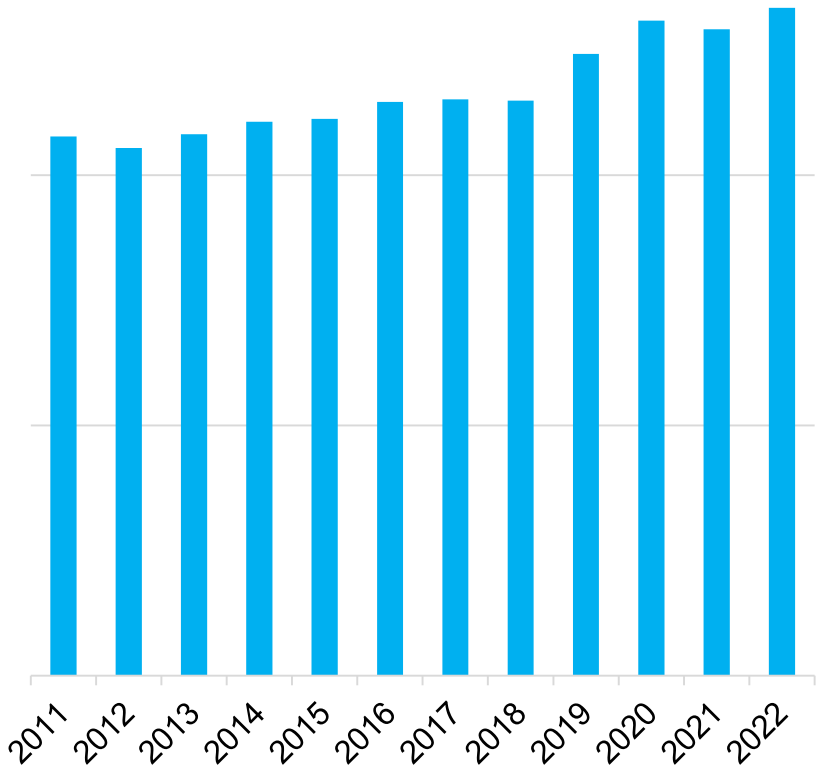
2018 Agrochemical Year



2021 Agrochemical Year

Nissan Chemical's General Agrochemicals excluding ROUNDUP

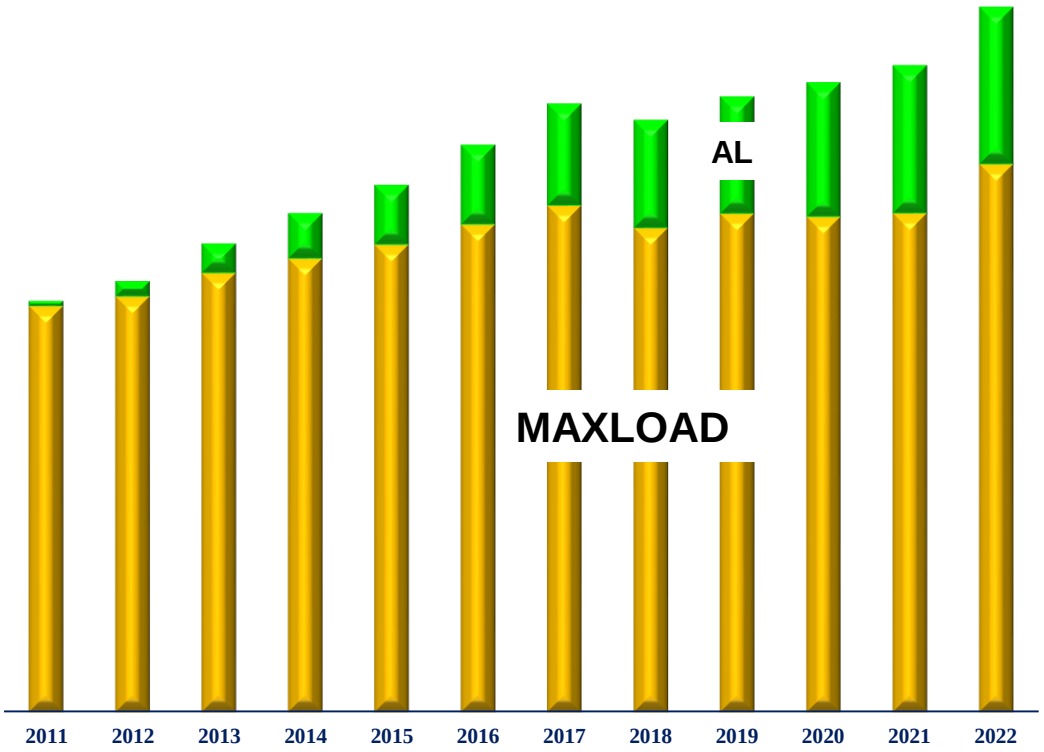
Trends in Nissan Chemical's General Agrochemicals Net Sales



*Agrochemical Year : October to September
2022: Forecast

ROUNDUP Sales

ROUNDUP Sales Trends



*Agrochemical Year : October to September
2022: Forecast

Sources of ROUNDUP's Growth

1. Overwhelming brand power

2. Due to the price raising of glyphosate in China price gap between generics and ROUNUP is shrinking

3. ULV5 nozzles for the boom sprayer accelerate shift from generics

4. Expansion of the herbicide market for general consumers

- **Growth rate over 3 years from 2019**
  General Consumer Market 33% (estimate)
  ROUNDUP AL 34%

Drugstores, supermarkets, etc.
Expansion to new business type

ROUNDUP Soy bean Pre-cultivation Trial (Fukuoka)
Spread on July 5, 2018 Photo taken on September 19, 2018

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ROUNDUP ML500ml→cultivate → sowing → soil treatment agent B

cultivate → sowing → soil treatment agent B

ROUNDUP Soy bean Pre-cultivation Trial (Fukuoka)
Spread on July 5, 2018　Photo taken on December 7, 2018

Nissan Chemical CORPORATION

ROUNDUP ML500ml→cultivate → sowing → soil treatment agent B

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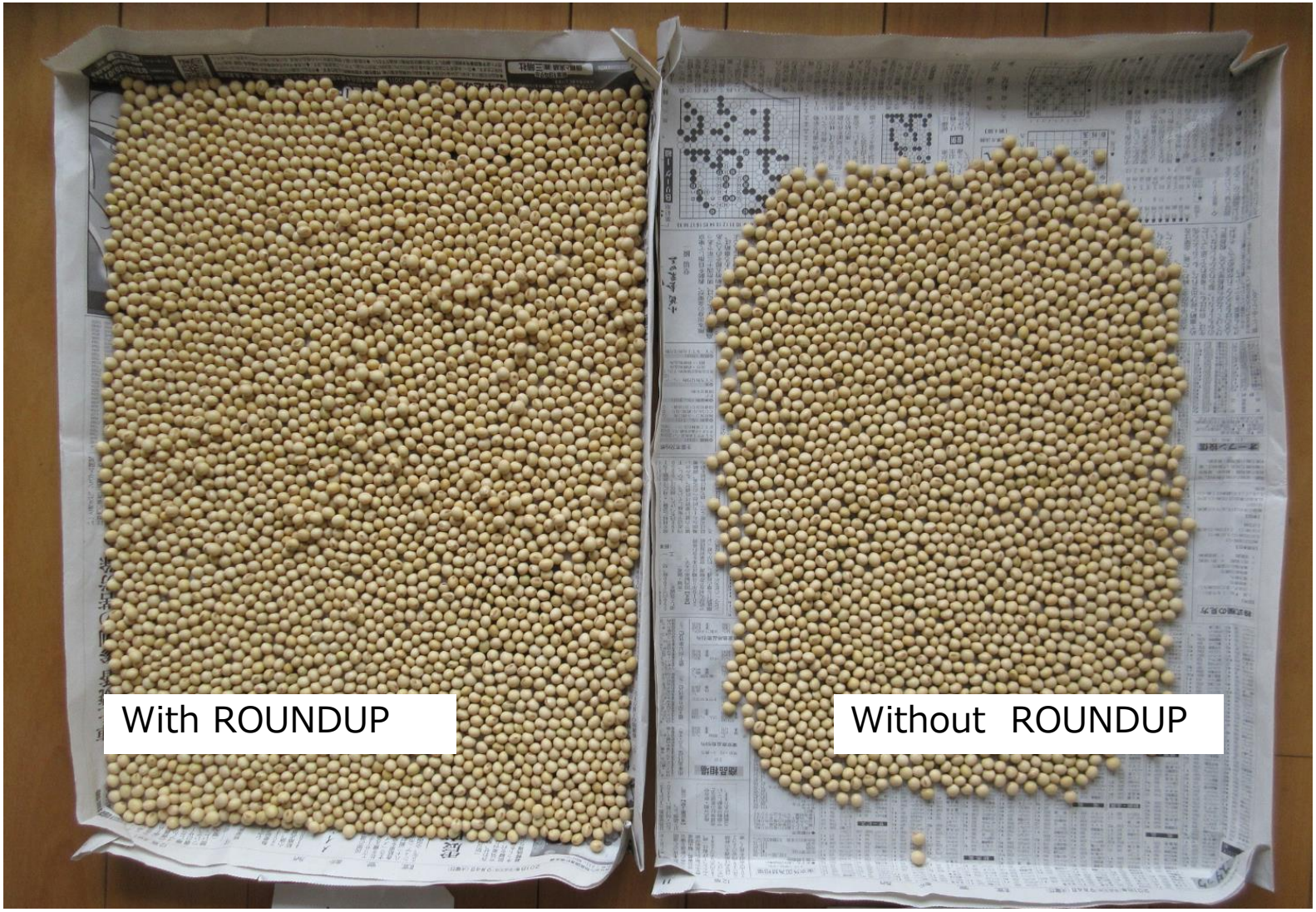
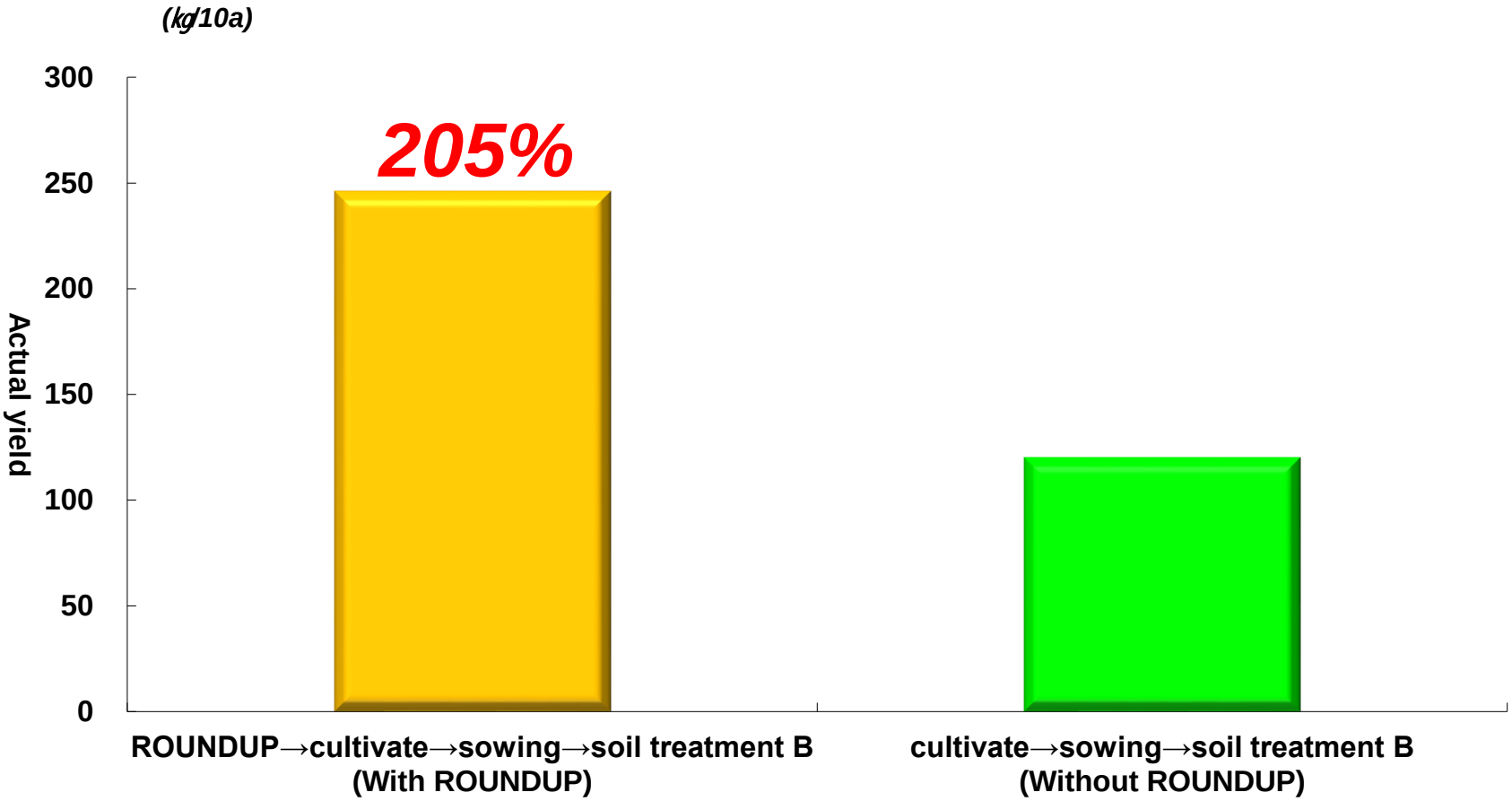


ROUNDUP Soy bean Pre-cultivation Trial (Fukuoka)

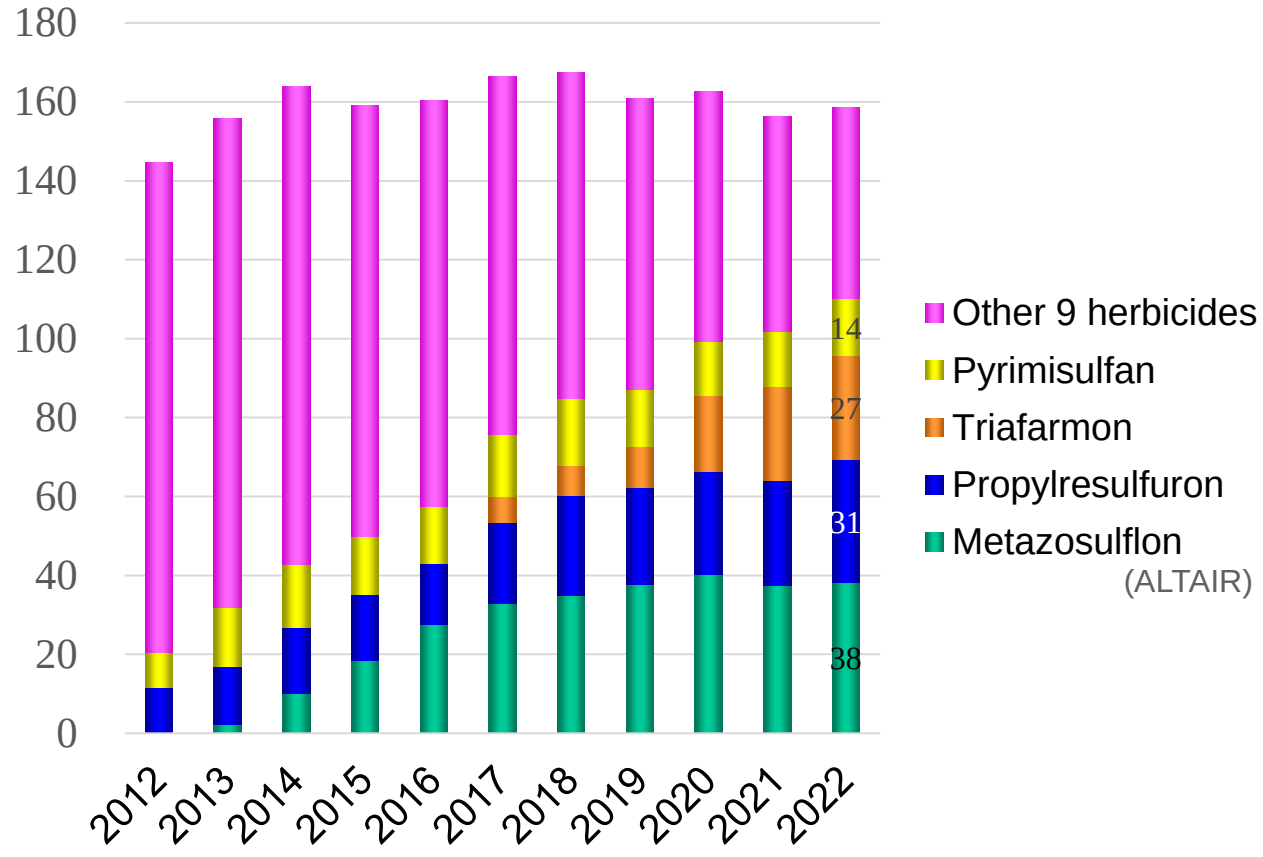
Yield Comparison Results (Adjusted to 10a, after 6mm screened out)



