



Access and Benefit Sharing Key Points for Policy-Makers

THE PHARMACEUTICAL INDUSTRY



Sarah A. Laird

November 2015

SUMMARY OF KEY POINTS



MARKETS, COMPANIES AND PRODUCTS

-  Revenues have increased steadily over the last 30 years, but in recent years growth has slowed in developed country markets while in 'pharmerging' markets it has increased.
-  The world's largest pharmaceutical companies are located in developed countries. Their earnings make them some of the wealthiest companies in the world.
-  The pharmaceutical industry has undergone significant consolidation over the last 30 years in order to increase growth and acquire new technologies, expertise and novel drug candidates.
-  Many of the industry's top-selling drugs have gone off-patent, resulting in reduced revenues in recent years. Patent expiries on small molecule products will reduce brand spending in developed markets by \$113 billion through 2017.
-  A top-selling pharmaceutical product can now generate more than \$5 billion in sales a year.
-  Specific disease areas and products differ significantly between developed and pharmerging markets.

TRENDS IN RESEARCH AND DEVELOPMENT

-  Spending on R&D has increased over the last few decades but productivity has gone down. The number of new drugs coming on the market each year has held roughly steady or declined since 1981.
-  Government contributions to pharmaceutical R&D remain high across the globe. In the US, for example, government funding contributed to 48% of all drugs approved by the FDA and 65% of drugs that received priority review between 1988-2005.
-  Drug discovery, including that on natural products, is increasingly done in smaller start-up companies, academia and government laboratories, with large companies undertaking development and marketing.

NATURAL PRODUCTS RESEARCH

-  Although support for natural products research in large companies has declined, the contribution of natural products to the development of new drugs continues, and between 1981-2013 an average of 31% of all new drugs annually were natural products.
-  Natural products research has undergone dramatic changes in the last 50 years, with significant implications for the speed, scale and focus of R&D, and the design of effective ABS measures.
-  Traditional knowledge, once the primary lead for the discovery of new medicines, is no longer a significant part of industry R&D.

INDUSTRY AND ABS

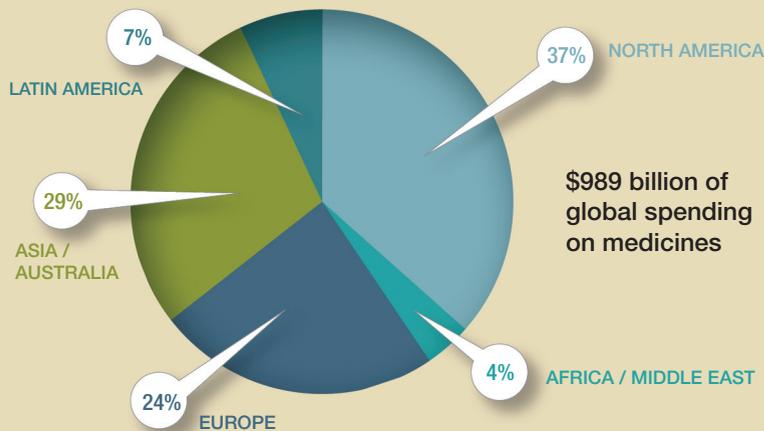
-  The pharmaceutical industry is more aware of the Convention on Biological Diversity than many other sectors, although this is more the case with large companies than with small. However, many concerns persist within industry about legal certainty and the need for new measures drafted to implement the Nagoya Protocol to reflect the scientific, business and legal realities of natural products research today.



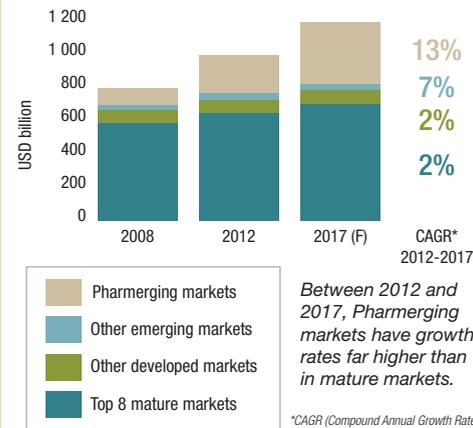
MARKETS, COMPANIES AND PRODUCTS



Revenues have increased steadily over the last 30 years, but in recent years growth has slowed in developed country markets while in 'pharmerging' markets it has increased.



Global growth rates



The world's largest pharmaceutical companies are located in developed countries. Their earnings make them some of the wealthiest companies in the world.

Top Companies

NORTH AMERICA

RANK	COMPANY	COUNTRY	2013 SALES (USD million)	2013 R&D SPENDING (USD million)	2013 TOP-SELLING DRUGS (USD million)
1			\$45,011	\$6,254	Lyrica (4,595) Prevnar (\$3,974) Enbrel (\$3,774)
2			\$37,519	\$7,123	Januvia (\$4,004) Zetia (\$2,658) Remicade (\$2,271)
3			\$26,475	\$5,810	Remicade (\$5,334) Zytiga (\$1,698) Prezista (\$1,673)
4			\$20,119	\$5,316	Cymbalta (\$5,084) Alimta (\$2,703) Humalog (\$2,611)
5			\$18,790	\$2,831	Humira (\$10,659) AndroGel (\$1,035) Kaletra (\$962)
6			\$18,192	\$3,941	Enbrel (\$4,551)
7			\$12,306	\$3,715	Reyataz (\$1,551)
8			\$10,804	\$2,056	Atripla (\$3,648)

