WSMI Regulator's Forum - October 19-20, 2017

Switzerland's Current Reclassification Experience and How to Mitigate Inherent Risks

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Ordinary Revision of the Therapeutic Products Act (Stage 2) & Therapeutic Products Ordinance Package IV

- **Facilitating market access:**
  Creating new and simpler access opportunities for certain medicinal product categories (especially medicinal products approved in an EU or EFTA country, medicinal products with traditional uses and medicinal products already approved in a canton, as well as various medicinal products used in complementary medicine);
  simplifying self-medication by modified allocation of the medicinal products to the different supply categories, and an easing of the supply requirements.

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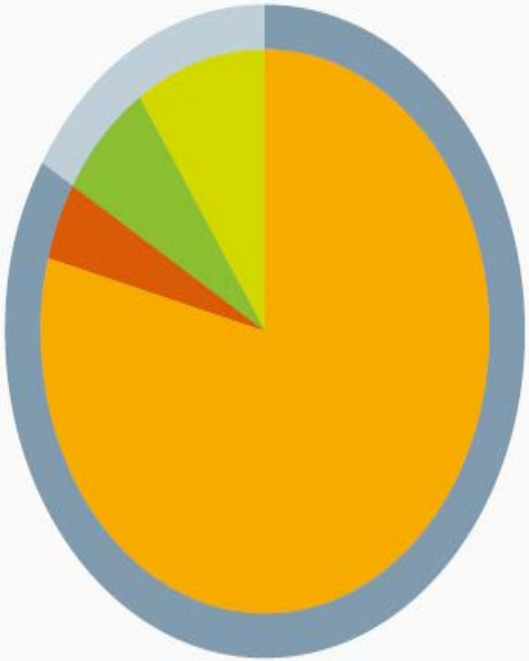
Baseline

Pharmaceutical market by reimbursability according to value

Market volume 2016: CHF 5,594.8 million (at ex-factory prices, 100%)



Reimbursable products
83.8% (CHF 4,689.0 million)

Prescription only
79.3% (CHF 4,439.6 million)

Over the counter
4.5% (CHF 249.4 million)

Non-reimbursable products
16.2% (CHF 905.8 million)

Prescription only
6.9% (CHF 386.7 million)

Over the counter
9.3% (CHF 519.1 million)

Source: Interpharma with database QuintilesIMS Switzerland, 2017.

A	**Rx no refill**
B	**Rx**
C	**Dispensed by Pharmacist**
D	**OTC - Dispensed with counselling**
E	**General Sales**

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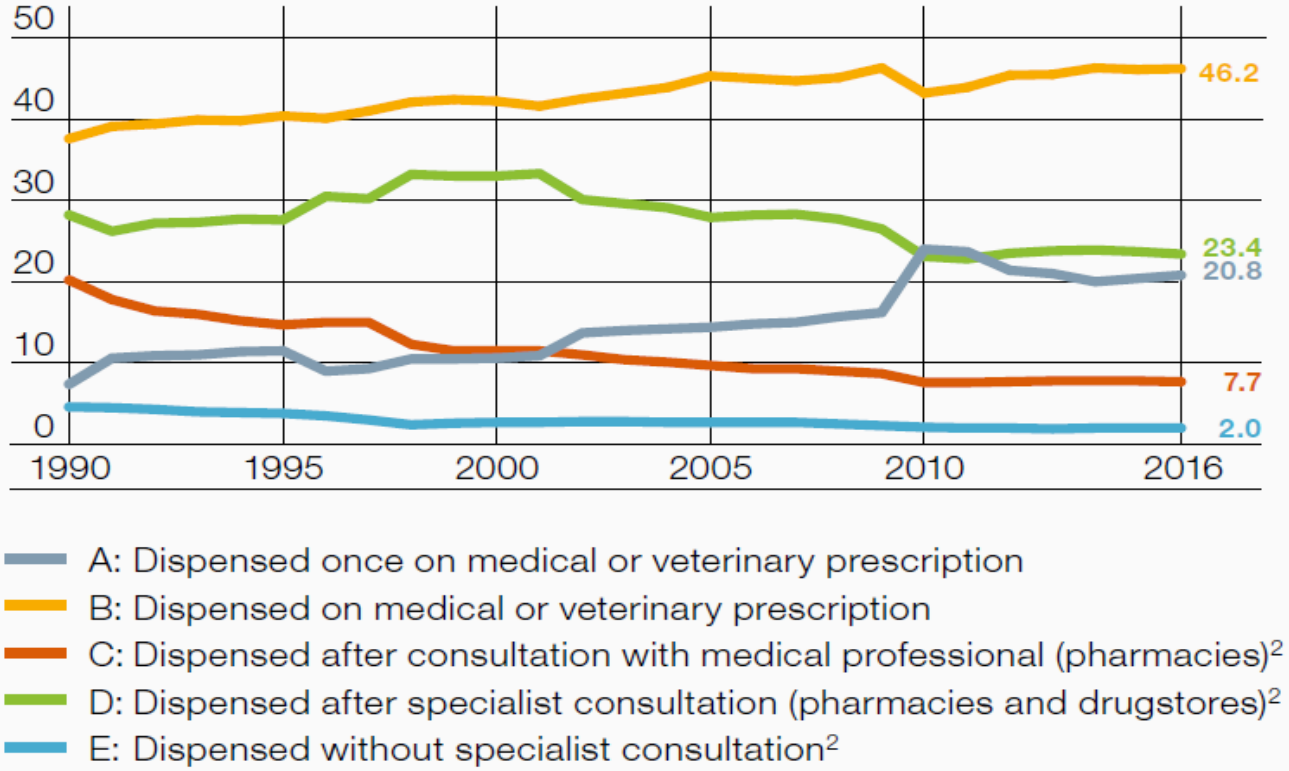
Dispensing

