POTENTIAL CONFLICTS OF INTEREST & COMPENSATION FOR TIME SPENT

CIOMS meeting on *Patient ~~involvement~~ Engagement in the Development and Safe Use of Medicines*

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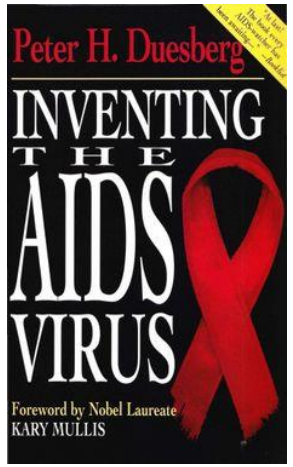
EURORDIS.ORG



What could influence our opinion?

Hearing on Advanced Therapies at the European Parliament (11 May 2006)

•KOL

- Key opinion leaders e.g. your scientific committee: Intellectual conflict of interest

• Politics, religion

- Influence of religions on our opinion vis à vis embryologic stem cells? Pre-natal screening? Abortion when teratogenic effect?

• Involvement in research

- Your organisation or yourself funded the first steps of an academic research: you strongly believe in a project. Participatory conflict of interest

• Social influencers

- Campaigns from science sceptical movements?
- DIY?
- Survivalists?
- Anti-vaccines?
- Other theories on patho-physiology?

• Funding, career

- Pharma?
- Government?
- Health insurers?
- Patents, IP rights, royalties?
- Applying to a job in pharma?

Financial or career conflict of interest

BE OPEN, transparent

Better to declare more than not enough

EXPLAIN

Where you’re coming from

STATE YOUR OWN

Conflicts. Your credibility will benefit

Case 1

- Regulators invited 2 patients to an oral explanation with the company (opinion likely to be negative)
- Two hours before the meeting, the company, patients and clinicians who had all been working on the product for years all together met in a hotel
- where
  - They reviewed all results from the clinical trials again
  - They coordinated what each one had to say at the meeting with regulators

- Independently from the funding issue:
  - The patients would not have spontaneously reported the pre-meeting they just had
  - Regulators agreed to listen and discuss with the 2 patients, as they were there anyway
  - Committee chair explained the situation to all experts before meeting started
  - But this had a negative impact on the contribution from patients (their credibility)
  - Need to educate industry and their consultants, but temptation will be there always

Case 2

- Patient organisation partner of a clinical trial sponsor (industry)
- Receives funding for a support programme
  - Trial participants meet with volunteers or staff at each trial visit
  - To help them stay in the trial (4 years)
  - And with a maximum adherence to treatment schedule (up to 100%)
- Having in mind that the organisation would continue receiving financial support from health authorities to prolong and expand the support programme to all future users, should the product be authorised
- Is there a conflict when regulators/HTA consult with
  - a representative of the organisation (board member or management)?
  - a "simple" member?
  - a trial participant?
- Difference between scientific advice and final evaluation?

Patients' organisations as co-developers – a logical evolution

You are never as well served as when you serve yourself
even if most patient groups don't have financial interests in the R&D of new products

- **Sanfilippo disease (A and B)**
  - **15 patient groups** gave a capital of $4,5 million to create Abeona therapeutics to develop a gene therapy
  - **Acquired** by another company for $45 million
  - Return on investment: 10x, development in progress
- **Cystic fibrosis**
  - **Cystic Fibrosis Foundation (CFF) granted** $150 million to Aurora Biosciences, later acquired by Vertex Pharmaceuticals with royalty rights to develop 2 products now authorised (ivacaftor, Lumacaftor/ivacaftor)
  - **Investment fund Royalty Pharma** purchased royalty rights for $3,3 billion to CFF
- **Duchenne muscular dystrophy**
  - **AFM-Telethon** gave €336,000 capital and €1,379,000 grant to Cellgene to develop a cell therapy
  - Company liquidated
- **HIV prevention**
  - **AIDES** received € 500,000 from Gilead to run a support programme for the Ipergay trial, as pre-exposure prophylaxis of HIV infection
  - Psychological type of conflict of interest within HIV+ groups?

