“Evaluating the Acceptability of Vaccine and Vaccination Programs: An Individual and Public Health Perspective”

FONDATION MERIEUX
MEETING REPORT


The Vaccine Acceptability meeting organized by Fondation Mérieux was held at “Les Pensieres” Conference Center from July 7 to the 9, 2008 in Veyrier du Lac, France. The meeting brought together foremost international experts from North America & Europe.

The following report summarizes the information provided during the meeting based on abstracts and speaker’s lectures, all procedure specifics are not detailed in this report.

Meeting Reporter: Valentina Picot
Table of Contents

I. Introduction
II. Meeting Objective
III. Summary of Scientific Agenda Lecture Presentations
   1. Welcome Address & Keynote Presentation
   2. Session I: Key Elements Supporting the Introduction of a New Vaccine
      • Chaired by: David Salisbury and Barbara Stoll
      • Lectures Briefings
   3. Session II: Understanding Willingness to Vaccinate
      • Chaired by: Zulfiqar Bhutta and Roger Glass
      • Lecture Briefings
   4. Session III: Understanding Willingness to be Vaccinated
      • Chaired by: Susan Rosenthal and Daniel Salmon
      • Lectures Briefings
   5. Session IV: How to Assess the Acceptability of Vaccination by the Vaccinees: The Concept of Patient Related Outcomes
      • Chaired by: Thomas Szucs
      • Lectures Briefings
IV. Annexes
   • Meeting Agenda
   • Press Release

Disclaimer
Information on this report was obtained from the lectures and abstracts given by the speakers as per scientific agenda on the Evaluating the Acceptability of Vaccine and Vaccination Programs a Fondation Mérieux meeting held on July 2008 at “Les Pensieres” conference center in Veyrier du lac, France. All graphs, flow charts and images were obtained from the speaker’s presentations to facilitate the comprehension on the subject. The information on this report was authorized as per signed authorization form by the speakers in question, a modified form of vulgarization of this information might require further speaker’s authorization. The information provided does not constitute a manual or technical sheet on the subject, it might have omissions, we cannot assure its completeness or accuracy, and should not be used for the diagnosis or treatment of disease. Commercial products and prototypes are named and illustrated for information purposes only. No endorsement or recommendation by the Fondation Mérieux or that of the organization partner or the meeting reporter are implied or should be inferred. They do not necessarily represent the views of Fondation Mérieux or that of the organization partner or the meeting reporter and have not been formally disseminated and should not be construed to represent any agency determination or policy.
I. Introduction

The introduction of new vaccines in vaccination programmes is based on public health needs, the assessment of the vaccine-preventable burden of disease both medical and social, and the safety and efficacy of the vaccine. This leads to the decision to recommend and fund vaccination programmes. With most vaccines intended to prevent childhood diseases, the success of vaccination policies essentially relied on the public awareness of the severity of the disease to be prevented and the willingness of health care professionals and the parents to actively protect their children against severe diseases.

But, despite recommendations and their proven efficacy or effectiveness, some vaccines remain underused, especially in older age groups. With more and more vaccine targeting new diseases less perceived as life-threatening or intended to adolescents, adults and/or the senior population, new factors will influence the level of implementation of vaccination programmes. They are, to a large extent, linked to the individual perception of the value of being vaccinated. These individual or general attitudes must be thoroughly analysed and understood as they will represent major drivers or barriers to the success of vaccination policies and their public health impact.

The two major players in this field are the health care professionals and the patients themselves, but they can be influenced by others stakeholders in the more and more complex environment of vaccinology.

The concept of acceptability of vaccination must also be introduced early in the development, regulatory and policy-making processes to introduce new vaccines. It includes not only sociological approaches but will also request the development of specific and validated tools to assess some of the patient-related outcomes linked to vaccination that will influence the acceptability of the programme.

The Mérieux Foundation is pleased to organize this meeting as a forum to better analyse and understand what could be the key success factors for the introduction of new vaccines and their adoption by the public at large.

The Foundation welcomes invited scientists, vaccinologists, representatives from industry and international institutions to Les Pensiéres Conference Center, in Annecy, France, from 7 to 9 July 2008, to attend "Evaluating the acceptability of vaccine and vaccination, an individual and public health perspective". Its purpose is to review the general principles leading to the introduction of new vaccines, to analyse the key elements which support the willingness to vaccinate by health care professionals and the willingness to be vaccinated by the population. This includes reviewing existing ways to assess these elements and the need to develop specific and validated tools, which could be used to support the development and registration of new vaccines, as well as recommendations and implementation of new vaccination programmes. Case studies related to newly introduced vaccines will provide practical examples and contribute to define a general approach.
II. Meeting Objectives

- To identify and understand the key elements underpinning the successful adoption of vaccination programmes by the population;
- To analyse the drivers and barriers that lead health care professionals to actively support vaccination policies: the "Willingness to Vaccinate";
- To analyse the elements that drive the acceptability of vaccination programmes by the target population: the "Willingness to be Vaccinated";
- To review the assessment methods for such parameters in a way that would be relevant to support policy making processes;
- To define a research agenda in this new area of vaccinology.
III. Summary of Scientific Agenda Lecture Presentations
The meeting was presented in sessions as follows.

2. Session I: What is a Model?
   a. Chaired by: David Salisbury and Barbara Stoll
   b. Lectures Briefings
   c. Discussion

3. Session II: What is the Expected Public Health Impact of Model Approach?
   a. Chaired by: Zulfiqar Bhutta and Roger Glass
   b. Lecture Briefings
   c. Discussion

4. Session III: Predicting the Impact of Interventions?
   a. Chaired by: Susan Rosenthal and Daniel Salmon
   b. Lectures Briefings
   c. Discussion

5. Session IV: The Future of Infectious Diseases Modelling
   a. Chaired by: Thomas Szucs
   b. Lectures Briefings

1. Welcome Address & Keynote Presentation

Christophe Longuet, Medical Director of the Mérieux Foundation welcomed the speakers and participants to “Les Pensières” conference center in Veyrier du Lac, France. He presented the foundation’s mission: to control infectious diseases in developing countries by supporting scientific research, sharing knowledge and supporting health infrastructures, patients and their families. The presentation allowed participants to better understand the scope and role of the Mérieux Foundation in disease control activities in developing countries.

1.1. Keynote Lecture
Principles of Vaccine Adoption (summary information taken from speaker’s ppt)
David Salisbury, Director of Immunisation, Department of Health, London, UK

Pressures for new vaccine introduction: International institutions, National authorities (GOs), Interest groups (NGOs), Professional organizations, Public at large, Opinion formers who influence the public at large.

Constraints on new vaccine introduction: Your own priorities are more important than anyone else’s - ability to influence prioritisation, Resource limitations at all levels, especially for preventative rather than curative services, Competing priorities for those implementing, Lack of receptivity at local level for problems of global, regional or national relevance - a predictable consequence of decentralisation.
Is there a need?, Is there a vaccine?, That is safe and effective?, Who should receive vaccines?, Would it be a good use of public funds?

**Is there a need? Information requirements:** Epidemiology of disease: Extent of burden in morbidity and mortality, Age of affected population, Projections for future disease burden, Clinical management of disease: Primary care implications, Secondary / tertiary care implications, Long term complications of disease and health requirements. Economic burden in time off work for affected or their carers.

**Annual cases of meningococcal infection England and Wales, 1992 - 1999.**
Is there a vaccine?
Not at the time of start-up.
Encouragement of manufacturers to collaborate with Phase II studies.
DH funding for Vaccine Evaluation Consortium in place.
Large increase in DH funding in 1997 to accelerate research.
Identification of specific policy related questions for DH funded research, separate to manufacturers' interests, eg giving men C conjugate at same time as MMR, or other vaccines.

Purpose of DH investment
To accelerate the availability of much needed vaccines.
To answer policy related questions that manufacturers would not necessarily address.
To hasten the process of license through generation of high quality data.
To evaluate vaccine effects in circumstances similar to routine use (e.g. immunisation of whole schools for adverse events).

Acquisition of resources.
Cost - benefit analysis.
Operational advantages.
Urgency / public health concerns.
Public / Professional pressures
Political dimension /Government priorities.