Dispensing categories over time

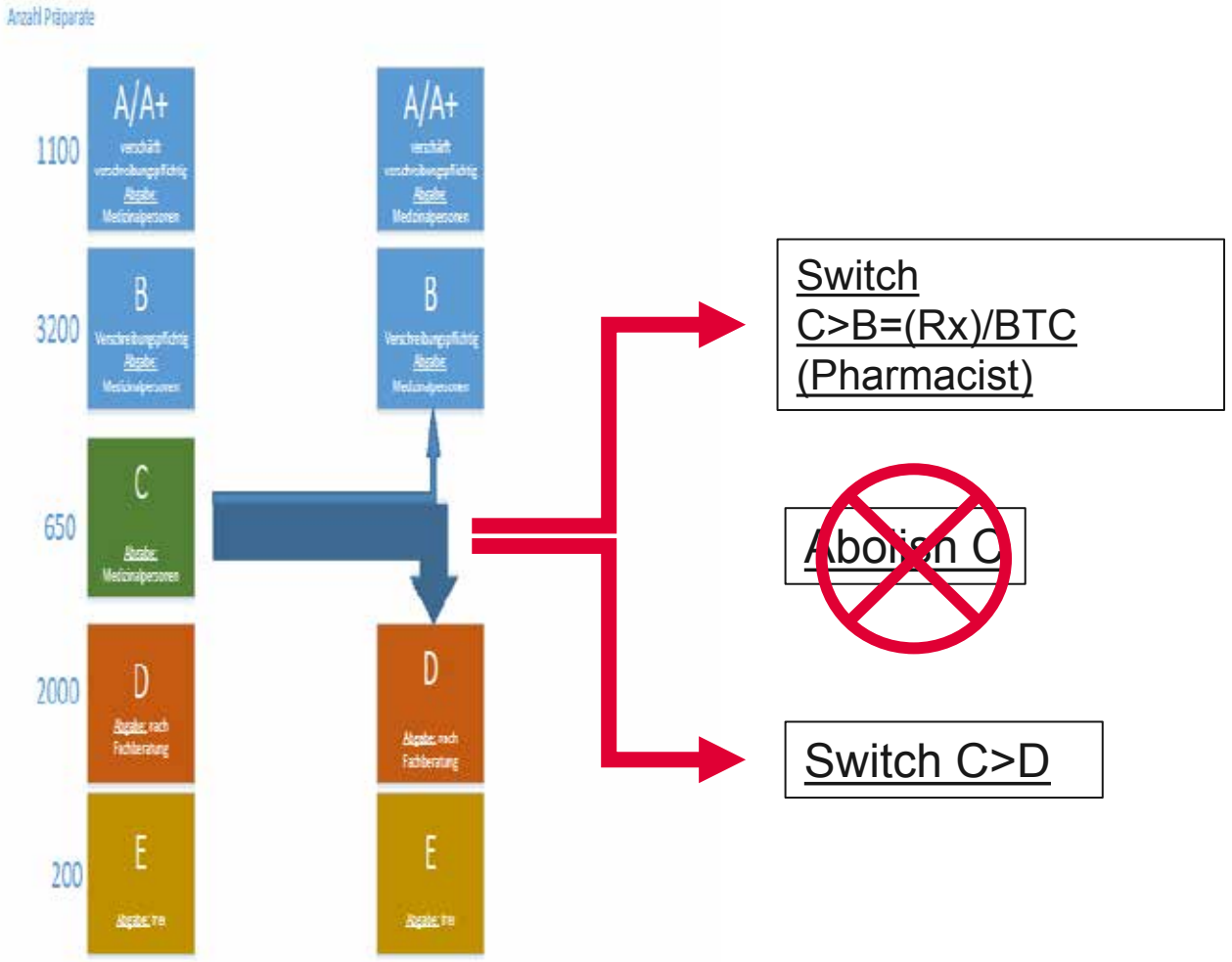
Medicines by dispensing category[1] (in %)



Source: Annual reports, various years, Swissmedic.