Société		Association		Capital	Subventions	Année
Anagenesis Biotechnologies	FR	AFM	FR	206 000 €	200 000 €	2013
Capricor Therapeutics	CA	CureDuchenne	US	1 000 000 $		2015
Catabasis Pharmaceuticals	US	Parent Project Muscular Dystrophy	US		na $	2014
Catabasis Pharmaceuticals	US	Parent Project Muscular Dystrophy	US		100 000 $	2015
Cellgene	CA	AFM	FR	336 000 €	1 379 000 €	2006
CombinatoRx	US	Charley's Fund + Nash Avery Foundation	US		3 000 000 $	2007
DART Therapeutics	US	Parent Project Muscular Dystrophy	US		300 000 $	2013
EspeRare Foundation	CH	AFM	FR		na €	2013
Halo Therapeutics (Akashi Therapeutics)	US	Charley's Fund	US		1 548 000 $	na
Halo Therapeutics (Akashi Therapeutics)	US	Charley's Fund	US		2 011 000 $	na
Halo Therapeutics (Akashi Therapeutics)	US	CureDuchenne	US		na $	2012
Halo Therapeutics (Akashi Therapeutics)	US	Parent Project Muscular Dystrophy	US		500 000 $	2014
Halo Therapeutics (Akashi Therapeutics)	US	Parent Project Muscular Dystrophy	US		100 000 $	2012
Halo Therapeutics (Akashi Therapeutics)	US	MDA + 15 associations	US	1 500 000 $		2014
Lexicon Therapeutics	US	CureDuchenne	US	5 000 000 $		2013
Phrixus Pharmaceuticals	US	Coalition Duchenne	US		67 374 $	2012
Prosensa	NL	AFM	FR		3 500 000 €	2003
Prosensa	NL	CureDuchenne	US	5 000 000 €		2014
Prosensa	NL	Parent Project Muscular Dystrophy	US		200 000 $	2014
Prothelia	US	Parent Project Muscular Dystrophy	US		46 000 $	2009
PTC Therapeutics	US	CureDuchenne	US		na $	na
PTC Therapeutics	US	Parent Project Muscular Dystrophy	US		50 000 $	2010
PTC Therapeutics	US	Parent Project Muscular Dystrophy	US		2 500 000 $	2004
ReveraGen Biopharma	US	CureDuchenne	US		na $	na
ReveraGen Biopharma	US	Parent Project Muscular Dystrophy	US		750 000 $	2015
ReveraGen Biopharma	US	Parent Project Muscular Dystrophy	US		49 991 $	2013
ReveraGen Biopharma	US	Foundation to Eradicate Duchenne	US		250 000 $	2015
ReveraGen Biopharma	US	Ryan's Quest Foundation	US		50 000 $	2015
Sanofi	US	MDA	US		60 000 $	2014
Sanofi	US	MDA	US		60 000 $	2015
Sarepta Therapeutics	US	CureDuchenne	US		250 000 $	2010
Sarepta Therapeutics	US	Foundation to Eradicate Duchenne	US		250 000 $	2010
Sarepta Therapeutics	US	Charley's Fund	US		2 450 000 $	2007
Sarepta Therapeutics	US	Charley's Fund	US		3 000 000 $	2009
Solid Ventures	US	Parent Project Muscular Dystrophy	US		na $	2014
Summit	UK	CureDuchenne + 5 associiations	US		1 500 000 $	2012
Summit	UK	Parent Project Muscular Dystrophy	US		250 000 $	2011
Synthena	CH	Association Monégasque Contre les Myopathies	MO		na €	na
Talem Technologies	US	Parent Project Muscular Dystrophy	US		70 531 $	2015
Tivorsan Pharmaceuticals	US	Parent Project Muscular Dystrophy	US		565 000 $	2012
Tivorsan Pharmaceuticals	US	MDA	US		1 000 000 $	2015

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•Main question

- Is there a problem for this discussion?

You DECLARE, someone will ASSESS

- Even just at the beginning of the meeting: never too late
- Not a black and white thing
- Should not exclude experts a priori in an automatic manner
- There is a value judgement

•question

As a patient, who do you trust more:
-) a physician involved in clinical trials and treatment guidelines development (with industry funding)
-) or a physician who never participated in a clinical trial or any research partly funded by industry
| COMPETENCE vs INDEPENDENCE

Need for a right balance: minimising conflicts, getting the expertise

What can be done?