ALTAIR Sales

Trends in Shipments of Major Ingredients
Used as the Parent of the Paddy Rice Herbicide
(ALS inhibitor*)

(ten thousand Ha)



*Agrochemical Year : October to September
2022: October to June

*ALS inhibitors kill weeds
by inhibiting the action of acetolactate synthase

Launched in 2021
Third-generation ALTAIR

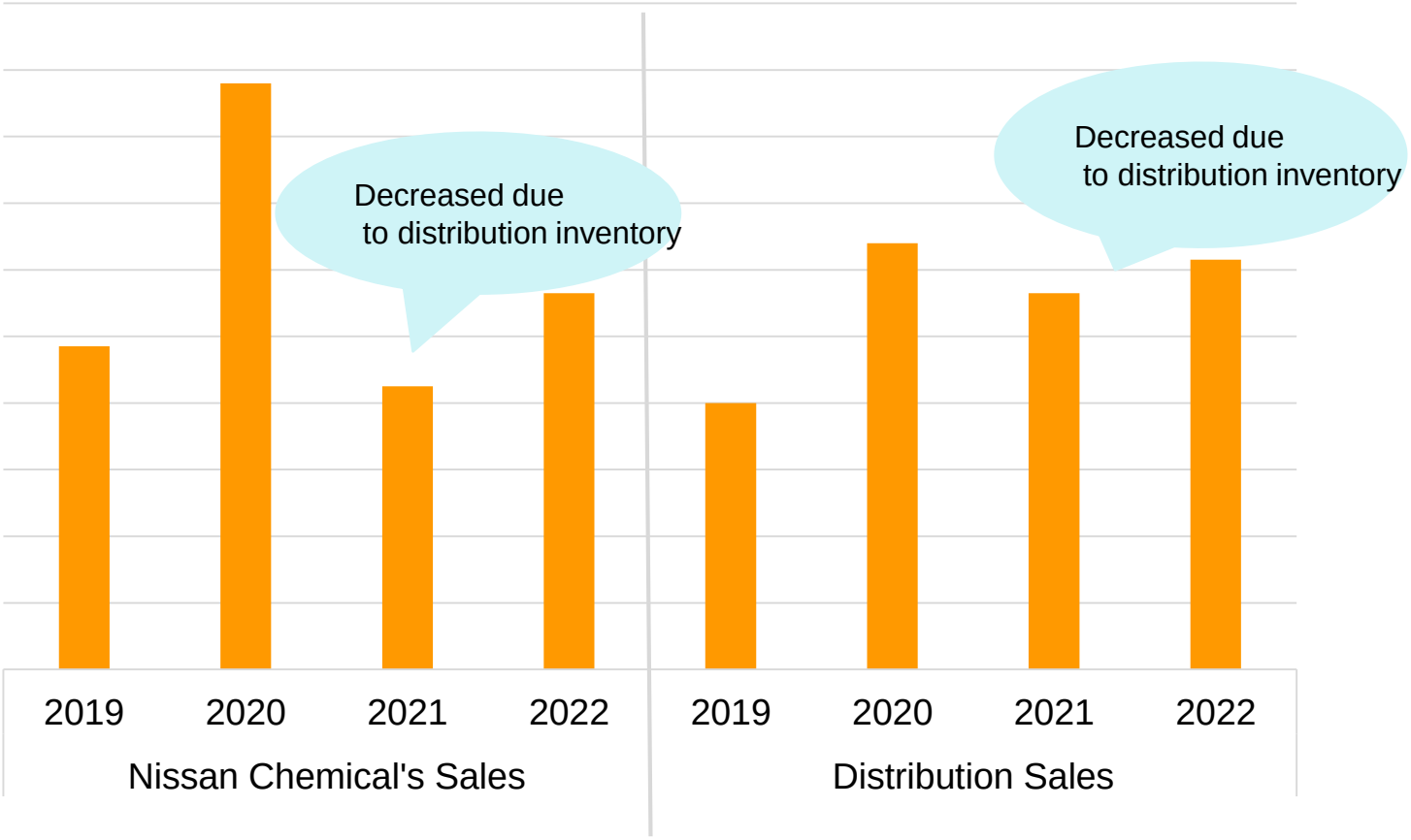
Weeding benefits of products containing ALTAIR

Test site: Paddy field in Hokkaido
Date of paddy rice transplantation : May 23, 2016
Date of chemical treatment : June 15, 2016
Date of photo taken : July 6, 2016
Major weeds: Barnyard millet, bulrush, etc.

GRACIA Sales

*Agrochemical Year : October to September

GRACIA Sales Volume



- Price of a competing product launched in 2021 are 17% lower than GRACIA's conventional standard (500ml). The impact is partly seen in 2022.
- Start to sell GRACIA‘s large-scale standard (5L) , which price is 20% lower than conventional standard, in 2023. Plan to strengthen sales after 2023.

GRACIA Promotion Images

Business Risks Managements

■**Strategy for Sustainable Food System MeaDRI (May 2021) Formulated by the Ministry of Agriculture, Forestry and Fisheries**

KPI of risk-weighted use of chemical pesticides*

- 10% reduction by 2030
- 50% reduction by 2050

*Risk-weighted use of chemical pesticides = API shipment volume multiplied by risk coefficient
Risk-weighted use of chemical pesticides is based on 23,300 in 2019 Agrochemical Year

Ratio of Nissan Chemical's risk-weighted use of chemical pesticides

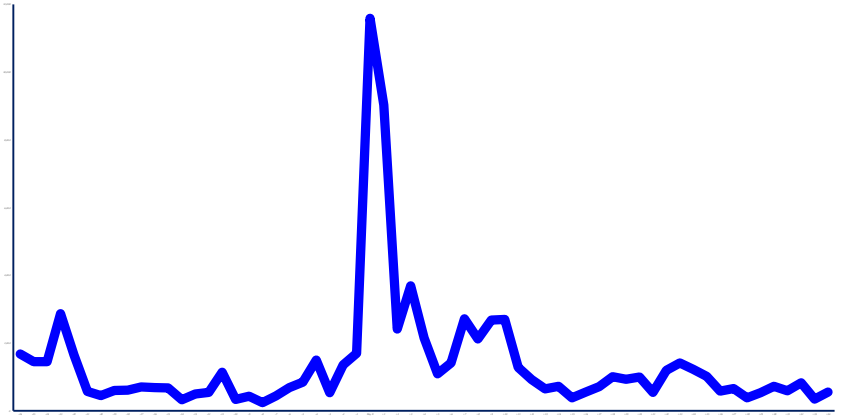
6.19%*

*Only for API contained in our major products, our own survey

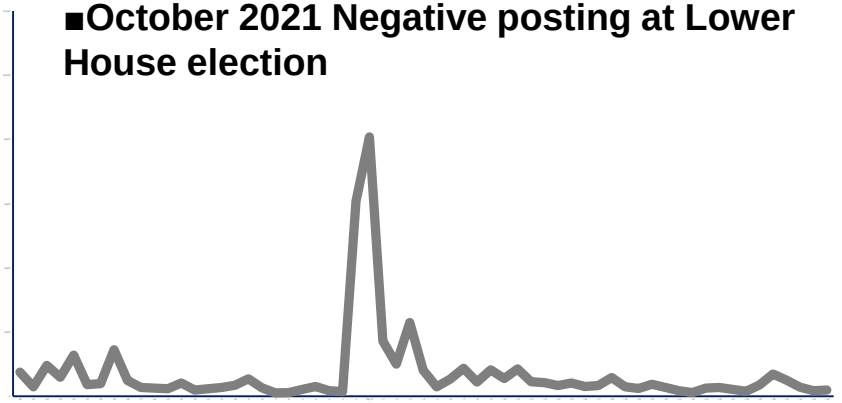
The impact of Strategy for Sustainable Food System MeaDRI is expected to be immaterial for the time being.

■**A slander post on social media to ROUNDUP**

■**July 2022 Negative posting at Upper House election**

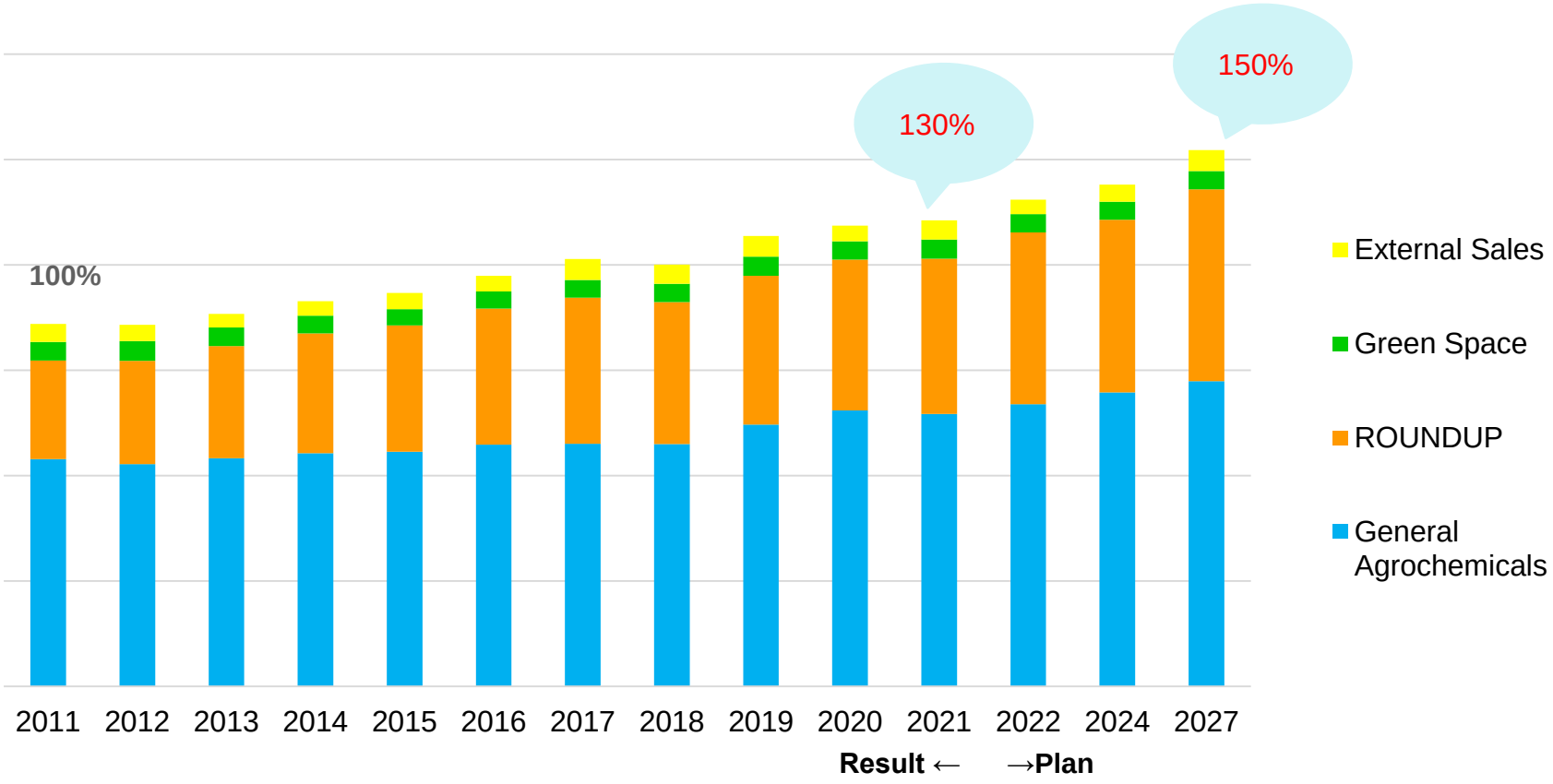


■**October 2021 Negative posting at Lower House election**



Domestic Sales (Medium-Term Business Plan)

※Fiscal Year: April to March



Domestic Sales Strategy

1. Strengthen sales of existing products
   - ROUNDUP, ALTAIR, GRACIA, etc

2. Enhance product portfolio
   - Expand sales of in-house paddy rice herbicide and active ingredients through NC-653
   - Acquire shares in the paddy rice box treatment agent market through NC-520
   - Increase share in paddy rice herbicide market through NC-656
   - Expand others and unannounced products

3. Maximize use of data marketing
   - Utilize selling place analysis data
   - Utilize ROUNDUP‘s home improvement store POS data

4. Prepare for the enlargement and consolidation of agricultural producers
   - Construct large-scale producer database
   - Implementate and utilize market surveys by our sales representative

5. Utilize digital communication tools
   - Shift from TV commercial to digital advertising
   - Start two-way communications with producers through Twitter
   - Strengthen information transmission abilities through YouTube

3. Oversea Sales Strategy

Contents

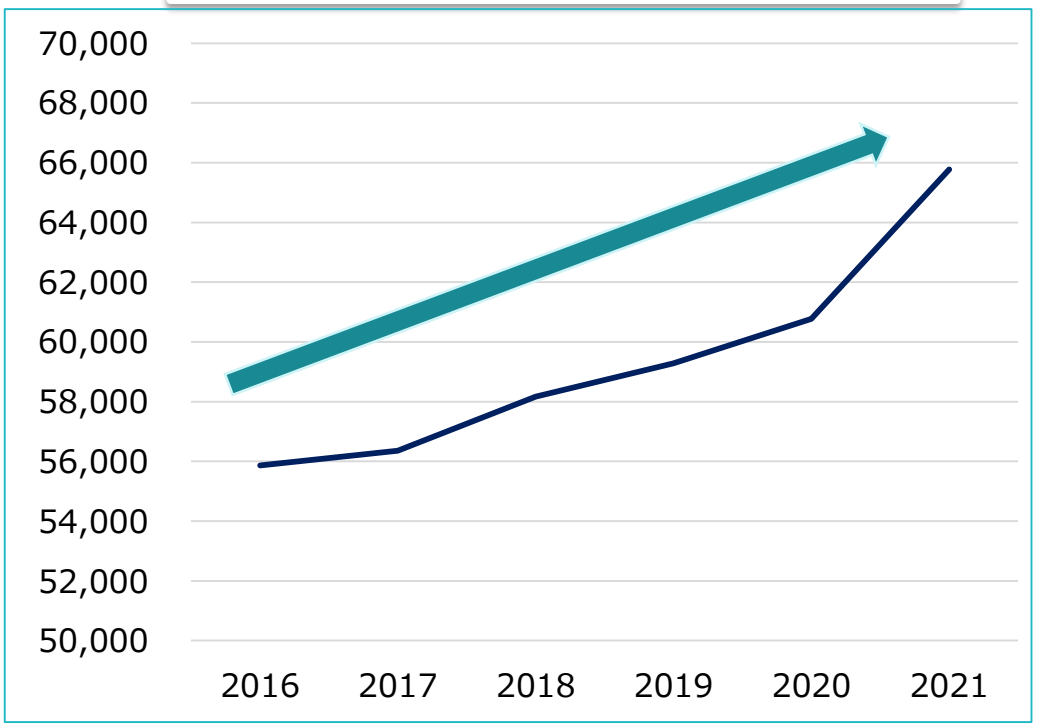
Global Agrochemicals Market

Global Agrochemicals Market Result in 2021 ($M)

Region	2021	2020	Growth Rate 21/20(%)
North America	10,333	9,837	5.0
Middle and South America	18,735	17,950	4.4
Asia	20,330	17,822	14.1
Europe	13,736	12,634	8.7
Middle East/Africa	2,641	2,526	4.6
Total	**65,775**	**60,769**	**8.2%**

