Past, Present and Future of the Pharmaceutical Sciences. A Personal View
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PHARMA 2030 – CURRENT AND FUTURE CHALLENGES
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A Joint Meeting of the Austrian Pharmaceutical Society (ÖPhG) and the Swiss Academy of Pharmaceutical Sciences (SAPhS)
What to discuss? A personal choice

• *Present state and Past performance? Impact of the Pharmaceutical Sciences*

• Did we lose something? Do we never learn? Are we too naive?

• Future: scenarios

• Emerging areas/Blurring borderlines/Science business models
General challenges for Pharma

And consequences...... for pharmaceutical scientists

Do you dare to tell guests at a birthday party that you work for pharma?
A drug made by Sanofi to treat epilepsy and bipolar disorders that was given to pregnant mothers resulted in up to 4,100 French children being born with significant birth defects, the French medical authority said yesterday.

During the 50 years from 1967-2016, between 2,150 and 4,100 children were born with at least one serious congenital disorder, after being exposed in the womb to a drug called valproate, according to a preliminary study from ANSM, France's drug regulator.

It was the first official estimate of the number of cases of birth defects linked to valproate in France. The drug has been sold in a number of global markets, including the US, China and the UK.

“The study confirms the highly teratogenic [capable of causing birth defects] nature of valproate,” Mahmoud Zureik, ANSM's scientific director and co-author of the report, told AFP news agency. “The figure of about 5,000 severe malformations is very high.”

The case has echoes of the thalidomide scandal — one of the darkest cases in pharmaceutical history — in which an estimated 10,000 children worldwide were born with malformed limbs between 1956 and 1963. Drugmakers were among those sued in the long battle to determine responsibility.

Sanofi, which from 2011 had warned the drug should not be used during pregnancy, said: “We are aware of the painful situations faced by families whose children have problems that may be related to their mother's treatment of anti-epileptic drugs during pregnancy.”

It added that as scientific knowledge on the risks associated with the use of sodium valproate, particularly during pregnancy, has increased it has been transparent with health authorities.

Valproate, introduced in France in 1967, is sold by Sanofi under the brand Depakine to treat epilepsy and as Depakote or Depamide for bipolar disorders.

The study found that the risk of major birth defects in children whose mother was treated with valproate for epilepsy was four times higher than the general population, and twice as high when the mother was treated with the same drug for a bipolar disorder. ANSM said this was because women treated for bipolar disorder were less exposed to the drug.

The US Food and Drug Administration warned healthcare professionals and women in 2013 that valproate sodium and related products, valproic acid and divalproex sodium, should not be taken during pregnancy.
IVORY TOWERS FALLING DOWN

Raise standards for preclinical cancer research

C. Glenn Begley and Lee M. Ellis propose how methods, publications and incentives must change if patients are to benefit.

……. Nevertheless, scientific findings were confirmed in only 6 (11%) cases .........

AND WHAT ABOUT ACADEMIA?

Believe it or not: how much can we rely on published data on potential drug targets?

Florian Prinz, Thomas Schlange and Khusru Asadullah
Can we do something about that?

Report commissioned by the Board of Pharmaceutical Sciences, FIP, the International Pharmaceutical Federation

Impact of the Pharmaceutical Sciences on Health Care in the last 50 years

PERSPECTIVES

Impact of the Pharmaceutical Sciences on Health Care: A Reflection over the Past 50 Years

MALCOLM ROWLAND,1,2 CHRISTIAN R. NOE,1 DENNIS A. SMITH,4,5 G. T. TUCKER,6,7 DAAN J. A. CROMMELIN,8 CARL C. PECK,2 MARIO L. ROCCI JR.,9 LUC BESANÇON,10 VINOD P. SHAH10

• Divided into six sections:
  - Drug discovery
  - ADME (absorption, distribution, metabolism, and excretion)
  - Pharmacokinetics and pharmacodynamics
  - Drug formulation (Pharmaceutics)
  - Drug regulation
  - Drug utilization
  each describing key contributions that have been made in the progression of medicines, from conception to use.

