Agrochemical active ingredients: better ways to make them

Presentation for
European Fine Chemicals Group
Budapest 2014

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Agenda

- Introduction
- Agriculture
- Global agrochemical industry
- Innovation
- Manufacture of agrochemicals
- A better way to make agrochemicals

[45 minutes]

Introduction

- My intention today is to persuade the European fine chemical industry, many members of which are represented here, to take a fresh look at where it's heading.

- The current business model is failing to sustain the industry AND it's failing to make the contribution to the global environment that it should be.

- I believe that the industry can recover much of its lost ground if it can persuade its customers in the bioscience sector* to reduce their reliance on captive production and let the industry do what it has done superbly in the recent past:

> *Develop and operate processes to manufacture its fine chemicals and maintain and improve those processes at the maximum possible efficiency*

*agrochemicals is the specific target for today's talk, but many of these remarks apply also to the pharma sector

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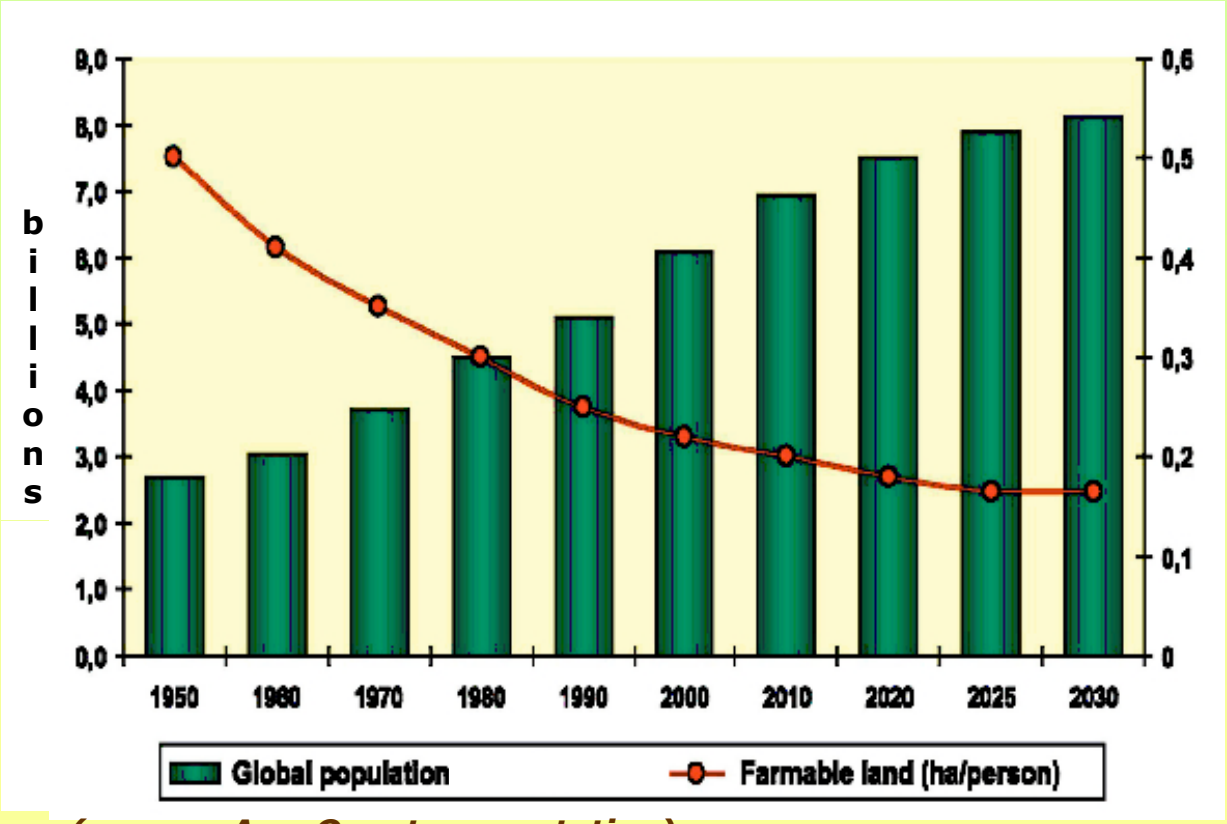
Agriculture

Why is innovation needed?

Decreasing area of agricultural land as the world's population increases, means productivity must improve



(source: AgraQuest presentation)

Keeping up with the constantly evolving challenges from agricultural pests is a vital part of this effort

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Global GDP (2012)

Source: UN statistics (2013)

Country **Note: trillion is 10^9**	***GDP USD trillions***
USA	16.2
China	8.4
Japan	6.0
Germany	3.4
France	2.6
UK	2.5
Brazil	2.3
Russia	2.0
Italy	2.0
India	1.9
Canada	1.8
Australia	1.6
Spain	1.3
Mexico	1.2
South Korea	1.1
Other 178	18.4
Global	**72.7**

Global value of food at the retail level (2012): USD 4 trn (of which Europe is USD 1.5 trn)

Source: US EPA (2013)

Global sales of chemical industry (2012): USD 3.13 trn

Source: Cefic Chemdata 2013

Global sales of fine chemical industry (2012): USD 20-30 bn

Note: captive production not included

It is clear that the fine chemicals industry is a very small part of the world's economy

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Estimates of global value of major crops (2012)

arranged by value per hectare

Crop	Global area (million ha)	Global production (mn. metric tons)	Average price (USD/metric ton)	Crop value USD bn	Crop value/ha USD/ha
bananas	10	100	935	94	9,400
potatoes	19	345	500	173	9,105
cassava	19	282	450	127	6,684
cotton	36	125	1,815	227	6,306
vines	8	62	750	47	5,875
sugar (beet)	7	240	560	19	2,714
maize	170	882	279	246	1,447
sugar (cane)	100	1,500	560	120	1,200
rice	159	466	400	186	1,170
soybeans	103	240	512	123	1,194
wheat	221	698	300	209	946
barley	50	134	264	35	700
oilseed rape	33	61	225	14	424

Source: Brychem/Agranova

Cereals are low agrochemical input crops, bananas are a high agrochemical input crop

This sub-total amounts to USD 1.62 trn
(total crop value ca. USD 2 trn)

