HTA in France and its impact in the National Health System

Dr. François Meyer
Advisor to the President,
International Affairs at HAS
Introduction
The French Healthcare system in a nutshell

• **National Health Insurance (NHI)**
  – Statutory, coverage > 90% of the population
  – Three major funds: salaried workers, rural workers, self-employed
  – Universal Medical Coverage (CMU) since 2000: for uninsured patients and supplementary coverage under threshold income

• **Supplementary Health Insurance:**
  – 92 percent of the population subscribe to supplementary health insurance

• **Which medical services are covered?**
  – Hospital care, ambulatory care, prescription drugs
  – For prescription drugs: Coinsurance level depends on the therapeutic value. 100%
Life expectancy at birth

Life expectancy at birth, total population


France
OECD
Poland
Health expenditures in 2 European countries
Expenditure trends

- France
- Poland

- Total health expenditure
  - % of GDP
  - Per capita (USD PPP)
  - 2000: 5k, 2.5k, 0k
  - 2005: 5k, 2.5k, 0k
  - 2010: 5k, 2.5k, 0k

- Public health expenditure
  - % of GDP
  - Per capita (USD PPP)
  - 2000: 5k, 2.5k, 0k
  - 2005: 5k, 2.5k, 0k
  - 2010: 5k, 2.5k, 0k

- Expenditure on pharmaceuticals
  - % of GDP
  - Per capita (USD PPP)
  - 2000: 1.5, 1, 0
  - 2005: 1.5, 1, 0
  - 2010: 1.5, 1, 0
Hospital Utilization, for All causes and for Circulatory Conditions, 2004

Source: OECD Health Data 2006 (October 2006).
HTA in France
HTA started in.. 1967

- Creation of a Positive list for reimbursed drugs
- A new drug will be reimbursed only if it has shown efficacy and either have improved clinical outcomes or have similar outcomes but induce savings.
- Committee set up to evaluate drugs

**MINISTÈRE DES AFFAIRES SOCIALES**

Décret n° 67-441 du 5 juin 1967 relatif aux conditions de remboursement des médicaments aux assurés sociaux.

Le Premier ministre,

Sur le rapport du ministre des affaires sociales, du ministre de l'économie et des finances et du ministre de l'industrie,

Vu le code de la sécurité sociale, et notamment les articles L. 249 et suivants;

Vu le code de la santé publique, et notamment les titres II et IV du livre V ;

Vu l'article 63 du décret n° 60-452 du 12 mai 1960 ;

Vu l'avis du conseil interministériel de coordination en matière de sécurité sociale ;

Le Conseil d'État (section sociale) entendu,

Décèrte :  

- Art. 2. — Les médicaments auxquels s'applique l'article L. 601 du code de la santé publique ne peuvent être remboursés ou pris en charge par les organismes de sécurité sociale, sur prescription médicale, ni être achetés ou fournis ou utilisés par eux qui s'ils figurent sur une liste des médicaments remboursables établie par arrêté du ministre des affaires sociales.

Art. 3. — Ne peuvent être inscrits sur la liste prévue à l'article 2 que les médicaments qui présentent une efficacité et qui sont présumés apporter une amélioration de la thérapeutique ou une économie dans le coût du traitement. A efficacité ou économie comparable, préférence est donnée aux médicaments qui résulteront d'un effort de recherche du fabricant.
Since then, HTA continuously developed...

- **Extension to other health technologies**
  - Procedures (decision maker: Health insurance funds. On the request of professional societies/unions)
  - Medical devices since 2000
  - Public health interventions (vaccines, screening programmes, other types)

- **In a continuously changing context**
  - Evidence based medicine, Clinical Practice Guidelines
  - Chronic Diseases
  - Early Access (and reimbursement) process started in mid 90s (Anti HIV drugs)
  - Introduction of DRG system in hospitals
  - Role of patient representatives
Haute Autorité de Santé
Set up in 2005

Afssaps
HTA for Drugs and Devices

ANAES
HTA for non-drug technology and public health actions

HAS
National French Authority for Health

Missions on products/technologies
HTA

Missions on practices
GCP
Healthcare pathways
Hospitals accreditation
Specialists certification
PCD
Patient safety
Comprehensive (‘Full’ HTA) vs Rapid HTA

