How to discover drugs ?

- ***Screening for activities, computational biology***

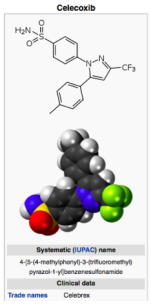
(large databases of structures, however no function)

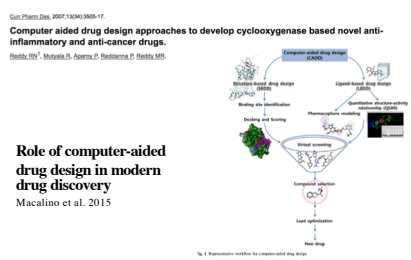
- ***Rational Drug Design***
  - **rational drug design** or more simply rational design, is the inventive process of finding new medications based on the knowledge of a biological target
- ***reverse vaccinology: when there is a need, fast response !***
  - **SARS CoV2**

High-Throughput Screening

- **High-throughput screening (HTS)** is a method for scientific experimentation especially used in drug discovery and relevant to the fields of biology and chemistry. Using robotics, data processing and control software, liquid handling devices, and sensitive detectors, High-Throughput Screening allows a researcher to quickly conduct millions of chemical, genetic or pharmacological tests. Through this process one can rapidly identify active compounds, antibodies or genes which modulate a particular biomolecular pathway. The results of these experiments provide starting points for drug design and for understanding the interaction or role of a particular biochemical process in biology
- 100,000 compounds per day.

ex: Cyclooxygenase inhibitor COX2 inhibitor (Celebrex®)





Fischer J, Ganellin CR (2006). **Analogue-based Drug Discovery**. John Wiley & Sons. p. 522

CONCLUSION

- Pharmaceutical innovation is a long and complex process.
- The pharmaceutical industry is a heavy industry with "blockbusters", flagship drugs that allow industries to earn billions, however
- Manufacturers are not interested in diseases but in the **drug markets**: there are rare diseases for which there are too few patients, hence the: "drug neglected diseases initiative" DNDI, moreover production of all drugs for environmental and economical reasons, switched to Asia
- The loss of environmental quality will creates a large « exposome » that shows how toxic our environement is

Drug neglected diseases initiative » DNDI

- Federation of public-private means to tackle these diseases
- In addition there is more and more opposition from public health NGOs to the practice of patents and licenses given the problems that exist in certain countries which cannot pay the royalties and decide to overrule manufacturers by manufacturing without a license
- (ex: **HAART**= highly active antiretroviral tritherapies)

Health Aff (Millwood). 2009 Jul-Aug;28(4):1103-13. doi: 10.1377/hlthaff.28.4.1103.

AIDS treatment in Brazil: impacts and challenges.

Nunn AS[1], da Fonseca EM, Bastos FI, Gruskin S.

Chapter 5
Brief History of french, Euro and US pharma industry

Context of the growth of the drug industry in France

- Until 2005: 5-7% annual growth since 2006: only 1% annual growth
- Sector concentration
- Closure of 140 Laboratories in 20 years or mergers and acquisitions in France
- Why such a decline?

The French pharmaceutical industry, yesterday and today Yesterday: Rhône-Poulenc

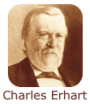
- Etienne Poulenc, born in 1823 enters as son-in-law in a business of mineral compresses for photography and therapy. He creates a factory in Ivry-Port. His three sons take over. One of the sons, Camille, engages in organic chemistry, thanks to strong research (Ivry-center). He established a new factory in Vitry in 1914, which supplied the armed forces with chemical and therapeutic products.
- In Lyon, a certain Debar founded in 1801 an import counter for dye extracts for textiles. Given increasing supply difficulties (Mexico, Brazil, Bengal) and the emergence of new technologies, he launched into artificial colors. Her nephew, Gilliard, teams up with a Swiss chemist to produce these dyes, then creates a factory in Saint-Fons, south of Lyon. The production of raw materials for powders and explosives rose from 4 tonnes / day in 1914 to 100 tonnes / day in 1917
- In 1928, a merger between Poulenc frères and the factories of the Rhône took place. Research is developing: plastics, artificial textiles, outlets in pharmaceuticals continue…

