



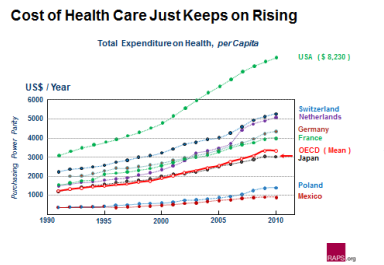
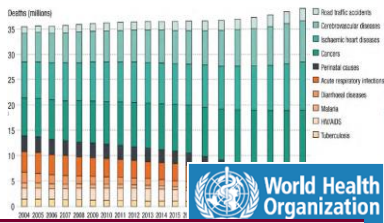
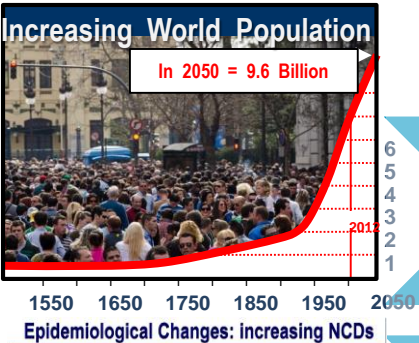
Global regulatory challenges to innovation

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Better Foods for Better Health - 5th Edition :
Microbiota & Health:
The challenges of a promising approach

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Changing HealthCare Paradigms ... Unmet Need - Opportunities - Challenges



→ timely, appropriate, affordable
healthcare solutions to patients/society



Global regulatory challenges to innovation

Build bridges in the **food drug continuum** between **regulated product categories** to address

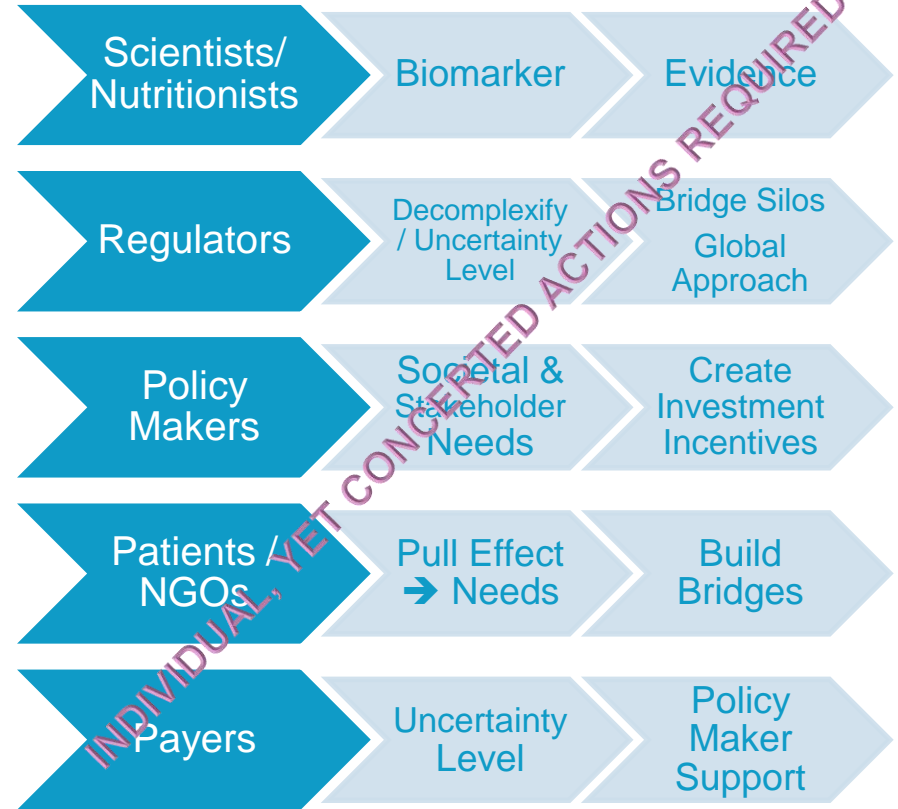
- **disruptive innovations** & create **incentives**, incl. market access
- gaps concerning **dietary disease management, disease prevention**

HealthCare Regulatory & Policy Framework Revisited

Regulations & processes expected to benefit society (consumers, patients), i.e.

- Science based & proportionate
- Predictable - clear, transparent, efficient, include precise timetables
- Enforceable
- Facilitating free movement of goods

Clearly define needs & build on **multi(ple) stakeholder** competencies



Setting the Frame for a Constructive Dialogue

- a Regulatory «Elevator Speech»

All that counts for product compliance
= meet «intended use»*
i.e. food, drug, device

be «SAFE → for its intended use»
[for drugs also RISK-BENEFIT]

«Not mislead consumer/patient»
i.e. CLAIM & related EVIDENCE
[for drug reimbursement also HEALTH ECONOMICS]

*Drug = «any substance(s) presented as
... treating or preventing disease»;*
in cases of doubt → it's a Drug!

Missing notion: «decomplexify» &
«incentivise» development to get a
compliant (food) product for «patients»

(1) to the market in a
«TIMELY» manner; «ROI»
→ Intellectual Property; «glocal» patient CTs...

(2) Define acceptable level for
«(UN-)CERTAINTY» of evidence
→ IT; Phase IV, post-market surveillance ...