A	Rx no refill
B	Rx
C	Dispensed by Pharmacist
D	OTC - Dispensed with counselling
E	General Sales

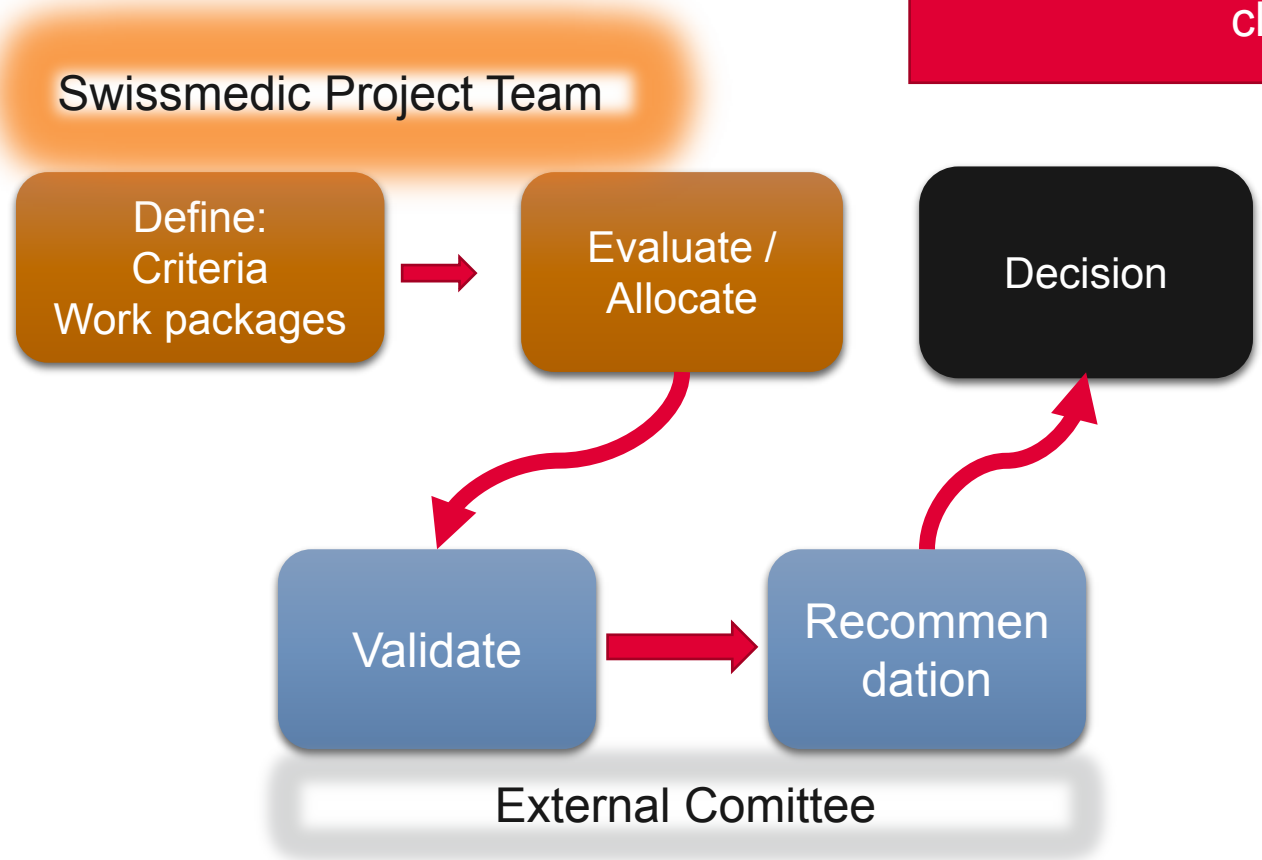
Reclassification



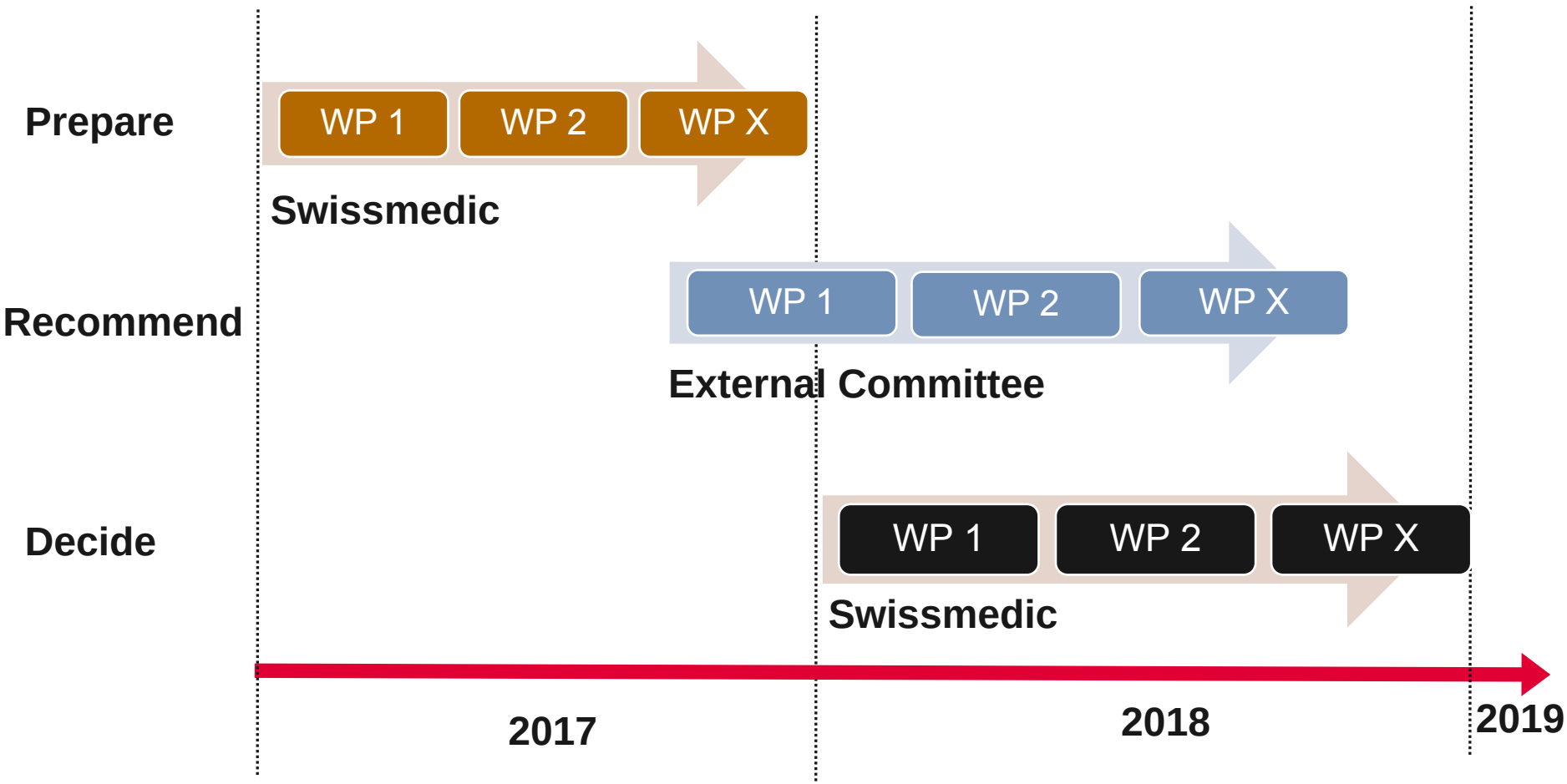
A	Rx no refill
B	Rx (& BTC)
C	~~Dispensed by pharmacist~~
D	OTC - Dispensed with counselling
E	General Sales

Process

Principles:
Scientifc (clin pharmacology), clinical



Rollout C > D/B


Prepare
WP 1
WP 2
WP X
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Recommend
WP 1
WP 2
WP X
External Committee
Decide
WP 1
WP 2
WP X
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2017
2018
2019

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To be considered

Dispensing point: requirements, qualifications,

Therapeutic index, critical dose?
Drug monitoring
DDI?