The French pharmaceutical industry, yesterday and today Today: Sanofi-Aventis

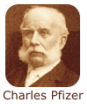
- Sanofi: the pharmaceutical group Elf, created and structured in 1973 a new pharmaceutical branch through the takeover of small laboratories (Labaz, Francis (IT), Moehs (ES)) active in basic and specialty chemicals (Clin-Midy) and vaccines (Institut Pasteur Production). The network already had 125 companies, 60 of which were abroad in 1982.
- Aventis: In Romainville, Genevoix had created a pharmaceutical factory in 1830. Mr. Roussel, business manager, produces blood products in the horse (Ecuries de Romainville). A pharmaceutical group, Roussel-Uclaf is created, which merged in 1973 with the German laboratory Hoechst, itself merging with the American Marion, and the whole will be taken over by Rhône-Poulenc who will have married Rorer (Rhône-Poulenc- Rorer) which will give Aventis
- Sanofi-Aventis will arise from the merger of the two. Pasteur-Mérieux Serums and Vaccines will become Sanofi-Aventis-Pasteur, one of the world leaders in vaccines

The American pharmaceutical industry: a giant -Pfizer

- Founded by **Charles Pfizer** and **Charles Erhart** in 1849



Charles Erhart (1821-1891)



Charles Pfizer (1824-1906)

42nd Str.

NYC

A year after arriving in New York from Germany in 1848, chemist Charles Pfizer joined forces with his cousin, confectioner Charles Erhart, to found the Chas in Brooklyn. Pfizer and Company Inc., a company specializing in chemicals, including tartar, borax and refined camphor. The company's first drug, santonin, was used as a dewormer. In 1868, the company moved to larger premises on Maiden Lane in the Wall Street neighborhood of Manhattan

Penicillin, an opportunity for Pfizer (and others ...)

- The start of the Second World War made the need for the development of a medicine to fight infections a pressing need. In 1928, in London, Sir Alexander Fleming had discovered penicillin. But, lacking a process to synthesize it in large quantities, it remained a simple laboratory curiosity..
- Several American companies are mobilized to solve the problem and, in 1942, the year when Pfizer was listed on the Stock Exchange, the company used its **fermentation expertise** to become the first to carry out mass production of this drug. Shortly after the Normandy landings, the miracle cure was used to treat the Allied forces and the world was propelled into the era of modern pharmacy
- In 1945, Pfizer was the world's largest producer of **penicillin** and encouraged its researchers to discover other microorganisms to fight infections. In 1959, after carrying out more than 20 million analyzes on some 135,000 soil samples from sites all around the globe, Pfizer launched the new antibiotic **Terramycin** - the first drug resulting from systematic research by Pfizer

Expansion, entry into vaccines

- In 1951, Pfizer began a decade of expansion around the world, including in Canada, in 1953. In 1959, it moved into the new premises of its global headquarters on 42nd Street East, in Manhattan, where it is located
- In the early 1960s, Pfizer was the main manufacturer of the new **oral polio vaccine**, the Salk vaccine. This vaccine is administered to some 60 million people and eliminates the fear of contracting this disease in North America. Simply called "Pfizer Inc", the company continued to develop innovative drugs throughout the 1970s and 1980s. Its sustained growth was further increased with the acquisition of Warner-Lambert in June 2000 and that of Pharmacia in 2003
- **The massive investment in research and development has enabled Pfizer to produce some of the most important current drugs and to spark ideas that will underpin the main treatments of the future. And with its ongoing commitment to improving health that translates into unwavering support for research and innovation, Pfizer will remain one of the world's leading pharmaceutical companies**.

Ensuring Survival in Times of Crisis: The Purchase of Wyeth (2009)

HEALTHCARE INNOVATION JANUARY 26, 2009 / 1:51 AM / UPDATED 13 YEARS AGO

Pfizer to buy Wyeth for $68 billion

- Threat of fall in turnover with loss of patent for Lipitor® / Tahor® $ 7.2 billion (USA, 2007), $ 7.85 billion (USA, 2006)
- Revenues from Lipitor fell further by 8% in Q4 2008 ($ 3.1 billion worldwide) compared to Q4 2007. In the US, Lipitor generated $ 1.6 billion, 13% less than compared to Q4 2007. International revenues $ 1.5 billion , (-2%). Represents 1/4 of sales
- Purchase of Wyeth: **Pneumococcal vaccines** (Prévenar®) ($ 2.5 billion in 2007)
- new products in Biotechnology Enbrel®: Etanercept is a TNF-alpha inhibitor; fusion protein associating the P75 fraction of the soluble TNF-alpha receptor with an Fc fragment of an IgG1. This medication is used in some inflammatory rheumatism in adults (RA) and children as well as in the treatment of psoriasis.