AFRICA / MIDDLE EAST

RANK	COMPANY	COUNTRY	2013 SALES (USD million)	2013 R&D SPENDING (USD million)	2013 TOP-SELLING DRUGS (USD million)
12			\$17,563	\$1,422	Copaxone (\$4,328)

EUROPE

RANK	COMPANY	COUNTRY	2013 SALES (USD million)	2013 R&D SPENDING (USD million)	2013 TOP-SELLING DRUGS (USD million)
1			\$46,017	\$9,360	Gleevec (\$4,693) Diovan (\$3,524) Lucentis (\$2,383)
2			\$39,143	\$8,294	Rituxan (\$7,503) Avastin (\$6,751) Herceptin (\$6,562)
3			\$37,701	\$6,117	Lantus (\$7,592) Plavix (\$2,460) LovenoX (\$2,262)
4			\$33,055	\$5,041	Seretide / Advair (\$8,251) Pediarix (\$1,349) Avodart (\$1,341)
5			\$24,523	\$4,269	Crestor (\$5,622) Nexium (\$3,872) Symbicort (\$3,483)
6			\$15,594	\$2,710	Kogenate (\$1,597)
7			\$14,886	\$2,090	NovoRapid (\$3,001)
8			\$14,468	\$3,247	Spiriva (\$4,719)

ASIA / AUSTRALIA

RANK	COMPANY	COUNTRY	2013 SALES (USD million)	2013 R&D SPENDING (USD million)	2013 TOP-SELLING DRUGS (USD million)
16			\$13,591	\$3,352	Biopress (\$1,256)
19			\$10,431	\$2,132	Prograf (\$1,755)
20			\$10,268	\$1,926	Benicar (\$2,116)



The pharmaceutical industry has undergone significant consolidation over the last 30 years in order to increase growth and acquire new technologies, expertise and novel drug candidates.

1980

Merck	Hoffman	Hoescht Roussel	Squibb	Sandoz	Glaxo	Pfizer
Schering-Plough	Genentech	Marion Merrill Dow	Bristol Myers	Ciba-Geigy	Wellcome	Parke-Davis
Organon		Rhone Poulenc	DuPont Pharma		Burroughs	Warner Lambert
		Sanofi	Merck DuPont		Smith Kline & French	Monsanto
		Synthelabo			Beecham	Searle

No Companies: (including Amgen and Johnson and Johnson) 33

Consolidation has been a continuing process

H-LaRoche Syntex	Hoescht	Squibb	Sandoz	SmithKline Beecham	Pfizer
Genentech	Sanofi/Synthelabo	Bristol Myers	Ciba-Geigy		Warner Lambert
	RhonePoulenc & Fisons				Monsanto Searle
	Marion Merrill Dow				Pharmacia Upjohn
					Lederle (AHP)
					Wyeth

Hoescht Roussel	Bristol-Meyers Squibb	SmithKline Beecham	Pfizer
Sanofi/Synthelabo		Burroughs-Wellcome	Pharmacia
RhonePoulenc & Fisons		Glaxo	Lederle(AHP)
			Wyeth

Merck	Hoffman LaRoche	Aventis		GlaxoSmith Kline	Wyeth
Schering-Plough		Sanofi/Synthelabo			Pfizer

2010

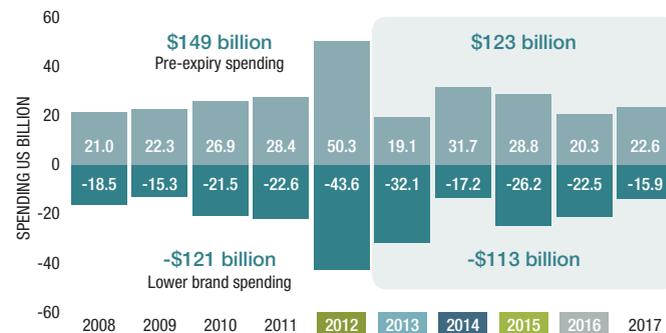
Merck 	Roche 	Sanofi-Aventis 	Bristol-Meyers Squibb 	Novartis 	Glaxo SmithKline 	Pfizer
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Many of the industry's top-selling drugs have gone off-patent, resulting in reduced revenues in recent years. Patent expiries on small molecule products will reduce brand spending in developed markets by \$113 billion through 2017.

Developed markets patent expiry 2008-2017



Protection expiry year	US	Japan	UK	France	Germany
2012	Plavix Seroquel Singulair Actos Lexapro Diovan Diovan HCT® Geodon Viagra Boniva	Nu Lotan Mylsee Preminent Haigou Seroquel	Lipitor Amias Seroquel Aricept® Singulair	Tahor Singulair Pariet Ixprim Aprovel	Seroquel Atacand Atacand Plus Sortis Aricept
2013	Oxycontin® Aciphex Zameta Xeloda Opana ER Asacol	Diovan Plavix Livalo Elplat	Viagra Xeloda	Seretide Coaprovel Xeloda Micardis Viagra	Viani Zometa Atmadisk Coaprovel Viagra
2014	Nexium® Cymbalta Cerebrex Symbicort Lunesta Restasis Evista Sandostatin LAR Actonel	Prograf Glivec Abilify	Abilify Ciprallex Risperdal Consta	Seroplex Abilify Ebixa Risperdal Consta LP	Axura Risperdal Consta Biopress Plus
2015	Abilify Copaxone Gleevec Namenda Provigil Combivent Zyvox Prezista Avodart	Zyprexa Adoair Alimta Spiriva Symbicort	Spiriva Cymbalta Alimta	Alimta Spiriva Copaxone Protelos Cymbalta	Spiriva Copaxone Alimta Cymbalta
2016	Crestor Benicar Benicar HCT Cubicin	Blopress Baraclude	Glivec Vfend	Glivec Cancidas Vfend	Glivec Zyvoxid Vfend



A top-selling pharmaceutical product can now generate more than \$5 billion in sales a year.



