HAUTE AUTORITÉ DE SANTÉ

Outlook and challenges for the future
A French perspective

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01

Breaking news

Pharmaceuticals: What's in the news ?

THE GUARDIAN Nov. 2010

At least 500 people are believed to have died from heart trouble linked to Mediator, sold in France from 1976 until last year.

Patients who took a controversial French weight-loss drug that caused the deaths of hundreds of people have filed a criminal lawsuit against the pharmaceutical giant Servier, in what could prove the biggest French healthcare scandal of the decade.

Despite fears over the drug's lethal side-effects, Mediator stayed on the market in France for over 30 years and was only banned in 2009.

Opposition politicians are now demanding a public inquiry, accusing the government and the state health regulatory body of being too close to the pharmaceutical industry and putting lives at risk to protect the profits of big business.

Mediator was recommended to overweight people with diabetes but also prescribed as an appetite suppressant to healthy women who wanted to lose a few kilos. Between its launch in 1976 and its ban in 2009 it was taken by more than 5 million French people, subsidised by the social security system.

Benfluorex

- January 15th : Report published by the governmental General Inspectorate of Social Affairs (IGAS).
  - "Inspectors have questioned how benfluorex was kept on the market despite it produced the same dangerous metabolite as an ingredient in anti-obesity drugs that were withdrawn from the market in 1997 for causing heart problems". (*Nature Med. Feb 11)*
- Health Minister pointed out the Company's responsibility but also "serious malfunctions" in the drug regulatory system.
- Role of whistleblowers: pulmonologist Irène Frachon, *La Revue Prescrire*
- Transparency committee gave advice, in 1999, to withdraw the drug from the reimbursement list. No delisting was decided, only price cuts.

Actions taken: 2011

- **January – June 2011**
  - Parliamentary hearings
  - IGAS second report suggesting changes in the drug evaluation system
  - “Assises du medicament” : Large consultation process, 6 working groups, launched February 17th
- **July – December 2011**

  Bill to be debated by Parliament
  - Health minister promised “urgent and radical measures to build a new health safety system so there would “not be a new Mediator tomorrow.”

02

Access to innovative/costly drugs in France

Access to innovative and expensive drugs in France

- **ATU Temporary Authorisations of Use**
  - Granted by Afssaps for drugs that have not yet received a MA
  - Restricted conditions
  - Covered by NHI
- **Expensive drugs in hospitals :**
  - List of expensive drugs for which hospitals will get reimbursemnent from the NHI funds
  - For all authorised indication and a list of not (yet) authorised indications
  - Similar system for off label use in ambulatory care (rare or chronic diseases)

Reimbursed indications for Expensive drugs in Hospitals

Authorised indication

Temporary Treatment Protocol

Not Accep-table

CANCERS DIGESTIFS	AMM	PTT	SNA
ALIMTA® - pemetrexed-			
▪ Mésothéliome péritonéal		X	
▪ Cancer colorectal métastatique			X
▪ Cancer du pancréas avancé ou métastatique			X
AVASTIN® - bevacizumab			
▪ Avastin® est indiqué chez les patients atteints de cancer colorectal métastatique, en association à une chimiothérapie à base de fluoropyrimidine.	X		
▪ Instauration du bevacizumab seul quelle que soit la ligne de traitement (cette situation ne concerne pas le traitement de maintenance)			X
▪ Cancer du pancréas			X
▪ Cancer colorectal en 1ère ligne en association au cetuximab			X
▪ Cancer colorectal en 1ère ligne en association au panitumumab			X

03

P&R in France

Marketing Authorisation

Criteria:

- **Pharmaceutical quality**
- **Efficacy**
- **Safety**

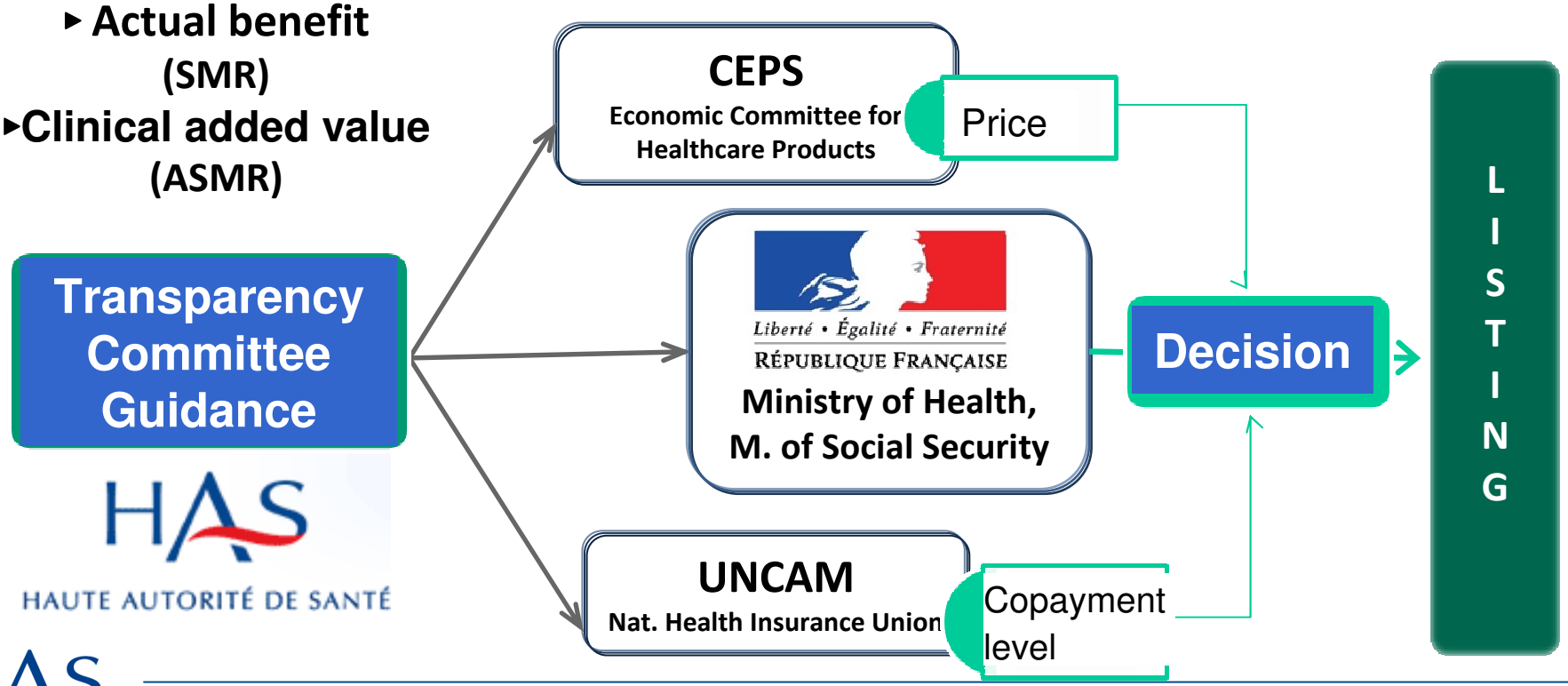
afssaps
Agence française de sécurité sanitaire des produits de santé

EUROPEAN MEDICINES AGENCY

Access to reimbursement

Criteria:

- **Actual benefit (SMR)**
- **Clinical added value (ASMR)**



HAS
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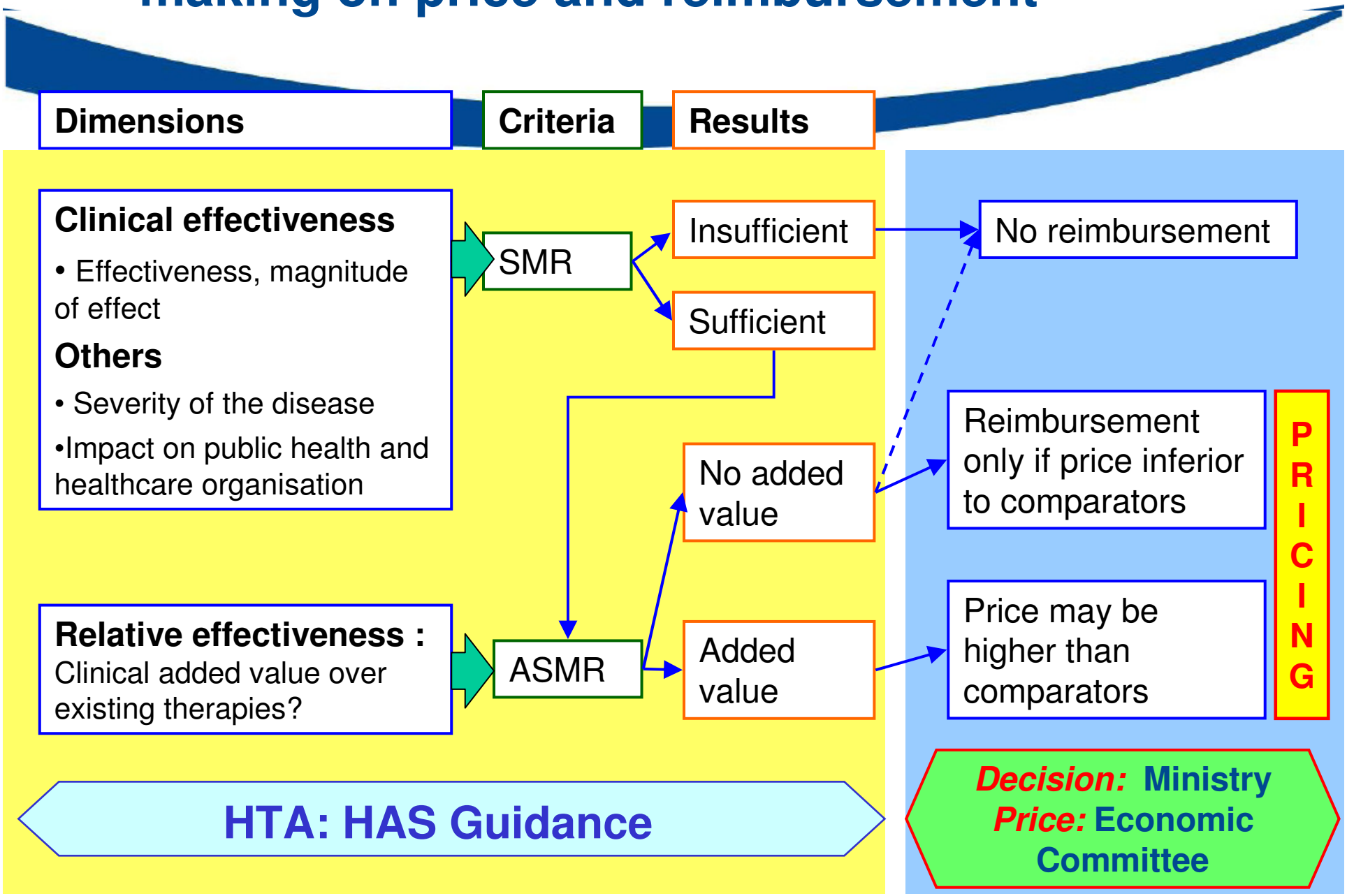
Initial assessment: From HTA to decision making on price and reimbursement