Introducing new vaccines / new policies
A complex multi-faceted task that requires the co-ordination of:
  - policy makers / programme management
  - public health experts
  - advertising & marketing experts
  - researchers
  - manufacturers
  - regulators
  - parents and health professionals

Introducing new vaccines / new policies.
Vaccine studies
Product selection
Disease Surveillance
Adverse Event monitoring
Supply arrangements
Call / recall programming
Coverage Measurement
Resources
Communication Strategy
Professional training materials
Vaccine failures
Impact assessment
Example:
Rate of invasive pneumococcal infection by age, England & Wales, HPA data.

Awareness of the pneumococcal campaign
Main message taken from pneumococcal campaign (unprompted).

- Get your child vaccinated/immunised: 33%
- Mention of a new immunisation/vaccine: 19%
- Protection against/prevention of diseases: 10%
- Wait to be contacted: 9%
- Available for children under 2: 8%

Diseases pneumococcal vaccine was thought to protect against (unprompted).

- Meningitis: 74%
- Blood poisoning/septicaemia: 58%
- Pneumonia: 52%
- Ear infections: 29%
- Don’t know: 11%
Perceived action to take for the pneumococcal vaccine (unprompted)

- Nothing/wait to be contacted: 72%
- Contact health visitor/surgery for more info: 11%
- Get more information from a leaflet: 8%
- Contact health visitor/surgery to make appt: 4%
- Visit immunisation website: 2%

Misleading information in different media as journals, internet, etc

It’s a fantastic breakthrough
DELT AT CANCER JAB FOR GIRLS

Cervical cancer vaccine ‘will encourage girls to be more promiscuous’

Delivery: Practical issues to consider

- Age of vaccination.
- Girls (and boys?).
- Catch-up campaign.
- School based programme vs GP practice.
- Parent and child acceptability.
2. Session I: Key Elements Supporting the Introduction of a New Vaccine

The Medical Needs
Paolo Bonanni, Department of Public Health – University of Florence – Italy

I like to begin with a quote from Prof. Ben van der Zeijst, WCVII 2006

“Today citizens assume that their governments have measures in place to protect them. Against childhood diseases and interpandemic influenza, but also against emerging infections and bioterroristic agents. Even travellers do not want to ‘lose time’ due to infections…..”

Vaccination is traditionally intended to protect against a given disease, i.e. to decrease its morbidity or mortality, or both. In addition, such a direct impact on the disease itself is expected to occur in a relatively short, foreseeable future and should be easily measurable through appropriate epidemiological surveillance. The ultimate impact is the elimination or eradication of the disease. It is unlikely that this rather straightforward paradigm is going to apply to a number of new vaccines. Indeed, the impact of new vaccination strategies will not only be a direct, short/medium term effect, but a broader long-term impact, not always easily measurable and leading at best to «controlling» a disease or its consequences. This new paradigm can be illustrated by several of the new vaccines (rotavirus, PV, pneumococcal conjugate, zoster, etc.).

To determine what are the drivers for decision making on vaccination programmes: there is a difference between the priorities regarding vaccination in the past and of today.

In the past
- Serious disease and death were triggers
- Few vaccines
- No pharmaco-economic analysis (self-evident advantage of vaccination)
- Preference for vaccination early in life
- High acceptance by parents
- Low costs

Today (from 2000 on)
- Many new vaccines in line
- Evidence Based Prevention (EBP) approach
- Parents more concerned about AE
- Higher technological content and higher costs

According to this, can be stated that vaccine-preventable diseases is an evolving concept: Traditionally, the effect of vaccination was measured as a reduction in the short term of: Deaths, serious sequelae, complications, and numbers of cases; this for well characterized acute diseases. The measurement is using standard surveillance methods, and the objective is the elimination or eradication of the disease.

Today, the impact of new vaccines is not only direct, short term, medical perse, and also is not easily measurable; usually leading to control rather than the elimination of the disease or its consequences.
Regarding chosen relevant efficacy endpoints, one can say that:

- The expected benefit of some new vaccines is not to reduce the incidence of a well-defined infection/disease, for example for the following disease the efficacy is to reduce complications, severe presentations, and hospitalizations, etc.
  - Some vaccines have more impact on disease complications or outcomes
    - Influenza: hospitalisation, societal impact
    - Rotavirus (RV): severe cases, hospitalisation, family disruption
    - Zoster: severity, post-herpetic neuralgia, social disruption
  - Need for clinical surrogate of protection when expected benefit is delayed
    - HPV: infection, pre-cancerous lesions and cervical cancer.

Some examples on the above saying are:
In the case of Influenza all age and risk groups are affected about 5% to 20% become ill each year. Several side effects such as in healthy children, otitis media, outpatient visits, antibiotics, school absenteeism and in healthy young adults, outpatient visits, antibiotics, work absenteeism, etc.

Taken into consideration all these aspects, the rationale for new influenza vaccination recommendations in the USA updated in 2006 were:

- Expanded vaccination to age groups 50-64 years and 6-59 months of age, this is expected to have an impact in reducing serious morbidity & mortality due to influenza in HR persons, to produce herd immunity; to provide personal & societal benefits to new groups and to promote better pandemic preparedness. (courtesy Dr. Kristin Nichol, modified)

Another example is that of Rotavirus gastroenteritis, a study entitle ‘Burden of Paediatric Rotavirus Gastroenteritis in Europe – Reveal Study” (Van Damme P. et al; JID, 2007), assessed the impact of gastroenteritis rotavirus in several European countries in children under 5 years of age. The study was done in three settings: The hospitals in the study area (N=12), all emergency rooms (N=16), and sample of GPs and/or paediatricians (N=139).

The outcome of the study brought out the following results:
- It was confirmed that about 40% of acute gastroenteritis is due to Rotavirus, as it was known.
- Importantly that more than 50% of hospitalisations and ER visits for acute gastroenteritis (AGE) are due to Rotavirus. (See graph below).
Following graph shows the impact of Rotavirus Vaccine on the RVGE Burden in Italy

Another example is that of the Human Papiloma Virus - HPV VLPs - which is an anti-cancer vaccine but not only as:
- First vaccine clearly perceived as directed against cancer (hep B in reality).
- Impact usually forecasted in the long term, BUT short-medium term impact possible on pre-cancerous lesions, cervical intraepithelial neoplasia (CIN 2/3 and CIN 1), on genital warts, and on number of diagnostic tests (repeat citology, colposcopy) and on related interventions (biopsy, excision, ablation or other)
- Relevant psychological impact of diagnostic procedures and treatment for frequently self-resolving low/medium-grade dysplastic lesions.

When studying the efficacy of this type of vaccines the issue is to choose clinically relevant efficacy endpoints.
A case study HPV vaccine: How to know if a vaccine will prevent cancer, since cancer is an unethical endpoint for clinical studies?
To choose the right endpoints is relevant to know well the natural history of the disease. In the case of the HPV vaccine: CIN 2/3 is the endpoint recommended by FDA and WHO, as this one is an oblige precursor of cervical cancer.

Also it’s important to bear in mind cross protection outcomes, and choosing clinically relevant efficacy endpoints with this regards. In the case of HPV vaccines of what is the best standard for proof of Cross Protection?
There are also some critical factors in the evaluation of the impact of new vaccinations.
• Herd immunity vs. direct protection.
• Induction and duration of immunological memory – duration of protection (sometimes correlates of protection not known - pertussis, HPV, etc.).
• Burden of disease is often lacking (e.g. rotavirus and Hib in developing countries).
• Cross protection between serotypes unknown.
• Possible emergence of non-vaccine type strains or of ‘escape mutants’

Previous experience shows all ‘unknowns’ usually hide greater vaccination impact.

Also strains for a given disease can change or be modified overtime, so there is an importance is keeping strict surveillance to look at is happening and eventually adding new strains or modified accordingly the current vaccine.

In terms of using immunological correlates of clinical protection as primary end points, following main issues to consider:
• To determine which is the protective level post-primary and post-booster.
• Determine seroprotective levels vs GMTs.
• The type of immunological testing being performed.
  – assay sensitivity
  – neutralisation or bactericidal activity
  – Characterisation of immune responses: class & subclass of immunoglobulins / functionality (e.g. avidity) of antibodies that have been elicited.
• Induction of immunological memory (priming), antibody persistence. The issue of how immunological memory can be triggered.
• Potential impact of pre-existing antibodies.
• Role of cellular / mucosal immunity.

There is a need to shift from the concept of prevention of disease to that of prevention of illness (also including consequences on social disruption, resource utilisation, protection of high-risk groups, family and community members, and impact on work absenteeism).