**Comprehensive HTA taking into account all domains** (Clinical, economical, ethical, legal…)
- Always performed for the assessment of Public Health Actions (eg various screenings methods)
- Drugs and devices: on the occasion of re-assessment of categories of drugs or devices
  - Drug-eluting stents
  - Statins
  - Growth hormones in children with normal levels of GH

**Rapid HTA for drugs an devices**
- Focused on the assessment of added clinical benefit (ASMR)
- Link between ASMR level and pricing
- Recent introduction of economics
Two characteristics of the French system till recent years

• **Main focus on the assessment of the added clinical benefit**
  – ASMR Amélioration du Service médical rendu
  – Level I (major) to IV (minor). Level V = no added clinical benefit
  – Consequence on pricing +++

• **Main focus on the quality of care, equity, patients rights to the best possible therapies**
  – Few, if any, negative decision for reimbursement if product treat severe disease with an additional clinical benefit
  – Cost not a limit if product brings individual clinical benefit
France: From HTA to pricing and reimbursement

**ASSESSMENT**

- Literature
- Dossier from Company

**Internal Assessors**

- Review of available data

**APPRAISAL**

- Specialist Committee

**HAS Guidance**

- Decision on P&R
  - Requirement of Additional Data Collection

**Economic Committee**

- Ministry of Health
- NHI funds

**HTA**
Initial listing: From HAS guidance to CEPS pricing

**Dimensions**

**Clinical aspects**
- clinical efficacy
- clinical effectiveness
- relative effectiveness

**Other aspects**
- disease characteristics
- target population
- impact on public health
- impact on healthcare organisation (qualitative)

**Criteria**

- Actual Benefit
  - Insufficient
  - Sufficient

- Clinical added benefit (CAB)
  - No CAB
  - Minor CAB
  - High to moderate CAB

**Results**

- No reimbursement
- Reimbursement only if price inferior to comparators
- Price may be higher than comparators
- European Price

**Decision:** Ministry Pricing: Economic Committee
## ACTUAL BENEFIT (SMR): reimbursement and copayment level

<table>
<thead>
<tr>
<th>SMR</th>
<th>Level of reimbursement by NHI</th>
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<tbody>
<tr>
<td>Important</td>
<td>65%</td>
</tr>
<tr>
<td>moderate</td>
<td>30%</td>
</tr>
<tr>
<td>minimal</td>
<td>15%</td>
</tr>
<tr>
<td>insufficient</td>
<td>NO REIMBURSEMENT</td>
</tr>
</tbody>
</table>
Si un médicament a plusieurs indications avec le même SMR, celui-ci n’est comptabilisé qu’une fois.
S’il possède des SMR différents, ils sont comptabilisés une fois dans chaque catégorie concernée. En 2012, 17 avis ont comporté 2 SMR différents et 7 ont comporté 3 SMR différents ce qui explique que le nombre de SMR formulés (247) soit plus élevé que le nombre d’avis rendus (216).
03

From HTA to pricing
Pricing committee (CEPS) Members

- **Chairperson, vice-chair person**
- **Ministry of Work, Employment and Health**
  - Representatives of: Director of Social Security, Director General for Health, Director of Care Provision
- **Ministry of Economy, Finance and Industry**
  - Representatives of DG for Competition, Consumer affairs and Combating fraud and DG for Competition, Industry and Services
- **NHI Bodies**
  - Representatives of CNAMTS, RSI, MSA
- **Union of complementary insurance companies**
- **Minister of Research**
Rules governing price setting

- **Primary considerations when setting prices:**
  - added clinical benefit (ASMR),
  - prices of comparators,
  - forecast sales volumes (clawback payments in case of overshooting)

- **Link between ASMR and price**
  - drugs that provide no added clinical benefit (ASMR 5) as assessed by HAS and no savings on treatment costs cannot be reimbursed
  - Drugs with ASMR 1-3: the price is not inferior to the lowest price in 4 European countries
Rules governing price setting

• **Spending objective: ONDAM**
  – Parliament adopts every year a national health spending objective (ONDAM),
  – indicative, not compulsory.