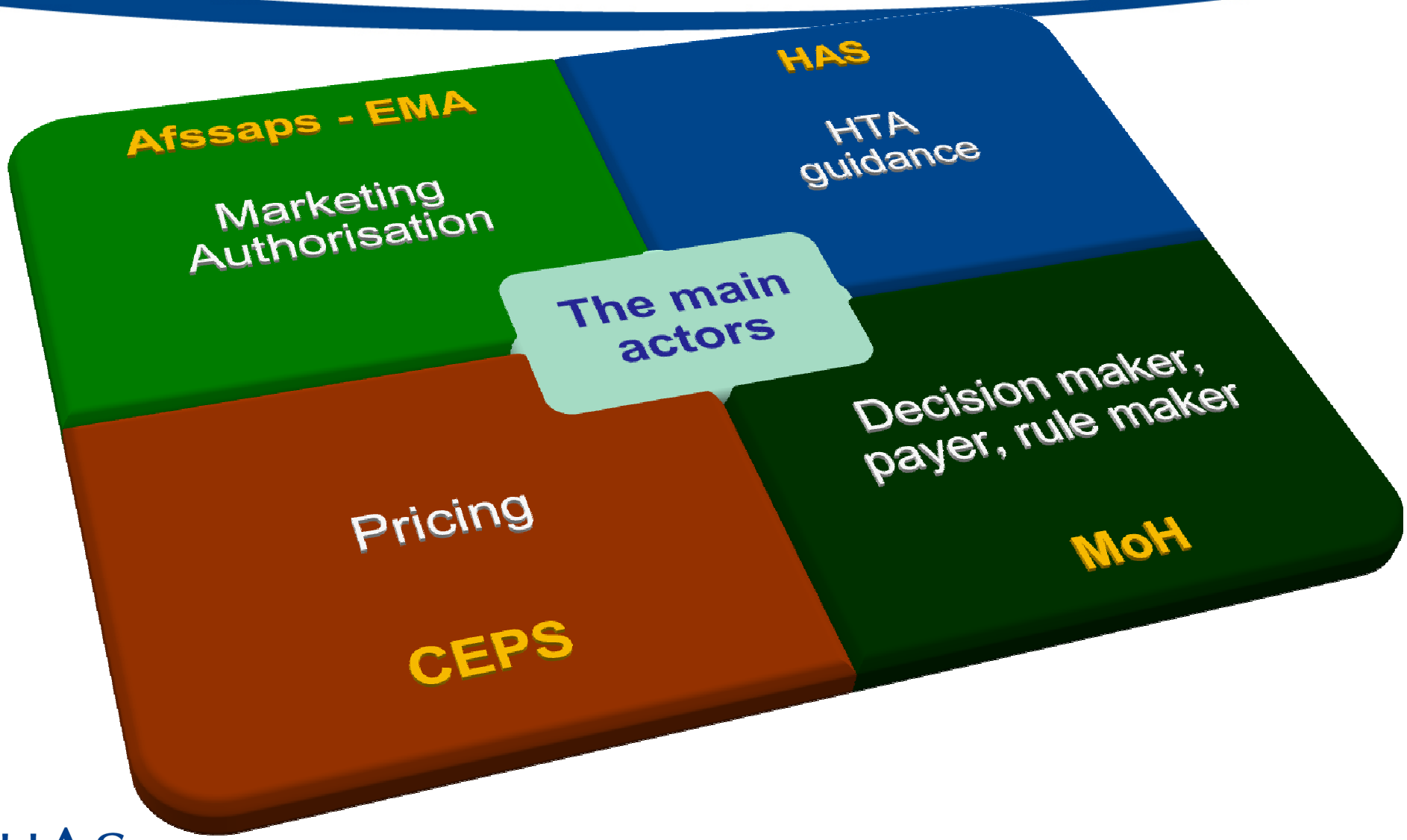
Drug pricing in France – The rules

- **Sale Price :**
  - Set by the Economic Committee for Health Products after negotiation with the company.
- **Account is primarily taken of:**
  - the 'ASMR' (**clinical added value**) of the medicine,
  - the prices of medicines serving the same therapeutic purpose,
  - forecast or recorded **sales volumes**
  - foreseeable and actual conditions of use of the medicine.
- **ASMR and price**
  - V (no added value) : can be listed only if it brings savings
  - Most innovative drugs (Level I and II, III) eligible for faster access at a better price (Price notification instead of negotiation)

04

Current situation and challenges in France

Market Access. Main actors in France



Marketing Authorisation

- **Pharmacovigilance Directive**
- **EMA Roadmap**

France

- **Afssaps: Prof. Maraninchi nomination**
- **Changes in Afssaps organisational structure expected**

HAS

Chairman of the Board :
Prof. Jean-Luc Harousseau
Managing Director :
François Romaneix

Pharmaceuticals (***Transparency Committee***)

Medical Devices, interventional and diagnostic procedures

Economic and Public Health Evaluation

H T A

Healthcare cover for long-term conditions

Medical information quality and dissemination

Accreditation of healthcare organisations

+ One Committee for Clinical Guidelines Validation

HAS: some changes

- **Appointment of Prof. Jean-Luc Harousseau as Chair of HAS Board**
- **Transparency Committee's end of term (March)**
- **Increasing activities in the field of the assessment of economic and other non clinical dimensions**
- **Increasing activities in European cooperation**