What is needed today as evaluation tools?
• Introduce and validate the most modern tests for the surveillance of infections (NAT, genotyping, serotyping sequencing, etc.).
• Implement the evaluation techniques of Evidence Based Prevention, through meta-analysis and systematic revision of efficacy and safety of vaccines.
• Expand a multidisciplinary approach (together with mathematicians, demographists and economists) to develop dynamic models on the epidemiology of disease and on the impact of new vaccination strategies.
• Explore new methods for the surveillance of social wellness, quality of life, impact on productivity.
• Learn and experience communication skills.
Another concept is how the prioritizations of interventions are balanced between costs and morbidity, an example shown in the following graph:

### Table 1. Scoring ranges

<table>
<thead>
<tr>
<th>Score</th>
<th>CPB range: QALYs saved, undiscounted</th>
<th>CE range: $/QALY saved, discounted</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>≥360,000</td>
<td>Cost saving</td>
</tr>
<tr>
<td>4</td>
<td>≥185,000 &lt;360,000</td>
<td>&gt;0 &lt;14,000</td>
</tr>
<tr>
<td>3</td>
<td>≥40,000 &lt;185,000</td>
<td>≥14,000 &lt;35,000</td>
</tr>
<tr>
<td>2</td>
<td>≥15,000 &lt;40,000</td>
<td>≥35,000 &lt;165,000</td>
</tr>
<tr>
<td>1</td>
<td>&lt;15,000</td>
<td>≥165,000 &lt;450,000</td>
</tr>
</tbody>
</table>

CE, cost effectiveness; CPB, clinically preventable burden; QALY, quality-adjusted life year.

The following graph shows how the interventions are prioritized to be justified for implementation or not, as observed for the diseases above or under the indented black line.

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**Future Vaccine Developments (L. Hessel / 9th ADVAC / Les Pensières 21 May 2008)**

* A solid scientific basis is critical for success, the likelihood that candidate vaccines will succeed as safe & effective vaccines depends on the scientific foundation, e.g. clinical and immunological endpoints
* Epidemiology studies (burden of disease), disease surveillance and health economic data are critical for guiding the vaccine development process, helping to identify high risk populations,
providing insight into changing epidemiology trends and anticipating post-licensure commitments.

**The perception of vaccines and vaccination in the next 10 years**

*Academic research should move beyond science and risk assessment through social and political analyses.
– Vaccinology bridges biomedical and social sciences.
*Vaccination is more a global social process than an isolated medical action, based on:
– the notion of community good or benefit.
– the relationship between the individual and the community, citizen and state, and health and disease.

> "Practical medicine is divided into two parts: a science which preserves health, and one which cures disease…. To preserve health is a thing that can be done better and with more certainty than restoring health once it has gone lost….”
> Bartolomeo from Salerno (12th Century)

**The Regulatory Process**

*Nora Dellepiane, Department of Immunization – Vaccine and Biologics – WHO
Geneva, Switzerland*

This talk will cover the following topics:

- Vaccines of assured quality
- Recommended regulatory functions and source of vaccines. WHO support to strengthen regulatory functions
- New vaccines: New challenges
- WHO innovative approaches to support strengthening of regulatory capacity

**Vaccines of Assured quality**

The WHO goal is to ensure that “100%” of vaccines used in all national immunization programmes are of assured quality.

Definition of “**Assured quality vaccines**”

National Regulatory Authority (NRA) independently controls the quality of vaccines in accordance with the six specified functions defined by WHO.

No unresolved confirmed reports of quality related problems.

Guided by Expert Committee on Standardization of Biologicals (ECBS) recommendations on safety, efficacy and quality issued in WHO Technical Report Series (TRS).

Part of the work of WHO is to provide regulatory guidance which is based on different approaches:

- Global written standards.
- Global measurement standards for testing vaccines.
- Support for the evidence base for standards.
WHO Global written standards
- Technical specifications that help define safe and efficacious vaccines. These are intended to be scientific and advisory in nature.
- Guidance for national regulatory authorities and manufacturers on international regulatory expectations for the production and quality control of vaccines, non-clinical and clinical evaluation of vaccines.
- Facilitate international harmonization of vaccine licensure.
- Living documents revised in response to scientific advances.

The WHO Recommendations on production and quality control of vaccines are advisory in nature; however, they are used as:
- The basis of national regulations in many countries to shape their own national regulations.
- They are also the basis for the assessment compliance performed by the WHO for the purposes of pre-qualification of vaccine supply by UN agencies.

Process to strengthen NRAs (Network of Regulatory Experts)
This is basically a program to work with regulatory authorities to strengthen their capacity. A five step capacity building program:

1) Benchmarking
2) NRA assessment of the regulatory functions in different countries.
3) Planning to address country gaps through the institutional development plan (IDP)
4) Implementation of plan that includes training courses (GTN), technical inputs, in country workshops.
5) Monitoring and evaluation to measure the progress and identify new needs if applicable.

This program started in 1997; today 86 countries have been evaluated under this program criteria.
When observing the vaccine pipeline is possible to see the impact that vaccination can have in reducing disease burden. In the pipeline there are Traditional vaccines (Tetanus, Pertussis, Polio) that are well known and do not have to confront major regulatory issues, vaccines underutilize (Cholera, Hepatitis, Rotavirus, HPV) that represent more challenges for
regulators and developers, and vaccines of the future (HIV, Malaria, TB) that are further more complex to regulators due to the many unknown processes.

**Some key messages:**
- The vaccine development pipeline is especially buoyant; some complex products are under development; specialist regulatory oversight is needed
- WHO is committed to support countries to ensure and sustain that 100% of vaccines used in all national immunization programmes are of assured quality – **NRA strengthening** activities and other innovative approaches are being applied to attain this goal.

**Regulation of new vaccines:**
- Responsibility now falls more on Developing Countries using these vaccines and less on Industrialized Countries where they are produced.
- Countries have insufficient expertise and experience to assess data and dossiers (Manufacturing, preclinical and clinical data, etc.).
- NRAs must acquire new skills.

**Clinical trials for new vaccines**
- Are being run in ANY country, no matter the expertise/strength of their National Regulatory Authority.
- Quality of the trials must be guaranteed.

**Responding to Challenges**
- Development of new support mechanisms for regulatory authorities.
- Development of new regulatory pathways.

**New Support Mechanisms for National Regulatory Authorities**
- Establishment of Developing Countries Vaccines Regulators Network (DCVRN) in 2004.
- Development of new Global Training Network Courses and country workshops on a needs basis.
- Sentinel Network to monitor safety during introduction of novel vaccines and DTP based combinations.

**Developing Countries Vaccine Regulators Network**

**Objectives**
Promote and support the strengthening of the regulatory capacity of NRAs for the evaluation of clinical trial proposals and clinical trial data through expertise and exchange of relevant information.

**Modus Operandi**
- Meetings twice a year
- Discuss critical aspects to be considered for the review of clinical data for registration of novel vaccines
- Develop procedures, forms and other relevant documents to harmonize regulation of clinical trials and evaluation of clinical trial data
- Exchange of information and mutual support
- Provide support to other countries in their region of influence (i.e. SA and Indonesia
African Vaccine Regulators Forum (AVAREF) established in 2006

Objectives
- To provide information to regulators of countries that are target for clinical trials
- To promote communication/collaboration between NRAs and Ethics committees and among regulators in the Region and others.
- To provide a resource of expert advise to regulators
- To identify needs for expert support to NRAs

Modus Operandi
- One plenary meeting per year (2 to date) plus support activities between meetings; joint WHO/HQ/AFRO activity
- 19 countries involved; NRA and National Ethics Committee representatives

AVAREF Achievements

An historical moment: For the 1st time in Africa, regulators and ethics committee members from Burkina Faso, The Gambia, Ghana, Ethiopia and Mali conducted an inspection of Good Clinical Practice (GCP) inspection of phase II observer-blind, randomized, active controlled clinical trial of meningococcal a conjugate vaccine at the Centre for Vaccine Development (CVD), Bamako, Mali; January, 2007.

Training Planning workshops for NRA strengthening
Twenty six countries
Senegal, Mali, Niger, Benin, Togo, RCA, Cameroon, Burkina Faso and Guinea (Ouagadougou May 2005)
Angola, Botswana, DRC, Malawi, Mozambique, Namibia, Rwanda, South Africa, Tanzania, Zambia and Zimbabwe (Gaborone Dec 2005).