Causes of Major problems of Pharma Industry

- **Patent Losses**
- **Trial issues**
- **Delisting Generics**
- **Development**
- **Price reductions**
- **Taxes on industry turnover**
- **Greater severity of health authorities**
- **Increase in R&D costs**

- The cost of developing a new drug doubles every 5 years
- Consequence, adapt R&D, which is changing (France: 11% turnover, 4 billion euros) everything that was easy to find was found
- Analyzing new knowledge in genomics and biotechnology requires medium and long-term investments

R&D costs

- Duration of product development: 12 years
- Development cost in the 80s = 200 Million Euro
- Current development cost = between 1 to 2 Billion Euro
- Pfizer strategy for 20 years: **development of blockbusters** (turnover> $ 1 billion)
- Fixed costs: research + clinical trials (very high)
- Huge investments but significant profitability as soon as fixed costs were covered by the proceeds of sales
  - Cost of producing an additional marginal box compared to the sale price
  - Very high marketing costs (France = 15,000 VM, 1 for 10 Practitioners)
  - products targeted at **mass pathologies** (hypertension, cholesterol, diabetes)

PFIZER AND BIONTECH ANNOUNCE FURTHER DETAILS ON COLLABORATION TO ACCELERATE GLOBAL COVID-19 VACCINE DEVELOPMENT

BioNTech GMP-certified mRNA manufacturing facilities in Europe

Pfizer scale-up manufacturing capacity

Pfizer will pay BioNTech $185 million upfront payments: $72 million cash and an equity investment of $113

milestone payments of up to $563 million for a potential total consideration of $748 million

Pfizer and BioNTech will share development costs equally.
Initially, Pfizer will fund 100 percent of the development costs, and BioNTech will repay Pfizer its 50 percent share of these costs during the commercialization of the vaccine.

BIONTECH

mRNA-based therapeutics--developing a new class of drugs

Some bitter failures ... and/or recent

- **Merck** Pain killer **Vioxx 2004**
  - Merck yanked Vioxx on Sept. 30 because a new study had found a higher rate of heart attacks and strokes in patients taking the drug than in those on a placebo. The move was a stunning denouement for a blockbuster drug that had been marketed in more than 80 countries with worldwide sales totaling $2.5 billion in 2003.
- **Pfizer** antiinflammatory **Bextra 2003**
  - Pfizer Agrees To Suspend Bextra Sales Due To FDA Risk Assessment For Rare But Serious Skin Reactions (New York - April 07, 2005) valdecoxib / NSAIDs
- **Sanofi-Aventis** antiobesity **Accomplia 2007**
  - rimonabant does not obtain its market authorization in the USA

- **Merck et Schering-Plough: anticholesterol Vytorin/Inegy 2008**
  - simvastatine + zetia not more efficient than simvastatine

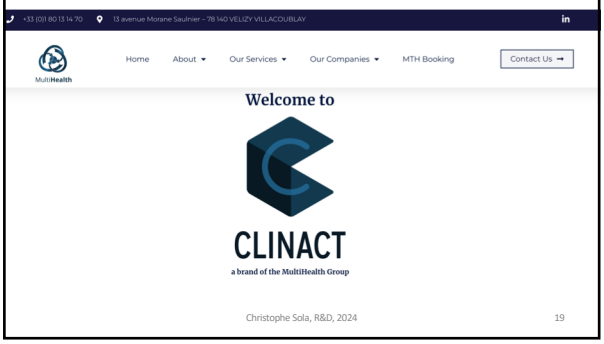
Chapter 6
What are CROs ? some CROs

AFCROs LES ENTREPRISES DE LA RECHERCHE CLINIQUE

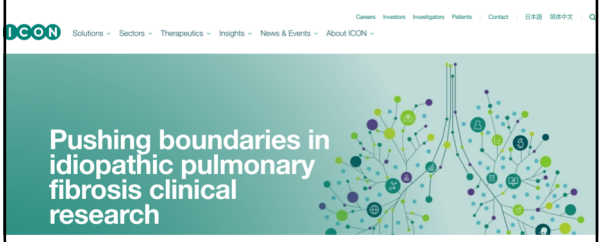
Accueil | Qui sommes-nous ? | Groupes de travail | Evènements | Devenir adhérent | Presse | Formations | Forum | Newsletters AFCROs

https://www.afcros.com/

https://multihealthgroup.com/clinact/ (groupe MultiHealth)