Source;Agbioinvestor

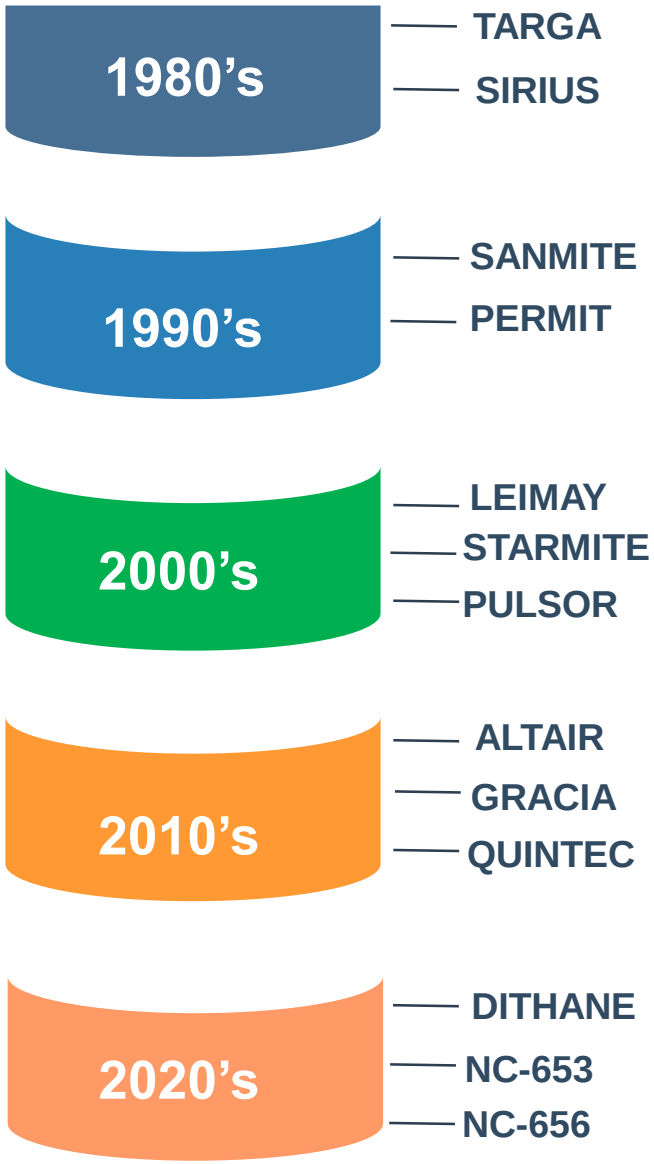
Global Agrochemicals Market Recent Records ($M)



Source;Agbioinvestor

16 to 21
+18% growth
CAGR : 3.3%

Product Portfolio

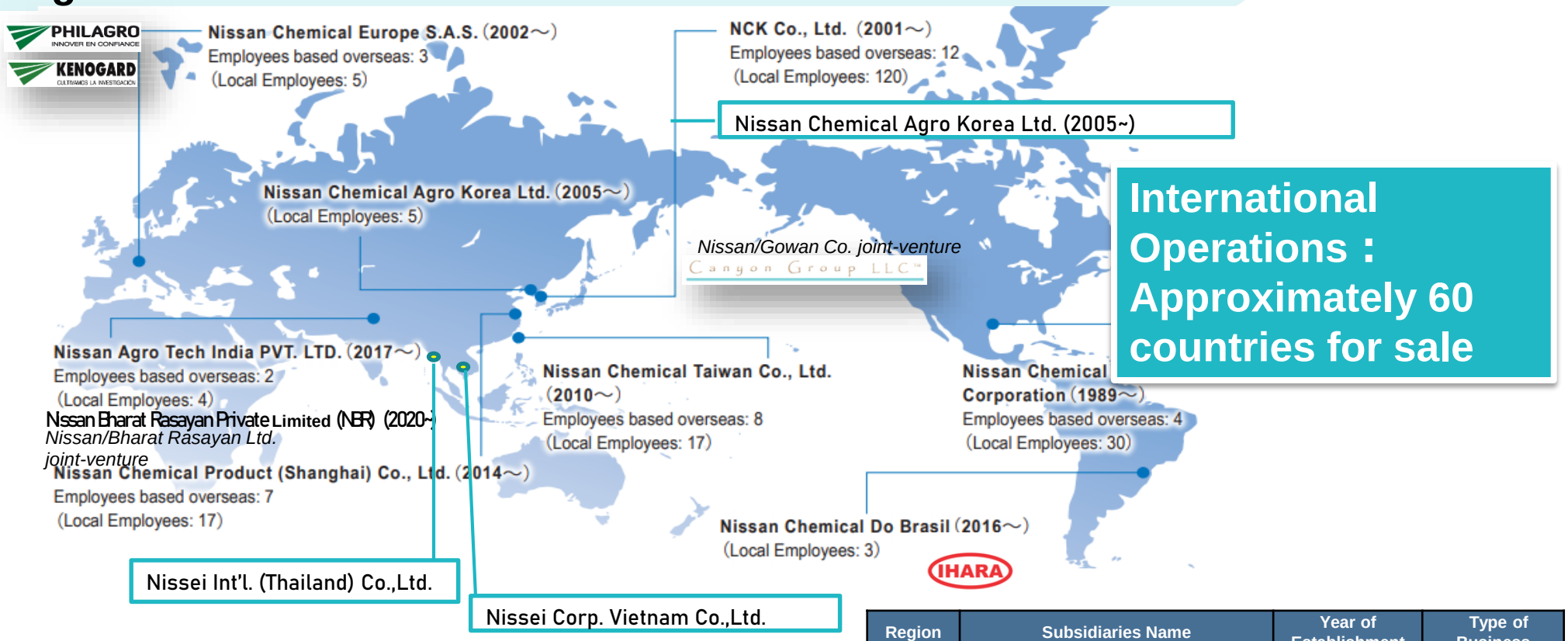


∗Except Japan

	Product	Active Ingredient	Registration	Countries
Herbicide	TARGA	Quizalofop	1987	49
	SIRIUS	Pyrazosulfuron	1989	25
	PERMIT	Halosulfuron	1994	36
	ALTAIR	Metazosulfuron	2011	7
	NC-653	Dimesulfazet		Developing
	NC-656	(Undisclosed)		Developing
Fungicide	LEIMAY	Amisulbrom	2007	47
	PULSOR	Thifluzamide	2010	12
	QUINTEC	Quinoxyfen	2019	17
	DITHANE	Mancozeb	2020	1(for Sales)
Insecticide	SANMITE	Pyridaben	1990	29
	STARMITE	Cyenopyrafen	2008	8
	GRACIA	Fluxametamide	2018	4

sold to over 60 countries

Overseas Subsidiaries and Agrochemical Business Model



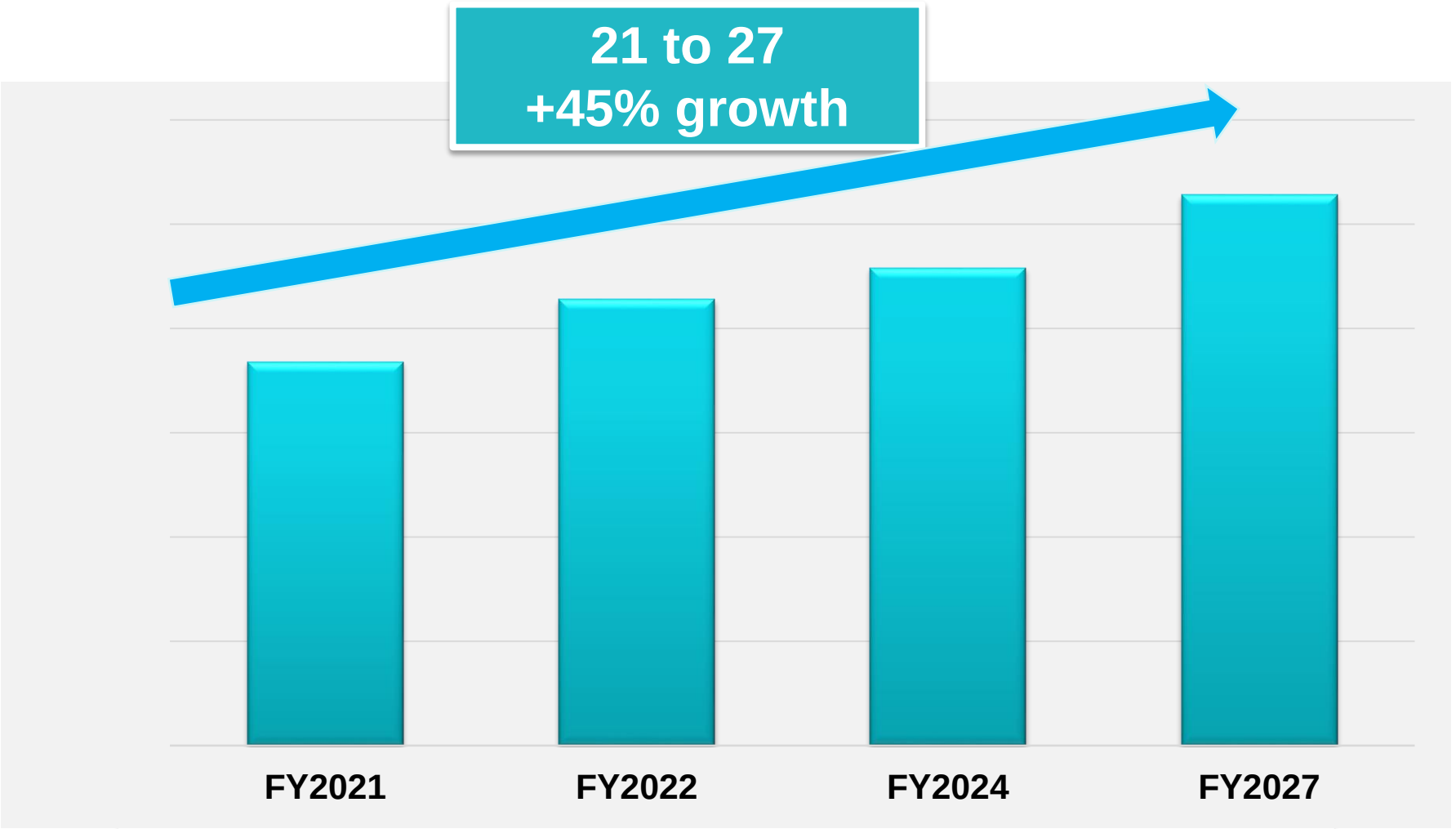
International Operations : Approximately 60 countries for sale

Nissan Chemical/Oversea Agrochemicals/ Basic Business Model : B to B

Nissan Chemical → Distributors each country → Sales channel each country → Farmers in each country

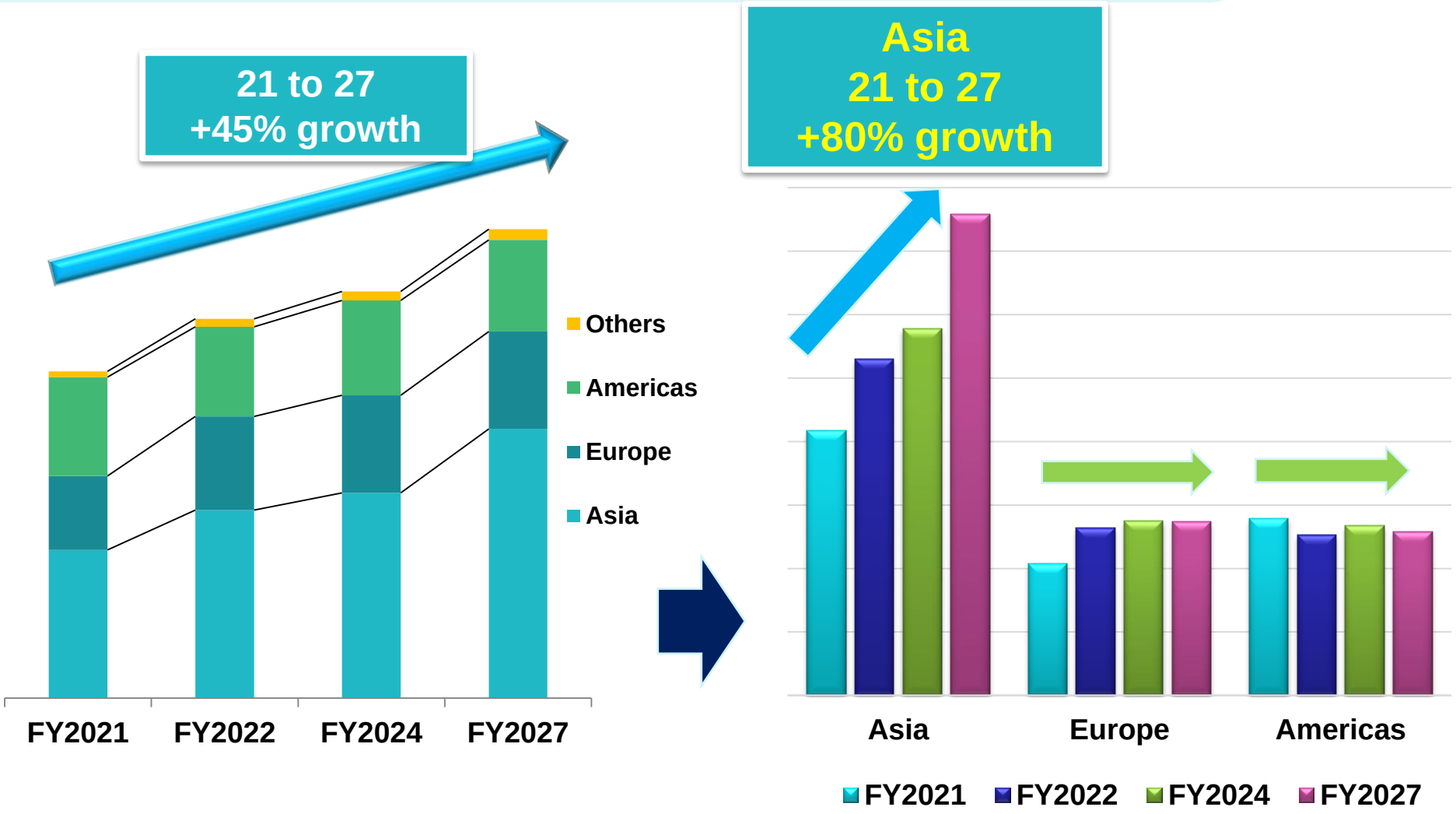
Region	Subsidiaries Name	Year of Establishment	Type of Business
Asia	Nissan Chemical Agro Korea Ltd.	2005	Service, Dist.
	Nissan Chemical Product(Shanghai) Co., Ltd.	2014	Service, Dist.
	Nissan Agro Tech India PVT.LTD.	2017	Service
	Nissan Bharat Rasayan PVT.LTD.	2021	Manufacturing
Europe	Nissan Chemical Europe S.A.S.(France)	2002	Service, Dist.
	Philagro (France)	1993	JV
	Kenogard (Spain)	1992	JV
Americas	Nissan Chemical Do Brasil	2016	Service
	Canyon(Gowan) USA	2004	JV
	Iharabras(Brazil)	2013	JV

Mid-term Plan Oversea Agrochemicals



Plan in 2027:+45% growth compared to 2021 result

Mid-term Plan Oversea Agrochemicals for each region



- Grow in Asia
- Maintain Americas and Europe

Key Strategy for each region

Asia

- Expand GRACIA sales in India, South Korea and South East Asia
- Differentiate TARGA from generics by launching mixtures in India
- Launching NC-653 and NC-656 in Asia during Stage-2

Europe

- Increase LEIMAY sales for multiple mixtures of multi-national companies
- Take care of Farm to Fork Strategy with new bio-products introduction

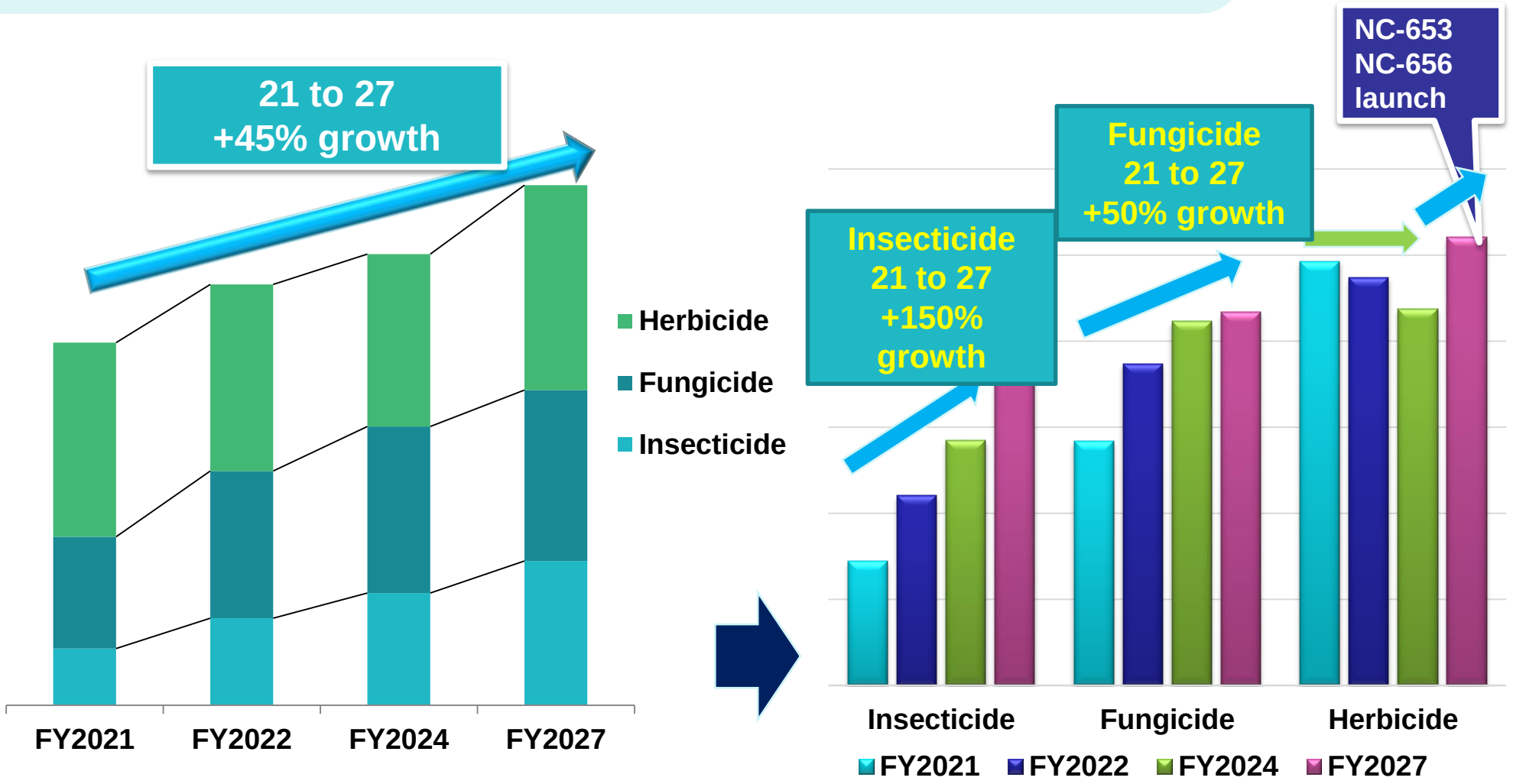
Americas

- Expand sales of post marketed products by strengthening current partnerships and the label expansions