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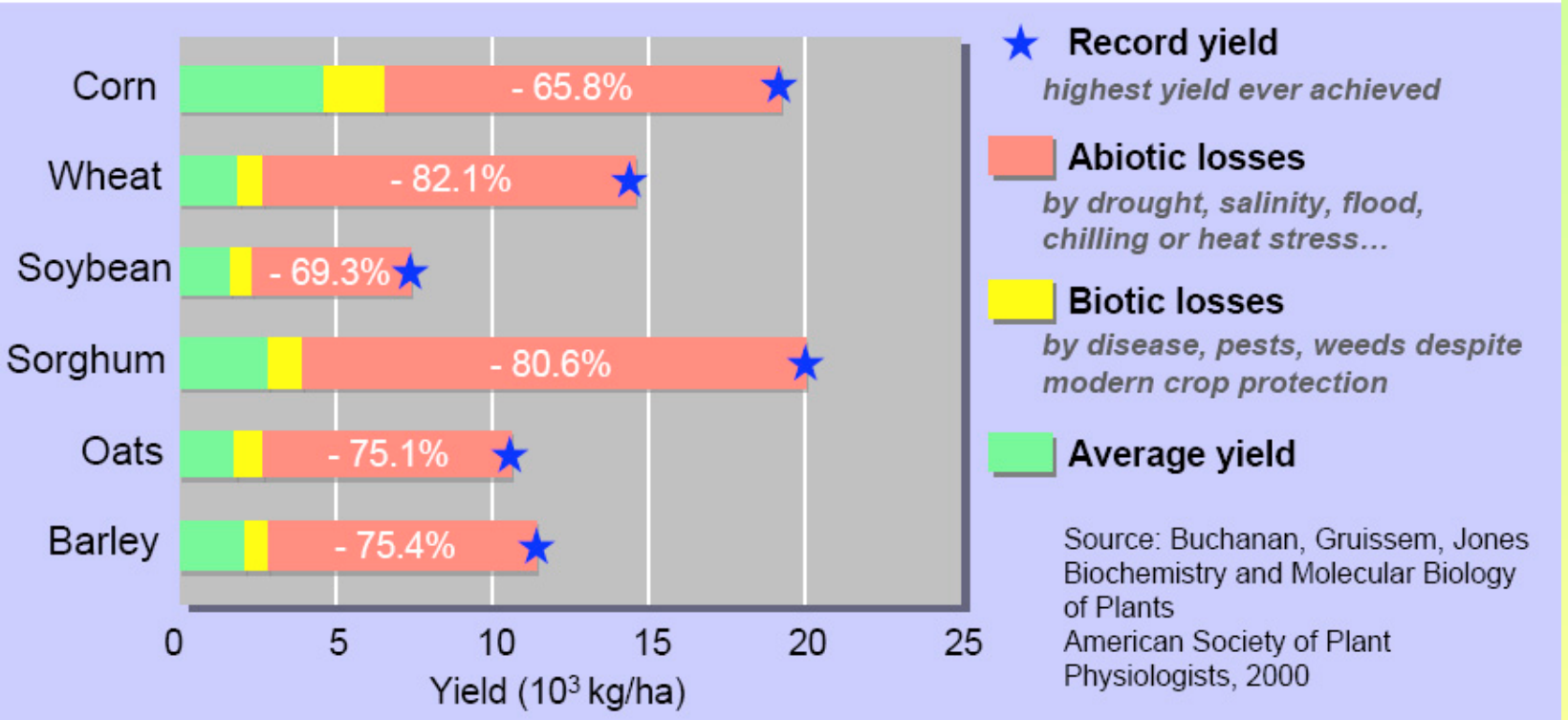
US Crop yields - climate

Pests are the least of farmer's worries!



Source: Presentation by Kenjiro Fukubayashi, Sumitomo Chemical Ltd

This slide presents an interesting insight into the broad picture of a farmer's struggle to bring in a successful crop.

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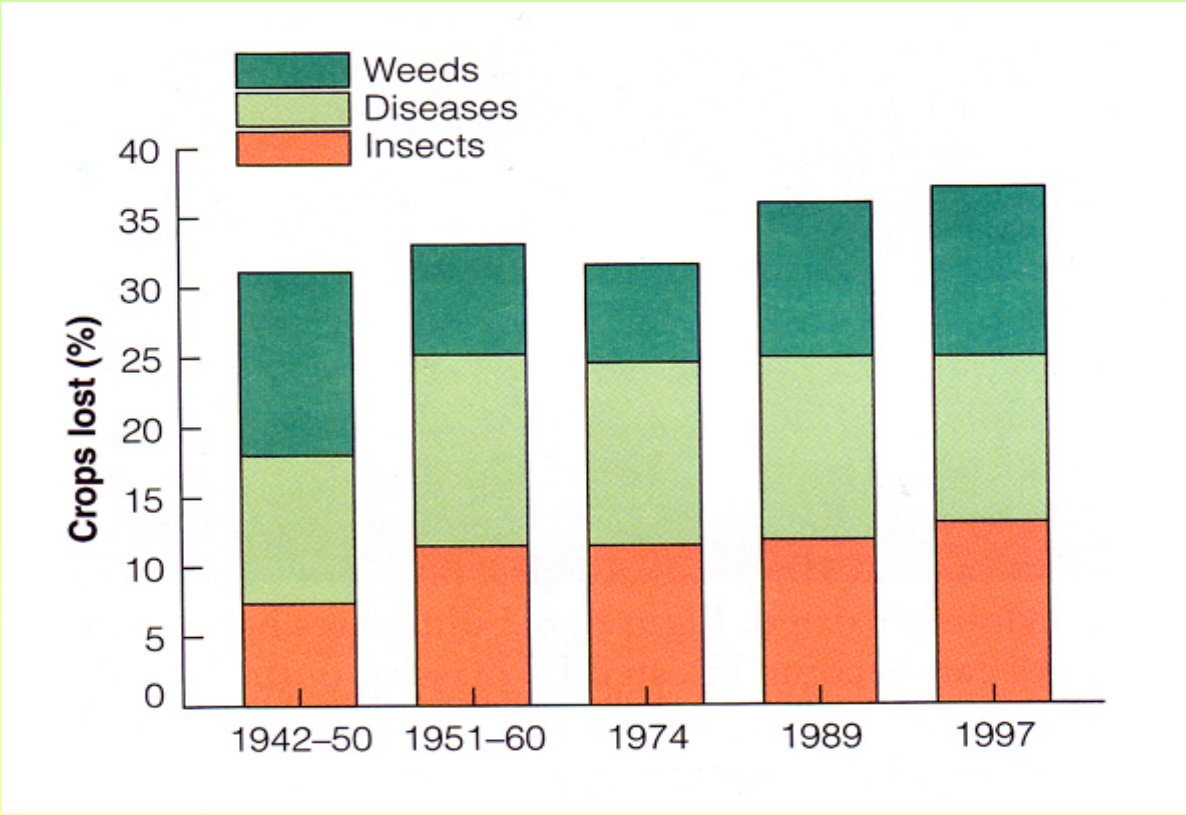
US Crop pest losses 1942-1997