Formulation / Application

Indication / Dose strength / Package

Age

Abuse Potential

Clinical practice experience

Consideration of similar medicinal products (known active substances)

Safety signals

Existing documentation (safety, efficacy, quality - B:R:U)

Risk mitigation (labelling, counseling)

Patient

Pictures: Shutterstock:540895525

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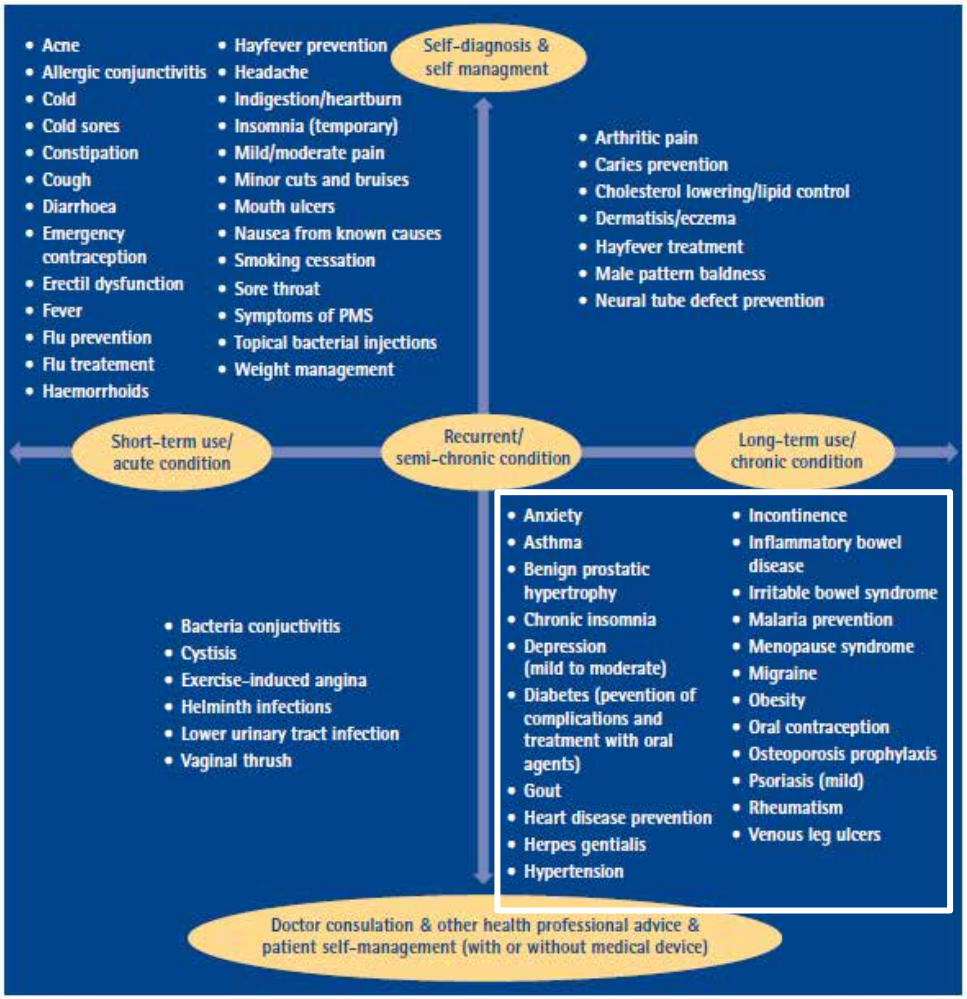
Switch Decision



SWITCH – Prescription to nonprescription medicines switch

Criteria (CH)
a) Pharmacological action (MoA)
b) Acute & chronic toxicity
c) Clinical experience (ADR, tolerability)
d) Indication
e) Abuse potential
f) Need for diagnosis & monitoring

ACCP

Review

A Decision-Analysis Tool for Benefit-Risk Assessment of Nonprescription Drugs

The Journal of Clinical Pharmacology
53(5) 475–482

DOI: 10.1002/jcph.22

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Network(ed)

ICH
harmonisation for better health

i-p-r-f.org
International Pharmaceutical Regulators Forum

IGDRP
International Generic Drug Regulators Pilot

World Health Organization

ACSS Consortium
Australia-Canada-Singapore-Switzerland Consortium

OECD
BETTER POLICIES FOR BETTER LIVES

PIC/S

EUPATI
European Patients' Academy on Therapeutic Innovation

Council of Europe
COUNCIL OF EUROPE CONSEIL DE L'EUROPE

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ICH

ICH HARMONISED TRIPARTITE GUIDELINE

PERIODIC BENEFIT-RISK EVALUATION REPORT (PBRER)

E2C(R2)

Current *Step 4* version

dated 17 December 2012

For PBRERs for products with several indications, formulations, or routes of administration, where there may be significant differences in the identified and potential risks, it may be appropriate to present risks by indication, formulation, or route of administration. Headings that could be considered include:

- Risks relating to the active substance;
- Risks related to a specific formulation or route of administration (including occupational exposure);
- Risks relating to a specific population; and
- Risks associated with non-prescription use (for substances that are available as both prescription and non-prescription products).