Other Area

- Launching GRACIA and LEIMAY in the Middle East

Mid-term Plan Oversea Agrochemical for each product



- Extension of Insecticide and Fungicide
- Maintenance of Herbicide
- Achievement of NC-653 and NC-656 launching

Key Strategy for each products

Insecticide

- Expand GRACIA sales in Asia
- Maintain market share of SANMITE in Americas

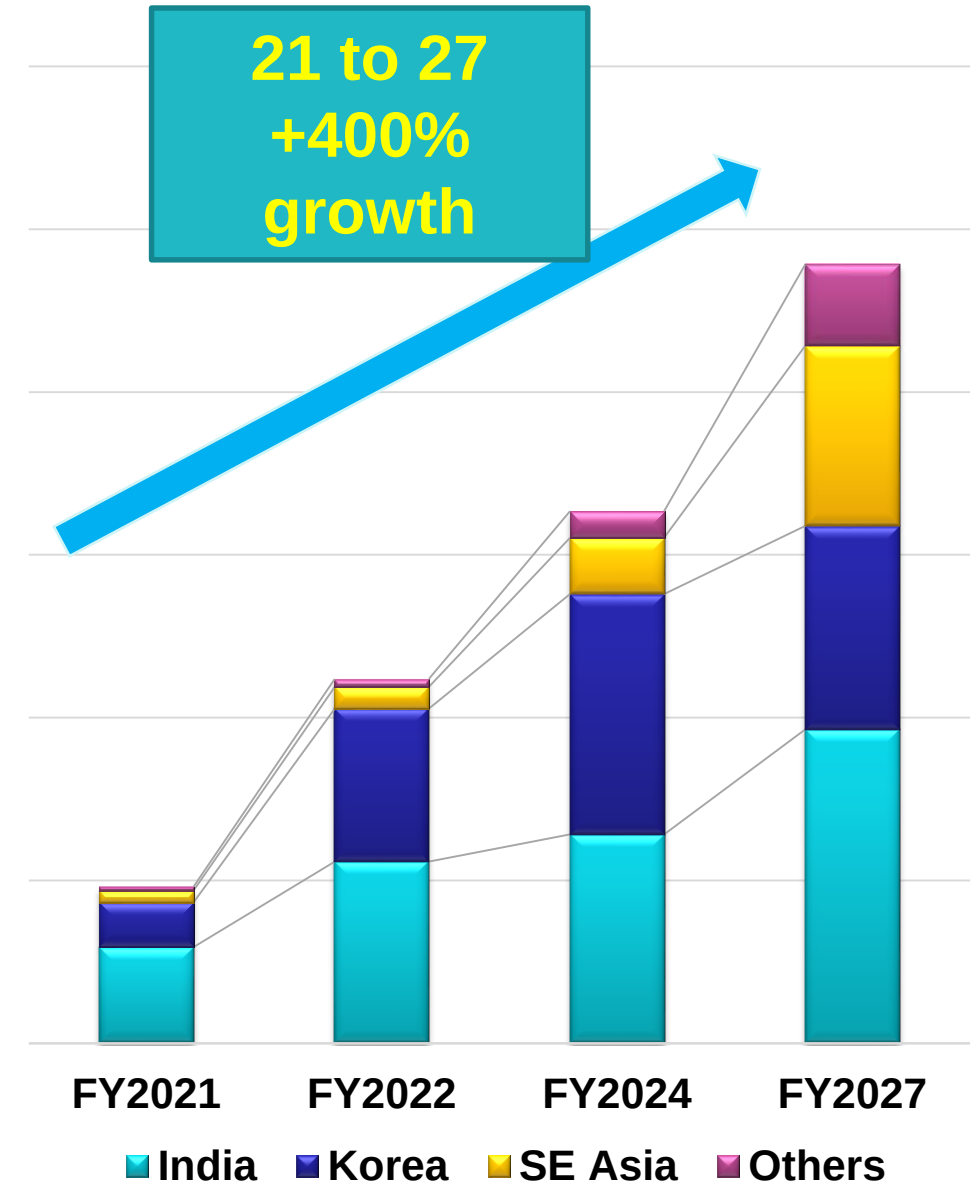
Fungicide

- Increase LEIMAY sales in EU for multiple mixtures of multi-national companies
- QUINTEC label expansion in North America

Herbicide

- Differentiate TARGA from generics by launching mixtures in India
- Maintain PERMIT sales by strengthening current partnership
- Launching ALTAIR in Bangladesh
- Launching NC-653 and NC-656 in Asia during Stage-2

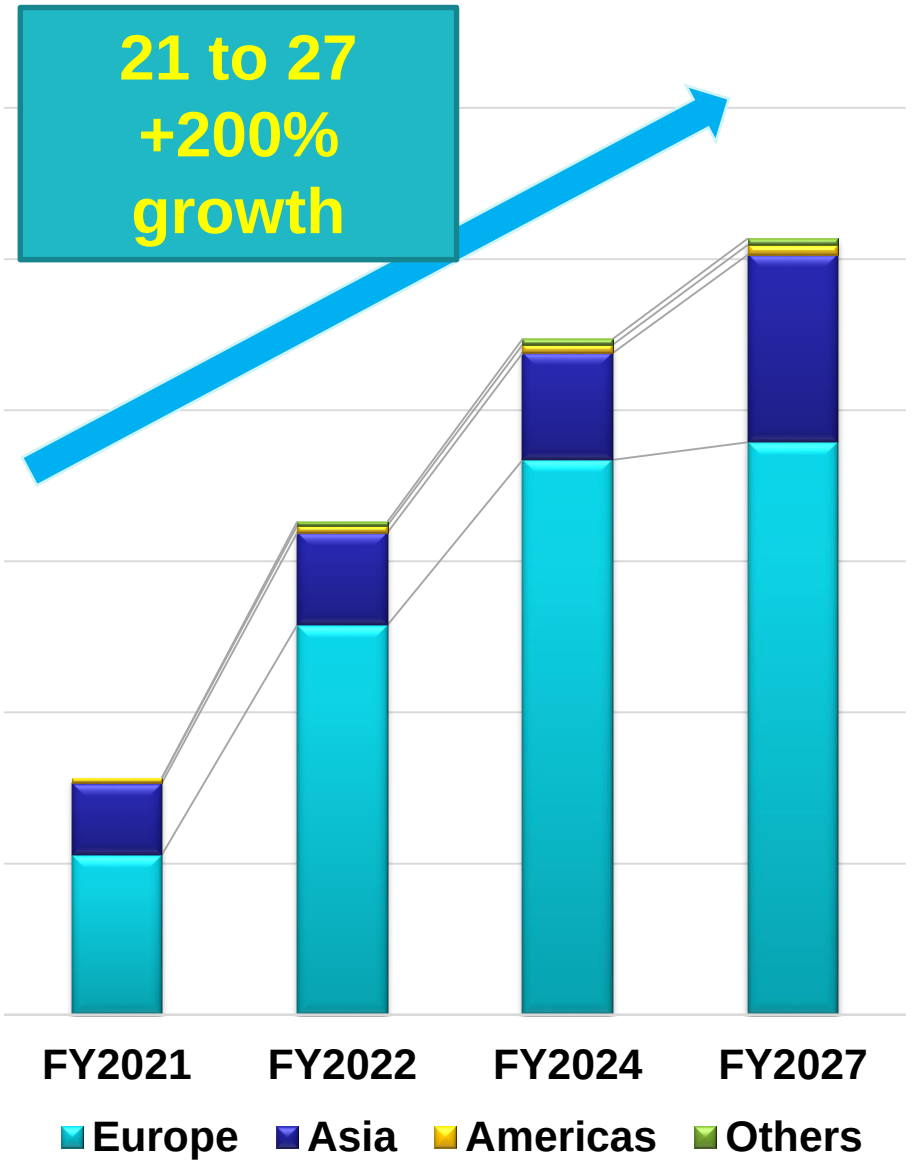
GRACIA Mid-Term Business Plan for each country and region



Key Strategies

- India (21 to 27:+200% growth)
  - Expand sales with multiple distributors and launching mixtures
- Korea
  - Recover by aggressive sales promotion
- SE Asia (21 to 27:+1,400% growth)
  - Expand sales in Indonesia and launching in multiple new countries
- Other regions (21 to 27:+800% growth)
  - Launching in multiple new countries

LEIMAY Mid-Term Business Plan for each region

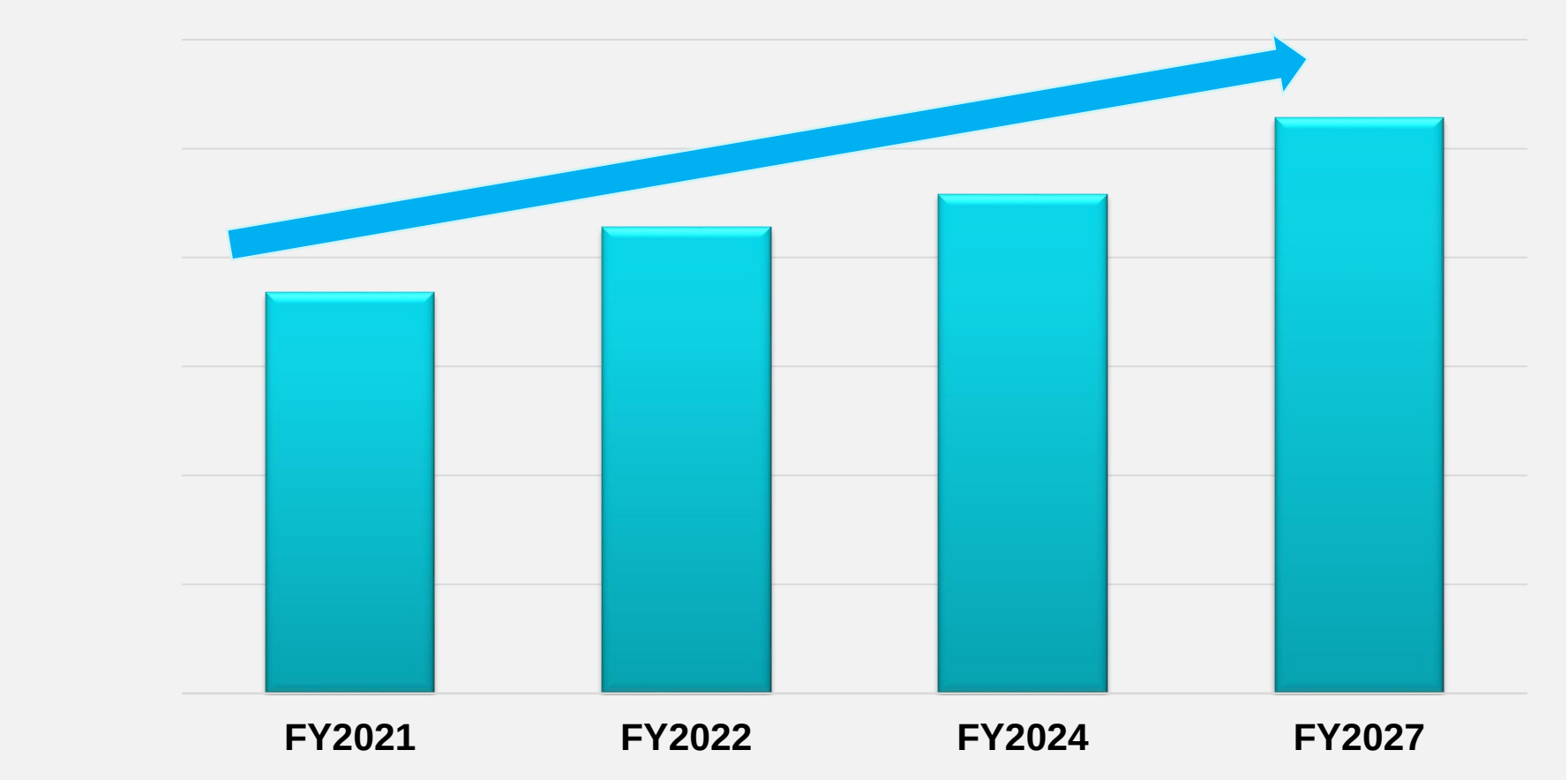


Key Strategies

- **Europe** (21 to 27:+250% growth)
  - Expanding mixtures to multinational companies
- **Asia** (21 to 27:+150% growth)
  - Launching mixtures in India

leimay®

Mid-Term Business Plan
Oversea Agrochemicals



21 to 27
To achieve +45% growth by steady implementation of the key strategies!

API of Animal Health Product Fluralaner

BRAVECTO series and EXZOLT, which contains the active pharmaceutical ingredient of Fluralaner invented by Nissan Chemical, are currently available in more than 100 countries.

I. Fluralaner

- **II. BRAVECTO**
- **III. BRAVECTO Plus**
- **IV. EXZOLT**

I. Fluralaner

- Invented by Nissan Chemical and supplied to MSD[1] as the active pharmaceutical ingredient of BRAVECTO and EXZOLT
- Currently, BRAVECTO series and EXZOLT are available in more than 100 countries
- Compound patent
  - Fluralaner's compound patent expires in March 2025, but many countries have a patent term extension system
    - Some EU countries including UK, France, Germany – already extended to February 2029
    - USA, etc. – applications under examination

II. BRAVECTO

- Developed and launched by MSD
- Veterinary medical products providing **12 weeks**[2] of continuous protection for dogs and cats against fleas and ticks with immediate effect, nearly **3 times longer** than any monthly products in the market.
- Chewable tablet for dogs
  - April 2014 EU, June 2014 USA, July 2015 Japan, July 2019 China
  - July 2020 monthly chews for puppies in USA
- Spot-on solution for dogs and cats
  - for cats: July 2016 EU, December 2016 USA, June 2018 Japan
  - for dogs: January 2017 USA and EU, January 2021 Japan

III. BRAVECTO Plus

- A broad-spectrum combination spot-on solution for cats to treat internal and external parasite infestations
  - July 2018 EU, December 2019 USA, January 2021 Japan

IV. EXZOLT

- A poultry medicine against red mite launched by MSD (administered via drinking water)
  - September 2017 EU, June 2018 Korea and Middle East etc., July 2021 Japan
- A cattle medicine
  - March 2022 approved in Brazil, May 2022 approved in Mexico

1. MSD: MSD Animal Health, the global animal health business unit of Merck
2. 8 weeks for *Rhipicephalus sanguineus* ticks

Sales Trend of Fluralaner

Nissan Chemical's Revenues are Consisted from Following Two Factors

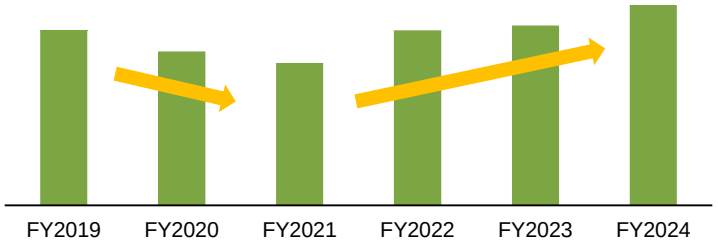
・Sales of Fluralaner to MSD as API[1] of BRAVECTO and EXZOLT products

・Running royalties received from MSD

1. API: Active Pharmaceutical Ingredient

FY2019-FY2024 Fluralaner Pro-forma Sales Image (including royalties)

(No change from FY2021 Presentation Materials announced in May 2022)



FY2019-FY2021: Actual, FY2022-: Outlook as of May 2022

- Inventory adjustments for Fluralaner were completed in FY2021.
- Plan a large sales increase in FY2022, due to the shipments shifted from FY2021 to FY2022. Assumed exchange rate is ¥115/$.
- Assumed exchange rate for FY2023 and beyond: ¥110/$.
- The mid-term plan for FY2027 includes the forecast of patent extensions and expirations by country and does not include the sales increase associated with the launch of newly developed BRAVECTO series and EXZOLT.