• **CEPS’ s task is to obtain the most advantageous price and financial conditions for the NHI system,**

• **whilst taking into consideration**
  – both the pharmaceutical market as a whole
  – and the limitations of the ONDAM budget,
  – as well as public health needs
  – and the obligation to treat all the companies equally.
Recent change: Additional information provided to the CEPS by HAS

- Assessment of efficiency will complement the assessment of the added clinical benefit

- Only for products claiming added benefit (ASMR level 1 to 3, major to moderate)

- Only if expected sales above 20M Euros per year
HTA process in UK, France, Germany
HTA: interface between science and policy making

Influence of culture and local regulations

- **UK:**
  - Importance of efficiency, cost-effectiveness
- **Germany, France:**
  - Importance on quality of the health care
- **Regulatory context:**
  - Defines the practical frame for HTA
  - Institution(s) in charge
  - Criteria to be applied
  - Which technologies will have to be evaluated by HTA bodies (All ? Selected ?)
France Germany UK: Institutions

<table>
<thead>
<tr>
<th>Country</th>
<th>HTA body</th>
<th>Set up</th>
<th>Recent or upcoming changes</th>
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<tbody>
<tr>
<td>UK</td>
<td>NICE</td>
<td>1999</td>
<td>Value based pricing To be implemented</td>
</tr>
<tr>
<td>Germany</td>
<td>IQWIG G-BA</td>
<td>2004</td>
<td>2011 AMNOG reform Introduction of HTA + pricing</td>
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<tr>
<td>France</td>
<td>HAS</td>
<td>2005</td>
<td>2013 introduction of economic evaluation new drugs &amp; MDs</td>
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- **France:**
  - HAS set up in 2005.
  - Grouping of the HTA activities under a single roof
  - Large remit including: Clinical practice guidelines, Definition of healthcare pathways for chronic diseases, missions on quality of care (including hospital accreditation) and patient safety (eg physicians certification), CPD…
The two main different systems in Europe

Determination of added clinical benefit

Price negotiation and decision

Health economics analysis (price proposed by company)

Decision based on the Cost/QALY estimate compared to threshold
Germany: The AMNOG process at-a-glance

**Pricing**: Federal Association of Health Insurance Funds

HTA = IQWIG and G-BA
UK: NICE Procedures

Assessment:

DH & NICE select and scope topic

HTA programme allocates TAR team & quality assures TAR production

Full text of TAR published in open access NIHR Journals Library title Health Technology Assessment and/or NICE website

Appraisal:

Consultees submit their evidence

NICE Appraisal Committee considers evidence and issues guidance

TAR: Technology Assessment Report

The relationship between assessment and appraisal
Recent and upcoming changes
NICE Value based pricing: proposed changes

Source: NICE Consultation Paper – Value Based Assessment of Health Technologies
Evolution of the French system

Determination of added clinical benefit

Price negotiation and decision

Towards a new criterion?

Introduction of economic evaluation to support decision on price
Towards a new criterion

A unique comparative indicator for both P&R

- Clear definition of objectives, relevant comparator(s), types of comparative studies
- Methodological approach combining semi-quantitative and sequential data
- Analysis includes efficacy, safety and practicability
ITR (relative therapeutic interest)
Process of the sequential evaluation

ELIGIBILITY ?
Comparator, end points
level of evidence (internal validity)

NO
ITR = -1

YES
Non inferiority
ITR = 0

Superiority invoked

Modulation by
tolerability and
practicality (-1,0,1)

 Improvement on
relevant end point
(0 to 3)

Final ITR
-1, 0, 1

Modulation by
Tolerability and
practicality (-1,0,1)

Final ITR
-1 to 3 or more
Why is France introducing Medico-economic assessment of drugs and devices?

