Microbiome et al.: Regulatory pathways for innovation at the food-drug continuum

Manfred Ruthsatz

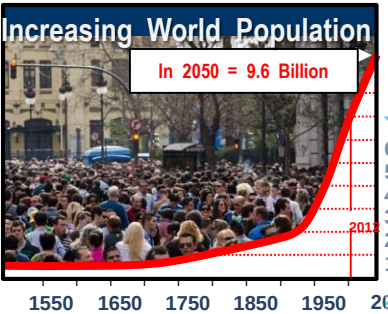
OECD Workshop - Microbiome, Diet and Health: Assessing Gaps in Science and Innovation

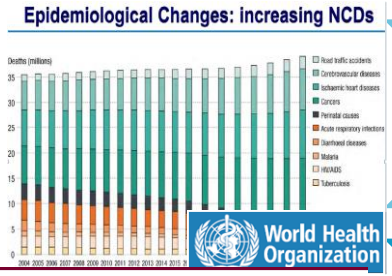
Brussels, May 30-31, 2016

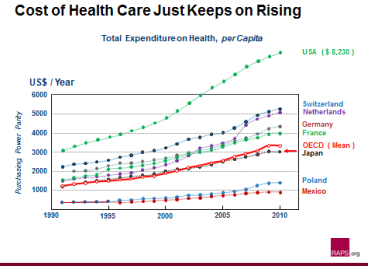
NestléHealthScience

Changing HealthCare Paradigms …

Address Unmet Need ➔ Opportunities & Challenges







«Pharma Model»

Treatment vs. Prevention

Blockbuster Market Access

Precision, Orphan drugs

«Nutrition Model»

Case Law Pharma Food

EFSA et al. Safety & Claims

«omics» (R)evolution Prevention

«Society Model»

Demographics

NCDs, Lifestyle & Prevention

HealthCare Costs

Disruptive Innovations

«-omics»/NGS/Diagnostics, Microbiome, nano, 3D Printing, IT/Big Data …

- Better understanding key role of Genetics, Nutrition, Medical Treatment & Lifestyle inter-connections

Gray Zones

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

NestléHealthScience

HealthCare Systems being dysfunctional by 20?!
- Get vested stakeholders out of silos to find concerted solutions

Stakeholder	Stuck with / in / on / - …	
Scientists/industry	**long-term investments**	resources, opportunity costs
Regulators	**current framework**	evidence / ltd. room for interpretation or switch categories
Policymakers/ Politicians	**short-term incentives**	vs. long-term vision
HCPs/Society	**treatment paradigm**	vs. disease prevention (primary, secondary, tertiary)
Payers	**current framework**	evidence & certainty incentive to pay
Patient/Society	-	not organized or vocal enough, not heard

3 Manfred Ruthsatz, OECD, May 31, 2016

Microbiome et al.: Regulatory challenges to innovation at the food-drug continuum

1. are current regulatory frameworks sufficient?
2. are there gaps to be addressed?
3. is there a need for an international approach?