Training Workshops and courses
- “Evaluation of clinical trials”, Pretoria, March 2005
- Regulatory forum on clinical evaluation of rotavirus vaccines (Botswana Dec. 2005)
- Joint review of CTA of Conjugate Meningitis A vaccine (Banjul Jun 2006)
- “Vaccine Regulation” (in French), M’bour, Senegal, March 2006
- “Surveillance of AEFIs” (in French) in Senegal (2006), Tunis (2007) and (in English) in Cape Town (RSA), 2006
- “Authorization & Inspection of Clinical Trials” in French in Ouidah in December 2006, and in English in Harare in July 2007
- “Good Clinical Practices” in English in Harare in July 2007
- Joint Inspection of Men. A Clinical Trials, Bamako, Mali, Jan. 2007*
- African trainees sent in 2006 to GTN courses on lot release in Lyon, France, and on GMP in Seoul, Korea.

New GTN courses
- GMP inspections. Training Center: KFDA, Korea
- Testing of Hib conjugate vaccines. Training Center: NVI, The Netherlands
- Authorization of Clinical Trials (Itinerant)
- GCP inspection course (Itinerant)
- Evaluation of Clinical data (Updated 2008) (Itinerant)
Lot Release (Updated 2007). Training Centers: AFSSAPS (in French) CDL Kasauli (in English)
Product Evaluation (under development)

New Regulatory Pathways
- Collaboration with EMEA for the establishment of Scientific Opinion procedure (Art. 58).
- Procedure for expedited review of imported prequalified vaccines for use in immunization programmes.
- Considering feasibility of establishing mutual support mechanism between NRAs in Asia for the regulation of JE vaccines.

Procedure for expedited review of PQd vaccines
It is intended for countries that source their vaccines through UN agencies, or who use the WHO prequalification as a basis for selection of vaccines for use in their national immunization programmes, importing them through direct procurement. It provides guidance on how NRAs of such countries can expedite the regulatory review for such products. Not intended to affect in any way post-approval activities in place in these countries. Countries intending to use the procedure should ensure that their national regulations contain provisions to allow to shorten the normal regulatory approval process.

Criteria for use
Scenario 1
For an expedited approval vaccines WHO-prequalified that are sourced through UN procurement agency.

Scenario 2
For an expedited approval of WHO-prequalified vaccines that are procured directly.

Requirements for licensing vaccines from PQ sources
Scenario 1
1. Check prequalification status
2. Submit product samples, product inserts, NRA lot release certificates from the country of origin, a list of countries where the product is licensed and marketed, and summary lot protocols of three final lots.
3. Visual inspection on samples
4. Review protocols (check specifications), labels, boxes and inserts against WHO model. Ensure presence of VVM
5. Prepare report of compliance (non-compliance)
6. If compliant, issue Certificate of Approval
7. Inform manufacturer and WHO
8. If novel vaccine with limited clinical data, review of clinical data may be needed

Scenario 2
1. Same as in scenario 1
2. Same as in scenario 1
3. Same as in scenario 1
4. Same as in scenario 1 in addition to ensure consistency with national tender specifications if different
5. Same as in scenario 1
6. Same as in scenario 1
7. Same as in scenario 1
8. Same as in scenario 1

**Outcome and timeframes for expedited review procedure**

**Scenario 1**
1. Waiver of fees from countries is requested
2. Total timeframe for evaluation should not exceed 30 days unless clinical data need to be reviewed, in which case timeframe is extended to 120 days
3. If info submitted by manufacturer is not complete, clock is halted awaiting completion.
4. Inform WHO that the procedure is being adopted. WHO will keep NRA informed of updates regarding PQ status.
5. Procedure applies to vaccines used in NIP
6. Countries should not stop use of PQ vaccines not yet registered in the country

**Scenario 2**
1. Same as in scenario 1
2. Same as in scenario 1. If country has testing capabilities and vaccine samples will be tested as part of the registration process, 90 days instead of 30 will be the timeframe for completion of procedure, except when clinical data need to be reviewed (120 days)
3. Same as in scenario 1
4. Same as in scenario 1;
5. Same as in scenario 1
6. Same as in scenario 1
Key Elements in the Introduction of a New Vaccine: The Willingness to Recommend

Claire-Anne Siegrist, Center of Vaccinology and Neonatal Immunology, University of
Geneva, President of the Federal Commission for Vaccinations, Geneva, Switzerland

Between the willingness to vaccinate and the willingness to be vaccinated, this talk will
address the willingness to recommend. National advisory committees on immunization are
considered, believe worldwide, as an independent group of experts in the of: Infectious
diseases immunology and microbiology, pediatrics, internal medicine, general practice,
epidemiology, public health, sometimes health economics, among others.

The Mission of the National Advisory Committees on Immunization is:

- Provide evidence-based recommendations for the use of vaccines in the general
  population or in high risk groups, including indication, age, number of doses /
  intervals, precautions and/or contraindications.
- Working with the staff responsible for the surveillance and prevention of transmissible
diseases.
- Independent of regulatory authorities.
- Reporting to the Chief of Public Health - at the national or district level.

WHO has generated guidelines on how these committees should function. In order to ad a
vaccine to a national immunization programme should address a number of key issues:
Policy and Programmatic issues, (see graph below).
For instance for Policy issues address public health priorities; disease burden, other
interventions besides vaccine, what is the efficacy, quality and safety of that given vaccine.
Programmatic issues address vaccine presentation, supply availability, programmatic strength,
other inventions, etc.
From this analysis can be determined whether a vaccine can be introduced, how can be
introduced, or wait for the vaccine to be introduce and why cannot be yet introduced.

From Speake’s slides, source from the Vaccine Introduction Guidelines issued by the WHO
All National Advisory Committees have to address an increasing number of questions, following a predefined transparent analytical framework for evidence-based vaccine recommendations. This framework was initially drafted in Canada and adopted in Switzerland in 2004. The content of these criteria might change a little among different countries.

1. Disease burden
2. Vaccine characteristics
3. Potential immunization strategies: Do we need to consider routine immunizations, what needs to be done to reach a programme target, what is the potential impact of the given strategies.
4. Cost-effectiveness
5. Acceptability of immunization program
6. Feasibility of immunization program
7. Capacity to evaluate the program
8. Open research questions, this does not mean research questions that should be opened all the time but important questions that eventually should postpone the introduction of a vaccine (unknowns).
9. Equity of the program
10. Legal considerations
11. Conformity of the recommendation

The compliance of these criteria might seem simple on paper, but is not in reality. To get a better understanding of the processes that implies the implementation of these criteria by the following examples.

**A complex process: selected examples...**

* Disease Burden:
- May we generate evidence-based recommendations without specific evidence of the national disease burden? WHO says yes, as this is not possibly applicable in all countries as for the case of HPV.
- If not, which evidence should be generated – and how?
  - Monitoring deaths, severe infections (hospitalizations), is relatively easy.
  - Monitoring out-patient issues is more difficult, for example we don’t know what is the disease burden of pneumococcal pneumonia, what about under-recognized diseases.
  - Disease severity? What is really the criteria for disease severity. Ex: shingles – pain post-herpetic neuralgia.
- How do we define whether, when, which resources should be allocated to the evaluation of a given disease burden?
  - For any licensed vaccine?
  - Based on certain criteria?
  - Which prioritization?

* Vaccine Characteristics
- On which evidence should the recommendations be based?

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<th></th>
<th>Availability</th>
<th>Exhaustivity</th>
<th>Credibility</th>
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<tbody>
<tr>
<td>Scientific literature</td>
<td>+++</td>
<td>+/-</td>
<td>+++</td>
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<tr>
<td>Files from industry</td>
<td>+++</td>
<td>+/-</td>
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<tr>
<td>Regulatory files</td>
<td>0 !</td>
<td>+++</td>
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</tbody>
</table>
Industry files related to vaccine characteristics are available for evaluation at the committees but they are often not exhaustive, and their credibility is being questioned especially when it relates to safety. Can we only rely on industry based files? Regulatory files are often more exhaustive and undergone a more thorough review are usually not available for immunization committees in many countries.

-How much is “sufficient evidence”?  
  - Examples: Do we have to know the duration of protection to recommend a vaccine. Ex: HPV, Zoster…
  - Compatibility with other vaccines (ex: HPV/Hep B), is an issue that is addressed completely different from one country to the other.

Taking the above into account enhancing the available evidence to support the “willingness to recommend” seems a very needed!

*Cost-Effectiveness: Health Economical Analysis*

-May we generate evidence-based recommendations without adequate evidence of the cost-effectiveness of interventions? And the answer is clearly No unless the program is not to be funded.