(as % of total crop)



Crop losses in USA (Pimentel 1991, 1997)

Some factors that drive this surprising fact:

- Farm subsidies prop up inefficient farmers
- Loss of useful AIs considered to be unsafe or too specialised to support registrations
- Concentration of costly R&D on major crops and pests

Although produced to justify banning chemical pesticides, this data is persuasive in showing the need for redoubling efforts to expand the use of all effective crop protection technologies

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Global agrochemical industry

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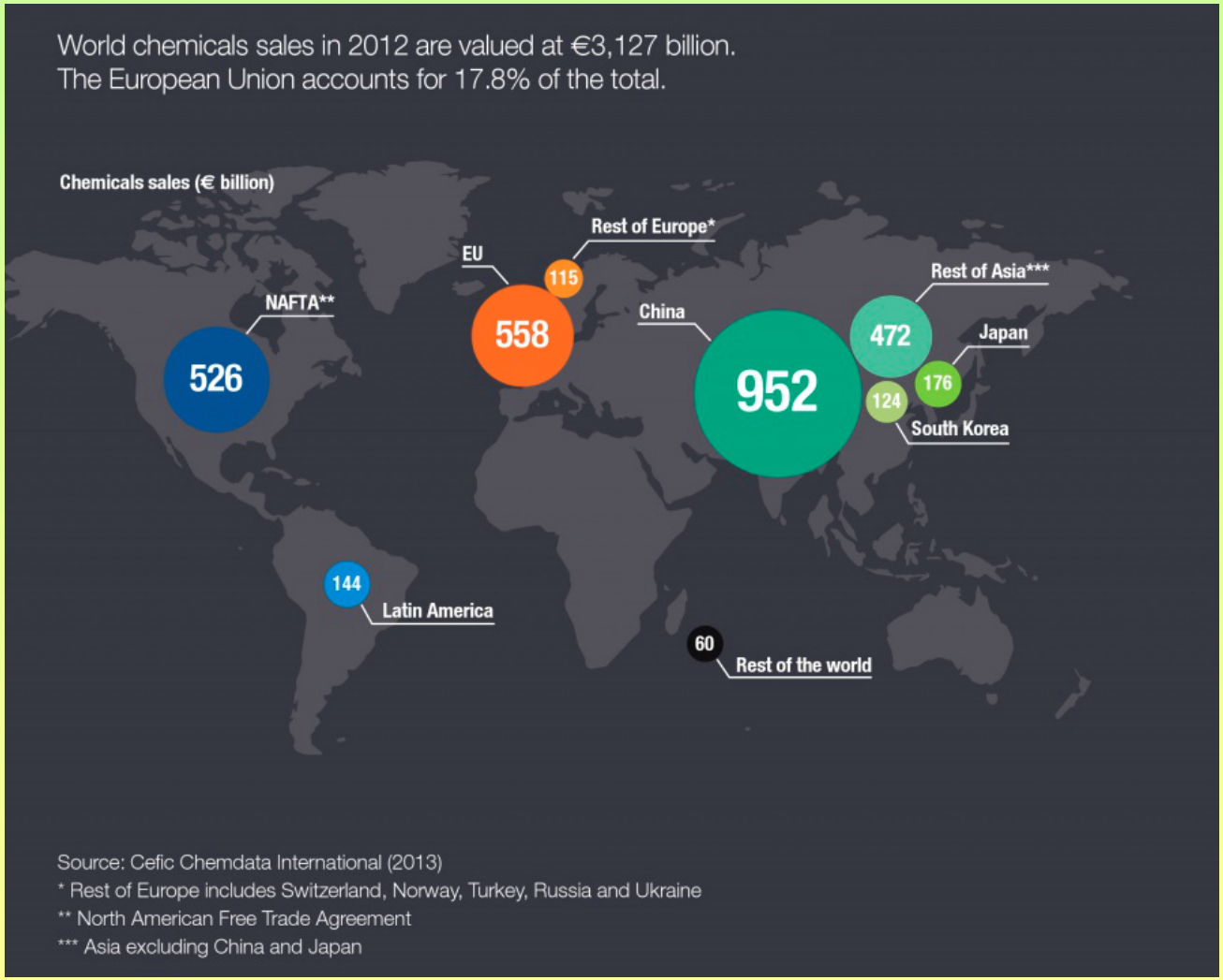
Global Chemical Industry



Global sales of China's chemical industry estimated at 30% of global total (2012)

Global sales of the fine chemical industry estimated at <1% of global total (2012)