BRAVECTO series and EXZOLT R&D

MSD is developing several pipeline products which contain the API of Fluralaner (including new type of BRAVECTO for pets and spot-on solution for livestock)

4. Biological Pesticides

Contents

Food: Governmental Policies

Governmental policies on agriculture (extract)

Country	Strategy	Pesticide・Risk	Fertilizer・Nutrition	Others
EU	Farm to Fork European Green deal	50% reduction by 2030	20% reduction by 2030	・50% reduction in food waste ・Achieved 25% organic agriculture
JPN	Strategy for Sustainable Food System MeaDRI	50% reduction by 2050	30% reduction by 2050	・Achieved 25% organic agriculture ・Net Zero CO_2 emissions
America	Agricultural Innovation	50% reduction by 2050	30% reduction by 2050	・Net Zero emission ・50% reduction in food loss

→ Environmental burdens reduction

Environmentally friendly agriculture

Nissan Chemical estimation on the regulations and industry's countermeasures

2027

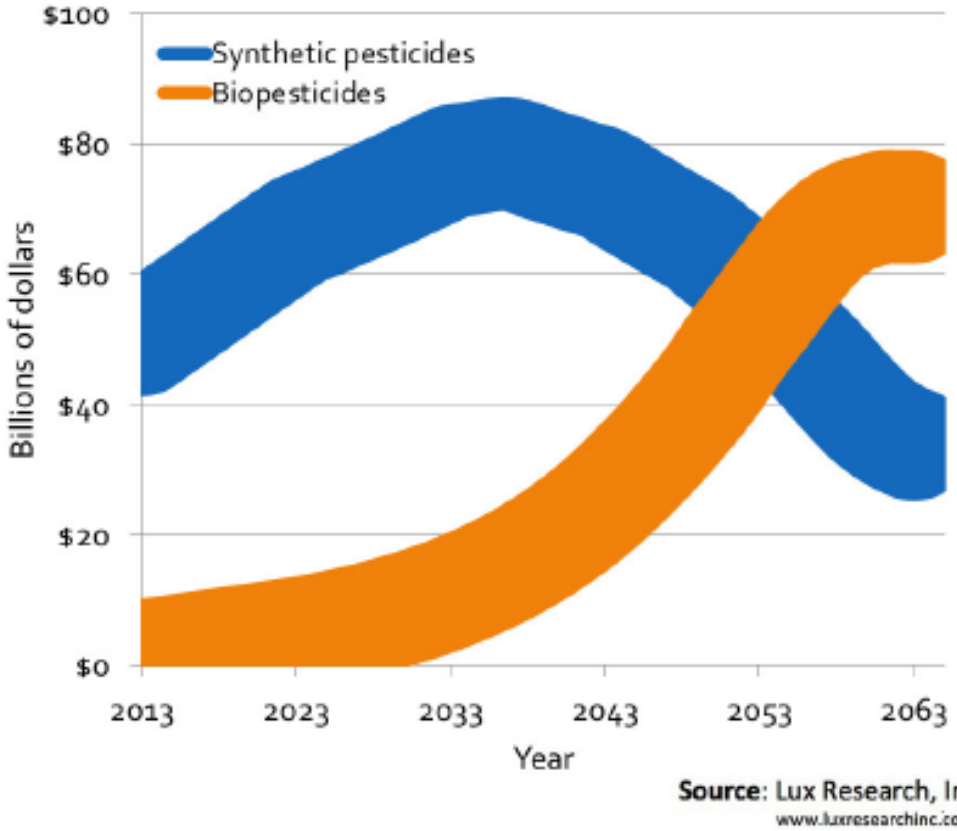
・The proceeding of re-evaluation/re-registration system and the tightening of regulations
・Development of chemical pesticides in compliant with such regulations
・Acceleration of development of agricultural materials other than chemical pesticides

→

2030

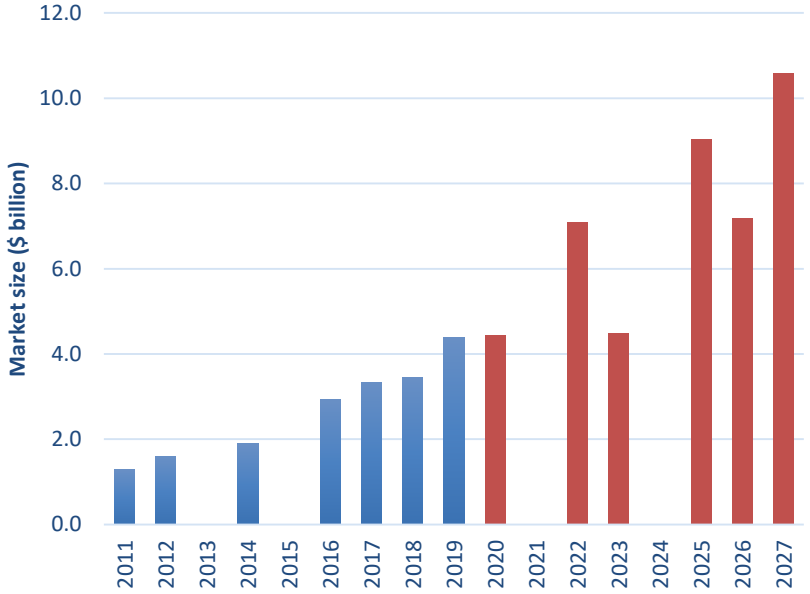
・Establishment of stricter registration system in each country (e.g. new system)
・Dissemination of eco-friendly agricultural materials
・Diffusion of biological materials

Biological Pesticides Market Forecast



(2015)

Actual and forecast estimates of the global biological pesticides market



Figures from
Biopesticides 2021
IHS Markit

Reversal of chemical and biological pesticides will occur around 2050

Other companies forecast show the same growth as Lux Research until 2027

Council for Science, Technology and Innovation in Cabinet Office, Japan (A)

Nissan Chemical CORPORATION

Bioeconomy Strategy Follow-up
～Implementation of a Bioeconomy Society ～
Expansion of bio-related market

Aiming for a total market size of 92 trillion by 2030, promoting market domain measures

Bioproduction
High-functional biomaterials,
Bioplastics, Bio production system, etc
【53.3 trillion yen】

Primary production
Sustainable primary production
System【1.7 trillion yen】
Large scale wooden architecture,
Smart forestry【1.0 trillion yen】

Health・Medical
Lifestyle improvement healthcare,
Functional foods, etc【33.0 trillion yen】
Biopharmaceuticals, Regenerative medicine
【3.3 trillion yen】

Initiative at each stage form production to consumption based on
‘’the Strategy ‘MeaDRI’’ and promotion of innovation such as carbon neutrality

Nissan Chemical modified and translated publicity of Council for Science, Technology and Innovation, June, 2021, Cabinet Office, Government of Japan

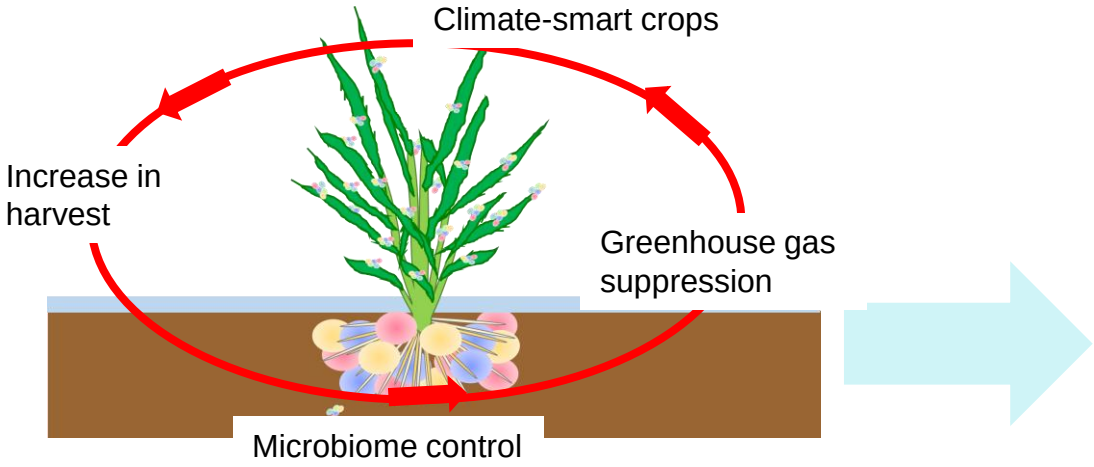
Council for Science, Technology and Innovation in Cabinet Office, Japan (B)

Sustainable Primary Production System
～Direction of Engagement～

1. Implementation of smart agriculture
2. Management to global environment (sustainable production)
3. Utilization of biotechnology

<Measures for global environment>

Expanding the reduced pesticide and fertilizer farming by full utilization of soil microbial functions with their complete elucidation

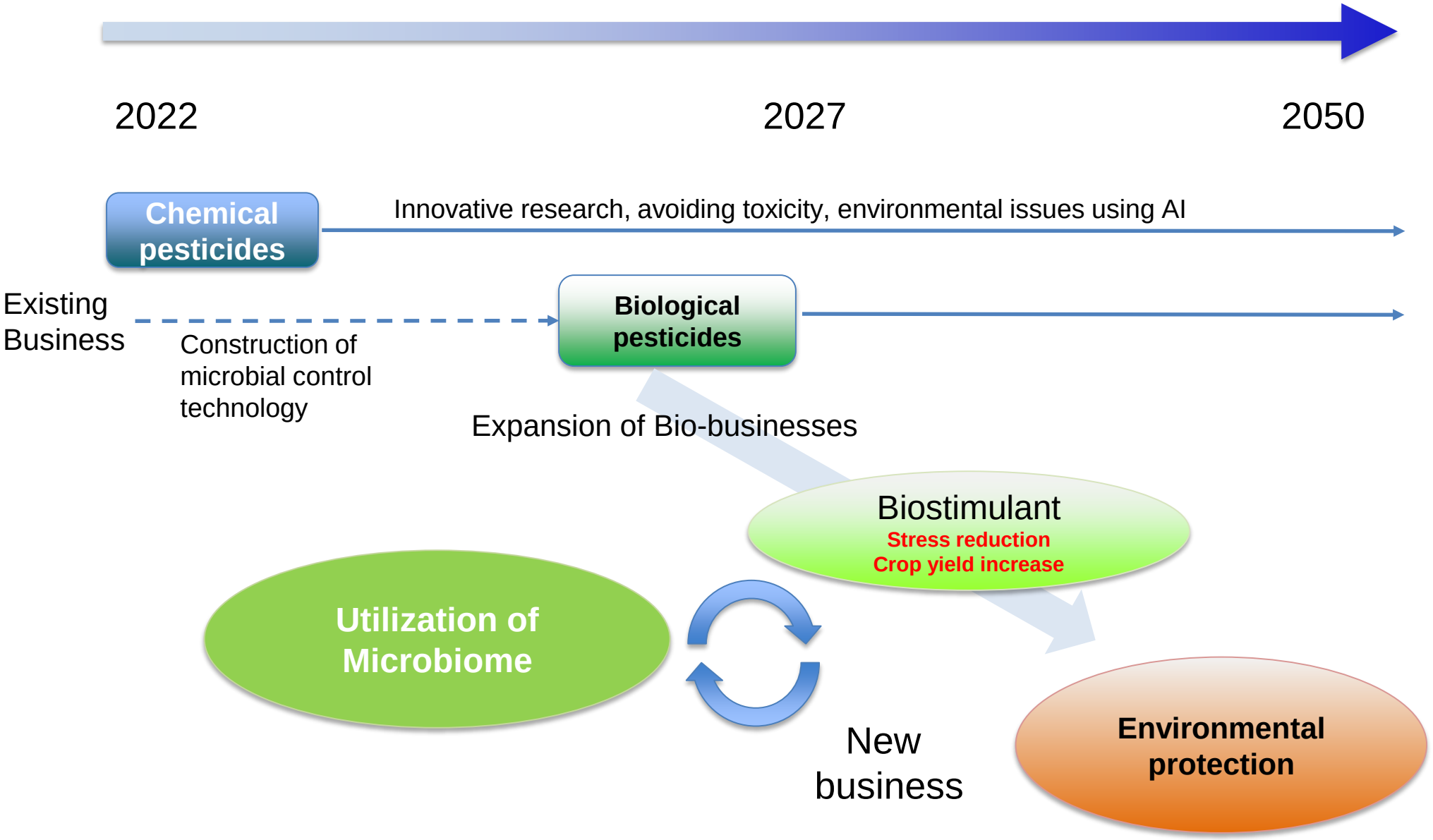


Sustainable production system

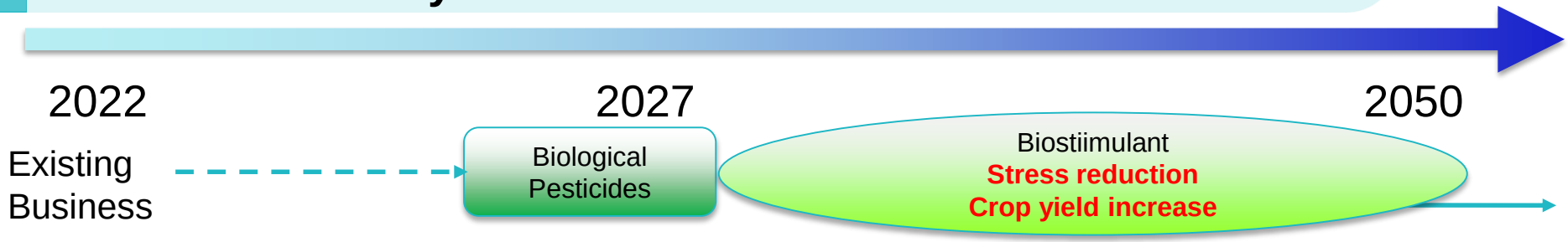
Integrated analysis soil microbiome and environment

Nissan Chemical modified and translated publicity of Council for Science, Technology and Innovation, June, 2021, Cabinet Office, Government of Japan

Nissan Chemical Research Plan



Biological Pesticides Development Strategy
- Current Activity -

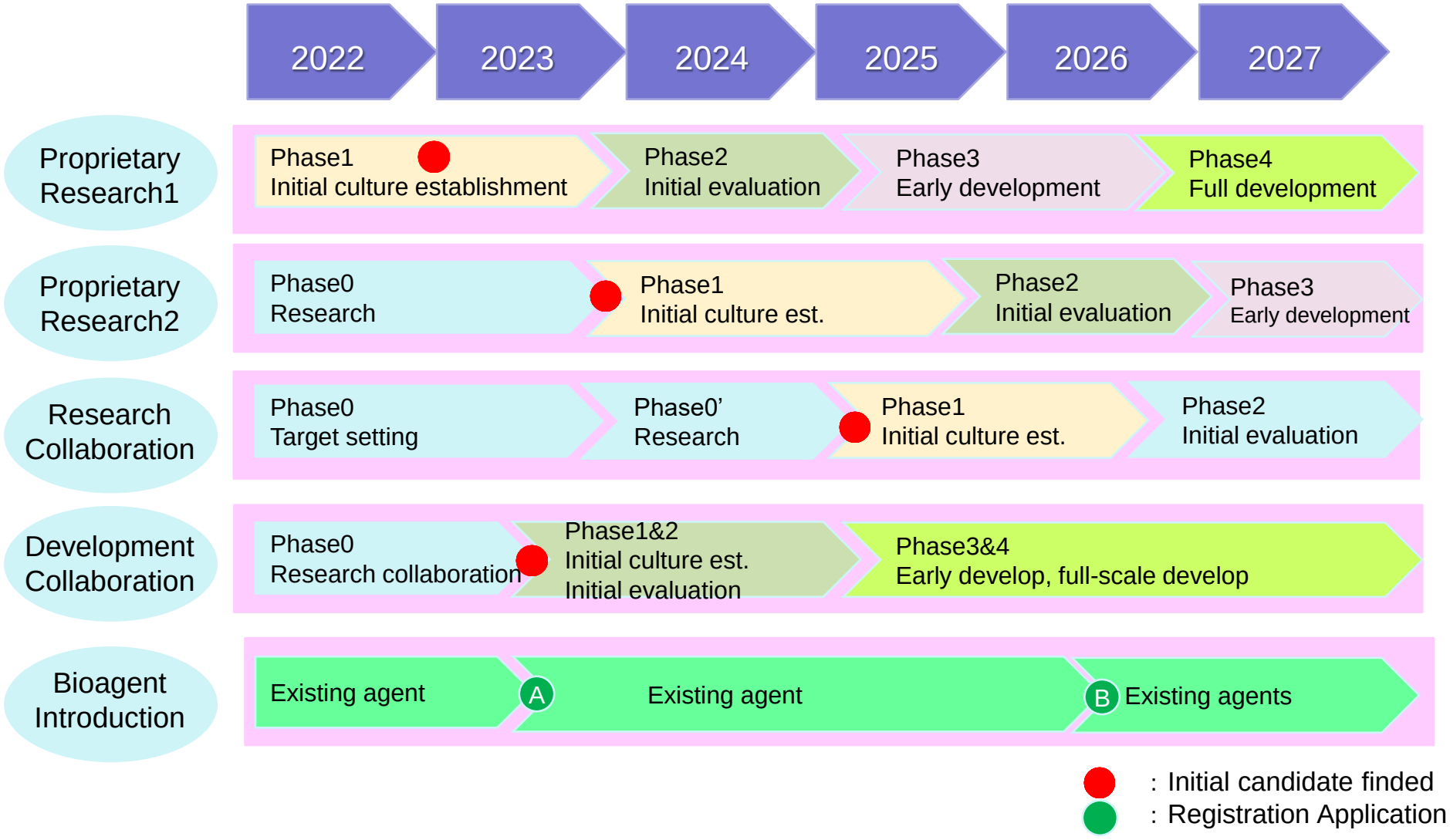


Actions on; Basic research, organization, registration, sales routes, etc

Organization	**Establishment of bio-research team in Biological Research Laboratories**
Research Collaboration	**Biological pesticides innovation, microbiome analysis technology**
Development Collaboration	**Optimization of collaborator's libraries**
3rd Party Product Introduction	**Introduction of existing products** **⇒⇒⇒ Expansion of sales, sales route, knowledge on registration system**