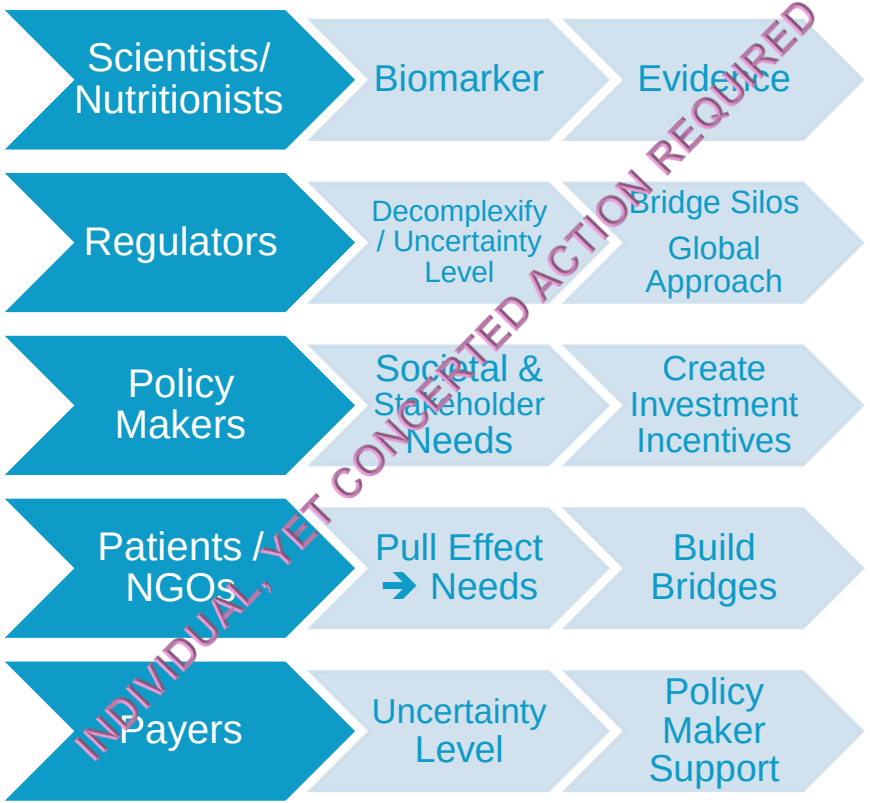
NestléHealthScience

A HealthCare Framework should benefit Consumers & Patients – The Task of a Multistakeholder Engagement

Regulations & processes to be

- 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



5 Manfred Ruthsatz, OECD, May 31, 2016

NestléHealthScience

Regulatory is Complex ➔ Simplify it to Incentivize Product Development
yet not so Complicated ➔ Product «Intended Use» Counts

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

Food-Drug «Borderlines» for the Regulator !
Food-Drug «Continuum» for Patient & Society !

Increase Flexibility between Food & Drug Frames for Innovative Solution-Focused Dietary Disease Management

Regulatory Design & 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; analytics; G(X)P; …); clinical endpoints*
- *Nutrient «cocktails» not adapted to [mono-]dose-response drug requirements*
- *Health vs. disease dosage continuum: nutritional ➔ pharmacologic ➔ toxic*
- *Patho-mechanism of action («DNR») proof for medical food, yet not drugs*