The global chemical industry had sales of USD 3,127 billion in 2012

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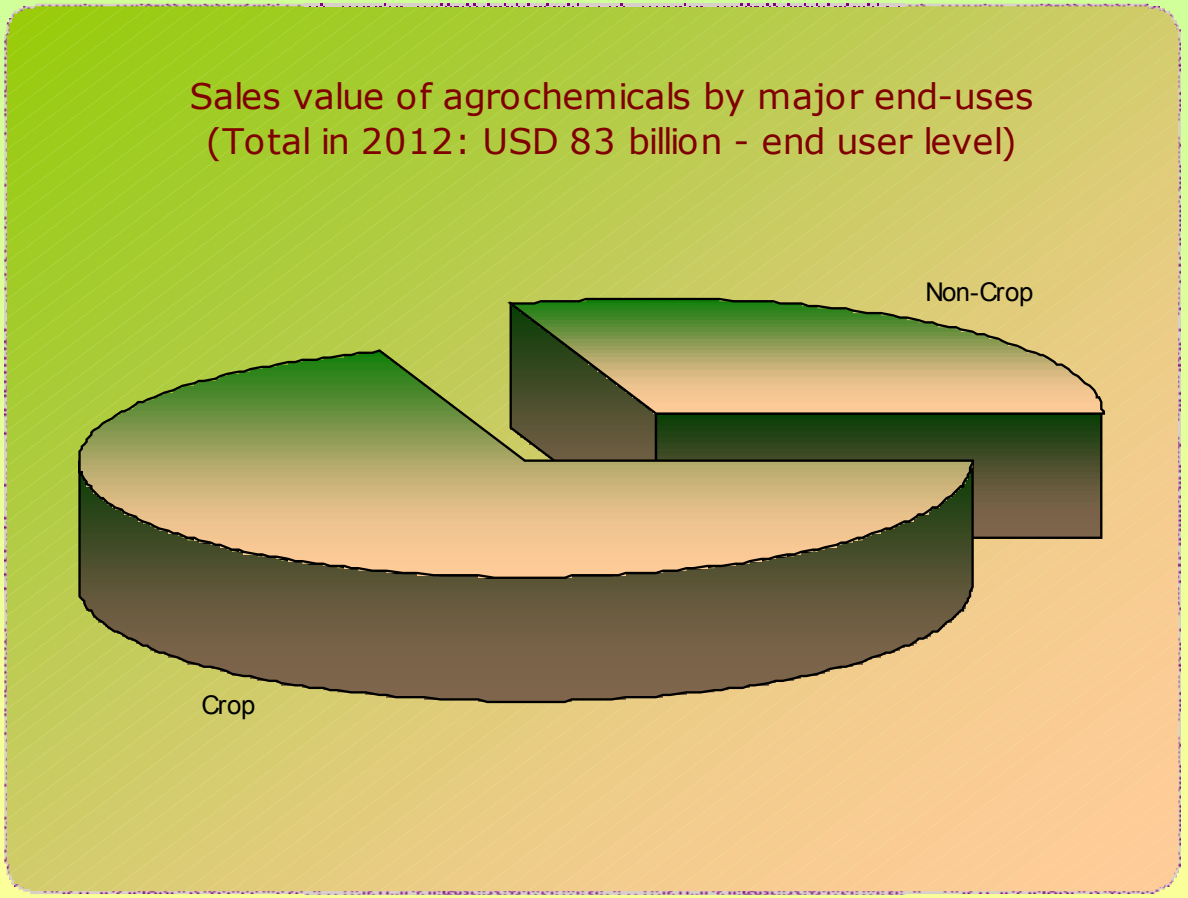
Global markets sales of crop and non-crop agrochemicals (2012)



Source: Agranova

Note also that crop protection chemicals account for less than 10% of farming inputs

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Global agrochemical sales, at ex-factory level. (USD million) 2012

Crop(s)	Herbicides	Insecticides	Fungicides	Others	Totals
Fruit & Vegetables	3,152	5,724	6,507	846	16,229
Cereals	4,426	540	2,229	341	7,536
Rice	1,675	1,423	1,147	125	4,371
Soybeans	3,718	381	1,146	30	5,275
Maize	3,084	945	221	46	4,296
Cotton	982	1,811	116	331	3,240
Sugar Beet	536	63	46	16	661
Oilseed Rape	581	112	105	39	828
Other Crops	3,710	1,783	1,500	506	7,499
Totals	**21,865**	**12,781**	**13,017**	**2,272**	**49,935**

Note that sales at the end user level would be approx. USD 58 bn.
The “others” category includes plant growth regulators, dessicants, nematicides, acaricides and molluscicides.

Source: Cropnosis

These estimates compare well with most market researchers, but appear to clash with data emerging from China - see later

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Major agrochemical companies and their global sales (USD million) 2004-2012

Agrochemical sales only		2004	2011	2012
Syngenta	Switzerland	6,030	10,162	10,710
Bayer CropScience	Germany	6,799	8,947	9,470
BASF	Germany	3,223	5,791	5,864
Dow AgroSciences	USA	3,079	4,605	5,017
Monsanto	USA	2,842	3,502	3,994
Du Pont	USA	2,518	2,856	3,172
Makhteshim-Agan	Israel	1,244	2,551	2,654
Nufarm	Australia	939	2,143	2,248
Sumitomo Chemical	Japan	865	1,723	1,669
Arysta LifeScience	Japan	685	1,485	1,557