- The economic context
- Increasing costs of expensive therapies without clear clinical superiority
- Very high cost of new therapies (including targeted therapies, orphan drugs)
- At all levels of the health-care system
  - health technologies (reimbursed drugs: <20% of healthcare costs)
  - appropriateness of medical choices and practice
  - organization of patient pathway
The objectives of medico-economic assessment

- Not just for reducing health-care expenses
- Not just for indicating the costs
- But to inform decision makers on possible disproportions between incremental costs and incremental effectiveness
- And provide them with a scientific and accurate guidance
The principles of medico-economic assessment

- Cost-effectiveness assessment
- Comparative assessment
  - Qalys used as a tool for comparing drugs

3. Incremental Cost-Effectiveness Ratio (ICER)
   Euros per Qaly at different prices

4. No predefined ICER threshold
   No consensus on the use of thresholds
   - How to define threshold?
   - One or more thresholds?
To provide the pricing committee (CEPS) with an assessment of clinical added value (individual benefit) and an economic opinion (collective benefit)
What use of HE in France in the frame of rapid HTA?

- **Product price** (decided by the company)
  - ICER Cost/QALY
  - Comparison to threshold
  - Decision on reimbursement taken by NICE

- **Product price** (proposed by the company)
  - ICER Cost/QALY
  - HAS gives advice
  - Price decided by Pricing Committee
New methods for evaluation?
Which adaptations for evaluations?

*Evaluation methods of clinical data*

**Benefit-risk initiatives**

- EMA Benefit-Risk methodology project
- PhRMA BRAT Framework and UMBRA Initiative
- ISPOR Risk-Benefit Management Working Group
- Consortium on Benefit-Risk Assessment (COBRA)
- European Federation of Statisticians in Pharmaceutical Industry (EFSPI) Benefit-Risk SIG
- IMI-PROTECT Benefit-Risk Integration and Representation Project

Innovative Medicines Initiative

- Public-Private Partnership between the European Commission and EFPIA
- Project PROTECT
  - PROTECT1 (Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium)
  
  “Improving and strengthening the monitoring of the benefit/risk of medicines marketed in the EU”
  including graphical representation of risk-benefit led by EMA with 31 public and private partners, 2009-2014
MCDA for Natalizumab (Tysabri®)

- Active drug: Natalizumab
- Indication: Relapsing remitting multiple sclerosis
- Regulatory history:
  - Approved 2004
  - License withdrawn 2005
  - Re introduced because of patient demand 2006
  - CHMP reassessed the PML risk and continue approval 2009
- Severe side effects: Progressive Multifocal Leukoencephalopathy
- Data source: EPAR (European Medicines Agency)
- Comparators: Placebo, Avonex, Copaxone
Results

- The Benefit-risk is the product of the weight and the value.
- Most of the Benefit-risk contribution is coming from prevention of relapses.
- Infusion site reactions are the worst risk
Plenary session: Should MCDA replace cost effectiveness analysis for evaluation of Health Care Coverage Decisions?

- MCDA for HTA: The Question Is Not Whether But Merely How To Do It
  Rob Baltussen, The Netherlands

- Why MCDA Should Not be Used: No Estimation of Opportunity Costs
  Karl Claxton, UK

- A Regulator’s Perspective on MCDA vs. CEA for Health Care Decisions
  Andrew Thomson, UK
Changes in the regulatory environment?
Adaptive Licensing: Taking the Next Step in the Evolution of Drug Approval

H-G Eichler\textsuperscript{1,2}, K Oye\textsuperscript{2,3,4}, LG Baird\textsuperscript{2}, E Abadie\textsuperscript{5}, J Brown\textsuperscript{6}, CL Drum\textsuperscript{2}, J Ferguson\textsuperscript{7}, S Garner\textsuperscript{8,9}, P Honig\textsuperscript{10}, M Hukkelhoven\textsuperscript{11}, JCW Lim\textsuperscript{12}, R Lim\textsuperscript{13}, MM Lumpkin\textsuperscript{14}, G Neil\textsuperscript{15}, B O’Rourke\textsuperscript{16}, E Pezalla\textsuperscript{17}, D Shoda\textsuperscript{18}, V Seyfert-Margolis\textsuperscript{14}, EV Sigal\textsuperscript{19}, J Sobotka\textsuperscript{20}, D Tan\textsuperscript{12}, TF Unger\textsuperscript{18} and G Hirsch\textsuperscript{2}

European Medicines Agency, MIT, Agence Français de Sécurité Sanitaire des Produits de Santé, Harvard Medical School, Novartis Vaccines & Diagnostics, NICE, Commonwealth Fund, AstraZeneca, Bristol-Myers Squibb, Singapore Health Sciences Authority, Health Canada, FDA, Johnson & Johnson, CADTH, Aetna, Pfizer, Friends of Cancer Research, Ohio Northern Univ. Raabe College of Pharmacy,
Current state: 1-step process
Adaptive Licensing: 2-step process
Adaptive Licensing: pros and cons

• **Pros: continuous approach of the evaluation**
  – Complete life cycle? Identifying obsolescence?