M&A

Subjects and Schedule in Mid-Term Business Plan (Vista 2027)



Microbial Technology Development by 2030

◆Microbial Screening meets Laboratory Automation
→Installing Microdroplet Screening Technology

◆Biomanufacturing meets Bioinformatics
→Analyzing and improving industrial strains

◆Microbiome meets Complicated Controls
→Understanding complicated microbial interactions and developing new products

◆Functional Material meets Synthetic Biology
→Designing Artificial biosynthetic pathway and microbial production

5. Pipelines

Contents

NC-653 (Dimesulfazet)

- ✓ Nissan Chemical in-house development API
- ✓ New herbicide for rice
  - → High crop safety
  - → Excellent control against herbicide-resistant biotype of *Schoenoplectiella juncoides* and hard-to-kill *Eleocharis kuroguwai*
- ✓ Will be launched in 2024
- ✓ Estimated peak sales will be 3.5 billion yen

NC-653 (Dimesulfazet)

【Rice herbicides of Nissan Chemical】

- SIRIUS (pyrazosulfuron-ethyl) ⇒ Launched in 1990
- ALTAIR (metazosulfuron) ⇒ Launched in 2012

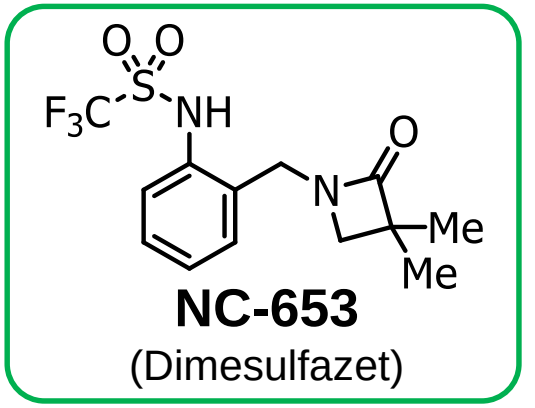
【NC-653 combinations】

- Product A contains NC-653 and others
- Product B contains NC-653, ALTAIR and another

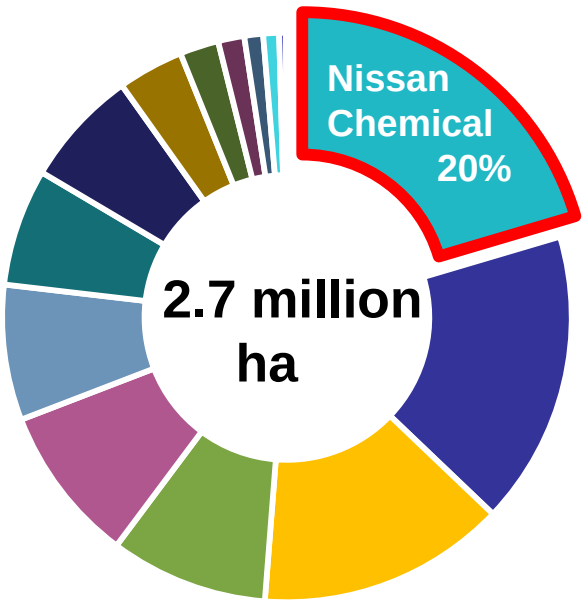
【Development of NC-653】

- Product A and B is under official trials
- Filed registration applications in 2022
- Developing next combinations

We will maintain and expand the top share in Japanese rice herbicide market with NC-653 following SIRIUS and ALTAIR



NC-653
(Dimesulfazet)



Herbicide treated area in Japanese rice (2021AY)

NC-653 (Dimesulfazet)

【Feature】

- ◆ Excellent control against R-biotype of *S. juncoides* which is becoming big problem in nationwide
- ◆ Good control against perennial sedges which were difficult to control by current herbicides

【Field Trial】

- 2019 field trial in Saitama pref.

Excellent control against all weeds including R-biotype of *S. juncoides*

NC-656

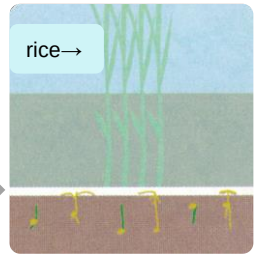
- ✓ Nissan Chemical in-house development API
- ✓ New rice herbicide
  - → Excellent efficacy against R-biotypes of grass weeds (*Echinochloa* spp., *Leptochloa* spp. and etc.)
  - → Foliar application herbicide
- ✓ Will be launched in 2027
- ✓ Estimated peak sales will be 10 billion yen

In-water application (Japan, Korea)

Global treated area : 14 million ha

ALTAIR etc.

Make a drug layer on the surface of soil and kill weeds.

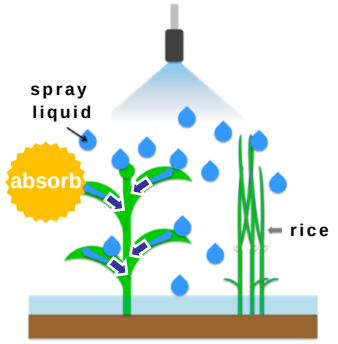


Foliar application (Other countries)

Global treated area : 28 million ha

NC-656

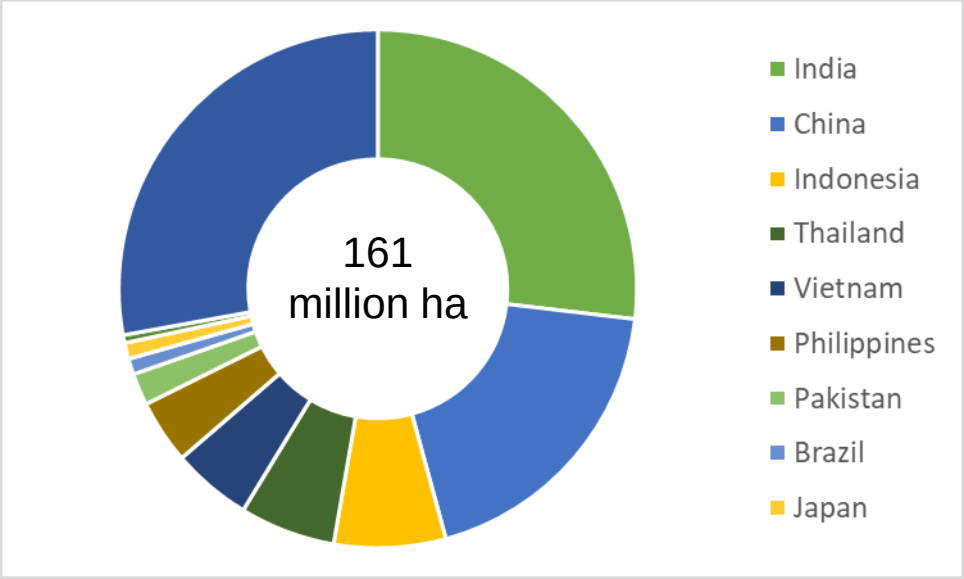
Spray to stems and leaves of weeds. Liquid absorbed from stems and leaves will kill weeds.



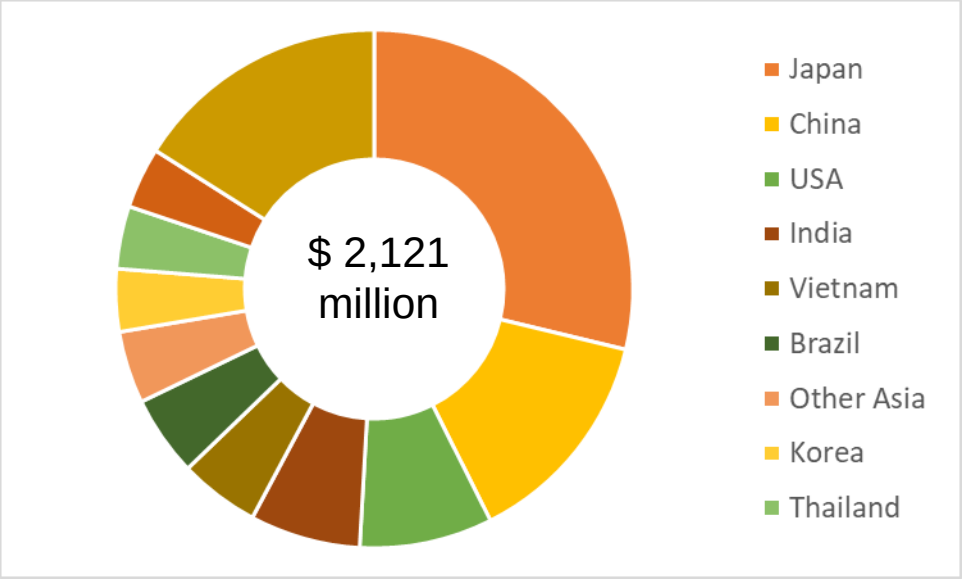
【Target market】

- NC-656 can be used in all global rice farming system including transplanting, wet-seeding and dry-seeding
- Developing in major rice herbicide market

Global rice cultivated area in 2020



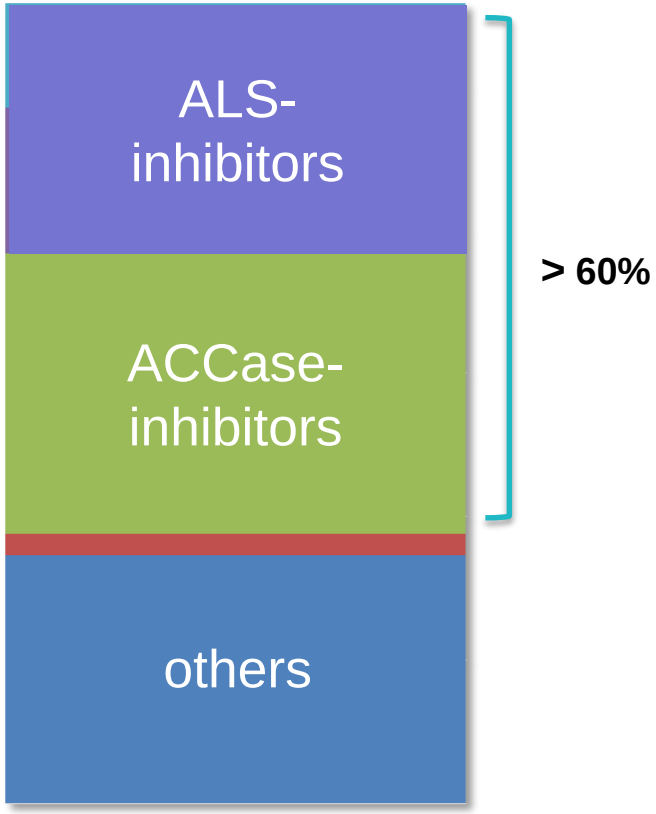
Global rice herbicide market in 2020



Source: AgbioInvestor-Crops 2020

Strength of NC-656

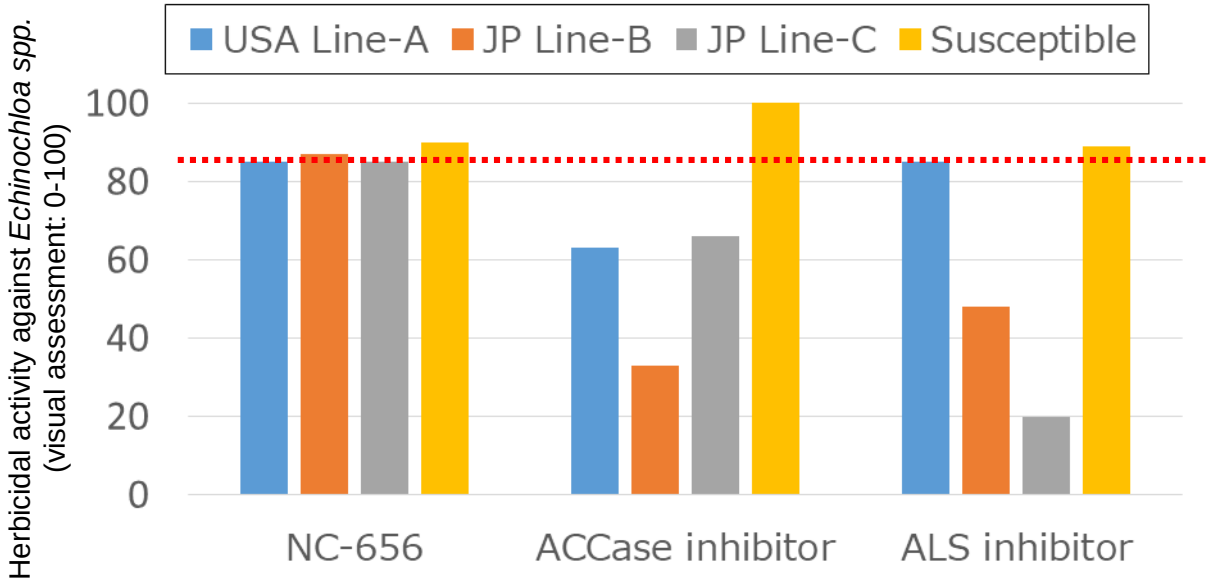
Foliar application herbicides for rice 28M ha (2018)



・ALS-inhibitors and ACCase-inhibitors occupied over 60% of rice foliar application herbicide market in 2018 (left)

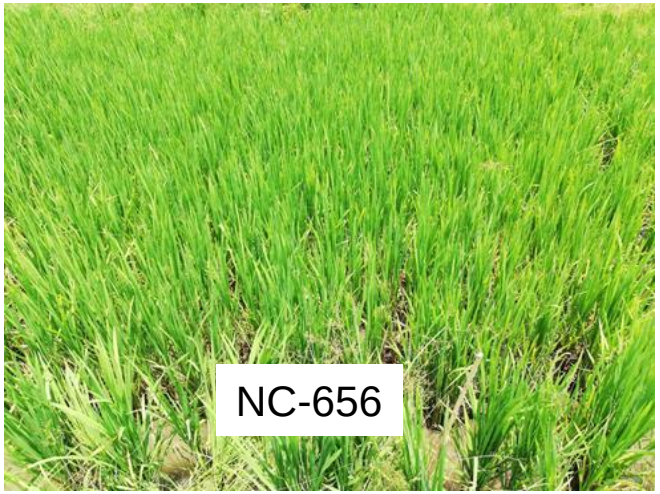
→ On the other hand resistant biotypes of grass weeds are increasing and making troubles for farmers

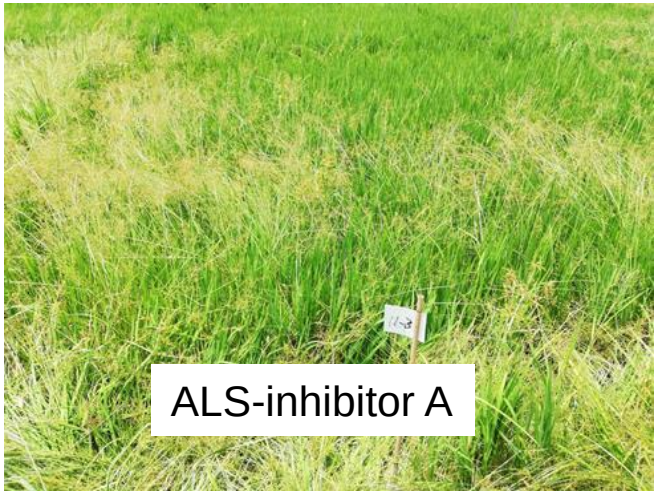
↓The MoA of NC-656 is HPPD-inhibitor which shows better control against resistant biotype to current herbicides (below)



NC-656 Field trial

2019 Field Trial in Vietnam





NC-656 controlled all weeds in the trial including R-biotypes

NC-520

- ✓ Developing with a partner
- ✓ New rice insecticide
  - → good control against planthoppers, beetles, and some lepidopteran pests
  - → several nursery-box treatment pre-mixtures
- ✓ Will be launched in 2025
- ✓ Estimated peak sales will be 2.5 billion yen

6. R&D of Chemical Pesticides

Contents

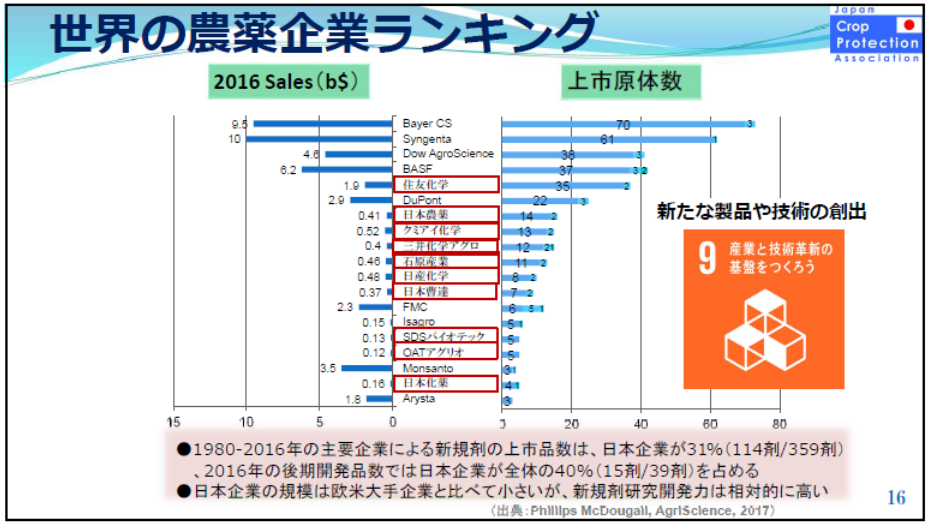
Agrochemical R&D in Japanese Companies

“Japanese companies have High R&D Capability for New Pesticides.”

