Global regulatory challenges to innovation

Manfred Ruthsatz

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

«Pharma Model»
- Treatment vs. Prevention
- Precision, Orphan drugs

«Nutrition Model»
- Case Law, Food Law
- Safety & Claims
- «omics» (R)evolution
  Prevention

«Society Model»
- Demographics
- NCDs, Lifestyle & Prevention
- HealthCare Costs

In 2050 = 9.6 Billion

Epidemiological Changes: increasing NCDs

World Health Organization

Cost of Health Care Just Keeps on Rising

- Disruptive Innovations & Grey Zones
  - Better understanding key role of Genetics, Nutrition, Medical Treatment & Lifestyle inter-connections

«-omics»/NGS/diagnostics, microbiome, nano, 3D Printing, IT/Big Data …

⇒ 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)
«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 pertinents 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 ...**

<table>
<thead>
<tr>
<th>Biological Drug</th>
<th>• … treatment, cure, prevention of IBD»</th>
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</thead>
<tbody>
<tr>
<td>FSMP/Medical Food (tube feeding or ONS)</td>
<td>• … dietary management of IBD»</td>
</tr>
<tr>
<td>Food Health Claim (EU NHCR Art.14; US)</td>
<td>• … risk (factor) reduction of IBD» («Disease Prevention»)</td>
</tr>
<tr>
<td>Food Health, S/F Claim (EU NHCR Art 13; US S/F)</td>
<td>• … normal bowel function/increase in faecal bulk»</td>
</tr>
</tbody>
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* incl. e.g. transfer from healthy to sick individuals
Medical Nutrition ➔ Disease Management

**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)


**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 …»**

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(sequences) 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 …)
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’