• **Cons: possibility of diffusion control following first authorization**
  – Impossible in numerous cases (example: new treatment for obesity)

• **Especially applicable for severe diseases with no alternatives in a small population**
  – Rare diseases
  – Transposable to medical devices?

• **Payer reservations**
  – Special dispensation mechanisms already in place
Use of observational (« real life ») data

• **IMI Get Real Project**
  - Objective: to better understand how real-world data can be used to improve the relevance of knowledge generated during development, e.g., through innovation in clinical trial design.
Promote cooperation and dialogue
Assessment of relative effectiveness of drugs

9 Methodological Guidelines

Endpoints used for REA of pharmaceuticals
1. Clinical endpoints
2. Composite endpoints
3. Surrogate endpoints
4. Safety
5. Health-related quality of life

Comparators and comparisons
6. Criteria for the choice of the most appropriate comparator(s)
7. Direct and indirect comparison

Levels of evidence
8. Internal validity
9. Applicability of evidence in the context of a relative effectiveness assessment

Link to the guidelines
http://www.eunethta.eu/outputs/methodological-guideline-rea-pharmaceuticals-clinical-endpoints
# Chosen guideline topics in JA2 – WP 7 – All technologies

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<tr>
<th>Topic</th>
<th>First author</th>
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<tbody>
<tr>
<td><strong>1. Elaboration period 2013 - 2014</strong></td>
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<tr>
<td>1. Internal validity of non-randomised studies (NRS) on interventions</td>
<td>IQWiG</td>
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<tr>
<td>2. Meta-analysis of diagnostic test accuracy studies</td>
<td>HIQA</td>
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<td>3. Economic evaluations</td>
<td>SBU</td>
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<tr>
<td><strong>2. Elaboration period 2014 - 2015</strong></td>
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<tr>
<td>4. Medical Devices</td>
<td>UMIT</td>
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<td>5. Personalised Medicine</td>
<td>OSTEBA</td>
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<td>6. Information retrieval in study registries and bibliographic databases</td>
<td>IQWiG</td>
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Are data produced during products development adequate?

- Development plans designed to satisfy needs for licensing
- Not always adapted for evaluation in view of reimbursement and pricing
- Sometimes impossible to conclude on effectiveness (clinical or cost effectiveness)
- Proposal: organise a dialogue between companies and HTA bodies
  - Companies present development plan and ask questions on the trial design (choice of comparators, endpoints, duration…) and on economic parameters
Multi HTA early dialogues
Current process

Main characteristics of the multi-HTA EDs:
- Confidential
- Non binding
- For new products with expected **added benefit**
- One indication per procedure

Main procedural steps:
- Letter of intent for selection
- Briefing book
- Face-to-face meeting

Content of the Briefing book:
- Development strategy, cost-effectiveness studies: **planned** studies
- **Prospective questions** and company’s position for each question relevant to the development plan
SEED: Shaping European Early Dialogues

- HAS (lead) + 13 partners
- Regulators, payers, patient representatives as observers.
- Sustainable process to put in place, including collaboration with EMA
- Kick-off meeting (D1): October 21, 2013
- Preliminary work: procedures and templates for Briefing Books (medicines, MDs)
- 4 EDs done, 6 to be done (till Spring 2015)

Model for permanent ED activity to be proposed
Conclusions? Some important points…

• **HTA: interface between science and policy making**
• **Methods should be robust AND adapted to context**
• **Various models of HTA across countries**
• **Judgments have to be made in a transparent way**
• **Importance of evolution of methodologies**
  – Use of observational data
  – New approaches such as MCDA…
• **Importance of dialogues**
  – Between HTA bodies, between HTA and regulators, with stakeholders