Proportion of launched and developed pesticides by Japanese companies in

1980-2016	launch	: 31%	(114 / 359)
2016	late-stage development	: 40%	(15 / 39)

Despite their small size, Japanese companies have excellent R&D capabilities



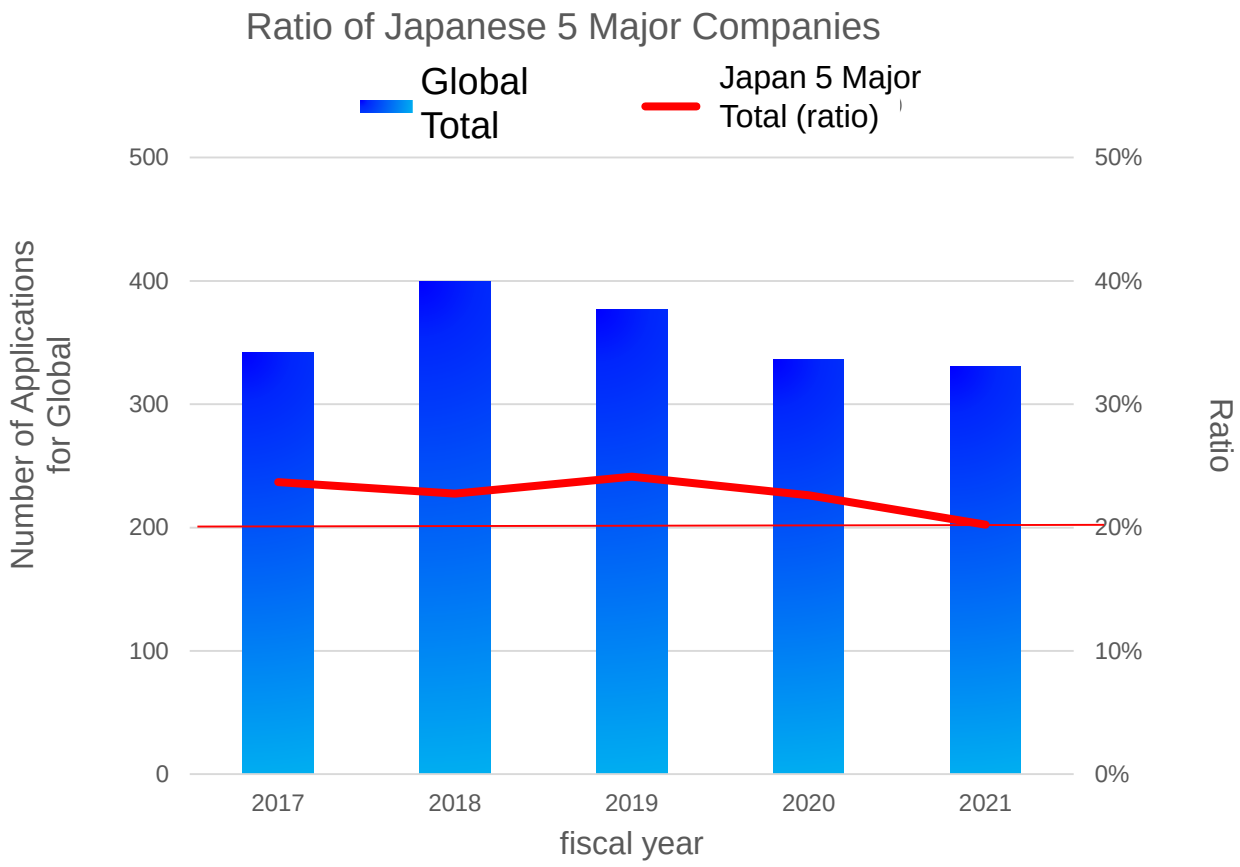
Red circled companies are Japanese

Source: JPCA, 8th Study Meeting on Crop Protection.

R&D Features in Patent Applications since 2017

Five major Japanese companies account for 20%

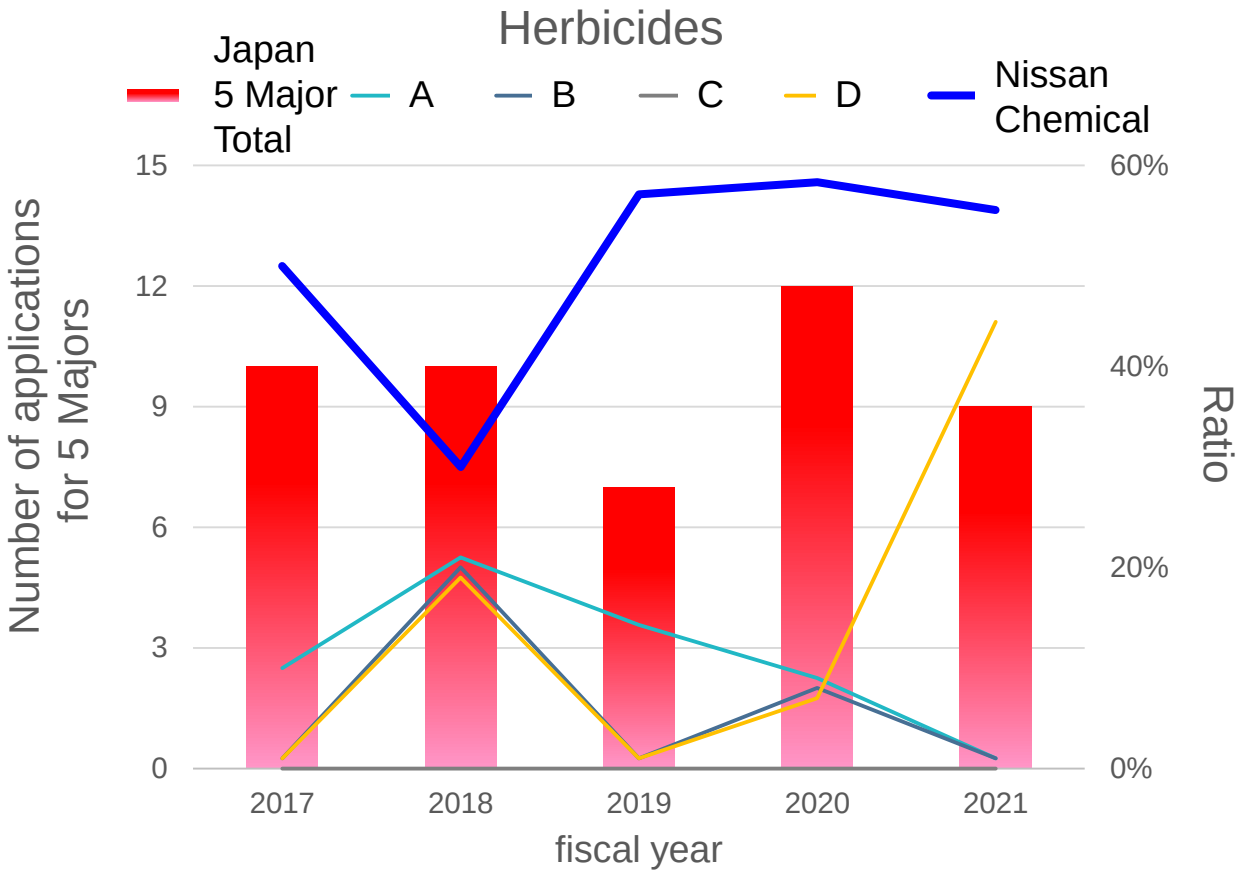
Continuous and vigorous development of New Pesticides in Japan



Our survey: Exclude duplicate substance patents in WO, EP, US, and JP

R&D Feature of Nissan Chemical

We have an advantage in the herbicide field, holding a foremost position in Japan



Our survey: Exclude duplicate substance patents in WO, EP, US, and JP

Our Strengths; Recent Products

	Launch (coming)	Concept
Animal Health products Fluralaner	2013	Novel Mode of Action Immediate effect against fleas and ticks 12 weeks effect
Insecticide Fluxametamide GRACIA	2018	Novel Mode of Action （IRAC Group30 GABA-gated chloride channel allosteric modulators）
Herbicide Dimesulfazet NC-653	(2024)	Major component of one-shot herbicides for paddy rice
Herbicide ISO application in progress NC-656	(2027)	Foliar application herbicide for global rice farming system Post-emergence grass weed control

Constant creation of “Original new products” as well as herbicides

Deepened Core Technologies

Precision + Power

Increase synthetic compounds by 30% ※1
Process Research : Cost reduction

Accurate Evaluation + Worldwide

Create original themes
Evaluate in over 10 countries※2
Test for safety evaluation in-house

Reliability + Challenge

Factory : Constructed new R&D facilities※3
Research : Biological pesticide and new formulation

※1 : 2018→2020　※2 : 2022　※3 : 2019 in Saitama Plant

Nissan Chemical CORPORATION

Our Roles

Creation of essential chemical pesticides suitable for social requirements

Farm to Fork

Contribution to food production by creating New Pesticides with people and environment friendly

Sustainable Agenda Vista2027

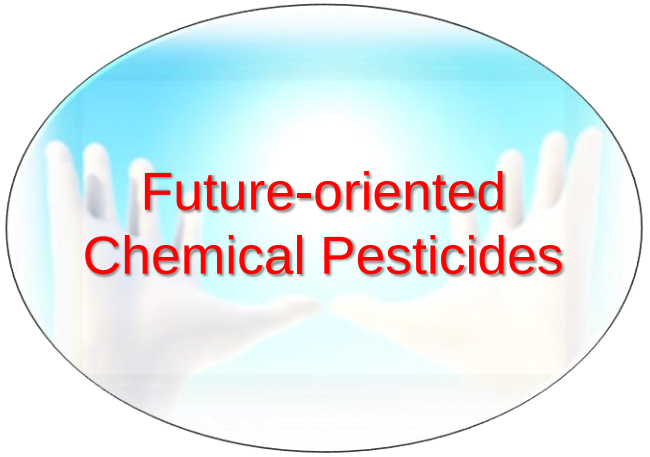
Sustainable Food Systems, MeaDRI https://www.maff.go.jp/e/policies/env/env_policy/meadri.html
Farm to Fork https://www.reneweuropegroup.eu/news/2021-09-10/farm-to-fork-strategy-overcome-environmental-challenges-create-economic-opportunities

Future of R&D

Deepening Technology
Power : Automation
Creativity : Global Perspective
Challenge : New Technologies

Tech Trend
Crop Protection with
pesticides not chemical

Biological Pesticides



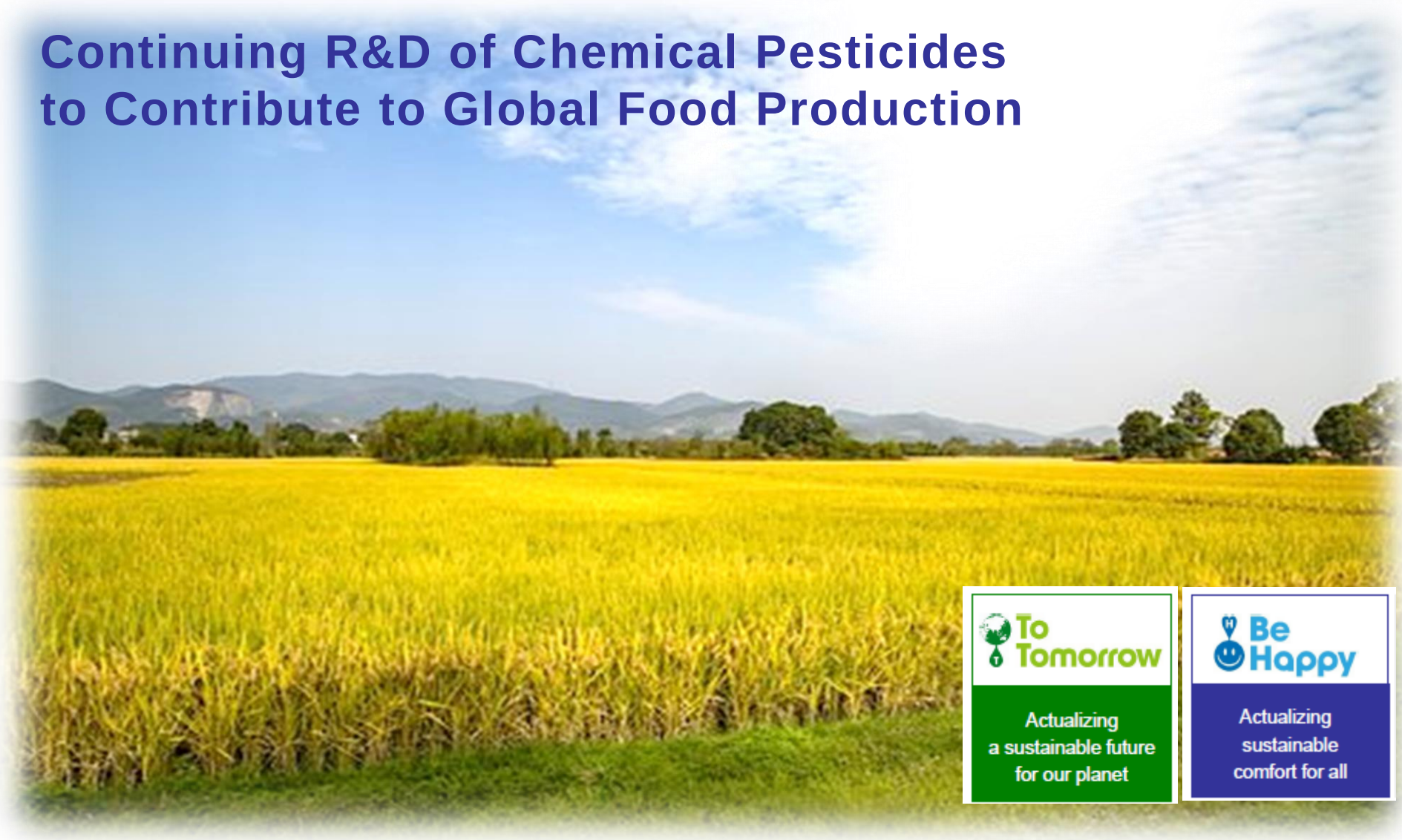
Digital Technology
AI Drug Discovery
Accelerate R&D

Pesticide Registration
Understand global regulations
Enhance safety evaluation

Eliminate Restricted Substance※
Consideration for elimination,
prohibition and restriction

※Treaty of Stockholm, Rotterdam, etc.