Gut Microbiome – A Great HealthCare Solutions Potential

- yet we need to address basic development issues to fit into current frame

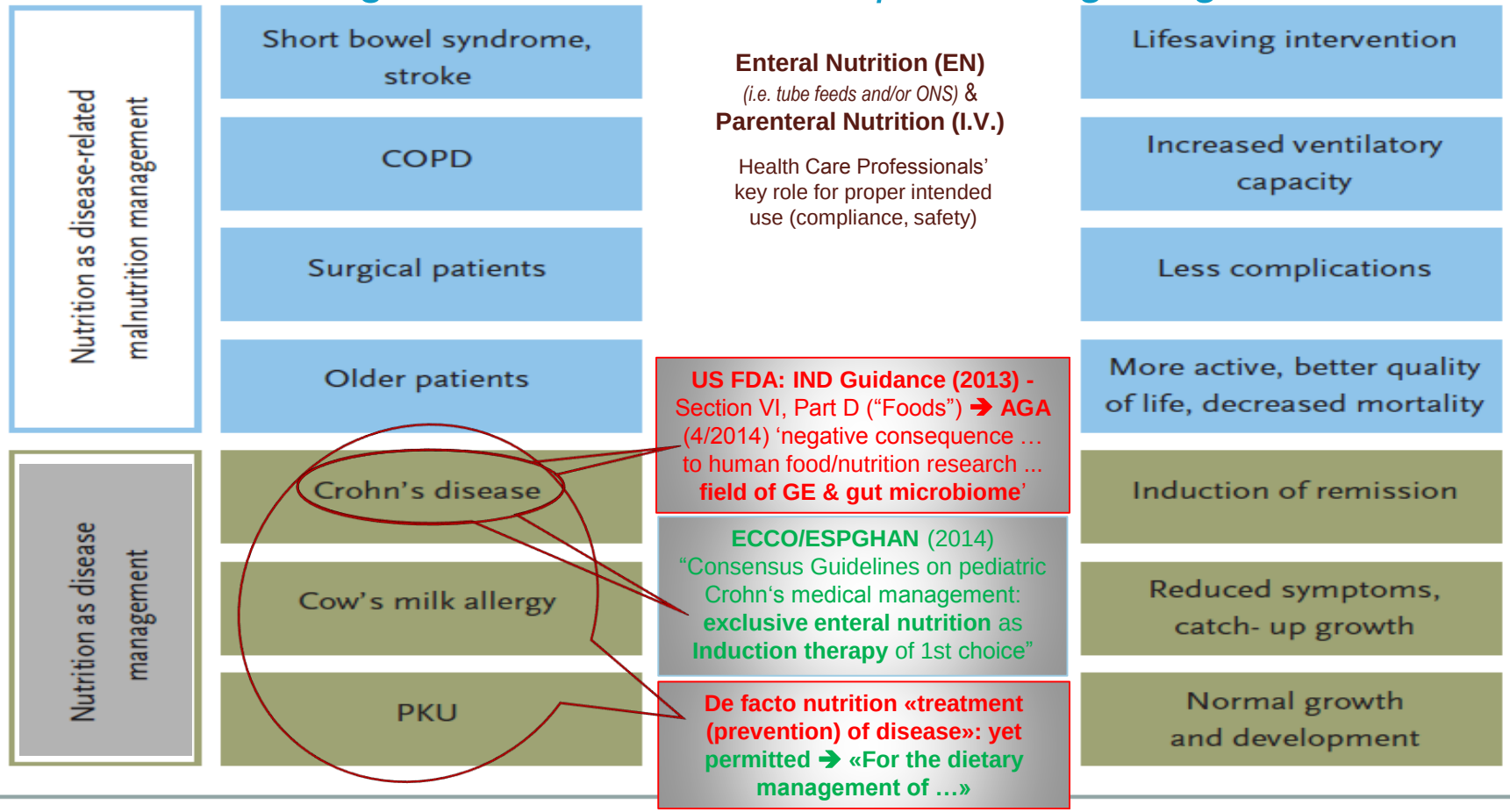
Base Line Thoughts	• Who are we dealing with, the Patient or Microbiome? a symbiosis? • What is a «Healthy Microbiome» / dysbiosis? health & disease impact
Disruptive Science	• Understand mechanism of action, functional equivalence, physiologically relevant endpoints, dynamics of microbiome • Gut microbiota - a determinant of individual metabolism, e.g. nutritional phenotyping to quantify “DNR”, nutritional needs
Quality, Safety, Efficacy	• What do we want to regulate? Safety 1st, e.g. free of major pathogens? Manufacturing: large scale; product consistency with live bacteria • 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)?

Example: «Modify* the Gut Microbiome for the …

Biological Drug	• **… treatment, cure, prevention of IBD / … C.diff. »**
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. FMT from healthy to sick individuals

Medical Nutrition ➔ Can be a de-facto Disease Prevention or Management/Treatment - *Complementing Drugs*



http://www.european-nutrition.org/images/uploads/pub-pdfs/Patient_perspectives_on_nutrition_.pdf

New Diagnostics require to revisit «Disease Prevention»

«Prevention of Disease = Medicine» !(?) ➔ **Diagnostics / «omics (r)evolution** creating new gray zones?
Where does health end, disease start (homeostasis)? What does it mean for early interventions & regulations?

PREVENTION Level	Definition (US NLM - Medical Subject Headings (MeSH)): **Methods to …**
Primary	… **avoid occurrence of disease.** *Most population-based health promotion efforts (e.g. vaccination)*
Secondary	… **diagnose and treat existent disease in early stages** before it causes significant morbidity
Tertiary	… **reduce negative impact of existent disease** by restoring function/disease-related complication

Already Status Quo:

Nutrition & Disease Prevention

Disease *(Symptom)* **Prevention**: e.g. Cow's Milk Allergy; PKU & other I.E.M.s; Crohn's Disease

Disease *(Risk Factor)* **Prevention**: sterols & CVD *(US, EU: few claims approved for foods («DR(F)RCs»))*

Prevention *(Disease Consequences)* - 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**»?