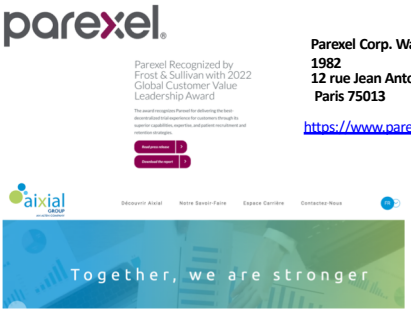


birth in 1990 (iconplc.com)



https://www.iconplc.com/

Icon Clinical Research

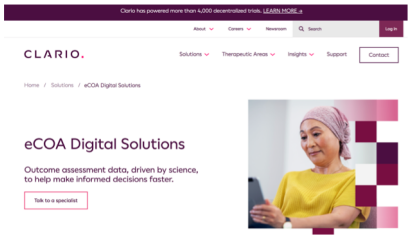


Parexel Corp. Waltham
1982
12 rue Jean Antoine de Baif
Paris 75013

https://www.parexel.com

Boulogne Billancourt
4 rue Danjou – Bâtiment B
92513 Boulogne-Billancourt Cedex
FRANCE T : +33 1 46 08 89 00

https://www.aixialgroup.com/
-biométrie
-affaires réglementaires
-vigilance



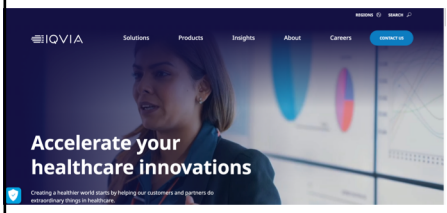
https://www.bioclinica.com/ in 2023 now https://www.clario.com/

21 employees
16 rue Montbrillant
69003 Lyon

RCTS, Vaulx en Velin, 69, 25 ans
39 rue du Plat, 69002 Lyon

https://www.rcts.fr/

https://www.iqvia.com. (formerly **Quintiles**)



IMS Health and Quintiles are now IQVIA

DMP= Dossier Médical Personnalisé

FORTUNE World's Most Admired Companies 2018

Optimed, Gières, 38, member of EUROFINS
https://www.eurofins.com/contact-us/worldwide-interactive-map/france/eurofins-optimed-clinical-research/

Mission TEC, Toulouse, 31

https://www.mission-tec.fr

MedPass, Paris
https://www.devicemed.fr/fournisseur/medpass-international

MedPass International
95 bis boulevard Pereire
75017 Paris
France

http://www.medpass.org

Contact :
Sarah SORREL
+33 (0)1 42 12 83 30
Medpass-NBD@medpass.org

Mediaxe, Clamart, 92 https://www.mediaxe.fr/

Chapter 7
R&D strategy
Agro Business versus Drug business
***What are the differences* ?**

History

- Drug industry in France historically comes from little behind-the-counter business, versus chemical heavy business (Germany).
- Compared to Germany, less SMEs in France (actually lot of Medium/big Size companies, start-up are more numerous in France)
- Agro-business comes from **Agriculture** = **Two different cultural worlds**
- USA is a world-wide leader in Pharma, Swiss is also an important political and major player too.
- Agriculture is of highly strategic economical interest for all countries (Carrefour versus « couche-tard... »)
- Drug industry too (sovereignty) as seen during the Covid crisis and today (drug shortage).

How to increase R&D Efficiency in Big Pharma ?

Schuhmacher et al. J Transl Med (2016) 14:105
DOI 10.1186/s12967-016-0838-4

Journal of Translational Medicine

REVIEW Open Access

Changing R&D models in research-based pharmaceutical companies

Alexander Schuhmacher[1*], Oliver Gassmann[2] and Markus Hinder[3]

(A) Activities to reduce portfolio and project risk
(B) activities to reduce R&D costs
(C) activities to increase the innovation potential.