Source: Cropnosis

Top six companies account for 80% global sales

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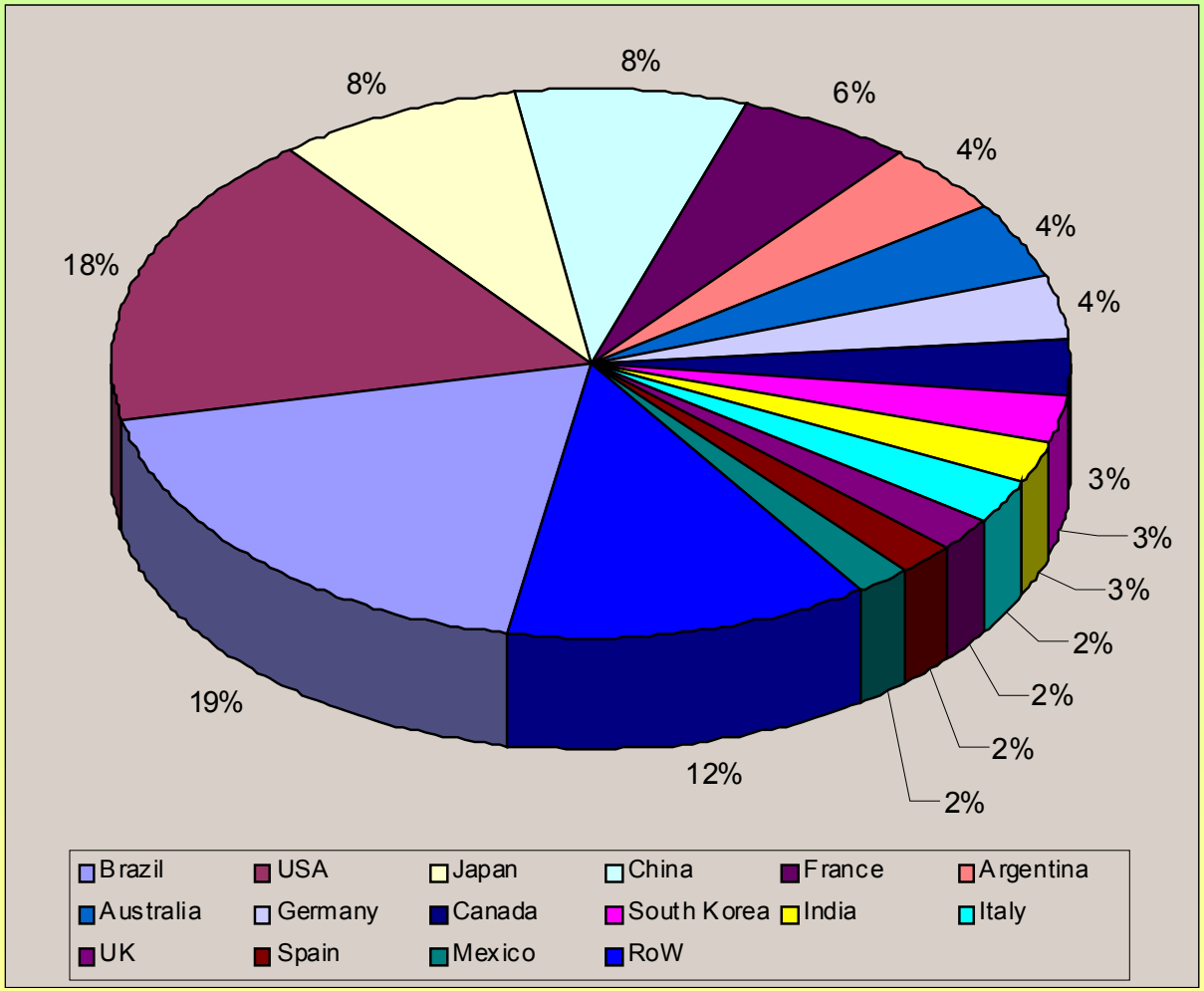
Global distribution of agrochemical sales by country as a percentage of global sales (2012)



Source: Cropnosis/Agranova

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Global seed sales (GM seeds, traits/biotechnology) by company (2010-2013) USD million

Company	***2010***	***2011***	***2012***	***2013***
Monsanto	7,743	8,583	10,008	10,260
DuPont	5,381	6,259	7,253	8,180
Syngenta	2,805	3,185	3,546	3,485
Vilmorin	1,413	1,707	1,759	1,848
Dow AgroSciences	780	1,075	1,365	1,588
KWS Saat	841	1,441	1,300	1,483
Bayer BioScience	910	1,140	1,236	1,294
Others	6,112	6,302	6,884	7,220
Total value	***25,985***	***29,692***	***33,351***	***35,358***

Source: Cropnosis Ltd

Major agchem companies have moved into seed and biotechnology and this has helped to maintain profits

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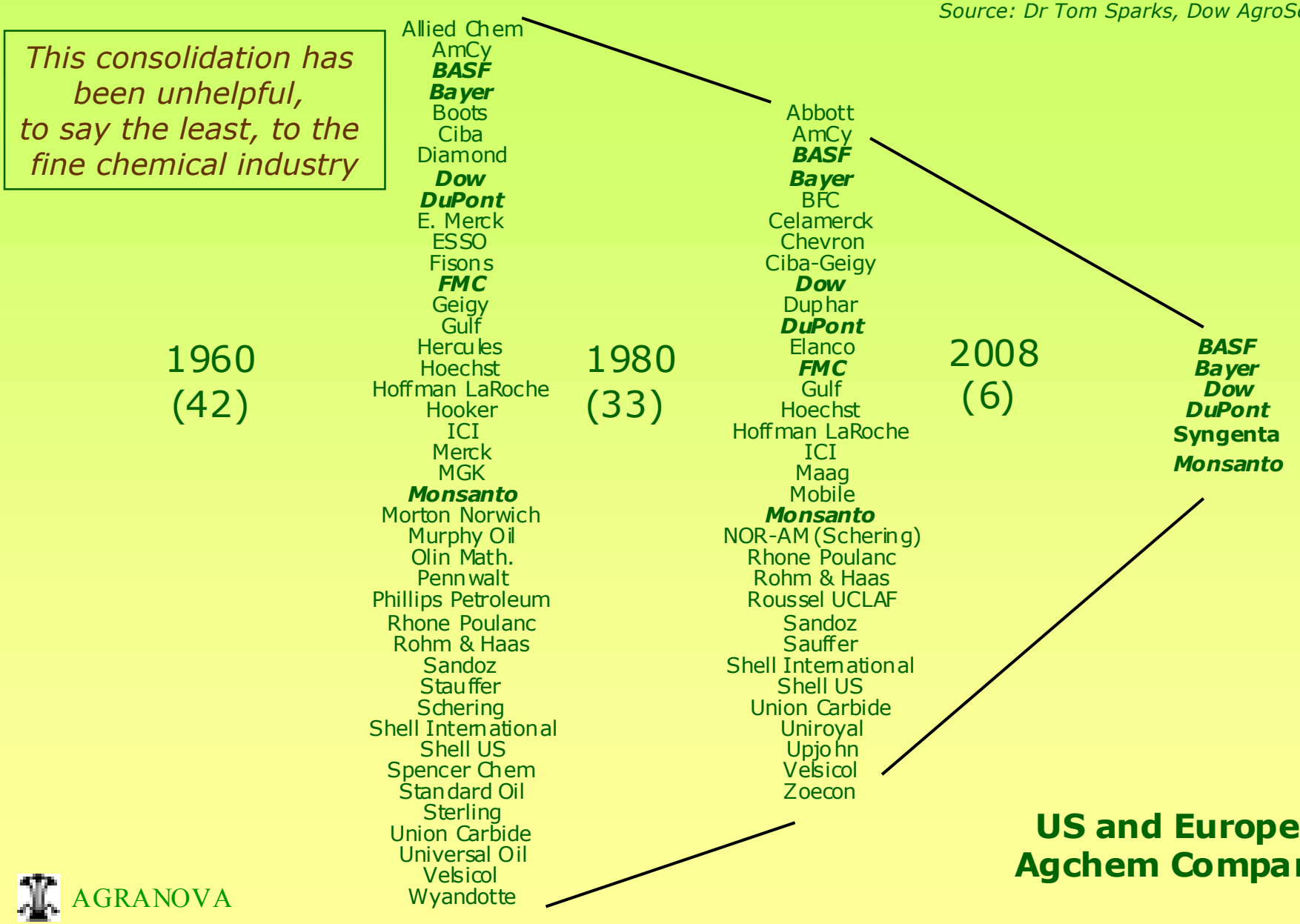
42 in 1960 contracted to 6 in 2008

Source: Dr Tom Sparks, Dow AgroSciences

This consolidation has been unhelpful, to say the least, to the fine chemical industry



US and European Agchem Companies

AGRANOVA

Regulation of the agrochemical industry

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Regulating agrochemicals - basic aim is to prove that:

They are effective in producing the desired agronomic outcome

Safe for the people using them, both in terms of acute and chronic toxicity, and that they pose no teratogenic or hormonal threats to people or animals.