Specific disease areas and products differ significantly between developed and pharmerging markets.

Top ten global products 2013

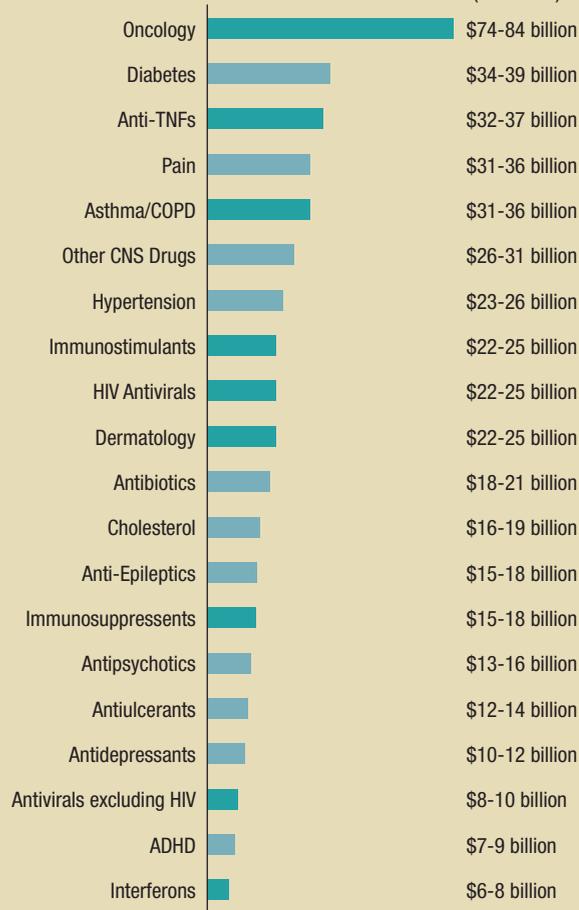
2013 sales (USD million)



Spending by therapy area (projected for 2017)

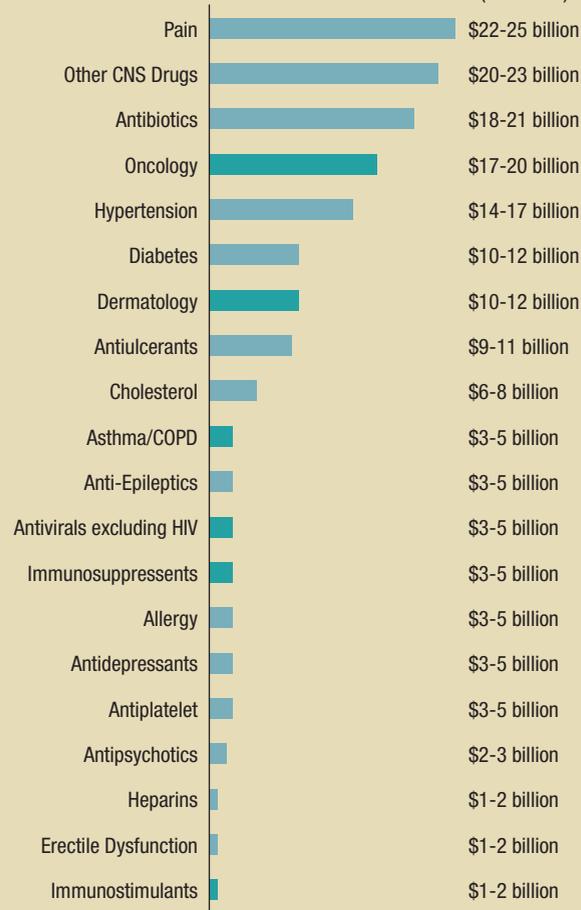
DEVELOPED MARKETS

Projected sales in 2017 (USD billion)



PHARMERGING MARKETS

Projected sales in 2017 (USD billion)