-If not, how should this evidence be generated?

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<thead>
<tr>
<th>Availability</th>
<th>Relevance</th>
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<tr>
<td>++</td>
<td>+/-</td>
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</table>
| This literature is occasionally available, but of little relevance because every country is different.

<table>
<thead>
<tr>
<th>Resources</th>
<th>Interest</th>
<th>Credibility</th>
</tr>
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<tr>
<td>+++</td>
<td>+++/-</td>
<td>?</td>
</tr>
<tr>
<td>+/-</td>
<td>?</td>
<td>+++</td>
</tr>
</tbody>
</table>

Important: What is “adequate evidence of the cost-effectiveness of an immunization program”?

**Example**: rotavirus immunization

- France: Birth cohort 0-3 years, Markov process. French databases, direct costs only.

- NL: Mass vaccination 0-4-year-old, Markov process. Dutch databases, including societal costs. At 100 € / child, 35’000€ / QALY saved. “Clear that mass vaccination can be attractive”. (Goosens Vaccine 2008).

- CH: “not fundable unless cost-saving including indirect costs”.

Taken the above example, we come back to the initial question: What is “adequate evidence of the cost-effectiveness of an immunization program”?

- Costs - budget impact? at which horizon?
- Criteria for cost-effectiveness ratio below which an immunization program could / should be recommended?
  - Cost per QALY saved? at which ratio? even for outcomes without permanent disabilities? discounting?
  - Should include or not costs?
- Relative importance of societal Cost-effectiveness versus individual health?
  - Ex: Men C in CH, chickenpox, HPV, zoster......, where we can find discrepancies in the way these vaccines are approached.

*Public Health vs. Individual Health*

In most countries **Routine immunization** is recommended where there are both public health + individual health benefits.

**For the prevention of:**

- High number of severe diseases (sequelae or death).
- Potentially severe diseases that may be rare but without alternative preventive or therapeutic strategies.
- Potentially severe diseases requiring high immunization coverage to protect those who may not be immunized, or that are recurrent because immunization was reduced.

**Targeted immunization** is the alternative to routine immunization, is vaccinating defined high-risk groups only, but this groups are often not well known, other form is **No recommendation** which means that the vaccine will be available but only on the private market.

**Exemples**: MenC in F, rotavirus in most EU countries, VZV in EU countries, HPV in certain EU countries...

To address the issue above describe in Switzerland a new level of recommendation was added **Complementary immunization**: This considering than from this vaccination the individual will benefit more that public health.

**For the prevention of:**

- Rare but severe diseases (Ex: Men C in CH).
- Relatively benign but frequent diseases. (Ex: Rotavirus in CH, could be in this categorie).
- Potentially severe diseases, but with alternatives (Ex: HPV > 20y in CH, could be in this categorie).
- Diseases without alternative strategies, regardless of their severity.

**Based on the above following two examples of physicians’ attitudes related to equity of access to interventions.**

- 2004: “How do Swiss physicians immunize their own children?”
  
  Answer: “All” their children are immunized against MenC, despite the fact that they have to pay out of pocket.
  
  This help us to generate a recommendation for: Complementary immunization against Men C to allow equity for children of non-physicians.

- 2008: “How would Swiss physicians welcome a recommendation of a complementary immunization against rotavirus?”
  
  - Considered rotavirus as a benign disease, their own children not immunized despite the vaccine was available in the market for more than a year.
  
  - Not willing to follow a recommendation - UNLESS vaccines were funded.
Bear this in mind the main challenges for the recommendation process can be:

- Sparse epidemiological data on national disease burden of vaccine preventable diseases.
- Absence / paucity of health-economics evaluation and disagreement on how it should be used.
- Public health versus individual health: Cost-effectiveness versus public demand.
- Open questions or controversies: long-term impact, safety? risks of replacement?

The recommendation process

1. A complex process that should be strengthened through better evidence-based assessment.
2. A complex process of independence versus dependence.

So reviewing what is the National Advisory Committees on Immunization:

An Independent group of experts whom are expected:

- To have limited contacts with the vaccine industry by fear of interest, and yet whose recommendation process requires evidence that is essentially generated by / available through the vaccine industry.
- To provide evidence-based recommendations including indication, age, nb of doses, intervals, etc and generate a strategy, strategies which have been previously set by the regulatory authorities based on the data generated by the industry in their clinical files.

There are a number of situations in Europe where recommendations are not followed according to regulatory requirements:

- Prevenar with the introduction of a 2+1 dose instead of a 3+1 in the regulatory files.
- Hexavalent with the introduction of a 2+1 dose instead of a 3+1 in the regulatory files.
- VZV. 2 doses vs 1 dose < 12y
- FSME boosters q 3-5-10y
- Compatibility issues

- To provide evidence-based recommendations which are likely not be followed by physicians Ex: Timeliness, Boosters, Vaccine scares.
- To provide evidence-based recommendations which may not be followed by political authorities or by those in charge of their financing.

Examples:

- Failure of introduction of the Pneumococcal conjugate vaccine in France.
- Rotavirus vaccine in Belgium, its introduction was decided by political authorities even before the National Immunization committee completed its work.
- HPV « recommended but not (yet) funded ».

Increasing work load...Shrinking prestige...No financial reward...The willingness to recommend: a complex process that requires full support
The Financial Sustainability of New Vaccine Introduction in the Poorest Countries: Evidence from the First Phase of GAVI
Patrick Lydon, World Health Organization, Geneva, Switzerland

This talk will be based on the GAVI experience on introducing new vaccines evidence from the first phase of this program in terms of the financing side.

**Global financing context**

There is difficulty to understand why financing for immunization is an issue when
- Vaccines are largely accepted as the "best buy" for the health sector, we normally hear that are cost-effective, etc.
- Financing is largely a national public responsibility.
- Vaccines are global public goods with many positive externalities (they are part of Millennium Development Goals -MDG, reduce poverty ...)
- Global financing context is positive (GAVI, IFFIm, AMC...)

Financing for vaccines and immunization still remains far from assured
- Many low-income countries continue to be donor dependant, particularly for vaccines.
- The result is volatile financing for immunization, and programmes vulnerable to any shifts in donor priorities.

**Vaccine Expenditures (% National Government Funded)**

As observed in the graph, all countries in dark blue are countries that are not funding any vaccines using their own domestic resources.


The above scenario give a sense of the context for vaccine financing in which GAVI performs, as the majority of these countries are GAVI supported.
Sources of Financing for Immunization

*Internal Public (50%)
- Government revenue
- Borrowing (loans)

*External Public (30%)
- Grant Aid Bilateral or multilateral
- Grant portion of an IDA loan
- Debt relief proceeds
- Budget support

*Internal Private (2%)
- Cost recovery schemes (user fees) Cross-subsidization (Bamako)
- Health insurance schemes
- Community health financing schemes

*External Private (28%)
- GAVI Fund
- Contributions (philanthropic, industry…)

*Innovative Financing (Innovating Financing Institutions such as the: International Facility for Immunization and the AMC).

To manage all these sources there are financing mechanisms to channel the money for purchasing vaccines, these organisms are such as:

- PAHO Revolving Fund (RF)
- UNICEF Vaccine Independence Initiative (VII)
- EU ARIVA Initiative
- GAVI Fund
- SWAp
- National Trust Funds

The Financing Challenge
Reaching Millennium Development Goals especially the MDG4 requires accelerating the introduction of new life saving vaccines in the poorest countries that have significant potential for child mortality reduction.

The problem:
- New vaccines are cost-effective but cost much more – from cents to several $.
- Increasing tension between "best-buy" for health and what is affordable for health systems. Often countries, especially poor countries their budget is not that big and cannot always accommodate with the increasing costs of vaccines.
- There is a need of a model to help accelerate the introduction of vaccines in poorest countries yet a model that is sustainable. G

What is a model for financial sustainability of new vaccine introduction in low income countries? Particularly important given many more vaccines available in the near future; The GAVI model intents to answer this need.
Vaccine development pipeline, denoting with the arrow vaccines that need further introduction or that will be introduced at some point.