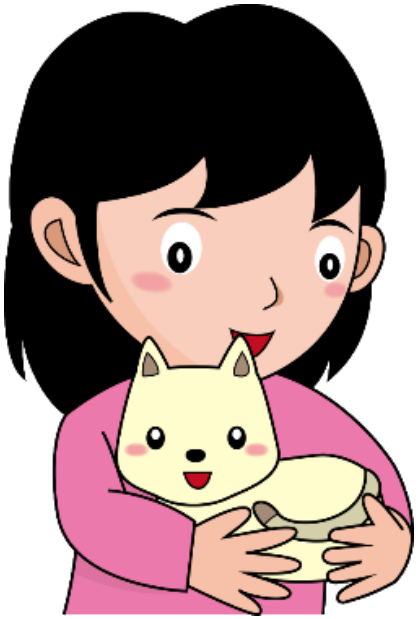
Continuing R&D of Chemical Pesticides to Contribute to Global Food Production



7. Safety research for pesticides

Contents

Why do pesticides not express their effects on humans?



Reason for not expressing

Species differences

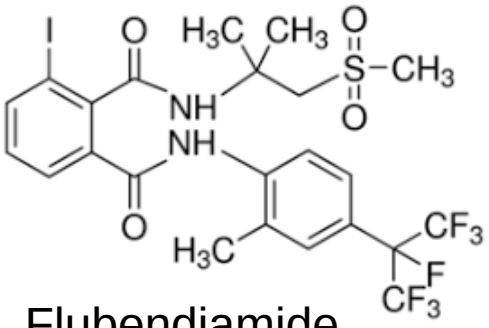
Different responses

Uptake differences

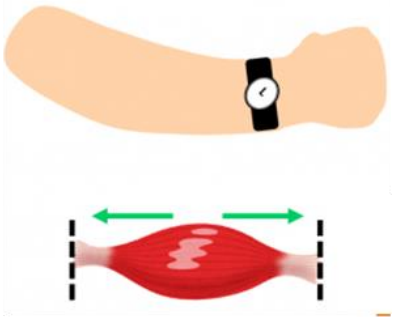
Different exposure level

Species differences: insect ryanodine receptor activators

○ Keeping on switch of muscle contraction in insects

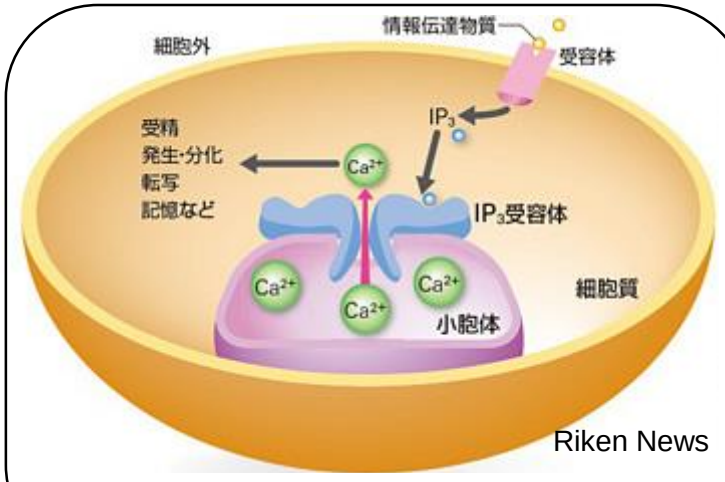


Flubendiamide
(Phoenix)



J Pestic Sci. 30:354–360 (2005)

Shrivel up and die



Riken News

Ryanodine receptor
(RyR)

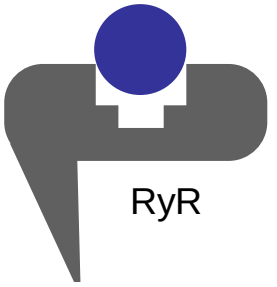
Insects

Flubendiamide

Binding and muscle contraction.

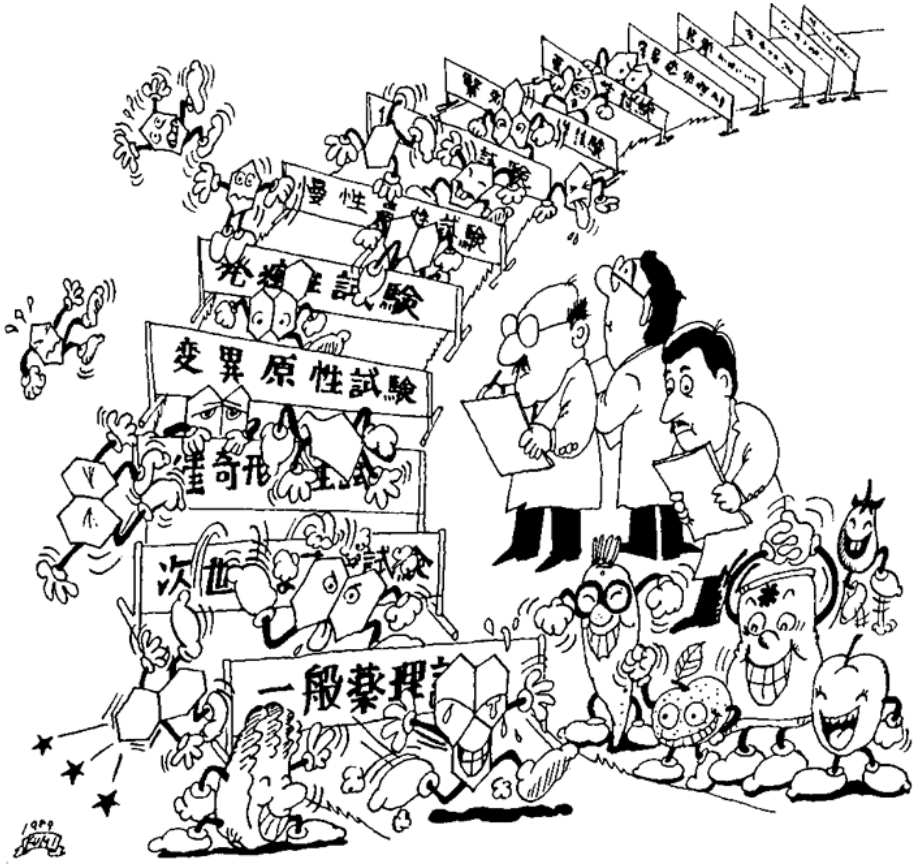
Mammals

Flubendiamide



Unable to bind, no muscle contraction.

Safety research in pesticide development



Targets affected by pesticides

Environmental organism

Consumer

Farmer

Safety data package for pesticide registration

○Toxicity

- Acute toxicity test — Rat
- Irritation test (Eye, Skin) — Rabbit
- Sensitization test — Guinea pig
- Immunotoxicity test (if required) — Rat
- Neurotoxicity test — Rat
- Developmental neurotox. test — Rat
- Delayed neurotox. test — Hen
- Sub-chronic toxicity test — Rat/Dog
- Chronic toxicity test — Rat
- Carcinogenicity test :Rat/Mouse
- Genotoxicity test
  - —Ames assay :Bacteria
  - —Chromosomal aberrations assay :Cultured cells
  - —Micronucleus assay :Mouse
- Reproductive test :Rat
- Teratogenicity test :Rat/Rabbit
- Pharmacological effect test :Rat/Mouse

○Metabolism/Residue/Physico-chemical

- Metabolism test (Plant, Soil, Animal)
- Hydrolysis/Photolysis in water test
- Residue test (Crop, Soil)
- Physico-chemical properties test
- Water pollution test (Paddy field)

○Useful plants and animals

- Effects Test for aquatic animals and aquatic plants

Safety Assessment of pesticides

Safety data package

The Cabinet Office
Food Safety Commission

Registration criteria

Ministry of the Environment

Pesticide Residue Standards

Ministry of Health, Labour and Welfare

Criteria for use

Ministry of Agriculture, Forestry and Fisheries

Environmental organism

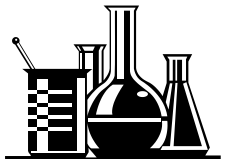
Consumer

Farmer

Development period for pesticides

Nissan Chemical CORPORATION

Screening | Early Development | Commercial Development | Launching



Manufacturing process considerations

Pilot plant

Green house trial

Field trial (small scale)

Field trial (large scale)

Physico-chemistry

Metabolism /Residue Preliminary study

Metabolism /Residue GLP study

Toxicity Screening

Toxicity Preliminary study

Toxicity GLP study

? years → ← 3 years → ← 8 years →

Serious toxicities for pesticide development

- Genotoxicity
- Endocrine disruption
- Teratogenicity
- Carcinogenicity
- Low NOAEL

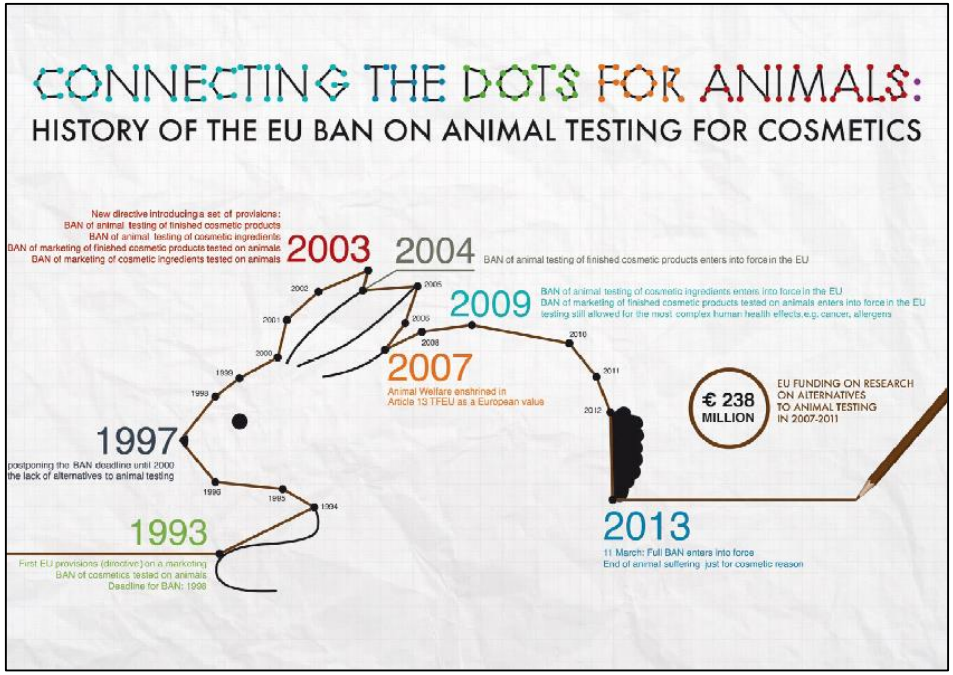
Accurate identification of these toxic-potential
in the screening phase/early development phase

Topics

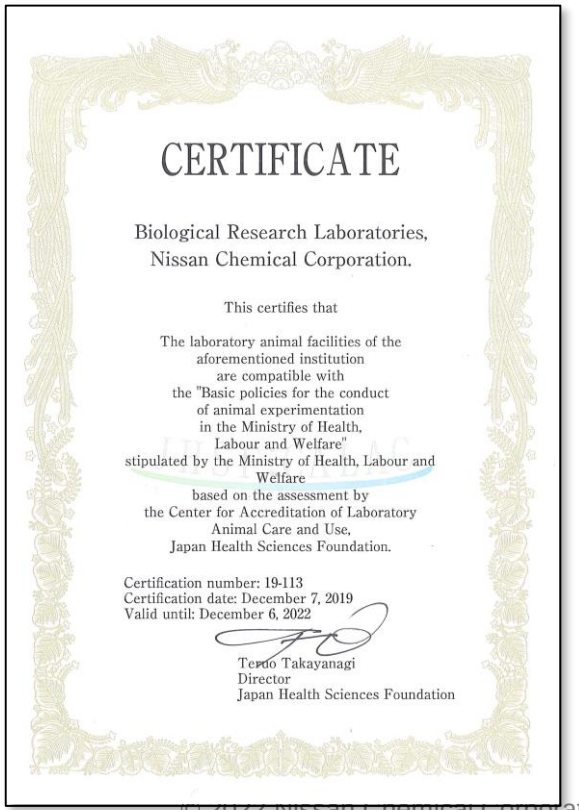
Animal Welfare

- Our response (Biological Research Laboratory)

- 2012: Set up the Animal Testing Working Group
- 2016: Certification of the Human Science Foundation
  (now the Japan Medical Information Centre)
- 2019: 2nd survey / certification continued.
- 2022: 3rd survey (in October)



An official website of the European Union



CERTIFICATE

Biological Research Laboratories,
Nissan Chemical Corporation.

This certifies that

The laboratory animal facilities of the
aforementioned institution
are compatible with
the "Basic policies for the conduct
of animal experimentation
in the Ministry of Health,
Labour and Welfare"
stipulated by the Ministry of Health, Labour and
Welfare
based on the assessment by
the Center for Accreditation of Laboratory
Animal Care and Use,
Japan Health Sciences Foundation.

Certification number: 19-113
Certification date: December 7, 2019
Valid until: December 6, 2022

Terdo Takayanagi
Director
Japan Health Sciences Foundation

Alternative method for sensitization: Support for listing in OECD Guideline

Nissan Chemical CORPORATION

- Participation in ADRA ring study
  - 2019: OECD TG 442C listed
  - 2022: OECD TG 442C added

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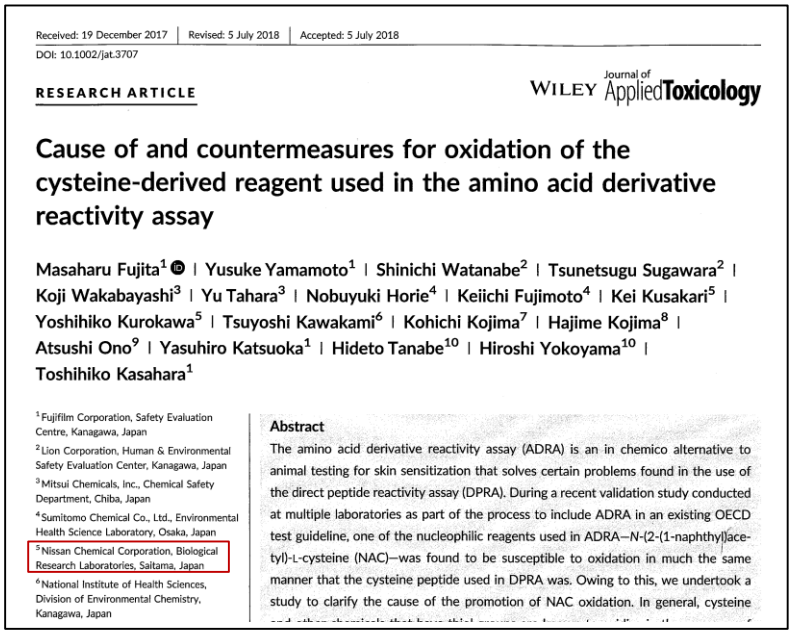
LION

Mitsui Chemicals

Nissan Chemical
CORPORATION

SUMITOMO CHEMICAL

OKAYAMA UNIVERSITY



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RESEARCH ARTICLE

Journal of Applied Toxicology

Cause of and countermeasures for oxidation of the cysteine-derived reagent used in the amino acid derivative reactivity assay

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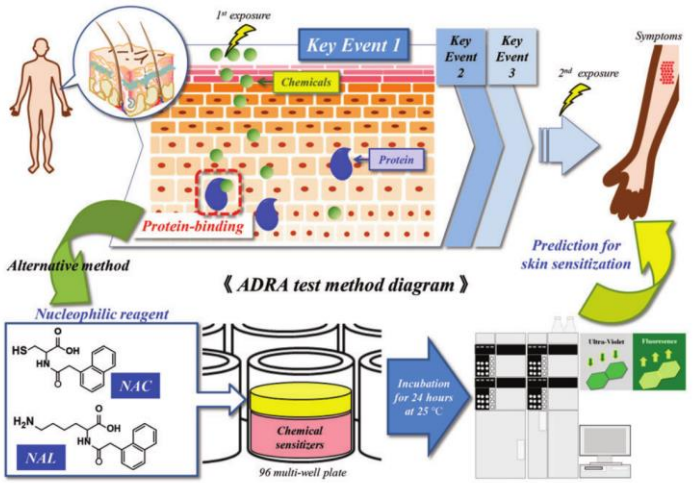
Abstract

The amino acid derivative reactivity assay (ADRA) is an in chemico alternative to animal testing for skin sensitization that solves certain problems found in the use of the direct peptide reactivity assay (DPRA). During a recent validation study conducted at multiple laboratories as part of the process to include ADRA in an existing OECD test guideline, one of the nucleophilic reagents used in ADRA—N-(2-(1-naphthyl)acetyl)-L-cysteine (NAC)—was found to be susceptible to oxidation in much the same manner that the cysteine peptide used in DPRA was. Owing to this, we undertook a study to clarify the cause of the promotion of NAC oxidation. In general, cysteine



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