BRAND 67%

GENERIC 21%

OTHER 12%

BRAND 26%

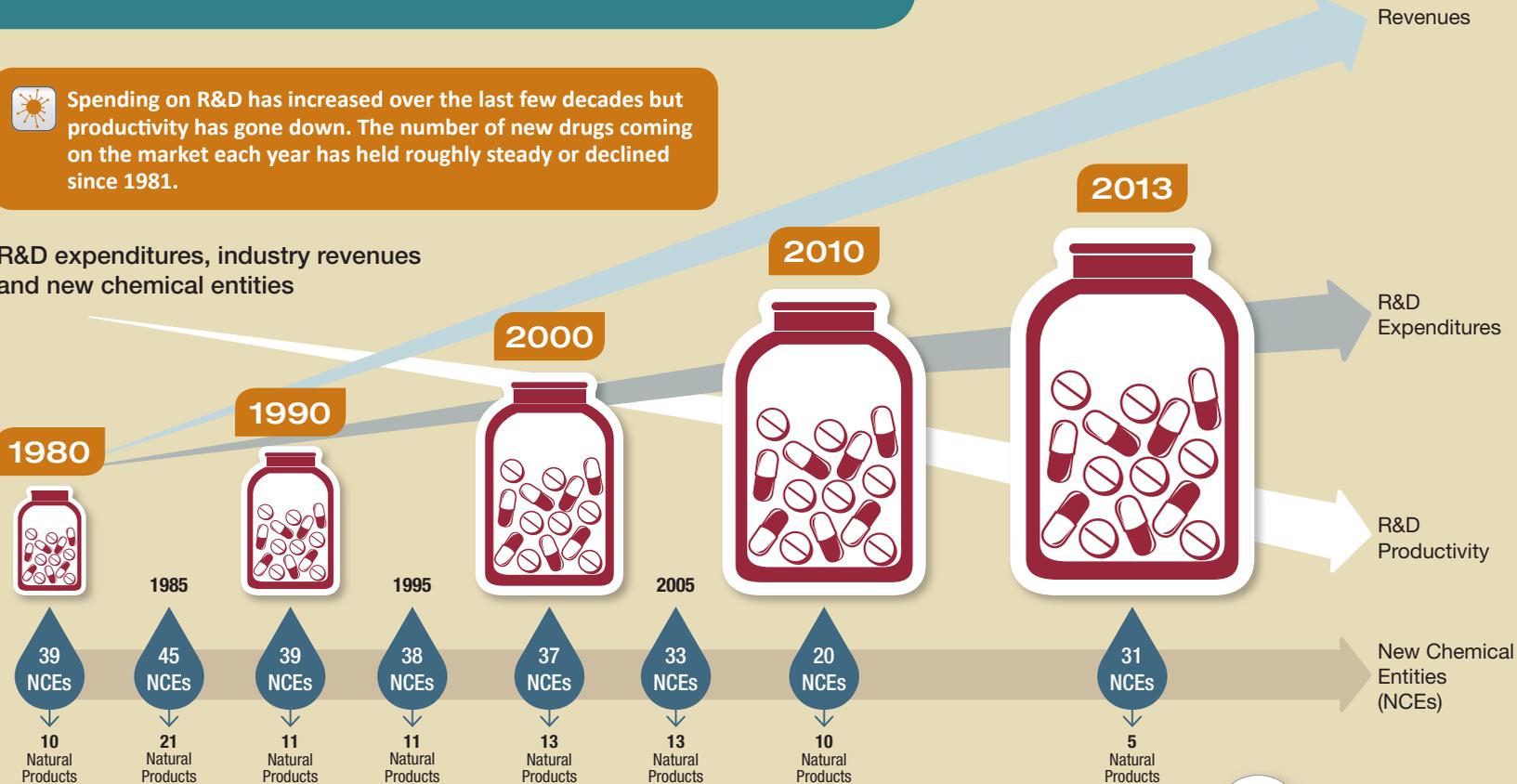
GENERIC 63%

OTHER 11%

TRENDS IN RESEARCH AND DEVELOPMENT

Spending on R&D has increased over the last few decades but productivity has gone down. The number of new drugs coming on the market each year has held roughly steady or declined since 1981.

R&D expenditures, industry revenues and new chemical entities



Government contributions to pharmaceutical R&D remain high across the globe. In the US, for example, government funding contributed to 48% of all drugs approved by the FDA and 65% of drugs that received priority review between 1988-2005.

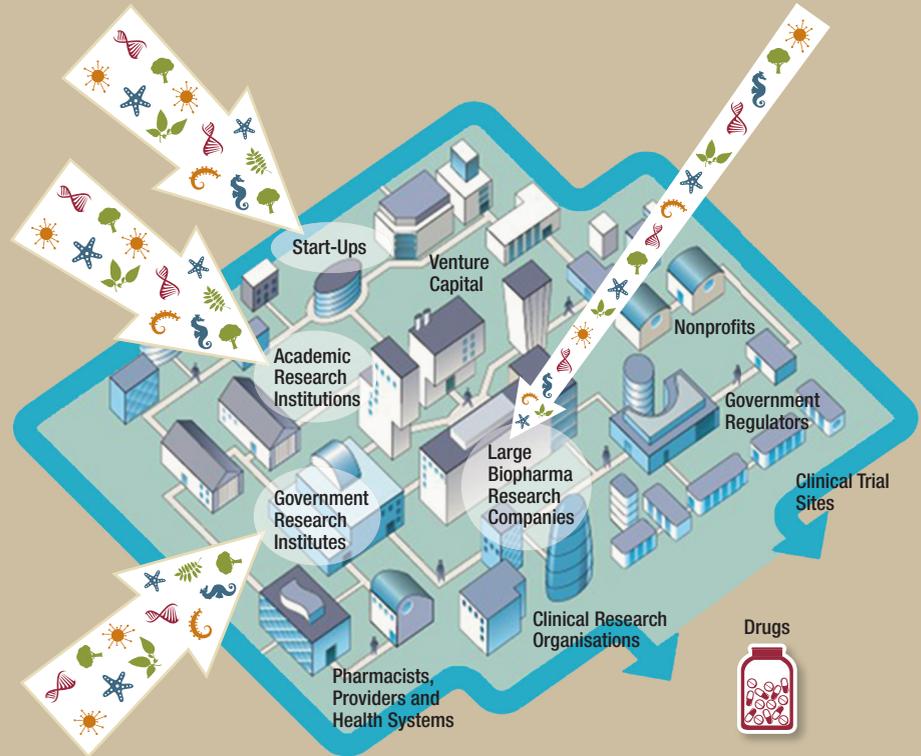
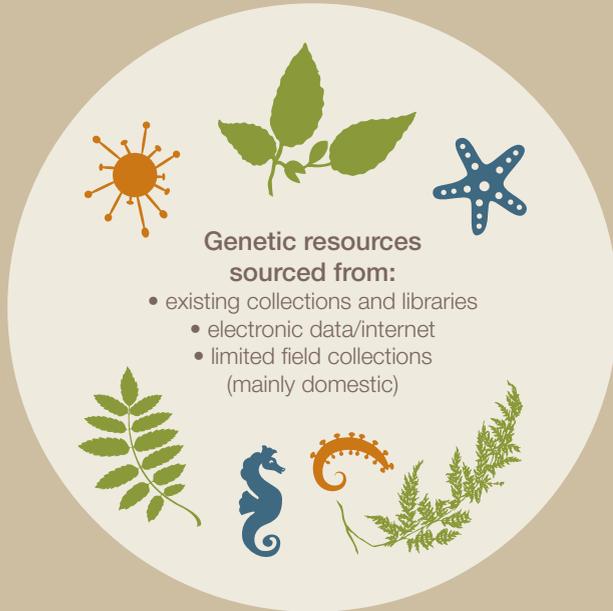
Public and industry biomedical R&D expenditures, 2012 (USD billion)