Provide a clear explanation of the methodology and reasoning used to develop the benefit-risk evaluation:

- The assumptions, considerations, and judgement or weighting that support the conclusions of the benefit-risk evaluation should be clear.
- If a formal quantitative or semi-quantitative assessment of benefit-risk is provided, a summary of the methods should be included.

Economic considerations (e.g., cost-effectiveness) should not be included in the benefit-risk evaluation.

REVISION OF M4E GUIDELINE ON ENHANCING THE FORMAT AND STRUCTURE OF BENEFIT-RISK INFORMATION IN ICH

EFFICACY - M4E(R2)

2.5.6.4 Benefit-Risk Assessment

When **describing** the benefit-risk assessment, the following additional aspects should be considered:

- The impact of the therapeutic context on the assessment, which may include information on the patient perspective if available. This discussion should consist of the following:
  - how the severity of disease and expected benefit influence the acceptability of the risks of the therapy.
  - how the medicinal product addresses a medical need.
- Key aspects of risk management that are important in reaching a favourable benefit-risk assessment, such as:
  - the proposed labeling.
  - whether non-responders can be readily identified allowing them to discontinue treatment.
  - other risk management activities, such as registries or restricted distribution systems.

There are many approaches available for conducting the benefit-risk assessment. This guideline does not prescribe a specific approach. A descriptive approach that explicitly communicates the interpretation of the data and the benefit-risk assessment will generally be adequate. An applicant may choose to use methods that quantitatively express the underlying judgments and uncertainties in the assessment. Analyses that compare and/or weigh benefits and risks using the submitted evidence may be presented. However, before using any method,

2.5 If applicable: Paediatric Investigation Plan (PIP)

2.6 Assessment 1

2.6.1 Preliminary Benefit-Risk Assessment

Not all submitted data have equal importance to the critical assessment of benefits and risk. It is acceptable to give preferential attention to the key elements and summarize other data by means of a short description.

The tabular Benefit-Risk Framework below is meant as a tool in the decision making process, it is not meant to replace free text descriptions of the benefit risk assessment.

- *The utility of the Framework needs to be determined from case to case.*
- *The Framework is meant as an aid and mental map to make the assessments more structured and more systematic, the tool cannot replace judgment.*
- *The Framework should aid the reader of the report to get an efficient overview and summary what were the key data, uncertainties, their interpretation and conclusions from all five dimensions which are driving the benefit-risk assessment.*

Refer also to Appendix 3 for further explanations about this Benefit-Risk Framework.

Decision Factor	Evidence and Uncertainties	Conclusions and Reasons
Analysis of Condition		
Current Treatment Options		
Benefit		
Risk		
Risk Management		
Benefit Risk Summary Assessment		

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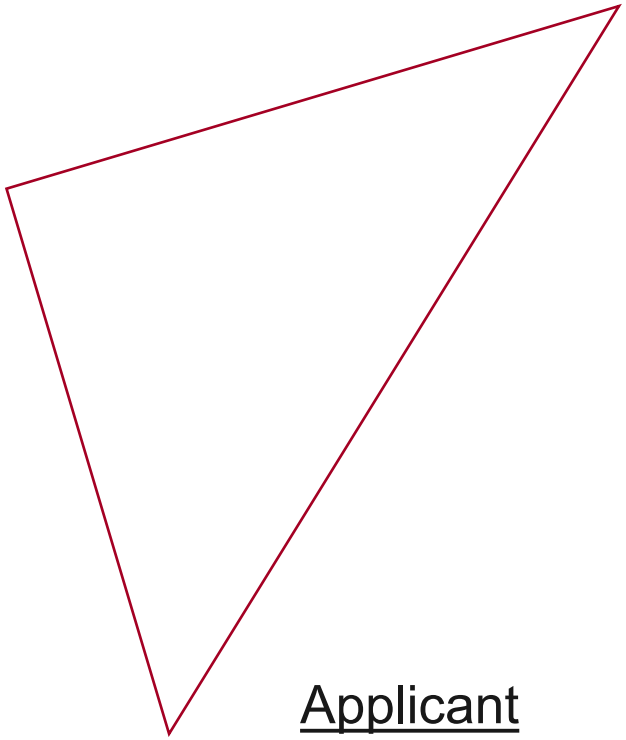
Stakeholders

