New modes of governing post-marketing surveillance
a contribution to responsible innovation?

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Tentative governance in emerging S&T

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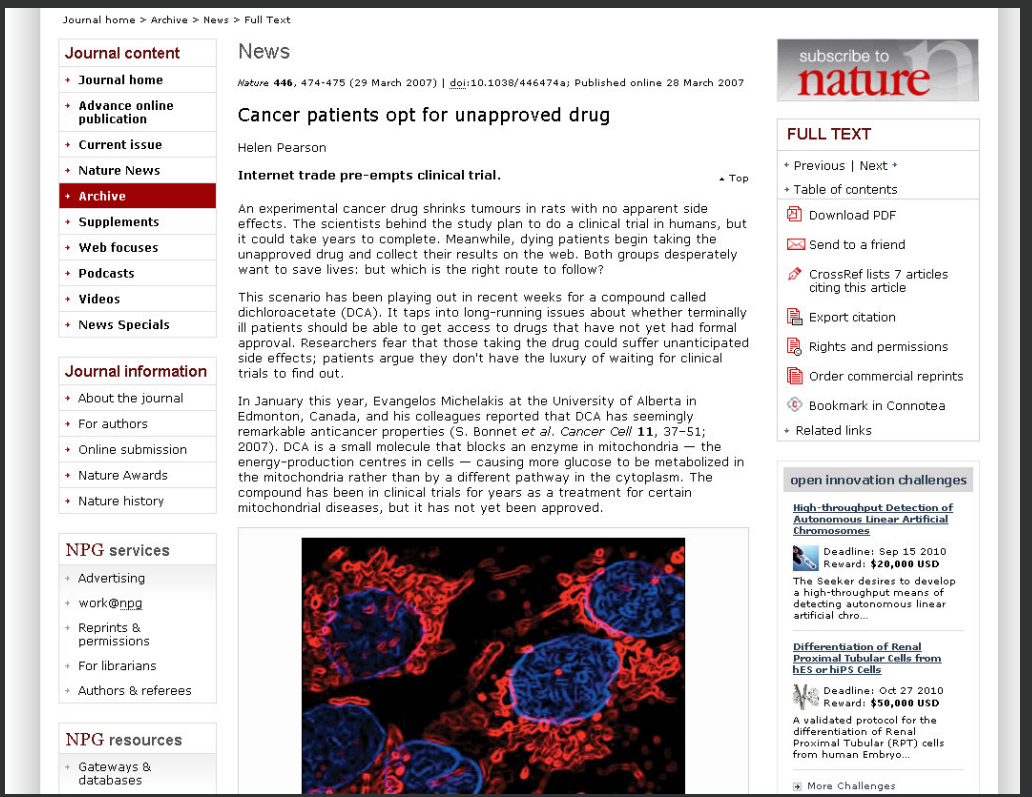
Universiteit Utrecht

Balancing act in pharma sector

"medically supervised guerrilla trials"



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News

Nature **446**, 474-475 (29 March 2007) | doi:10.1038/446474a; Published online 28 March 2007

Cancer patients opt for unapproved drug

Helen Pearson

Internet trade pre-empts clinical trial.

Top

An experimental cancer drug shrinks tumours in rats with no apparent side effects. The scientists behind the study plan to do a clinical trial in humans, but it could take years to complete. Meanwhile, dying patients begin taking the unapproved drug and collect their results on the web. Both groups desperately want to save lives: but which is the right route to follow?

This scenario has been playing out in recent weeks for a compound called dichloroacetate (DCA). It taps into long-running issues about whether terminally ill patients should be able to get access to drugs that have not yet had formal approval. Researchers fear that those taking the drug could suffer unanticipated side effects; patients argue they don't have the luxury of waiting for clinical trials to find out.

In January this year, Evangelos Michelakis at the University of Alberta in Edmonton, Canada, and his colleagues reported that DCA has seemingly remarkable anticancer properties (S. Bonnet *et al. Cancer Cell* **11**, 37–51; 2007). DCA is a small molecule that blocks an enzyme in mitochondria — the energy-production centres in cells — causing more glucose to be metabolized in the mitochondria rather than by a different pathway in the cytoplasm. The compound has been in clinical trials for years as a treatment for certain mitochondrial diseases, but it has not yet been approved.

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open innovation challenges

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A validated protocol for the differentiation of Renal Proximal Tubular (RPT) cells from human Embryo...