Do not produce unacceptable levels of contamination of the crops to which they are applied (minimum residue levels set by statute)

Do not produce contamination of the environment leading to toxicity to people or non-target organisms

If only it was so simple :>)

Regulating agrochemicals in the EU has become a major industry

- European companies have allowed the "tail to wag the dog"
- Helped to stifle innovation in chemical process development
- Result is that producers are locked into processes that were developed quickly to ensure the original product launch was not delayed
- There are precious few incentives to improve the chemistry and so it is often relatively inefficient. This locking-in continues even when production goes East.
- Means that there are far more effluents with which to deal, creating (ironically) more environmental problems

John Chapman will elaborate on the regulatory system, with all its bells and whistles

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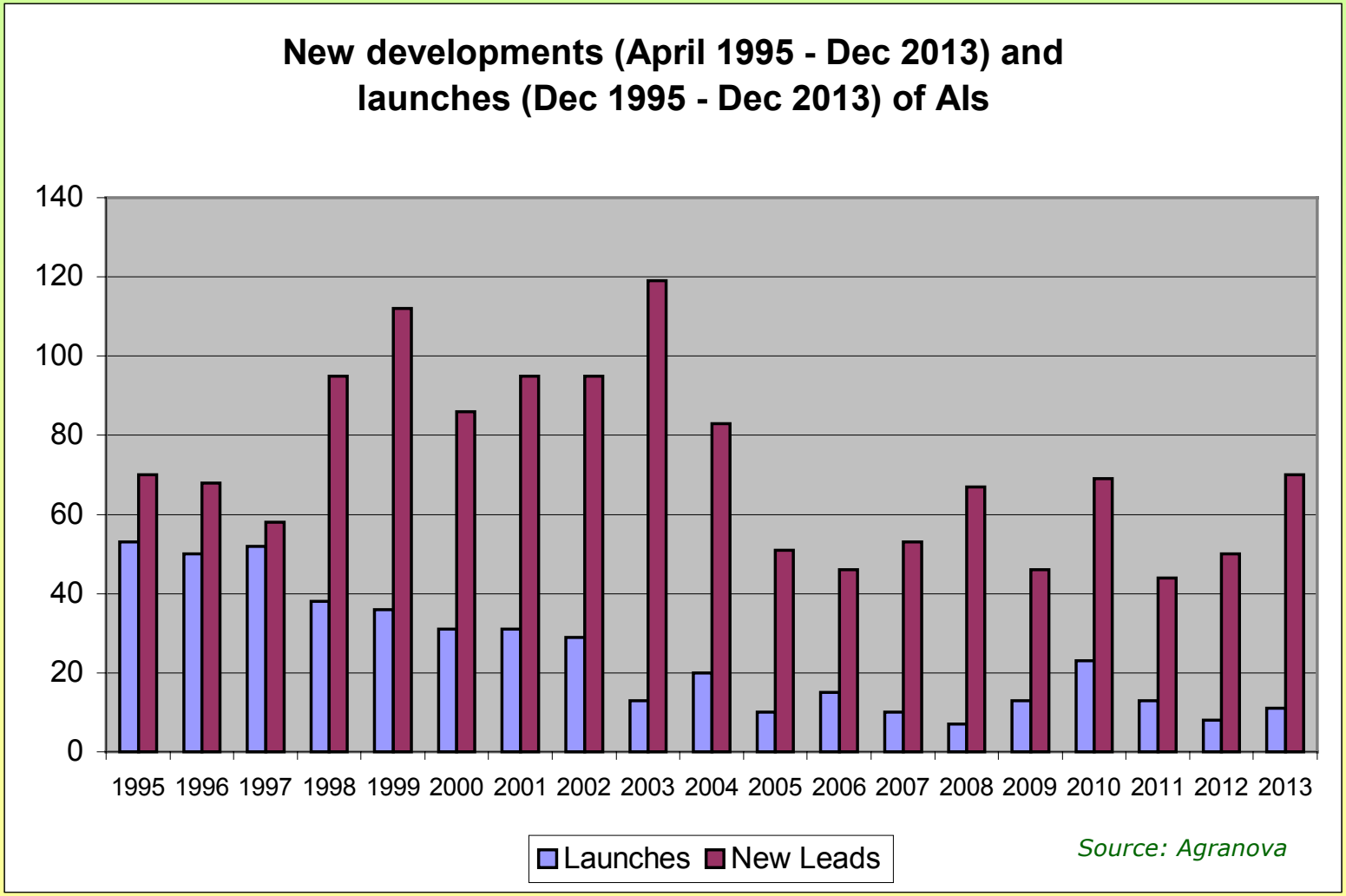
Innovation

Annual rates of innovation and commercialisation of novel active ingredients and biological agents



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Taking up the burden of discovery

NEW LEADS (agrochemicals) 2009-2010

USA	13	Herbicides	10
Europe	10	Insecticides	28
Japan	19	Fungicides	16
China	12	Other	3
RoW	3		

Source: Ag Chem New Compound Review (Vol 28) 2010

- In the late 1990s-early 2000s Japan took over from the USA and Europe as a major source of new leads
- China's R&D effort emerged in the mid-2000s as a new centre for discovery.