The GAVI Model (2001-2006)
Initially the GAVI was aiming of accelerating the introduction of Hepatitis B and Haemophilus influenza type b (Hib) vaccines in 72 countries with GNI per capita of less than $1,000.
The model for financial sustainability
- Create a global fund for vaccines (GAVI Fund of over $1 billion)
- Stimulate demand by guaranteeing 5 years worth of free vaccines
- Increased volume would lower prices to affordable levels after 5 years
- This period would be sufficient to plan the transition of financial responsibility and ensure financial sustainability
The GAVI Model (Phase I)

Observing the diagram on the side, the model aims to provide funds at the beginning, vaccine prices likely will go down, then governments and partners will work out to provide vaccines for the country, and GAVI can move on to settle the same model for the accelerating the introduction of vaccines in other needed countries.

Part of the model requires that through GAVI the countries developed:
The tools for countries
  – The financial sustainability plan (FSP).
  – Current and 10 year forecasts of costs, financing and gaps.

To understand how well did the model work?
A Review of findings was done:
  – Expenditures on immunization
  – Sources of variation
  – Immunization Financing
  – Trend in vaccine prices
  – Financial sustainability

The analysis on data & methods
  – For 50 countries with good regional representation FSP tool data was extracted into an online Immunization Financing Database.

**Immunization Expenditures**
Expenditures are on the rise. With an average of $17.5 per child during 2005-2010 with HepB and Hib vaccines (see graph below):
  – This is up from their current spending of about $6 to sustain coverage with basic vaccines.
  – This means an average scale up by a factor of 2 to 3 depending on income group.
  – So according to the graph the proportion to scale up on expending is of about 11$ which is a big amount in relation to their current expenditures.
Main source of variation in the expenditures is mainly linked to:
  – Changing expenditure profile - largely driven by new vaccines (> 50%)
- Poorest countries tended to introduce the more expensive combination of GAVI supported vaccines (HepB-Hib).
- Other source of variation.

Changing Expenditure Profile
Changing expenditure (see graph below), light blue represents the introduction of new vaccines and thus account for an important part of the new expenditure profile. Cost largely driven by new vaccines (about 50% - up to 75% in some cases) and will vary with the type of new vaccines. There is a whole series of non-vaccine costs that also rise with the introduction of new vaccines, some examples:
- Plus $1 dollar more per child for the pentavalent vaccine.
- Plus $2 - $3 dollars more for rota, pneumo.

Also there are other sources of variation.
Sources of Variation

Cost per child will vary according to:

- >$30 per infant in small countries (Max = $42) and <$5 in large countries (Min=$3)
- Even for similar coverage levels.

Shared health systems cost and delivery strategies.

Development, income and coverage.

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<tbody>
<tr>
<td>For countries &lt; $1,000 GNI per capita</td>
<td>% DTP3</td>
<td>$ per infant</td>
<td>Factor of increase in cost</td>
<td>% Total immunization expenditures</td>
<td>% Total immunization expenditures</td>
</tr>
<tr>
<td>Fragile States</td>
<td>47%</td>
<td>$5.4</td>
<td>3.0</td>
<td>+18%</td>
<td>+51%</td>
</tr>
<tr>
<td>Poorest</td>
<td>65%</td>
<td>$5.8</td>
<td>2.8</td>
<td>+41%</td>
<td>+35%</td>
</tr>
<tr>
<td>Intermediate</td>
<td>84%</td>
<td>$6.3</td>
<td>2.5</td>
<td>+53%</td>
<td>+25%</td>
</tr>
<tr>
<td>Least Poor</td>
<td>86%</td>
<td>$10.1</td>
<td>2.0</td>
<td>+63%</td>
<td>+17%</td>
</tr>
</tbody>
</table>

As per above graph we can observe that: Non vaccine cost per child varies according to different forms of coverage.

- Cost coverage relationship is non-linear
- Indication of economies and diseconomies of scale happening at different levels of coverage
- Would imply different levels of investment to reach higher coverage levels
- Draft findings. More research is needed to confirm these.
Immunization Financing
The graph exhibits the expenditures and contributions of each funding.

Immunization financing also on the rise
- Majority of the increase from national governments (>20% increase).
- GAVI has become a major source of additive financing, particularly in the poorest of the poor.
- This is a concern for the sustainability of the program.

Still a $4 funding gap per child remains
- For completing the HepB and Hib agenda - despite GAVI monies.
- Variability in gaps linked to level of government funding.
- Concerns about financial sustainability in the poorest of the poor.
- Financial transition is far from assured.

Where are some of the funding gaps? (see side graph)
- For the 2008-2010 period 40% unfunded ($4) as earlier explained.
- Most of the gaps are for vaccines, supplies and logistics (55% - 30%).
- Important gaps are for service delivery (23% - 43%).
- For the 2008-2010 period, needs for campaigns are not included in these figures, important funding gaps for the polio, measles….

Vaccine Prices and Volume
- Most important factor of success of the GAVI model and financial sustainability is a reduction in the price of vaccines to affordable levels. However, as an example, for the pentavelant vaccine from 2001 to 2006 there was not enough value to bring prices down significantly.
- The US$ price of HepB and Hib combination vaccines increased between 2001-2006.
- The price - volume effect of the model is unclear in the absence of a healthy competitive vaccine market.
  – Worked for HepB but not Hib combination vaccines.
  – Promising trends for the future.

Sustaining Gains
Lessons learnt:
No drop in price of combination vaccines over the period of 2001 – 2006 due to:
  – Cost implications of new vaccines still important
  – Important funding gaps to finish the agenda
  – Countries threatening to drop the vaccines if GAVI did not come up with solutions.

Although there were some modest increases in financing non-GAVI funding, governments started to put more budget allocations towards vaccine it was not enough to actually cover for everything, the planning horizon too short and donors were not able to make multiyear commitments in sustainable way.

The foresee solution to actually sustain the gains was to:
Support evidence-based priority setting & decision-making
  – Hib Initiative and ADIPs
Stimulate downward pressure on vaccine prices
  – GAVI long term procurement strategy (demand side).
  – Emerging suppliers study (supply side).
Revision were made to the GAVI model
  – Co-financing model for GAVI Phase II
Revised GAVI Model (2007-2015)

In this revised model:
- Countries will need to co-finance vaccines from the onset.
- The level of co-financing will heavily subsidized, this will vary depending on income levels and development status.

Until 2010 co-financing groups have been categorized in levels as:
Fragile state:
- Countries in crisis
- $0.10 per dose
Poorest:
- <$ 1000 GNI pc & LDC
- $0.20 per dose
Intermediate:
- <$ 1000 GNI pc not LDC
- $0.30 per dose
Least Poor:
- $> 1000 GNI pc today
- $0.30 per dose (+15% a year)

The GAVI Model (2001-2006) – Summary
Between 2001-2006, GAVI succeeded in accelerating the introduction of HepB and Hib vaccines in over 55 of the poorest countries.
While the benefits outweigh the costs, financial sustainability is far from assured.
- Not a failure of the model itself.
- Scaling up with new vaccines in poor countries had greater than expected cost implications on immunization programmes – and not just for vaccines.
- A healthy competitive vaccine market with high demand can lower vaccine prices.
- More time is needed to plan a financial transition away from GAVI Fund resources.

Reference: www.who.int/immunization_financing
Health Infrastructure and Logistics: The Backbone of Immunization Programs
Michel Zaffran, Senior Adviser, WHO/IVB & Director, Project Optimize, Geneve, Switzerland

This talk will address the infrastructure, supply Chain & logistics needed for immunization programs “the backbone of immunization”.

The following diagram show in quick glance what is needed for immunization programs to take place, a process that covers not only the delivery of vaccines from the manufacturer to the children, but also requires an information system that goes throughout the chain and reports backs to feed up the system properly.

Infrastructure, Supply Chain and Logistics
A network of people and equipment operating within a range of standard operating procedures. Objective: is to have availability of vaccines and immunization technologies:

- in the right quantities
- at the right place
- at the right time
- in the appropriate conditions of quality in the point of delivery

A supply Chain System needs to rely on accurate:

- Forecasting of needs.
- Procurement of right vaccine quantities system.
- Well establish warehousing and distribution systems including transport.
- Information Systems
  - Target population and its location
  - Storage capacity at all levels
  - Population data
  - Vaccines quantities used and lost
For a good system to operate it needs high levels of performance required first at the Central Level.