More Challenges

Balancing act in pharma sector

Yahoo Finance (extracted: 15-02-2010)

Balancing act in pharma sector

- Need for fast drug innovation vs. public demand for risk-free drugs
- Most stringent: accelerated approvals

- Less pre-market data → need for more post-market data

Governance problems

- Uncertainty about safety risks
- "Either going too fast or too slow"
- Facilitating bandwagon effect
- Approve unsafe drugs (and risk public outcry) vs. disapprove valuable treatments (and withhold it to patients)
- Collecting information/signals
- Creating incentives/sanctions
- Facilitating collective learning and innovation

Governance problems

- Stakeholders have different:
  - Perspectives, underlying norms and values
  - Incentives
  - Ways of articulating their demands (e.g. on an epistemological level)

Niches created

- Meeting 'unmet medical needs'
- Based on less comprehensive data
- Showing positive risk-benefit balances
- More data expected in the near future
- Accelerated approvals (US), conditional approvals, approval under exceptional circumstances (both EU)
- Post-marketing commitments ('specific obligations')

→ Specific regulatory pathways create protected spaces

Aim and research question

To what extent do new modes of governing post-marketing surveillance lead to a 'responsible' balance in the context of these niches?

Two building blocks:

- governance in niches (political)
- learning processes in niches (cognitive)

Building block (1): governance

Developing aspects of governance:

- Patterns of interaction
- Exchange of information
- Power relations
- Network rules
- Role perceptions
- Incentives
- Openness

Building block (2): learning

- Epistemic culture: shared visions/perspectives/valuation of knowledge (type, sources, etc.)
- Different levels:
  - Demand articulation (needs, problems, expectations)
  - Second-order learning (ontological and epistemological)
- Normative end point: shared narrative strengthens niche

Methods

- 2 case studies
  - Conditional approvals
  - HIV and pandemic influenza
- Based on extensive desk research and interviews, complemented with the results of expert workshops
- Dutch/European focus

Case 1: HIV

- Early 1980s: desperate for treatment
- Experimental drugs and ‘buyers clubs’
- Vocal patient community
- Strong influence on ‘science’: accelerated approvals, surrogate endpoints, compassionate use (Epstein)
- Late 1980s and 1990s: first, accelerated approvals (e.g. AZT)

Case 1: HIV

- New governance structures of post-marketing surveillance:
  - Amsterdam Cohort Study
  - HIV Monitoring Foundation
  - International adverse effect studies (e.g. DAD)
  - Spurred methodological innovations
  - Coincide with care innovations
  - Nationaal Aids Therapie Evaluatie Centrum (Natec)
  - 'Inadvertently ignoring' existing pharmacovigilance structures
  - Post-marketing in the surgery

Case 1: governing HIV

Aspects of governance:	HIV:
• Interaction pattern	• "Urban", frequent, known
• Info exchange	• Quick, various sources (// Internet)
• Power relations	• Distributed
• Network rules	• Re-inventing (formal) rules
• Role perceptions	• Everyone is lay expert
• Incentives	• Advancement to cure and prestige
• Openness	• Forced open by patient community

→ **Small, closed community**

Case 1: learning HIV

- Convergence on problem definition, openness to solutions
- Co-evolution of S&T knowledge and post-marketing
- Shared narrative and vision about dealing with disease, safety and S&T
- Shared norms: “nothing about us, without us”; agreement on ontological and epistemiological level
- There are minority groups

Case 2: pandemic influenza

- Quick reaction by companies, governments, PV-centres, etc.
- Discussions about risk-benefit, ‘panic mongering’ and role pharmaceutical industry

Case 2: governing pand. influenza

Aspects of governance:

- Interaction pattern
- Info exchange
- Power relations
- Network rules
- Role perceptions
- Incentives
- Openness

Pandemic influenza:

- Once-off but quick
- Quick through specialised channels
- Top-down
- Existing rules, but expedited
- Critical voice is not taken serious
- Averting pandemic/disaster
- Technocratic, one-way communication

→ **Militaristic drills**

Case 2: learning pand. influenza

- Limited involvement of large variety of 'critical groups': religious, critical, pro-individual choice, holistic, free-riders.
- Grassroots, bottom-up website
- No closure, different interpretations on ontological and epistemological level remained (experience vs. figures)
- Dominant PV-culture reacted: more attention and effort for pharmacovigilance, etc.

Conclusions

- Different modes of governance:
  - Small closed scene vs. militaristic drills // self-regulatory vs. strong role for government
- Co-evolution of niches and S&T of diseases
- Learning is occurring:
  - Shared narrative: stressing 'sense of urgency' // need for protective space
  - Responsible balancing act?
- Tentative governance in niche context

Questions?

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