Research into new insecticides has become dominant, as a result of the changing centres of R&D

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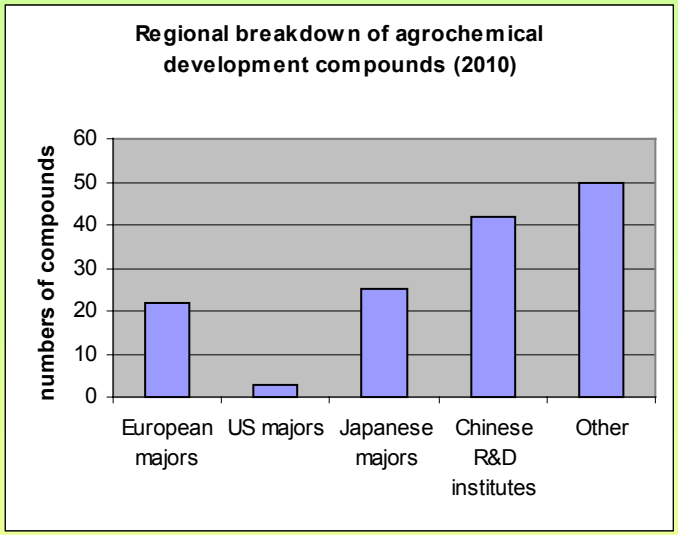
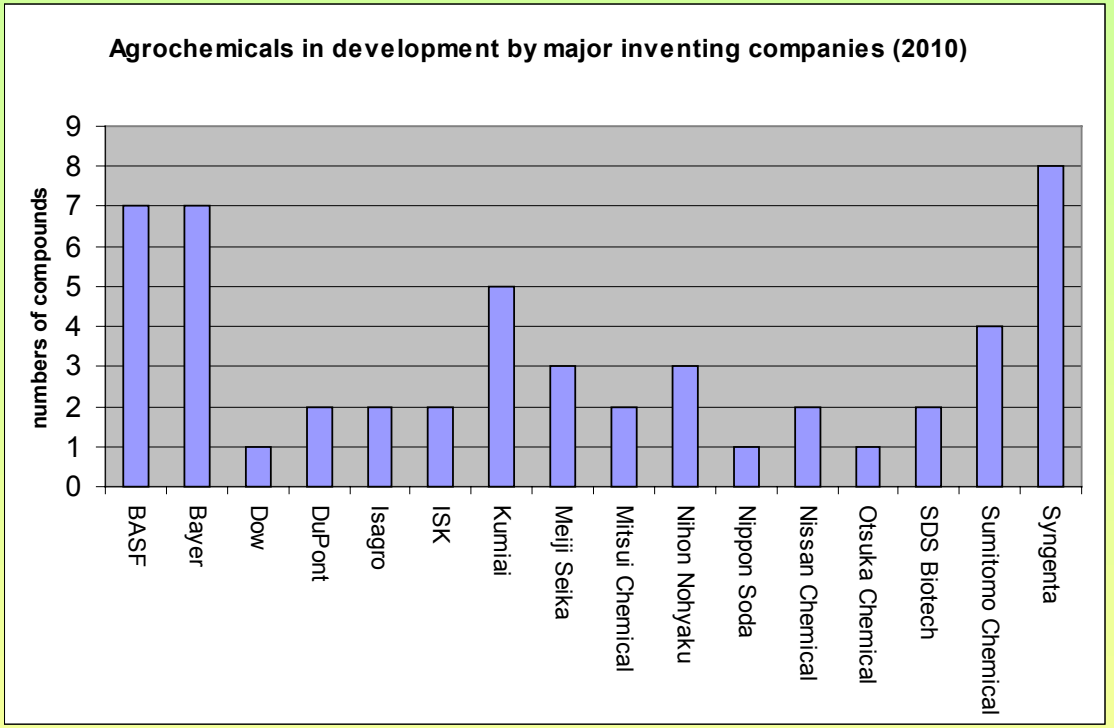
R&D pipeline - discovery groups



The striking decline in US agrochemical research is the result of the emphasis on GM crop research. However, over-dependence on a limited range of tolerant herbicides has its dangers, as illustrated by the emergence of glyphosate resistance, particularly in the USA.



Source: Ag Chem Base 2010 (Agranova)

- In 2010 pipeline contained around 325 development products
- R&D no longer dominated by the major agrochemical companies*
- 142 chemical compounds have been identified (see graphs above) of which 44 have known modes of action

* However, this analysis neglects quality of AIs

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Manufacture of agrochemicals

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Production of AIs is still dominated by major agchem groups

- Key active ingredients made on own facilities, with 1-2 back-up contract manufacturers
- AIs for older, less important products outsourced
- Raw materials and intermediates usually sourced from appropriate specialists
- Chemical process innovation largely limited to captive groups, which produce "patent swamps" to protect the technology
- Trends over past 10-15 years has been to favour toll-manufacture over custom synthesis (to retain tighter control of technology)
- This has led to "dumbing down" of fine chemical industry
- Many major agchem companies have, nevertheless exposed their key technologies to Asian competition.

European fine chemicals industry has lost out in this process

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The shift of innovation towards Asia has favoured Asian fine chemical producers

- Chemical process innovation remains in Japan, thanks to its successful agchem companies
- Early intermediates and pilot quantities of AI supplied by Japanese producers
- Scale-up of production has been carried out in China, and to a far lesser extent, to India
- Technologies remain in Asia, even when major agchem companies license AIs
- During the past five years, China has emerged as a major producer of agrochemicals and their intermediates*

** A recent report by China's CCPIA claimed that the **sales of its top 100** agrochemical companies rose from USD 8 bn in 2011 to **USD 15.9 bn in 2014** (March-March financial years).*

Again, the European fine chemicals industry has been the main loser in this rapid industrial progress

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Fine chemical companies that supply the life-sciences industry

(Source: Jan Ramakers)

Company	*Location of HQ*	*Revenue 2011 (USD millions)*
Evonik	Germany	2,870
Lonza	Switzerland	2,250
DSM	Netherlands	1,250
BASF	Germany	700
Saltigo (Lanxess)	Germany	695
Albemarle	USA	490
SAFC	USA	380
Weylchem	Germany	360
Novasep	France	350
Siegfried	Switzerland	320
Vertellus	USA	290
Cambrex	USA	260
Dow	USA	250
Aesica	UK	240
Tessenderlo	France/Italy	225
Sumitomo Chemical	Japan	200
Omnichem	Belgium	170
Zach System	Italy/France	165
Wacker	Germany	155
Boehringer Ingelheim	Germany	140
Isochem	France/Hungary	150
PCAS	France	140
CABB	Switzerland	135
Arkema	France	120
Nippon Soda	Japan	115
Many, many others		63,680
Top 25 lifescience fine chemical producers		**12,420**