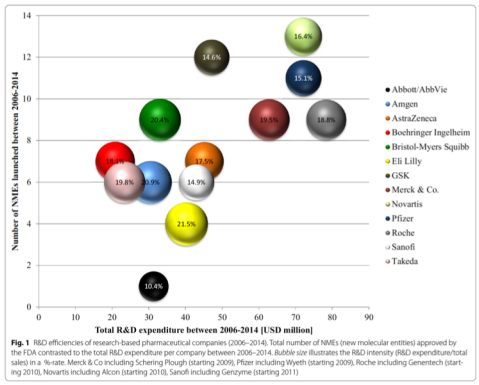


Fig. 1 R&D efficiencies of research-based pharmaceutical companies (2006–2014). Total number of NMEs (new molecular entities) approved by the FDA contrasted to the total R&D expenditure per company between 2006–2014. *Bubble size* illustrates the R&D intensity (R&D expenditure/total sales) in a %-rate. Merck & Co including Schering Plough (starting 2009), Pfizer including Wyeth (starting 2009), Roche including Genentech (starting 2010), Novartis including Alcon (starting 2010), Sanofi including Genzyme (starting 2011)

 Schuhmacher et al. 2016

The 'innovation gap' haunts Big Pharma, and the race is on for the next blockbusters

The next big innovation wave is out there, and as pharmas expect massive losses without enough internal R&D to fill those shoes, smaller biotechs beckon.

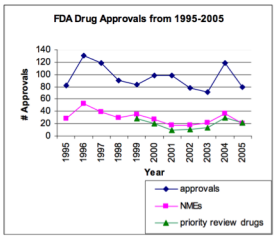


Figure 1 FDA drug approvals have remained flat

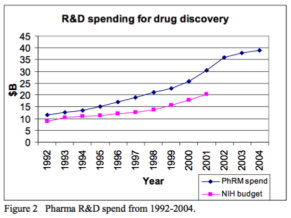
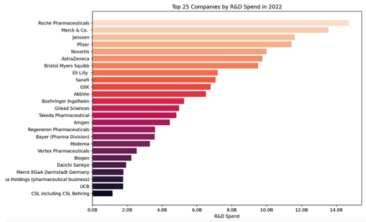


Figure 2 Pharma R&D spend from 1992-2004.

https://www.pharmavoice.com/news/innovation-gap-pharma-blockbuster-drug-biotech/622804/
https://citeseerx.ist.psu.edu/document?repid=rep1&type=pdf&doi=b3b23901ff6b8f3726f819d9d6e7336f2a545244

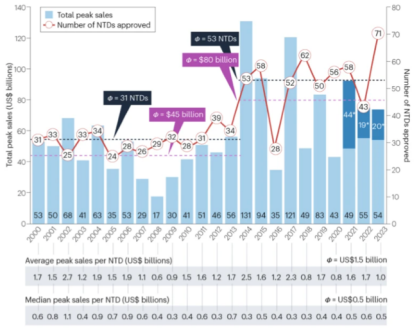
Pharma's top 20 R&D spenders in 2021.

Companies	R&D Spend	R&D as a percentage of revenue
1. Pfizer	$13,829,000,000	17.0%
2. Roche Pharmaceuticals (division of Roche Group)	$13,342,082,240	27.1%



2022

https://www.drugdiscovertrends.com/top-pharma-rd-spenders-2022/



M. Baedecker et al. 2024 and https://doi.org/10.1038/d41573-023-00001-3

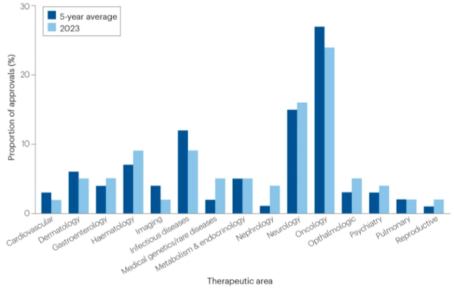


Fig. 2 | CDER approvals by therapeutic area. Indications that span multiple therapeutic areas are classified under only one, based on which FDA office and division reviewed the approval application. Sources: *Nature Reviews Drug Discovery*, FDA