- Those in contact with industry (e.g. fundraisers) and representatives consulted by authorities could be distinct persons within our organisations
- Information on funding / revenues available and open for public scrutiny (not just on request) – still too rarely done
- Diversify sources and avoid dominant positions
  - Consider a reserve fund in case you have to stop financial relations with a company
  - The % of revenues from one single company should not be too high
- Wash out period: when thinking to be consulted by regulators / HTA, stop any relation with company at least one year ahead of the consultation
- Refrain from being in contact with company or its consultants before or after any consultation with regulators / HTA
- Demonstrate independence: e.g. public hearing with travel costs covered by the company and the patient talks against the product

https://www.eurordis.org/financial-information-and-funding#tabs-4

Acknowledgements | **Revenue** | Expenses | Corporate revenue

EURORDIS Revenue 2017

Expand All Collapse All

Revenue	Amount (€)	Percentage
⊞Patient Organisations	882 796	16%
⊞Individuals	1 038 157	19%
⊞European Commission	1 392 730	25%
⊞Corporates	1 788 093	32%
⊞Not for Profit Organisations	25 000	0%
Event Fees	112 721	2%
⊞Miscellaneous	354 367	6%
Sub-total	5 593 863	100%
Recovery of provisions	24 350	
Total Revenue	5 618 213	

Acknowledgements | Revenue | Expenses | **Corporate revenue**

EURORDIS Corporate Revenue 2017

Expand All Collapse All

Pharmaceutical & Biotechnology Companies

Company	Amount (€)	% of Revenue
⊞**ABLYNX**	**10 000**	**0,18%**
⊞**ACHILLION**	**26 000**	**0,46%**
⊟**ACTELION**	**45 000**	**0,80%**
EURORDIS Black Pearl Awards	35 000	0,63%
EURORDIS Round Table of Companies	10 000	0,18%
⊞**AEGERION**	5 000	0,09%
⊞**AGIOS**	5 000	0,09%
⊞**AKCEA**	**10 000**	0,18%
⊞**ALEXION**	**25 000**	**0,45%**
⊞**ALNYLAM**	**35 000**	**0,63%**
⊞**AMGEN**	**5 000**	**0,09%**
⊞**AMICUS THERAPEUTICS**	**15 000**	**0,27%**
⊞**ASTRAZENECA**	**10 000**	**0,18%**

EURORDIS RARE DISEASES EUROPE

PROTECT YOURSELF

Extract from EURORDIS's Policy on financial support by commercial companies*

To avoid the risks inherent in a relationship between an NGO and commercial companies, the following activities are never funded by commercial companies of the health sector:

- *All activities related to governance, mainly the Board meetings and the General Assembly*
- *The salaries of the staff dedicated to advocacy work (mainly the CEO and the European Public Affairs Director and Advisors)*
- *All activities related to EURORDIS representation in different fora, such as the EMA Committees or the EU Committee of Experts on Rare Diseases*

*: http://download2.eurordis.org/documents/pdf/eurordis-policy-commercial-support.pdf

Fair compensation of your activity as an expert

- Europe: EURORDIS proposes 450-900 € per meeting day (average 600 - 450 approximates the compensation for time spent for experts who evaluate research projects DG Research)
  - Both for members who are volunteers or paid staff (for the latter, the amount can be paid to the organisation, partly or fully)
  - In addition to travel and subsistence costs
- The rate could be adapted based on average salary in country of residence to account for different GDP/inhabitants
  - Some authorities propose 1,200 € /day
- No distinction between different statutes of individuals (retired, active, self-employed, compensated, volunteer, paid staff)
  - but be aware of possible fiscal consequences (loosing you disability benefits)
- EMA: per diem for experts (105€/meeting day), doubled for patients who are not staff of their organisation but unpaid volunteers

Other possible solutions
French labour market legislation "Code du Travail"

- **Article L3142-S1: days off to be engaged**
  - "When a salaried employee, who is a member of an association (…) is appointed as representative of that association to be on a body – advisory or otherwise – instituted by legal or regulatory provision by a state or regional authority, the employer must grant him or her the necessary time to participate in meetings of that body."
  - E.g. Ethics committee, scientific committee at ANSM or HAS
- **Article L3142-S2: days off are compensated**
  - "The salaried employee benefiting from leave of representation who is subject as a result to a reduction in pay receives from the state/regional authority an allowance compensating, wholly or partially, the reduction in pay."
- **Article L3142-S3: limit of 9 days a year**
  - "The period of leave of representation must not exceed nine days in a year. It may be divided into half days"

To conclude

Denver Principle of patient advocacy (1983): *"To be involved at every level of decision making, in all decisions that affect our lives"*

Participate in all forums with equal credibility as others – *declare interest, respect confidentiality, avoid insider trading*

Engagement principles should be the same than for other experts: *"to be treated on the same basis"*

Being part of the decision making imposes responsibilities on us – and legal liability

Thank you for your attention

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