• Common thread: application of translational science to improvement of drug discovery, development and therapy.
Formulation Sciences: Timeline of introduction of key concepts and developments

MDI = metered dose inhaler
DPI = Dry powder inhalation
OROS = osmotic release oral system
EPR = enhanced permeability and retention effect
PAT/QbD = process analytical technology
Quality by design

BCS/Biowaiver

Bioavailability

Drug Targeting/ Nanoparticles/proteins

Pegylation of proteins/ nanoparticles

Transdermal


FIP 2012
Contributions of pharmaceutical sciences during past 50 years

- From description to mechanistic prediction.
- Targeting for specificity of action.
- Building druggability qualities into design.
- Optimising drugs, products, and dosage regimens for patients through PK/PD modeling.
- Building quality and reproducibility into drug delivery systems and products.
- Ensuring regulation reflects scientific developments.
- Delivering better medicines, including generics, to patients.

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Insulin and the dog
and how to move fast!

Those were the days......
Publication early 1922

Nobel prize Banting 1923

Courtesy of Alexander Florence
Oral/rectal administration of insulin was and is a challenge

Ethics: ‘Tempora mutantur et nos mutamur in illis’

To the Editor of the Lancet.

SIR,—With reference to the annotation with this heading in your issue of Feb. 23rd I should like to ask whether insulin has ever been tried by the rectum. If not, perhaps readers who are in a position to do so would try this route, giving watery or oily suspensions of small bulk after an evacuation of the lower bowel, and publishing their results.

I am, Sir, yours faithfully,
H. H. KING,
Central Research Institute, Kasauli, Major, I.M.S.
March 20th, 1924.

To the Editor of the Lancet.

SIR,—Major H. H. King will find in THE LANCET of Oct. 6th, 1923 (p. 777), that a negative result was obtained by my colleagues and myself after administering insulin per rectum in a case of diabetes. The necessary control experiments were carried out.

I am, Sir, yours faithfully,
E. P. Poulton.
Delivery of Biologicals: Do we have to stick to the needle?
Needle phobia is a recently defined medical condition that affects at least 10% of the population. The etiology of needle phobia lies in an inherited vasovagal reflex of shock, triggered by needle puncture.

- Victims of needle phobia typically experience a temporary anticipatory tachycardia and hypertension, which on needle insertion turns into a state of shock - bradycardia and hypotension, accompanied by pallor, diaphoresis, tinnitus, vaso-vagal syncope (fainting), and sometimes cardiac arrest and death.

- Because persons with needle phobia typically avoid medical care, this condition is a significant impediment in the health care system.

- That’s why a confirmed needlephobia is a reason for health insurances to incure the expenses of needlefree devices.
After all those years, still no orally administered protein medicine
THE RISE AND FALL
of MODERN MEDICINE

JAMES LE FANU, M.D.

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Did we lose something?

- The precautionary principle or precautionary approach states if an action or policy has a suspected risk of causing harm to the public or to the environment, in the absence of scientific consensus that the action or policy is harmful, the burden of proof that it is not harmful falls on those taking an action.
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• *Future: scenarios*
• Emerging areas/Blurring borderlines/Business models in science
Pharmaceutical Sciences in 202?

A scenario analysis

Daan Crommelin, Pieter Stolk, Bert Leufkens
Pharmaceutical Sciences?
Applications in the private sector

The oil industry in the early 70s, assumptions:

1. Oil would remain plentiful;
2. Prices would remain low.

But: What if an accident in Saudi Arabia led to the severing of an oil pipeline? What would happen to global supply and prices?

1973 – Yom Kippur war / oil embargo:
1979 – Iranian Revolution
1980-1988 – Iran/Iraq war
1990 – Iraq invades Kuwait
And so on…
We are not accustomed to think in exponential terms, but some developments are exactly like that...