M. Baedecke et al. and https://doi.org/10.1038/d41573-023-00001-3

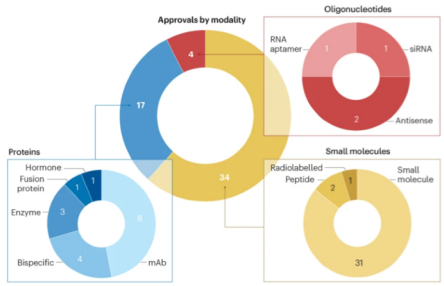


Fig. 3 | CDER approvals by modality. Small molecules, including peptides of up to 40 amino acids in length, and oligonucleotides are approved as new molecular entities (NMEs). Protein-based candidates are approved through biologics license applications (BLAs). mAb, monoclonal antibody; siRNA, small interfering RNA. Source: *Nature Reviews Drug Discovery*.

M. Baedecker et al. or https://doi.org/10.1038/d41573-023-00001-3

Food companies global R&D spending lowest among top sectors

By Ahmed ElAmin III, 12-Dec-2005

Related tags: research and development, Unilever, Nestle

Related topics: Supply Chain

The food industry continues to sit at the bottom of the pile when it comes to investing in research and development, an annual study shows.

The study, published every year by the European Commission, shows food producers worldwide are still last on the list of the top 15 sectors when it comes to spending on R&D, even as their sales continue to show sluggish growth in many markets.

The relatively low spend also contrasts with the size of the sector. For example it is the largest manufacturing sector in the EU.

RELATED NEWS:

Oil cost squeezes Kerry's margins

Industry to hold science pow-wow on innovation research

Royal Cosun announces indicative 2006 sugar beet price

Teagasc pushes Ireland towards greater food innovation

pharma R&D budget
= **10 x** Agro-Food R&D

Food Companies Continue to Spend on R&D as Plant-Based Food Movement Rages On

FN Media Group Presents Microsmallcap.com Market Commentary

NEWS PROVIDED BY
Microsmallcap.com →
23 Dec, 2020, 08:50 ET

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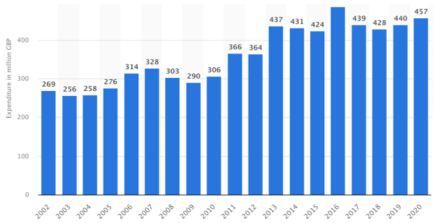
Food Research
Call to Action on Funding and Priorities

https://www.ift.org/-/media/policy-advocacy/files/ift-whitepaper-012720final.pdf

In 2018, total private industry R&D expenditures for agriculture and food were **$20.7 billion in the U.S. and $6.7 billion in the EU**

In 2021, research and development spending in the pharmaceutical industry totaled some **238 billion U.S. dollars** globally. 24 oct. 2022



Research and development expenditure in food, beverages and tobacco product businesses in the United Kingdom (UK) from 2002 to 2020

https://www.statista.com/statistics/411117/food-beverages-tobacco-united-kingdom-uk-research-and-development-spend/

What Is R&D In The Food And Beverage Industry?

- Developing new ingredients or formulas
- Creating a new flavour or product range
- Improving the food or drink's nutritional content, taste or texture
- Developing new samples or prototypes
- Devising ways to cut costs without reducing product quality
- Creating healthier product lines, i.e products with less fat or sugar
- Coming up with ways to more sustainably package and transport a product
- Devising ways to lengthen a product's shelf life
- Developing better ways to minimise contamination
- Coming up with innovative ways to deal with scrap, spoilage and waste

The use of sustainably-sourced ingredients

Targeted marketing

Reducing waste

1. New, not just improved products
2. Increased speed to market
3. Products in response to pandemic
4. Targeted health claim marketing
5. Waste reduction
6. Sustainable ingredients

https://www.myriadassociates.ie/news/2020/what-is-rd-in-the-food-and-beverage-industry

https://www.grandeciq.com/blog/rd-innovations-in-food-and-beverage-manufacturing

United States Department of Agriculture

USDA

Economic Research Service

Research Investments and Market Structure in the Food Processing, Agricultural Input, and Biofuel Industries Worldwide

Economic Research Report Number 130
December 2011

Keith O. Fuglie
Paul W. Heisey
John L. King
Carl E. Pray
Kelly Day-Rubenstein
David Schimmelpfennig
Sun Ling Wang
Rupa Karmarkar-Deshmukh

https://www.researchgate.net/publication/292384143_Research_investments_and_market_structure_in_the_food_processing_agricultural_input_and_biofuel_industries_worldwide

main conclusion : « Industry concentration on the rise ».