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Fine chemical companies that supply the agrochemical industry (key technologies)

Company	*Location of HQ*	*Involvement with the agchem sector*	*Specialities, technologies*
Evonik	Germany	small	Amino acids and chiral synthesis
Lonza	Switzerland	modest	Generalist, ketene-based, pyridines
DSM	Netherlands	small	Generalist
BASF	Germany	modest	Generalist
Saltigo (Lanxess)	Germany	significant	Generalist, phosgenation, nitration
Albemarle	USA	significant	Aromatic ethylation, catalysis
Weylchem	Germany	modest	Acetylene chemistry
Novasep	France	modest	Azides, large scale SMB
Siegfried	Switzerland	modest	Nitrations
Vertellus	USA	significant	Pyridine chemistry (gas phase)
Dow	USA	modest	Pyridine chemistry (gas phase)
Wacker	Germany	modest	Ketene-derived intermediates
Isochem	France/Hungary	significant	Phosgene, chloroformates
PCAS	France	modest	Generalist
CABB	Switzerland	significant	Nitration, sulphur chemistry
Alzchem	Germany	significant	Guanadines, pyrimidines

Source: Agranova

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Leading Chinese agrochemical companies

Company	Agrochemical sales (USD mn) Agranova estimates				CCPIA estimates
	2009	2010	2011	2012	2013
Sinochem	800	850	1,100	1,200	-
ChemChina Agrochemical	550	600	650	700	-
Zhejiang Xin'an (Wynca)	295	296	331	430	577
Zhejiang Jinfanda	210	230	254	260	574
Nutriechem Laboratory	-	-	-	-	573
Sichuan Leshan Fuhua	-	-	-	-	492
Jiangsu Yangnong Group	215	235	285	310	488
Hubei Sanonda Group	230	218	265	290	466
Redsun Group	110	136	198	230	-
Shandong Weifang Rainbow	152	168	190	200	450
Shandong Binnong Technology	115	148	235	255	383
Jiangsu Lianhe Technology	-	-	-	-	360
Nangtong Jianshan	-	-	-	-	353
Jiangsu Changlong Chemicals	160	70	173	180	332
Shenzhen Noposion	190	226	243	255	280
Jiangsu Good Harvest Weien	89	105	124	140	260
Shandong Qiaochang Chemical	170	167	175	185	214
Jiangsu Kwin Group (Kesheng)	50	69	180	190	176
Jiangsu Langfeng (Suhua)	92	103	131	135	165
Anhui Huaxing Chemical	128	134	130	135	125
Shenghua BIOK Group	93	105	103	100	117

Source: Agranova / CCPIA

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Most of these companies generate the majority of sales by exporting AIs and intermediates to the USA, Europe and Japan

A better way to make agrochemical actives

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A little bit of history

- The modern fine chemical industry began in the 1860s, spawning the modern pharmaceutical industry (1880s), the chemical industry (1900s) and the agrochemical industry (1940s).
- The main treatments for crops prior to the advent of the fine chemical industry in 1940s were sulphur, copper salts, brine, detergent solution and plant extracts like Derris.
- As the sales of the chemical and bioscience companies grew, they became major industries during the latter part of the twentieth century.
- Investor power displaced technological control of these industries towards the end of the century, leading to industry consolidation around valuable products.
- Investors saw fine chemicals as a cost centre to be minimised, rather than the "geese that were laying the golden eggs".
- Since the turn of the century, the fine chemical industry has become part of the service sector, with little control over its profits or future.

Today, it is the bioscience industries, rather than the fine chemical industry, that attracts the majority of organic chemists

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Current technical problems

- Far too much capacity for any given technology

> Lanxess could supply the world's current demand for fine chemicals derived from phosgene, whereas actual capacity is > 5 x what is needed

- Average process efficiencies are far too low, with an average active ingredient probably generating 1-2 times its mass in organic by-products, 5-8 times its mass of solvent for recovery (if possible) and 10 times its mass of aqueous waste needing disposal.

> Not nearly enough good engineering solutions are being adopted in fine chemical manufacture. Too many flexible plants, not enough continuous and catalysed reactions

- Insufficient ingenuity and too much repetition of old technologies

> Too much copying, regulatory "locking in", lack of time and resources being applied to generate and maintain the best process economics

European fine chemical industry is well positioned to recover some of what has been lost

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What an independent fine chemical industry could bring to agrochemical manufacturing

- An industry dominated by organic chemists will continuously develop new and improved processes *because that's what they care about*.
- The fruits of cutting costs can be equitably shared between the industry and its customers, providing the funding needed to ensure a vibrant industry.
- Investors can continue to reap returns at the finished product stage and their short-term interests reconciled with the long term needs of a technology and capital intensive industry.
- Independent, European fine chemical producers can be counted upon to observe proprietary rights because customers will have better legal redress to European companies that fail to observe them.

Our customers will not be easily convinced, but now is as good moment to make the attempt

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What will be the costs of an independent fine chemical industry?

Higher returns required by the industry can be accommodated by its customers because better designed processes will deliver benefits:

- Reliable, local production that conforms to increasingly stringent regulatory demands
- Processes will be more efficient and better engineered
- Environmental load will be reduced
- Through consolidation, unnecessary capital investments in chemical plants can be avoided

As the relative cost advantages enjoyed by Asian suppliers decrease, European fine chemical companies can emphasise these advantages to their customers.

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Conclusion

- The European fine chemical industry retains the scale and power to become its own master once again.
- As an industry, we should persuade our customers to relinquish responsibility for manufacturing active ingredients, wherever possible.
- The industry should consolidate, but should also reduce its scale so that the necessary dynamism can be recaptured (given improved profits, the need to be part of a bigger, less nimble organisation is reduced).
- More collaboration rather than repetition of facilities should be encouraged
- Differentiation by ingenuity of a company's chemists and engineers to devise the most efficient technologies should become the key determinant of success
- Our customers might again develop a respect for what our profession can offer and pay the industry accordingly

Europe cannot defend its industries by hiding behind a wall of regulation;
it needs to engage with the world and beat them using its proven ability
to innovate and commercialise world-beating technologies.

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Thank you for listening

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