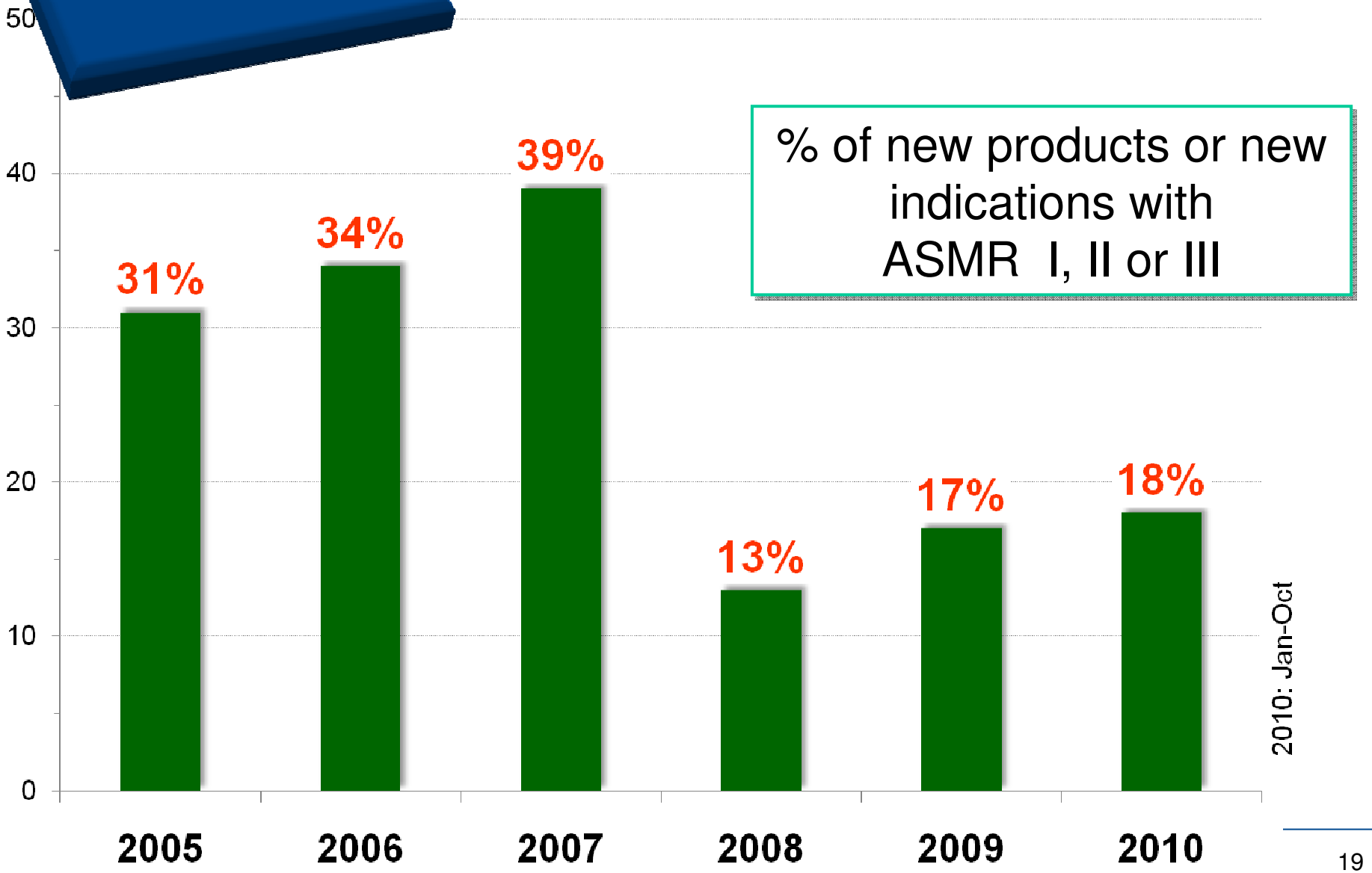
Economic assessments

- **Drugs : development of MTAs in addition to STAs :**
  - Statins (published)
  - Growth hormones in children without GH deficiency
  - Antihypertensive agents (started)
  - Treatments for Type 2 Diabetes (planned)
- **Devices :**
  - Drug eluting stents
  - Self monitoring devices for anticoagulants
- **Procedures..**
- **19 economic reports issued in 2009**