Drug discovery, including that on natural products, is increasingly done in smaller start-up companies, academia and government laboratories, with large companies undertaking development and marketing.

The ecosystem of life sciences R&D



“ We can work here, and collect microorganisms from marine water and soil in our local environment. In any microenvironment the vast majority of bacteria are for the most part unknown. This wouldn't apply to extreme environments that tend to select for very specific types of bacteria. When I worked at Lederle, anyone who went on a trip was given a plastic bag to collect soil samples. But now we know we can find spectacular microbial diversity here. This wouldn't be true for plants, but it is definitely true for microorganisms. It would take us lifetimes to sort through what we can get our hands on from this region, so there is no need to collect overseas.

– Chief Scientific Officer, small biotech company in the US

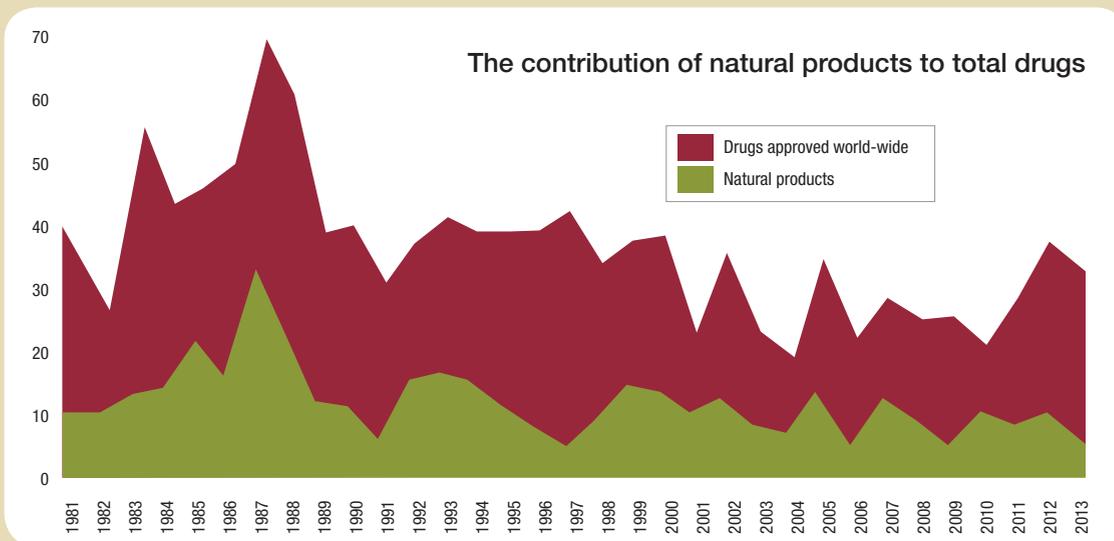
“ Collaborations provide a biotechnology company with money and resources while providing the pharmaceutical company access to cutting-edge technologies. In addition, by collaborating with multiple partners, pharmaceutical companies today decentralise parts of their R&D activities. This decentralisation provides a mechanism by which companies can (1) evaluate multiple new platform or product opportunities without increasing the size and cost of their own operations and (2) effectively increase the bandwidth of their operations.

– Phil Kearney, Director of Licensing and External Research, Merck Sharp and Dohme