Patients
- Self-diagnose
- Self-treat
- Self-manage

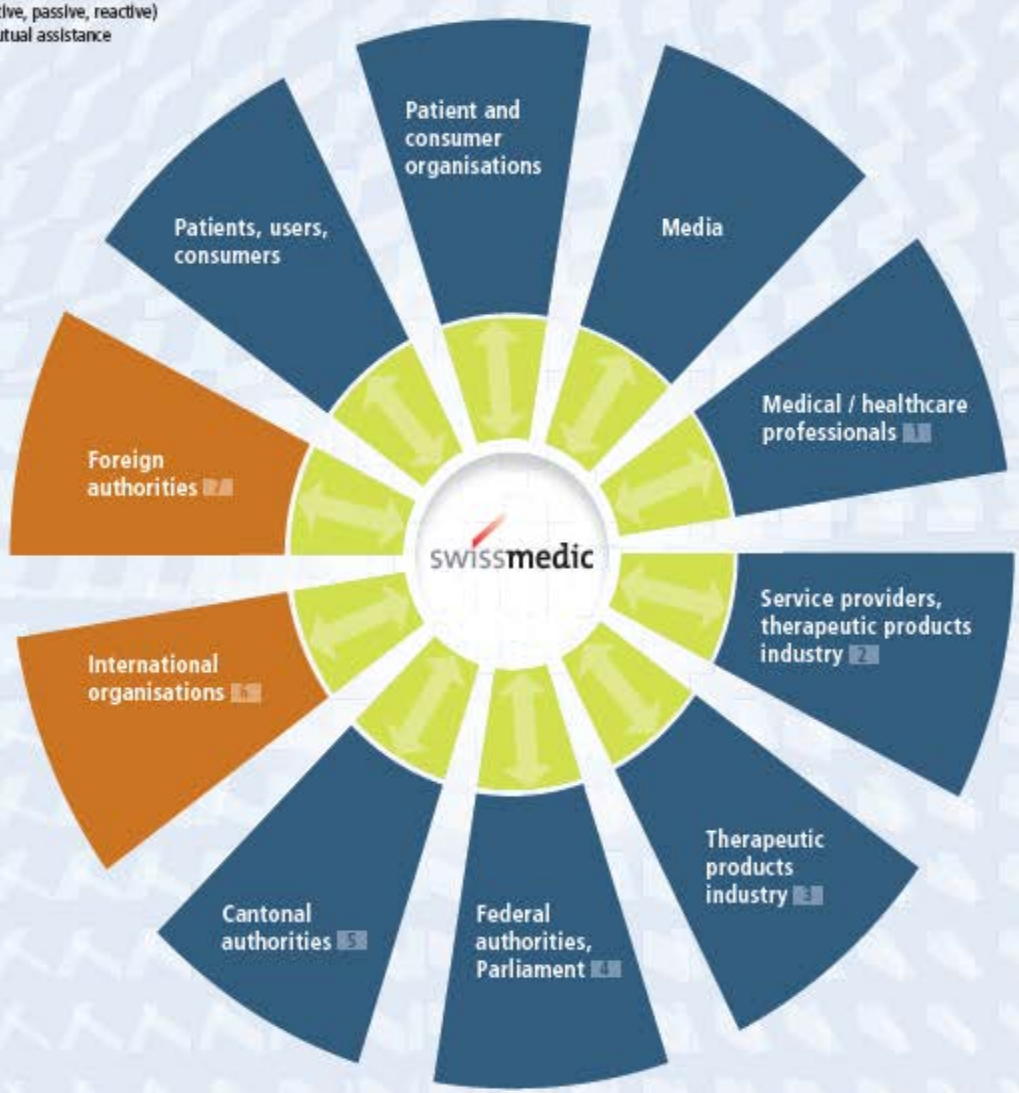
Regulator
- B:R:U
- Label / PI
- Communication



Applicant
- Ø PBRER
- Ø Quality
- Ø Distribution

Focal points of the collaboration

- Provision of information (active, passive, reactive)
  Exchange of information, mutual assistance
  Co-ordination, collaboration
- National
- International



1
- Physicians / Veterinarians
- Pharmacists
- Druggists
- Others

2
- Initial / further training institutions
- Contract research organisations

3
- Associations
- Firms

4
- Parliamentary commissions / delegations, etc.
- National authorities (Federal Office of Public Health, Federal Food Safety and Veterinary Office, State Secretariat for Economic Affairs, etc.)