HAS

HTA guidance

Drugs with clinical added value



% of new products or new indications with ASMR I, II or III

Economic Committee

- **New head to be appointed soon**
- **2009 report :**

  ASMR-rated drugs in expensive classes
  - uninterrupted rise in prices of the most expensive medicines not possible anymore.
  - access to these highly profitable markets constitutes sufficient benefit for the innovating companies, whilst it is not necessary or justifiable for NHI system to take on further costs

Medicines with no ASMR

- **A drug without ASMR should bring savings**
- **Particular situation and current debate**
  - Drugs with a new mechanism of action that have not shown to be superior to the reference products at the time of licensing
  - No ASMR granted, but considered as useful alternative treatments by HAS.
  - 'CEPS 2009 : *When treatments costs of the **old reference products are very low** and hence incompatible with the costs required to market more recently developed drugs, the committee is sometimes obliged to make an exception, as it is allowed to do according to the case law, and to grant an ASMR rating*

Orphan Drugs

Orphan drugs expenditures 2009

- Total 930 M€ (+14%)

By therapeutic domain :

- Cancer (MM, CML) 490 M€
- Enzyme/Protein repl. therapies 180 M€
- Pulmonary arterial Hypertension 130 M€
- Various 130 M€

• By sales levels and proportion of expenditure

- 13 Drugs with annual sales > 30 M€ ≈ 700 M€
- ≈ 50 Drugs with average sales < 5M€ ≈ 230 M€

Source : CEPS annuel report 2009

OMPs : CEPS conclusions

- **The committee is therefore naturally questioning the value of continuing to provide support and special benefits for medicines that make a high turnover when their profitability on the market is at least as firmly guaranteed as that of most non-orphan medicines.**

Minister of Health

- **Possible changes of the status of HAS guidance document**
  - In the case of a listed drug for which HAS Transparency Committee considers that it should be delisted (SMR became insufficient) : delisting should happen automatically ?
- **New legislative/regulatory/organisational frame for drug evaluation in France?**
- **Consequences at European level?**

Joint Action

- **HAS appointed by French government to participate in EUnetHTA Joint Action**
- **Active involvement, particularly in 2 work packages :**
  - WP5 Relative Effectiveness Assessment (REA) of Pharmaceuticals (CVZ, co-lead HAS)
  - WP7 New Technologies. Facilitating Evidence Generation and Collaboration on (Pre-coverage) Assessments (HAS lead partner)

International cooperation - Objectives

- **Reduce duplication of work and unjustified differences in the outcomes of the assessments**
  - EUnetHTA Core HTA
  - CAVOD
- **Enhance quality of the assessments**
  - Methodological guidelines (eg on relative effectiveness assessment of pharmaceuticals)
- **Reduce uncertainty**
  - Data collection after launch of a product :
    - EUnetHTA Work Package 7 on New technologies
    - EMA post marketing studies on safety and efficacy
- **Enhance the quality of the data submitted**
  - Scientific advice? Guidelines ?

International Cooperation - Challenges

- **Practical aspects**
  - Guidelines production: time consuming process, participation of all future users needed
  - Stakeholder involvement
  - National / Local procedural constraints
- **Cultural, societal, ortanisational aspects**
  - RCTs vs other methods : technical and cultural aspects to be taken into account…
  - Pros and cons of Scientific Advice activities.
  - Judgements have to be made… Subjective appreciation of relevance will not be eliminated…
- **Step by step approach needed**

Conclusions: Future context for drug assessment/appraisal?

- **French context:**
  - Importance of the future changes yet unknown
    - organisational aspects,
    - evolution of the French model of ASMR-based pricing ?
- **European Context**
  - Definition of realistic objectives for the Joint Action 2
  - EMA – HTA working together :
    - Scientific Advice
    - Post marketing data collection
    - Other areas
  - What's next : Governance of the future permanent cooperation (CBHC Directive)

Thank you for your attention

http://www.has-sante.fr