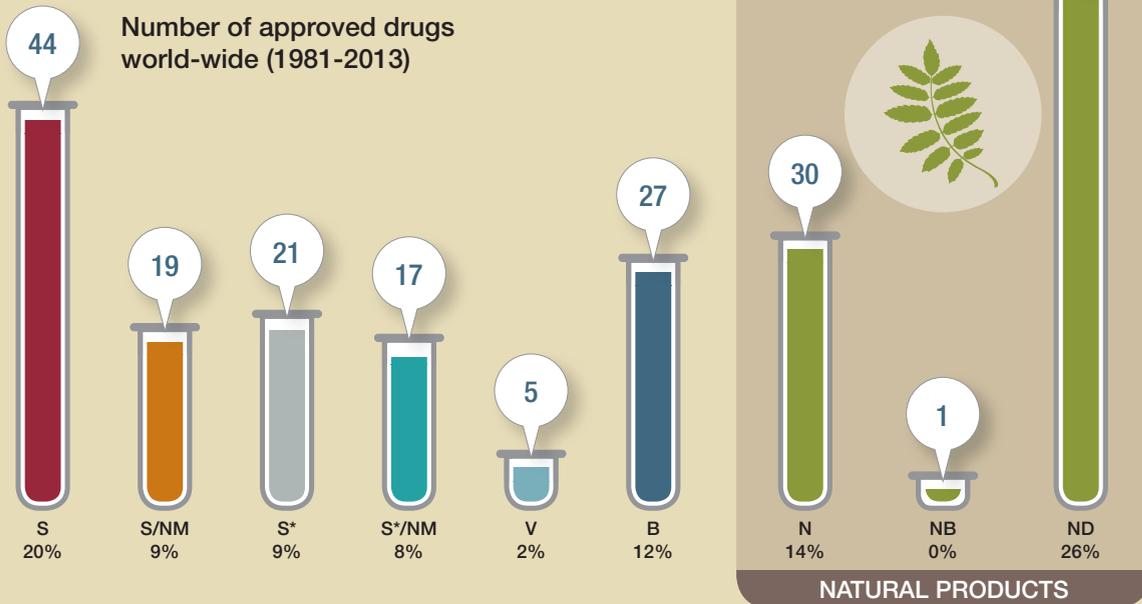
NATURAL PRODUCTS RESEARCH



Although support for natural products research in large companies has declined, the contribution of natural products to the development of new drugs continues, and between 1981-2013 an average of 31% of all new drugs annually were natural products.



44 Number of approved drugs world-wide (1981-2013)

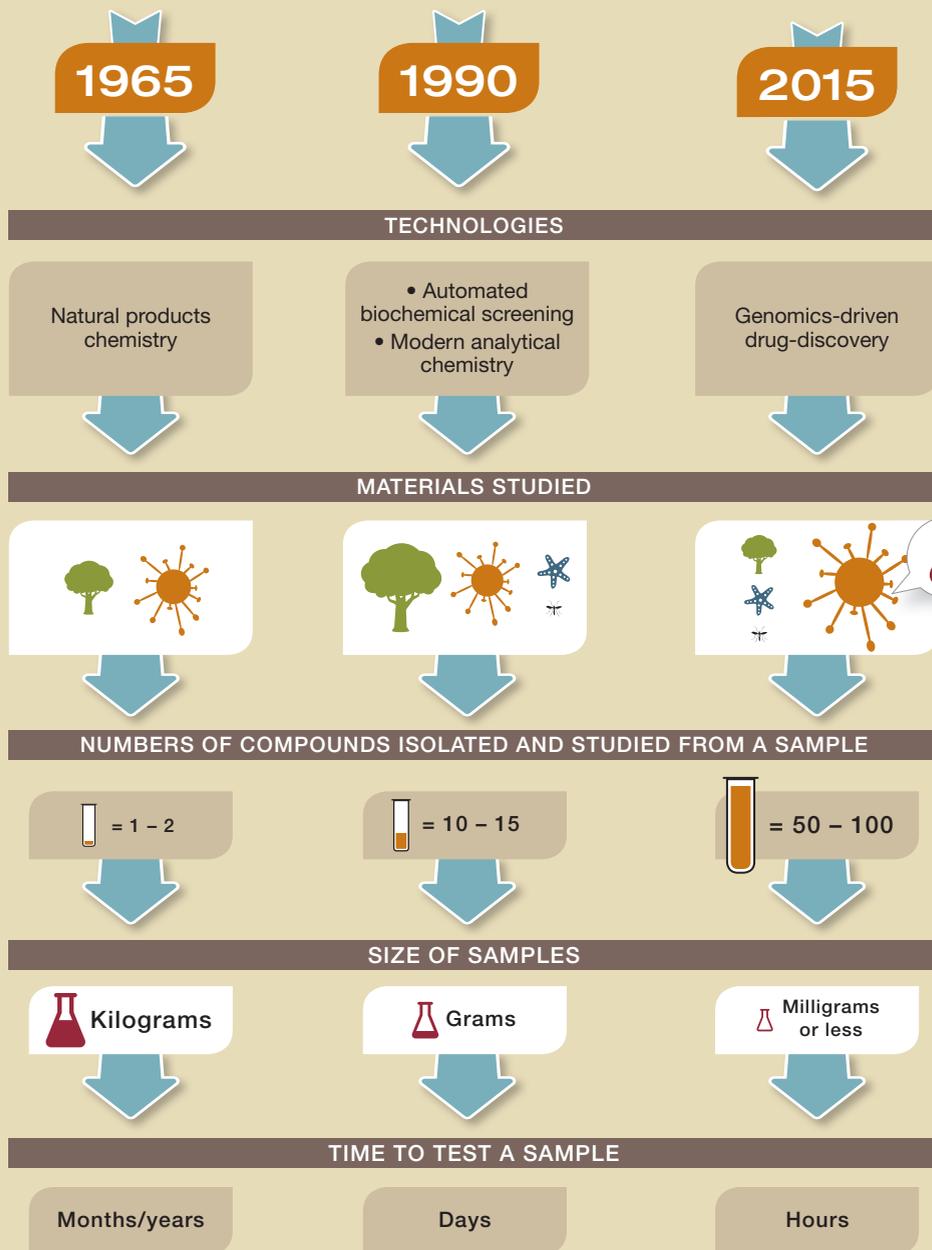


KEY

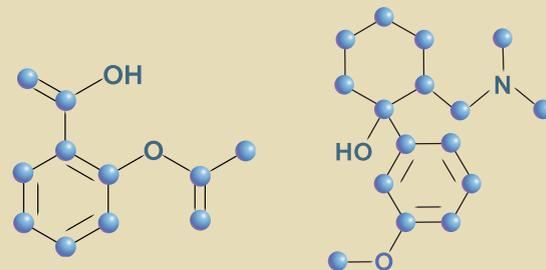
S	Totally synthetic drug, often found by random screening/modification of an existing agent
S/NM	Totally synthetic drug/Natural Product mimic
S*	Made by total synthesis, but the pharmacophore is/was from a Natural Product
S*/NM	Made by total synthesis, but the pharmacophore is/was from a Natural Product/Natural Product mimic
V	Vaccine
B	Biological; usually a large (>45 residues) peptide or protein either isolated from an organism/cell line or produced by biotechnological means in a surrogate host
N	Natural Product
NB	Natural Product 'botanical' (in general these have been recently approved)
ND	Derived from a Natural Product and is usually a semisynthetic modification

Source: Newman and Cragg, 2012

TRENDS IN NATURAL PRODUCT RESEARCH AND DRUG DISCOVERY



Natural products research has undergone dramatic changes in the last 50 years, with significant implications for the speed, scale and focus of R&D, and the design of effective ABS measures.