Eroom's Law in pharmaceutical R&D. The number of new drugs approved by the FDA per billion US dollars (inflation-adjusted) spent on R&D has halved roughly every 9 years. Scannell et al., 2012

the number of transistors on integrated circuits doubles approximately every two years
A turkey before and after Thanksgiving. The history of a process over a thousand days tells you nothing about what is to happen next. The naïve projection of the future from the past can be applied to anything.
Scenario analysis

- Scenario planning is about changing minds, not making plans
- Scenarios are not forecasts
- Scenarios are learning devices to take a long view and to open mental maps
- Think the unthinkable

Charles Darwin
(1809 - 1882)

And keep in mind:
It is *not* the survival of the fittest.....
It is the survival of those who can *adapt best*
The world (of pharmaceutical sciences) out there is in a constant change anno 2009

• Rethinking the drug discovery and development process
• Therapeutic gaps are at the menu chart
• Rethinking the regulatory system
• Safety first/precautionary principle
• Payers in the hot seat
• Biologicals are changing the landscape
• Patient demand and societal mistrust
• Emerging countries
• Recessions, financial crisis

Time for an update????

About 30 experts, including: investors, industry professionals, academics, regulators, NGOs
What is the most important driver for the future?

1. Molecular biology, biomarkers, genomics
2. Information and other new (material) technologies
3. Rethinking pharma business model
4. Funding and investing models, risk sharing
5. Regulatory constraints and opportunities
6. Health care environment, payers in the hot seat
7. Therapeutic gaps, unequal access
8. Patient/public advocacy, zero risk culture, ethics
9. Demographics, longevity, chronic diseases
10. Globalization, emerging markets (BRIC countries)
11. Financial system

Update....... Add drivers
What is your number 1, 2 and 3?
Based on expert input we created 2 axes for scenario drivers

**Attitude towards treatment and prevention of diseases**

- Non-pharmacological vs Pharmacological

**Science Culture**

- Dominance of entrepreneurial science vs Dominance of vocational science
The 2 x 2 scenario matrix is the basis for the 4 scenarios narratives

- Decline of traditional pharma companies;
- Focus on devices and lifestyle technologies;
- New types of businesses emerge at interfaces.

- Big pharma has disappeared. Focus of big companies on confirmatory trials/production/marketing;
- Drug development in SMEs and public institutes.

- The patent cliff has been crossed: big pharma dominant in innovation, SMEs as suppliers of early-stage developments;
- Governments are partners through PPPs.

- Separation of professions/industry vs academia
- Companies focus on niche markets in which added value can be shown best
- There is strong pressure to contain drug prices in major markets.

September 2010
Which scenario do you prefer?

2 x 2 scenario matrix based on the dimension 'science culture' and the 'Approach to the treatment and prevention of diseases', with the four scenarios located inside the matrix.

Choose from the following scenarios:

- **Scenario 1**: Filling the pipeline
- **Scenario 2**: Fusion
- **Scenario 3**: Decline of the titans
- **Scenario 4**: Pharmacological expenditure constraints

**Science culture**

**Treatment and prevention of diseases**

**Le nozze di Figaro**

**Faust**

**Zauberflöte**

**Gotterdammerung**

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Which scenario do you think is most likely?

- Scenario 1: Filling the pipeline
- Scenario 2: Fusion
- Scenario 3: Decline of the titans
- Scenario 4: Pharmaceutical expenditure constraints

The scenarios are based on the dimensions 'Science culture' and 'Approach to the treatment and prevention of diseases'.
One of the fundamental tenets of scenario analysis is that it is probably better to **conduct** a scenario analysis than to **read/hear** about it!
FROM THE ANALYST’S COUCH

Pharmaceutical sciences in 2020

Daan Crommelin, Pieter Stolk, Luc Besançon, Vinod Shah, Kamal Midha and Hubert Leufkens
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Quick, quick, I must hurry. 
There go the people. I must follow them as I am their leader

Alexandre Ledru-Rollin, France 1807-1864
(thanks to Mike Powell, Sofinnova)