We require Multi-Stakeholder Innovation & Need Based Actions to Revisit HealthCare Regulatory & Policy Framework

1. Build Bridges behind common goal

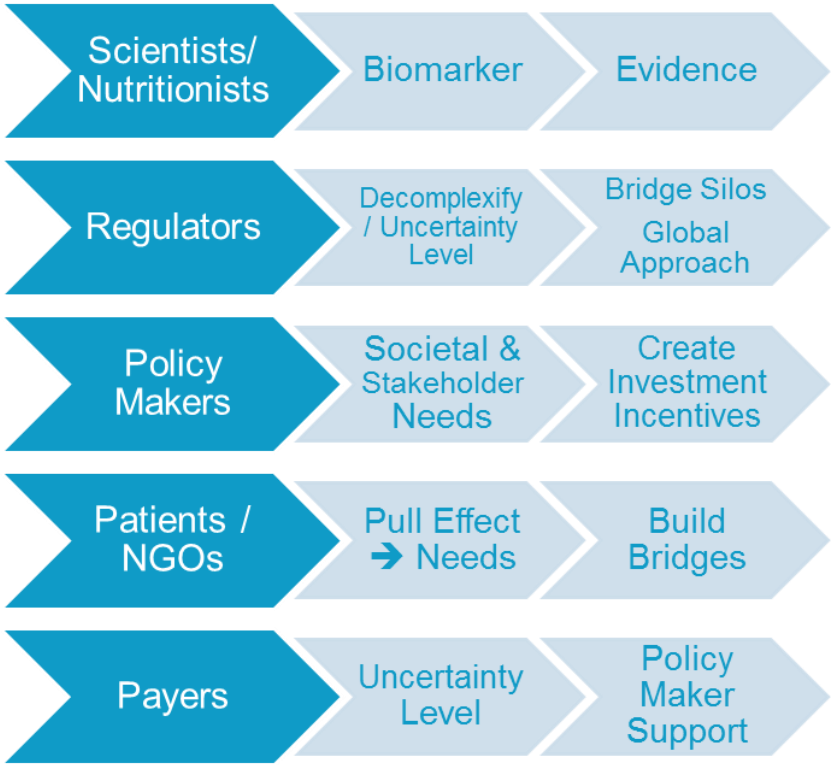
- Foster investment into new/disruptive science, solutions

2. Refine Food Drug Continuum

- Disease Prevention (primary, secondary, tertiary)
- Flexibility for nutrients («Less is More»): remove technical development barriers (Quality/Safety, not disease based)

3. Medical Food/FSMP Specifics

- Dietary Disease Management & Therapy
- Strengthen «Certainty»: Phase IV evidence vs Pre-market registration; define level of uncertainty
- Strive for Global Convergence; Market Access
- Incentivise Use Pathways: expand existing solutions (DR Malnutrition: EN vs. PN; HEOR; treatment vs. prevention)



NestléHealthScience

An Example of a Successful Multi-Stakeholder Model in Progress

ONCA

‘Every patient
who is malnourished or
at risk of undernutrition
is systematically screened

and

has access to appropriate,
equitable, high quality
nutritional care’

NestléHealthScience

Conclusion – Actions to Enable 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

Simplify ➔ "Phase IV" Market Access

Nutrition & Disease Prevention
(primary, secondary, tertiary)
Management/Therapy Stratification
Microbiome

Accelerate policy making to catalyse incentives & investments for developing healthcare solutions

Leverage **Multistakeholder** Expert Venues

Facilitated by **Glocal Platforms**
(WHO/Codex, EU, US … - OECD, RAPS, Mérieux …)

Glossary

Acronym	Category
CMC	Chemistry Manufacturing Control
CVD	CardioVascular Disease
DNR	Distinctive Nutritional Requirements
DR(F)R Claim	Disease Risk (Factor) Reduction Claim
G(X)P	Short for GMP, GCP, GLP, i.e. Good Manufacturing, Clinical, Laboratory Practices
HEOR	Health Economics Outcomes Research
S/F Claims	Structure Function Claims (USA)