(3) Nutrition for Disease Prevention,
Therapy & Holistic approaches
(Drug + Nutrition + Services)

*Wording is key. notion includes also the nature of
the effect (e.g. physiologic, pharmacologic, toxic)

Regulatory Design, Silos & Gaps



«Intended use» designed @ very start of development:
‘changing horses midstream?’ →
~ start from scratch to meet compliance requirements



«Disruptive innovations» in dietary disease management:
difficulty to meet all category requirements in switching frames

- ❖ *Nutrition vs. drug CMC (monographs; G(X)P; analytics, ...); clinical endpoints*
- ❖ *Nutrient «cocktails» not adapted to [mono-]dose-response drug requirements*
- ❖ *Health vs. disease dosage concept: nutritional → pharmacologic → toxic*
- ❖ *Patho-mechanism of action («DNR») proof for medical food, yet not drugs*

Gut Microbiome – some pertinent PTCs & Qs



Base Line Thoughts

- Who are we dealing with, the Patient or Microbiome?
- What is a «Healthy Microbiome» / dysbiosis? health & disease impact

Disruptive Science

- Understand mechanism of action, functional equivalence, physiologically relevant endpoints, dynamics of microbiome
- Gut microbiota - a determinant of individual metabolism, e.g. nutritional phenotyping to quantify “DNR”, nutritional needs

Safety & Efficacy

- What do we want to regulate? Safety 1st, e.g. free of major pathogens?
- Fiber or probiotic effects on the microbiome, always a nutritional effect?
- Classify «non-gut» related systemic microbiome effects alike?

Gold Standards, Precedents, Analogies, Learnings

- Pro-, Pre-, Symbiotics / Antibiotics
- First 1000 days, functional ecology, variability
- The payers’ view(s)?

IBD example: «Modify* the Gut Microbiome for the ...



Biological Drug

- ... treatment, cure, prevention of IBD»

FSMP/Medical Food (tube feeding or ONS)

- ... dietary management of IBD»

Food Health Claim (EU NHCR Art.14; US)

- ... risk (factor) reduction of IBD»
(~«Disease Prevention»)

Food Health, S/F Claim (EU NHCR Art 13; US S/F)

- ... normal bowel function/increase in faecal bulk»

* incl. e.g. transfer from healthy to sick individuals

Medical Nutrition → Disease Management

Nutrition as disease-related malnutrition management

- Short bowel syndrome, stroke
- COPD
- Surgical patients
- Older patients

Enteral Nutrition (EN)
(i.e. tube feeds and/or ONS) &
Parenteral Nutrition (I.V.)

Health Care Professionals' key role for proper intended use (compliance, safety)

- Lifesaving intervention
- Increased ventilatory capacity
- Less complications
- More active, better quality of life, decreased mortality

Nutrition as disease management

- Crohn's disease
- Cow's milk allergy
- PKU

US FDA: IND Guidance (2013) - Section VI, Part D ("Foods") → AGA (4/2014) 'negative consequence ... to human food/nutrition research ... field of GE & gut microbiome'

ECCO/ESPGHAN (2014)
"Consensus Guidelines on pediatric Crohn's medical management: **exclusive enteral nutrition as Induction therapy of 1st choice**"

De facto nutrition «treatment (prevention) of disease»: yet permitted → «For the dietary management of ...»

- Induction of remission
- Reduced symptoms, catch-up growth
- Normal growth and development

Disease Prevention & Disruptive Science: New Issues?

Diagnostics / «omics (r)evolution creating new gray zones?

Where does health end, disease start (homeostasis)? What does it mean for early interventions & regulations?

Prevention of Disease = «Medicine», yet different levels to consider (US NLM)

- **Primary** ~: avoid occurrence of disease (e.g. vaccination)
- **Secondary** ~: treat existent disease in early stages before it causes significant morbidity
- **Tertiary** ~: reduce negative impact of existent disease (illness) by restoring function/ disease-related complication

Prevention of Disease via Nutrition (Therapy), is already Status Quo

- **Disease (Symptom) Prevention:** e.g. Cow's Milk Allergy; PKU & other I.E.M.s; Crohn's Disease
- **Prevention of Disease (Risk):** sterols & CVD (US, EU: few claims approved for foods («DR(F)RCs»))
- **Prevention of falls & hip fracture in osteoporosis**

Consequences for patients & society?

Nutrition: to what extent are

- **Developers** ready to invest into complex nutrition & disease studies, i.e. uncertain success with ltd. **incentives/ ROI** (incl. development costs; access)?
- **Regulators & Payers** ready to accepting limited evidence & related «**uncertainty**»?

Conclusion – Actions to Ensure Innovation



Demographics & Co(nsequences) require Microbiome as a key ally for an innovative disease management

Disruptive innovations → better understanding of interconnections:

Genetics, Nutrition, Medical Treatment & Lifestyle

Healthcare regulatory & policy frameworks are largely sufficient, yet inconsistent or unprepared in some cases

Disease Prevention (primary, secondary, tertiary);
Dietary Disease Management, Nutrition Therapy;
Stratification;
Microbiome

«Accelerate» market access & ensure incentives for investing into developing healthcare solutions

Leverage Multistakeholder expert venues (WHO, EU, US ...), facilitated by global platforms (Mérieux, OECD, RAPS ...)

Better Foods for Better Health - 5th Edition : Microbiota & Health: The challenges of a promising approach

Merci !
Thank you !

- ... This year, the Symposium will:
- present new perspectives from the microbiota approach to prevent or cure disease
 - evaluate the opportunities of novel scientific models based on microbiota studies
 - discuss the need for new, harmonized tools to assess nutrition efficiency and safety;
 - provide a platform for increased dialogue between Regulators, Academia and Industry'