Several aspects are looked (see above graph) to determine high performance, these aspects are assessed with a tool developed in collaboration with the Unicef, following the aspects considered:

- Building, Equipment and Transport
- Vaccine Arrival management
- Storage Capacity
- Temperature control
- Equipment Maintenance
- Stock Control
- Distribution system

Following some data that was generated on regarding performance aspects on Central stores from 42 countries. (see side graph)

- The physical infrastructure is usually taken care of.
- Weaknesses are concentrated in the areas of management, maintenance and training.
High levels of performance compliance is required not only at the central level but at all levels.
Vaccine Arrival
Storage Capacity
Temperature Control
Building, Equipment and Transport
Equipment Maintenance
Stock Control
Distribution
Proper management of diluents
Adequate knowledge and use of Vaccine Vial Monitors
Adequate Knowledge and implementation of Multidose Vial Policy
Vaccine Wastage – tools in place for monitoring

Another tool has been developing by the WHO to assess the management of vaccines in the countries. It is observed that at the central level management compliance is better achieve that at the periphery.

New Vaccines imposed New Logistics Challenges in infrastructure, supply chain and etc.

This graph shows that both the cost and the volume per dose when moving to new vaccines the costs and volume per dose is increasing which implies more logistics (storage, transport, etc).
Implications - Central level Storage Capacity

The graph basically shows the level of storage for the given vaccines at the Central level there is a strong difference for the different vaccine associations among the different regions (RO) (EM =Easter-Mediterranean, AF= African, AM = America, WP= Western-Pacific, SEA = SoutEast Asia).

The implications at the peripheral level also are important as there are different storage capacity issues that affect countries in different manner.

Project Optimize - Immunization systems and technologies for Tomorrow
In partnership WHO – PATH – funding of the Gates Foundation
Project Rationale:
Logistics systems are being challenged:
  • New vaccines and drugs in the pipeline
  • Little spare cold chain capacity in LMICs
  • Suboptimal product profiles for vaccines and supporting technologies

Short-term fixes occur in the absence of long-term planning:
  • Need for guiding vision of how developing-country logistics systems should look in 2025
  • Need to plan for greater integration of health care service support systems

Develop a comprehensive, long-term approach
  • A shared vision of future support systems for health services that will address the challenges of management, storage, transport, and use of vaccines
    -Downstream: through more cost-effective and well-managed systems
    -Upstream: by advising on/influencing product characteristics
  • Generating evidence, building consensus, and launching activities to initiate the realization of this vision
    -Target product profiles, standards, performance specifications
Objective
Develop a comprehensive, long-term approach

- A shared vision of future support systems for health services that will address the challenges of management, storage, transport, and use of vaccines
  - Downstream: through more cost-effective and well-managed systems
  - Upstream: by advising on/influencing product characteristics

- Generating evidence, building consensus, and launching activities to initiate the realization of this vision
  - Target product profiles, standards, performance specifications
  - Regulatory requirements
  - Policy changes
  - Demonstration projects in countries

Example: Vaccine presentation

**Issue:** how to optimize presentation, volume and wastage

**Presentation:**
Relate to primary packaging.
Obvious increase of packed volume from single to multi-dose presentations.
Wastage more problematic (MDVP, session size, …).

![HepB presentation graph](image)

Example: Distribution Systems

**Issue:** how to address the issues of vaccine distribution?

- Ex 1: Moving Warehouses
  - Mozambique – Village Reach
  - Zimbabwe – Delivery Team Topping Up (DTTU)
  - Check supplies, link with maintenance and data collection

- Ex 2: McKesson Model
  - A lower levels, independent drivers are contracted out to distribute the commodities to the end point

- Ex 3: Integrated distribution systems
  - Linking with other health commodity distribution systems
  - Private sector: Snowman in India delivering Polio vaccine
  - Back-loading: Vaccines there, flowers back…Comoros
Cold Chain - Landscape Analysis

Expanding vaccine storage requirements
- 8 to 10 fold increase in vaccine volumes to distribute
- Revision of secondary packing of vaccines needed (bundling of multiple boxes)
- More/larger cold-rooms
- Revision of sub-national transport required
- Larger Health Center refrigerators, larger carriers, new technology
- Flexibility for storage in controlled ambient conditions could help relieve cold chain pressure

Changing energy preferences
- Absorption type refrigeration (kerosene/Gas) least efficient, phasing out
- Well performing solar electric without batteries needed to replace absorption—soon
- Potential for passive and intermittent cooling and heat protection—requires research

Upgrading information technology
- Cool-chain MIS software applications should be web-based for better national connectivity
- Bar-coding and potentially RFID technology could improve product ID, inventory, other tracking
- SMS, PDAs and GPS/RS could be used to aid remote data collection & interaction

Optimize: Areas of Work

Optimizing Today: Output: Supporting ongoing efforts to address immediate problems in immunization

Optimizing Tomorrow: Output: Finding innovative solutions to existing problems in immunization

Optimizing the Future: Output: Visionary solutions for optimizing immunization in 2025
Ensuring the Willingness to Vaccine: The Role of Professional Societies
Jean-Pierre Michel, Department of Rehabilitation and Geriatrics, Geneva Medical School and University Hospitals, Switzerland

Between 1999 and 2050 the expected increase of both 60+ and 80+ year of age European populations should reach 160%. Concerted efforts of professional geriatric societies are essential in forecasting the near future needs of care.

As per the above graph, in the countries in pink about 20% of the population is over the age of 60, in contrast countries in yellow have a percentage of people over 60 years below 10%. This allows us to imagine how the world will change in age over time, and the impact of this in the near future, (see follow graph).
The world will age with time in developed and developing countries. As earlier mentioned only in Europe by the year 2050 the population over 60 years of age will reach to 160%.

The national gerontological societies and the national geriatric societies in Europe have joined to work together to address the issues related to preventable infectious diseases. The reason is that the burden of especially few diseases in the aging populations is significant, these disease are the following:

<table>
<thead>
<tr>
<th>Life threatening diseases</th>
<th>Tetanus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Flu (with the spectrum of the H5N1 virus)</td>
</tr>
<tr>
<td></td>
<td>Peumoccocal</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Quality of life issues</th>
<th>Herpes Zoster</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Travel-related risks</th>
<th>Hepatitis A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hepatitis B</td>
</tr>
<tr>
<td></td>
<td>Diphtheria</td>
</tr>
</tbody>
</table>

| Regional risk            | Tuberculosis                     |
All the above mentioned diseases have vaccines available for administration in the aging population.

**The present talk will address the following issues:**

1. Why the actual vaccines are so badly considered in the old and very old adults?
2. What involvement can have European geriatric societies?
3. Vaccines and « healthy ageing »

1. **Why the actual vaccines are so badly considered in the old and very old adults?**

When considering the existing guidelines, it is observed that the group of 60+ years is considered as a homogeneous group, vaccines are not tailored to address this group. (see graph)
This is very inadequate when considering that life expectancy today of people over 65 is long and is expected to increase with time. For instance the life expectancy over 65 y.o. in France, is as per following table:

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2050</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>17.6 y</td>
<td>21.9 y</td>
</tr>
<tr>
<td>Women</td>
<td>22.1 y</td>
<td>25.7 y</td>
</tr>
</tbody>
</table>

[Source: Insee, fr/fr/ppp/fr/projpop0550]

Not only considering life expectancy but also health quality of life which strongly impacts the life cycles and makes this population group very heterogeneous.

Another concern is the poor vaccine coverage & protection in Europe. In the following study in 11 European countries on vaccination uptake of 65+ y.o. taken into consideration the WHO goal of 2006 of up to 50% uptake it is observed that several countries were not reaching or barely reaching this goal, and if the WHO goal in 2010 is of 75% uptake, we can conclude that we are far from reaching it.

[Flu vaccination uptake among the 65+ age group]

[Source: TNS Health survey 2006/2007]
Also the data from cohort studies has given many conflicting results about the efficacy of vaccines in this age group.

![Table of Vaccines and Age Groups]

All this conflict also comes from the numerous vaccine policies in the different European countries; these differences in vaccine administration programs do cause an impact likely in vaccine efficacy.

2. What involvement can have the European geriatric societies?

One aspect is filling up the gap between vaccine recommendations, the discontinuity of vaccines recommendations, and increasing the willingness to vaccinated and be vaccinated; this as part of preventive medicine strategies.

To achieve this vaccine working group was constituted (EUGMS & IAG-ER) by members of both associations, specialist in vaccinology, immunology, vaccine programs, geriatricians and other relevant experts. The aim of the working group was to come up with consensus guidelines for a new vaccine program for the aging population.