“

The approach we are using more and more, and now predominantly, is to leverage the biosynthetic pathways in microorganisms to address chemical problems in terms of drug discovery, and to find new compounds, or even old compounds, and then to use genetic engineering to change those compounds to make them better drug candidates. This is really the trend in natural product science... The days of going out and collecting things – whether sponges, plants, or soil samples for microorganisms – and searching for new chemicals for drug leads on a mass scale by turning the crank a lot, those days are behind us. There is still value there, but we need to be smarter about how we do this. Over the last 10-15 years the scientific community has come to realise that the real value in organisms is the genes that enable organisms to make the compounds that they do. Bioprospecting in the 1990s emphasised the organism, but it really isn't the organism anymore, it is the genes, and we need to incorporate this into our models for benefit-sharing.

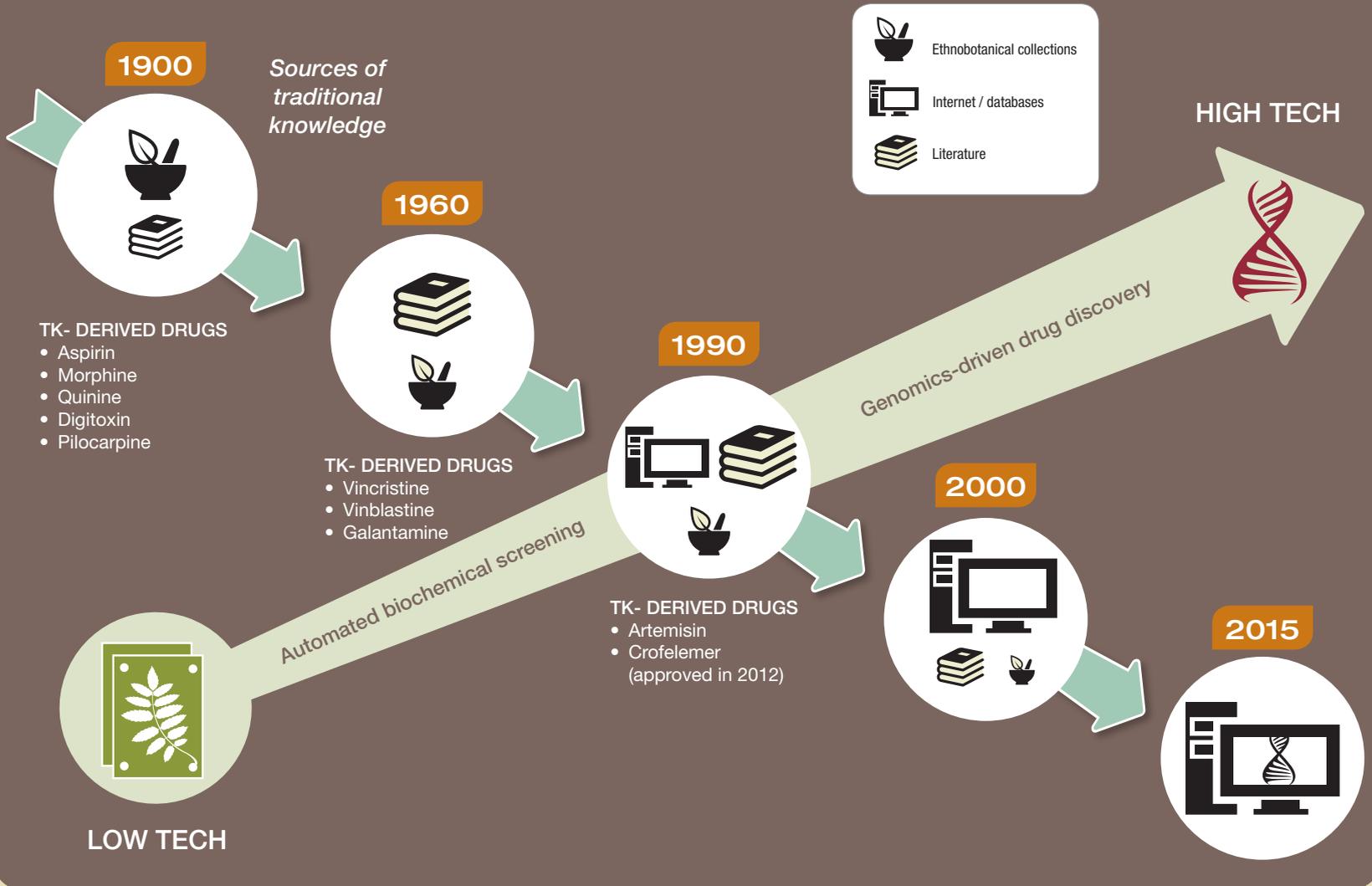
– Head of Natural Products Unit, large pharmaceutical company



Traditional knowledge, once the primary lead for the discovery of new medicines, is no longer a significant part of industry R&D.