Fuglie, Keith O., Paul W. Heisey, John L. King, Carl E. Pray, Kelly Day-Rubenstein, David Schimmelpfennig, Sun Ling Wang, and Rupa Karmarkar-Deshmukh. Research Investments and Market Structure in the Food Processing, Agricultural Input, and Biofuel Industries Worldwide. ERR-130. U.S. Dept. of Agriculture, Econ. Res. Serv. December 2011.

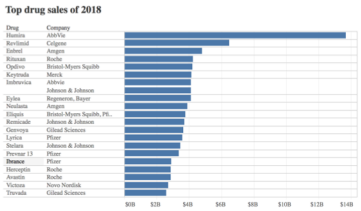
Drug Markets: from chemistry to biotechnology

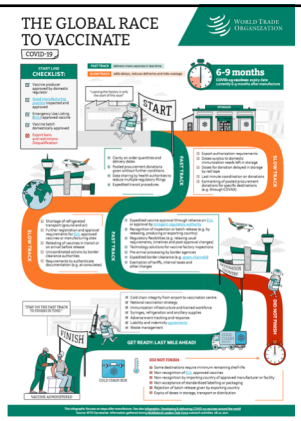
- **20** drugs in the United States accounted for $319.9 billion in sales in 2011. **Heart disease, Antiaggregant, Depression (Lipitor** 7 billion$, **Plavix** 6,8 billion$)

http://www.businessinsider.com/10-best-selling-blockbuster-drugs-2012-6?op=1#ixzz2loyf2m7D

https://www.fiercepharma.com/special-report/top-20-drugs-by-2018-u-s-sales

immunosuppressor anticancer drugs





Cultural value comparison : Food Ind.

- **Food**
  - Funny and pleasure products or commodities
  - Convivial (more Informal)
  - Creative /Product Driven
  - No tight links in teams (seed model= *Network*)
  - Branding independence
  - Finance driven : **High volumes/Low added value**
  - High differentiation of brands
  - Low added value of food safety compared to post marketed drug survey (quality is a prerequisite), i.e. controled process is insured, no health risk

Cultural value comparison : Drug Ind

- **Drug**
  - Not so Funny (keep healthy !)
  - Rigourous (more Formal)
  - Process driven (Quality/Pharmaceutical process)
  - Tight links in teams (health= death proximity)
  - Brand is less important that Firms History !
  - Finance driven =**Low to High Volume/High added value**
  - low differenciation of brands (« *me too* »)
  - **High value of Novelty**
  - **High value of Research** (even post-marketed)
  - Responsability of Pharmacosurvey teams in long lasting history of the drug, i.e. independent of drug quality, scientific risks is always present thoughout drug market history
  - High value of drug safety, i.e. surveillance must be insured , if health risk high potential financial loss

Food R&D innovation

- ***Process Innovation***
  - **Improving financial yields**

  How ?
- ***Product Innovation***
  - Marketing
  - New niche
  - New brand
  - New product

Food R&D : mainly technology ?

- ***Food technology*** is a branch of *food science which deals with the actual production processes to make foods*
- ex: **Extrusion cooking** (EC)
  - **Extrusion** is a process used to create objects of a fixed, cross-sectional profile
- ex: **Supercritical fluid extraction** (SFE)
  - decafeinated coffee

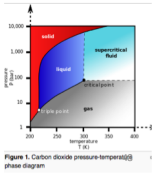


Figure 1. Carbon dioxide pressure-temperature phase diagram

Food and Ingredients : from processed to ultraprocessed food

Ultra-Processed Foods: Definitions and Policy Issues

Michael J Gibney

Institute of Food and Health, University College Dublin, Dublin, Ireland

Current development in Nutrition, 2018

« The global concern is that rising incomes, urbanization, and employment levels,the rise of consumerism, and the time scarcity that arises from long working hours together with long school and work commutes, are all contributing to the transformation of social structures, such that an increasing proportion of processed foods are consumed »

Seeds and Industry

- **Tomato seeds**

The influence of technological changes on the industrial tomato sector

Paolo DE CASTRO, Roberto DELLA CASA
Fruit and Vegetable Observatory, Nomisma, Bologna (Italy)

- Tomato harvesting methods
- Tomato ripening
- Tomato processing technology

1. ***Ketchup***, one of the most popular condiments in the US, is a half a billion dollar industry.