5
- Cantonal offices (e.g. Cantonal Inspectorates)
- Cantonal Pharmacists
- Cantonal Medical Officers, Cantonal Veterinarians
- Conference of Health Directors

6
- World Health Organization (WHO)
- International Conference on Harmonisation (ICH)
- European Commission
- Council of Europe
- Organisation for Economic Cooperation and Development (OEDC)
- Pharmaceutical Inspection Co-operation Scheme (PIC/S)
- European Free Trade Association (EFTA)
- Others

7
- Australia
- Brazil
- Chinese Taipei
- Germany
- Ireland
- Israel
- Japan
- Canada
- Liechtenstein
- New Zealand
- Singapore
- South Korea
- USA
- Others

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‘Stakes’

	Patient	Regulator	Applicant
Benefit	• Empowered • Preference • Improved access	n/a	Distribution channel
Risk	• Unintended & intended misuse	Mandate	Liability
Un-certainty	• Correct diagnosis (delay)? • Application? • Co-medication	**Communication** (patient information) Consumer literacy	Guidelines

Special cases:

- St. John’s wort
- Corticosteroids
- PDE-5 inhibitors
- Antimicrobials

BMJ 2017;357:j2460 doi: 10.1136/bmj.j2460 (Published 2017 May 24)

FEATURE

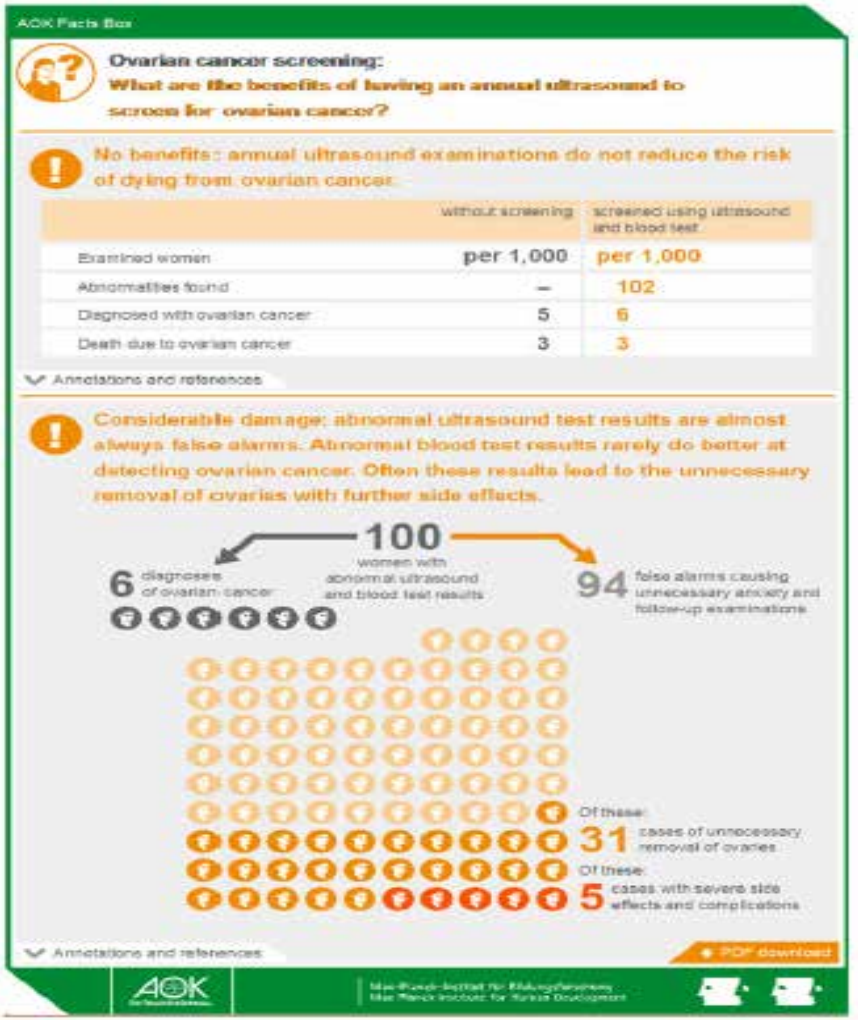
How new fact boxes are explaining medical risk to millions

Smart "fact boxes" that communicate evidence based information on the benefits and harms of drugs and health screening are being rolled out to millions of people in Europe. **Gerd Gigerenzer** and **Kai Kolpatzik** report

Gerd Gigerenzer *director*[1], Kai Kolpatzik *head*[2]

[1]Harding Center for Risk Literacy and Center for Adaptive Behavior and Cognition, Max Planck Institute for Human Development, Berlin, Germany; [2]Department of Prevention, General Local Health Insurance Fund (AOK-Bundesverband), Berlin, Germany; Correspondence to: G Gigerenzer gigerenzer@mpib-berlin.mpg.de

An alien investigating healthcare on Earth would be quite puzzled. We spend billions on clinical studies but fail to ensure that patients and physicians are communicated the results transparently.[1] Instead they get persuasion, marketing, and, in some countries, misleading direct-to-consumer advertising.[2 3]



Assembling the data

In general, fact boxes report the results from a randomised trial or, if available, a systematic review; provide quantitative, evidence based information about benefits and harms; use absolute numbers rather than relative risk reductions or other formats that are known to confuse patients and physicians; and