Use of traditional knowledge in drug development





The pharmaceutical industry is more aware of the Convention on Biological Diversity than many other sectors, although this is more the case with larger companies than with smaller. However, many concerns persist within industry about legal certainty and the need for new measures drafted to implement the Nagoya Protocol to reflect the scientific, business and legal realities of natural products research today.



The CBD has had a cooling effect on natural products research, but it will not stop a company from going forward. There are ways to work with the treaty, the best being working directly with academic and other partners... Our collaborators do the work to get the agreements in place and so it isn't too cumbersome and we came up with a good agreement. The real test of the agreement didn't happen because we didn't get a drug out of it... But we could operate, the research could continue.

– Head of Natural Products,
large pharmaceutical company



I've always maintained that natural product drug discovery and development is an international collaborative effort – no one country is dominant. That is why I think if source countries can develop viable and not too restrictive policies this can be a win-win situation for everyone. If policies are too restrictive, particularly with microbes as a source of new chemistry and potential new drugs, companies will just study the microbial resources they have in their libraries or their own backyards. The microbial area makes protecting countries' rights very tricky, since companies can find compounds discovered in microorganisms from one country in another – much more so than for plants. This is why NCI's policy has always been that the place where the original collection and discovery was made is the one that should benefit, and this is even more important today.

– Gordon Cragg, retired from Natural Products Branch,
US National Cancer Institute

SOURCES

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IMS Health, 2013. Pharmmerging Markets: Picking a Pathway to Success; IMS, 2014. Global Outlook for Medicines through 2018; Pharmaceutical Executive, 2014. Pharma 50 Insight: The Accelerating Growth of Specialty Markets; Van Arnum, P. 2014. IMS Offers a Subdued Outlook for Global Pharmaceutical Industry at DCAT Week '14. DCAT Connect, March 25; Datamonitor, 2009. Big Pharma Mega-Mergers 1995-2014; Baum, R. 2011. Changing Pharmaceutical Paradigms. Chemical and Engineering News, October 4; Kearney, P. 2011. What is the Future for the Big Pharma Model? AFG Venture Group Dispatches.

Page 4

Newman, D.J. 2015. pers. com.; IMS Health, 2013. Thought Leadership, September; IMS Health, 2014. Top 20 Global Products 2013; IMS Health, 2014. Global Outlook for Medicines through 2018; Kearney, P. 2011. What is the Future for the Big Pharma Model? AFG Venture Group Dispatches; Noor, W. 2014. The Long Tail. PharmExec.com; Pharma Voice, 2014. Specialty Drugs: An Evolving Commercial Model; Van Arnum, P. 2014. IMS Offers a Subdued Outlook for Global Pharmaceutical Industry at DCAT Week '14. DCAT Connect, March 25.

Page 5

IMS Institute for Healthcare Informatics, 2013; www.drug.com, 2014; IMS Health, 2014; Staton, T. 2014. The Top 10 Patent Losses of 2015, FiercePharma, www.fiercepharma.com, December 17; Krishnan, A. 2011, Drug Patents Expiration in 2011 and 2012 – A Bumpy Ride Ahead for Big Pharma as Big Drugs Lose Patent Protection. IHS Healthcare, pharma blog; Alazraki, M. 2011. The 10 Biggest-Selling Drugs that Are About to Lose Their Patent, February, www.dailyfinance.com.

Page 6

PhRMA, 2015, www.phrma.org; Chakma, J., Sun, G.H., Steinberg, J.D., Sammut, S.M. and Jagsi, R. 2014. Asia's Ascent – Global Trends in Biomedical R&D Expenditures. The New England Journal of Medicine 370(1):3-6; EFPIA, 2014. www.efpia.eu; Shah, A. 2014. Pfizer and AstraZeneca: Innovation Will Not Follow Acquisition. Seeking Alpha, May; Newman, D.J. and Cragg, G.M. 2012. Natural Products as Sources of New Drugs over the 30 Years from 1981 to 2010. Journal of Natural Products. www.pubs.acs.org/jnp.

Page 7

PhRMA, 2015. www.phrma.org; Kearney, P. 2011. What is the Future for the Big Pharma Model? AFG Venture Group Dispatches; Noor, W. 2014. Pharm Exec's Pharma 50 in 2014. PharmExec.com, June 9.

Page 8

Newman, D.J. and Cragg, G.M. 2012. Natural Products as Sources of New Drugs over the 30 Years from 1981 to 2010. Journal of Natural Products. www.pubs.acs.org/jnp; Newman, D.J. and Cragg, G.M. in press.



www.abs-initiative.info



www.bio-economy.org.za



www.peopleandplants.org

The Access and Benefit-Sharing Key Points for Policy-Makers series has been produced to provide governments, companies, researchers, communities and others with background information to assist with the development of access and benefit-sharing measures to implement the Nagoya Protocol. The briefs are organised around central, key points on trends and practices in markets, research and development, and ABS. More detailed information on these sectors can be found at: www.bio-economy.org.za; www.abs-initiative.info; www.peopleandplants.org; CBD Bioscience at a Crossroads policy briefs: <https://www.cbd.int/abs/policy-brief/default.shtml/>; and in the upcoming book: <http://www.routledge.com/books/details/9781138779099/>

Acknowledgements: Sincere thanks are due to the many individuals who contributed comments and insights to the pharmaceutical industry brief. In particular, we would like to thank Bruno David, Gordon Cragg, Frank Koehn, David Newman and Sheo Singh. Thanks are also due to Paula Wood for her design and Jaci van Niekerk for her support and assistance in this process.

For further information please contact:
abs-initiative@giz.de