2. ***Ketchup*** is originally a spicy fish sauce called Ke-Tsiap from east Asia. It was brought west in the 17th century and by the early 1800's recipes for ketchup as we know it started to appear in cookbooks.

3. H.J. Heinz Company is the world leader in ***Ketchup*** sales, with a 60% market share in the US. It sells over 600 million bottles of ketchup annually.

4. Nutritionally, ***Ketchup*** , as well as other cooked tomato products, is a good source of the anti-oxidant lycopene. Lycopenes are beneficial in the prevention of prostate and colon cancers. This is one of the rare cases where cooking a raw vegetable actually improves the bio-availability of a nutrient instead of reducing it.

5. 25% of ***Ketchup*** is sugar!! Now you know why kids love it, and consider ***Ketchup*** the main part of a meal, with the rest of the food serving as a condiment.

6. ***Ketchup*** is also high in salt. a single teaspoon contains almost ten percent's worth of the daily maximum recommended value of sodium.

7. The ingredient list for Heinz ***Ketchup*** is:

Tomato Concentrate , Distilled Vinegar, High Fructose Corn Syrup, Corn Syrup, Salt, Spice, Onion Powder, Natural Flavoring.

If you were wondering why corn syrup (a cheaper sugar than table sugar) appears twice, a possible answer could be that by splitting the sugar ingredient into 2 separate ingredients, it doesn't appear in the second place in the list, psychologically reducing the fear of buying the product. We're still trying to figure out what that Natural Flavor is. Spice too.

8. The FDA strictly regulates what products may be called ***Ketchup***; especially important are viscosity and the presence of tomatoes and tomato solids.

9. In 2005, after urging by Heinz and several other tomato product manufacturers, the FDA allowed tomato product labels to tout health claims, due to the aforementioned lycopenes. The ruling includes ketchup as well as tomato pasta sauces and marinades.

10. Squeeze bottle were introduced in the 1980's to solve the problem of ***Ketchup*** not flowing out of glass containers.

11. Not everyone is a big fan of ***Ketchup***. In the Netherlands, mayonnaise is the condiment of choice with french fries.

One Health Crisis example: drug industry, the Mediator example

- **Mediator**
  - Failure of the health authorities
  - Lack of ethics of Industrial (roles mixed up)
  - Need of « *lanceur d'alerte* » (Dr. Irene Frachon)
  - Time passes…
  - Unsolved : Chronic crisis
  - Follow-up : public committes to assess individual damages

Another Health Crisis example:the Covid-19

- **No masks (change of paradigm in strategy)**

in 2013, the general Secretary of defence and nationale safety (SGDS N) published a note entitled « *Doctrine pour protéger les travailleurs contre les maladies hautement pathogènes à transmission respiratoire* » [2]. This note established that the national stock of masks as managed by EPRUS (now part of Santé publique France) concerned only surgical protective masks used by sick people and their contacts whereas the stockage of masks for workers concerns their companies, whether public or private


Haut Conseil de la santé publique

AVIS

relatif à la stratégie à adopter concernant les stocks de l'État en masques et en équipements de protection individuelle (EPI)

6 août 2021


PREMIER MINISTRE

Secrétariat général de la défense et de la sécurité nationale

Doctrine de protection des travailleurs

face aux maladies hautement pathogènes à transmission respiratoire

https://www.fmfpro.org/penurie-de-masques-aux-origines-des-decisions-d-etat/

file:///Users/christophe.sola/Downloads/hcspa20210806_strpoulestodemasetquideproinddel.pdf

Other Crisis example: Food safety

- **Germed seeds** (summer 2011)
  - Fast alert (Germany), 5 weeks.
  - Fast tracking (first accused : cumcumber)
  - Rapid diagnostics : E. coli O104:H4 (risk assessment)
  - 30 Deaths
  - Laboratory investigation (not found in seeds though)
  - Solved : acute crisis
  - Follow-up : First problem with bio agriculture