The following is consensus proposition:
Proposed EUGMS and IAGG-ER vaccine programme for the old adults

<table>
<thead>
<tr>
<th>Retirement age (55-70 y.)</th>
<th>(after assessment of the vaccine status)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- TdaP or Td vaccine</td>
<td>- Pneumococcal vaccine</td>
</tr>
<tr>
<td>- Influenza vaccine</td>
<td>- Herpes Zoster vaccine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Each year after the retirement age (after assessment of the vaccine status)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Influenza vaccine</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>New medical/injury event (after assessment of the vaccine status)</th>
<th>Multiple hospital stays (after assessment of the vaccine status)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Td or TT vaccine</td>
<td>- Pneumococcal vaccine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nursing home admission (or age of Nursing home admission)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- DT or TT vaccine</td>
<td>- Pneumococcal vaccine</td>
</tr>
<tr>
<td>- Influenza vaccine</td>
<td>- Herpes Zoster vaccine</td>
</tr>
</tbody>
</table>

Another aspect is about Increasing Flu vaccination rates among high-risk population groups. A meta-analysis study that evaluates 14 studies about the effectiveness of the impact of three types of interventions provided the following results:

1. **Patient focused interventions (N = 6)**  
   *(In-person, mail or telephone reminder)*  
   OR = 1.85 [1.25-2.75]

2. **Provider focused interventions (N = 4)**  
   *(Office based reminder systems)*  
   OR = 2.06 [1.70 -2.48]

3. **Mixed interventions (N = 14)**  
   *(Provider incentive systems, small group consensus programmes, organisational changes)*  
   OR = 2.50 [1.75-3.58]


The study shows that the provider role of following and reminder systems are very key to enhance vaccine coverage rates. Thus is very important to better inform and train vaccine providers in this context, to improve the willingness to vaccinate of the providers.

Besides the above said, it’s very important to think globally taking into consideration with this herd immunity. No only focussing on the provider but on the relationship between the child and old age prevention programs, and this includes the health care workers.
Surprisingly vaccine coverage of health care workers is lower than other target groups, as observed in the following graph.

A study performed by *ROTHON-TONDEUR M et al (Aging 2006; 18: 512-6)* regarding health care workers (HCW) vaccination uptake, showed that the factors associated with Non vaccine uptake were: Lack of motivation, lack of knowledge, organizational problems. This indeed has an impact in the willingness of the HCW of promoting vaccine uptake into patients.

Strategies to increase immunization rates among HCWs in LTCFs

<table>
<thead>
<tr>
<th>«Chipping away at the goal»</th>
<th>«The price is right»</th>
<th>«Slower gains»</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yearlong education</td>
<td>Pay staff a bonus for receiving vaccinations</td>
<td>Get the leadership involved</td>
</tr>
<tr>
<td><em>Personal benefits</em></td>
<td><em>Flu Busters Team</em></td>
<td></td>
</tr>
<tr>
<td>Obtaining staff buy-in</td>
<td>Staff education</td>
<td>Know your staff</td>
</tr>
<tr>
<td><em>Workload benefits</em></td>
<td><em>For hesitant staff members</em></td>
<td></td>
</tr>
<tr>
<td>Positive incentives</td>
<td>Make it easy</td>
<td></td>
</tr>
<tr>
<td><em>Luncheon</em></td>
<td><em>If fear of shots; intranasal vaccine</em></td>
<td></td>
</tr>
<tr>
<td>+ 24% to + 85%</td>
<td>+ 85%</td>
<td>+ 47%</td>
</tr>
</tbody>
</table>

Complement Notes taken from Abstract:

Why focusing first on vaccines in the ageing and aged adults?
Nowadays, preventable infectious diseases still represent the major cause of clinical and concurrent medical events, hospital admissions and death in this population originating increased care costs. The very low vaccine coverage over the age of 60 y. is linked to a) the actual discrepancies existing in vaccine recommendations between European countries b) the absence of detailed consensual vaccine guidelines for individuals whose mean life expectancy at 60 is at least 20 years in Western Europe c) the discussed efficacy of vaccines in this age group d) the non understanding of the usefulness of a herd immunity by the health care professionals whose willingness to vaccinate or be vaccinated is dramatically low.

The European geriatric professional societies‘vaccine involvement
Following the WHO and European Community vaccine initiatives and fixed goals, the EUGMS* and IAGG-ER** decided to stimulate an interdisciplinary working group to propose consensual vaccine recommendations for the ageing and old adults to enable maintenance of life-long protection against preventable infectious diseases, contributing to “healthy ageing”.
These recommendations are designed to complement existing information. After their publication in a major medical peer review journal, they will be transmitted to the 27 national geriatric societies constituting the EUGMS and IAGG, translated in each country language and locally promoted.

Expected outcomes
An increased long life vaccine coverage favouring healthy ageing will lead to a decreased incidence of preventable infectious diseases in the extreme old age.

* EUGMS: European Union Geriatric Medicine Society
** IAGG-ER: International Association of Gerontology and Geriatrics – European Region
Assessing the Willingness to Vaccinate: Methodological Approaches
Marion Stephen, Directrice Adjointe, IPSOS Santé, France

The talk will discuss different approaches that are being taken at IPSOS health to assess the willingness to vaccinate, this will include what are the: Key indicators, the different methodological approaches, examples of interview flow.

In terms of key indicators
First is needed to identify the criteria that will promote the willingness to vaccinate as:
- Identify the drivers for Proactive Physicians to vaccinate or prescribe a vaccine
- Identify the barriers to vaccinate
- Understand which are the most determining drivers and barriers explaining the prescription of a vaccine.
- Physician’s profiles: understand who will be the ‘early adopters’, the ‘followers’ and the ‘cautious’ physicians towards a specific vaccination
- To know what’s in the physician’s minds in terms of:
  ✓ Knowledge / Information
  ✓ Representations
  ✓ Attitudes (motivations and barriers)
  ✓ Opinions

All this information is correlated to the actual behaviours.

In terms of the different methodological approaches
This can be done with the use of a broad range of complementary methods to perform the assessment.
- « Qualitative » Surveys: frequently done out of a few numbers of interviews but with a very long discussion and questionnaires, often face to face, aiming to:
  In-depth understanding of drivers and barriers
  Attitude analysis
  Emotional dimensions

- « Quantitative » Surveys: Large number of interviews with close ended questions, this surveys aim to:
  Hierarchy of barriers and levers
  Measure the level of motivation
  Determine the profiles of prescribers / non prescribers

- “Statistical” analysis can be applied to the surveys through:
  Typology
  Linear regression
Methodology

Qualitative: One-to-one depth interview or focus groups

In the Depth One to One Interview

- They allow to observe and explain individual reactions, and to highlight a global attitude.
- They provide very specific and individual qualitative information and not only a global vision due to the leadership effects of a focus group.
- They highlight the precise motivations and barriers of the different profiles of physicians

Focus Groups

They are notably effective:

- In using liberating, un-inhibiting projective techniques such as “role playing”, personification, or lateral thinking.
- In helping the participants in the groups to react / interact, formulate, express and ‘test’ some messages or motivations.
- In unearthing the underlying imagery, emotions, attitudes, drivers etc. of individuals, as well as evaluating the propositions, their positive cues and limits (group situations tend to magnify the critical mindset and in this sense provide useful directional information).
- In high-lighting the different existing points of view, making the individuals face with each other and react to others’ opinions.
- In generating creative propositions to improve willingness to vaccinate.

This method is by far the most effective when creative routes are expected at the end of the day.
Exemple of Interview flow
Physicians (quantitative and qualitative)

What is important to know when conducting a survey among physicians is the following.

- To use as much as possible homogeneous methodologies in the various countries involved in the study; it is important to go as much as possible through a common mode of administration across countries in order to be as comparable as possible.

- To take into account the local specificities to choose the most adapted method:
  - To build the most representative samples.
  - To obtain the most precise answers according to cultural specificities.

For these reasons, the methodology may vary from one country to another, but overly the same method will be used in a vast majority of countries.
Methodology

Qualitative: How do we recruit physicians

Physicians are screened on the following criteria:
- They are screened to get a sample of “experts” (High frequency of Px), of “followers” (Middle frequency of Px) and of “cautious” (Low frequency of Px).

Simple but key criteria will be used to identify and screen physicians from each category: for example attitude toward a specific vaccination (those who prescribe in higher quantity, those who started to prescribe, non prescribers…)

Additional criteria:
- Working full time
- In active clinical practice since 5-25 years
- > 70% of the time is spent on patient care
- Vaccine prescribers
- Other screening criteria may be added.

The size of the sample has to allow us:
- to conduct a precise analysis, in depth on the key indicators for each target (GPs, pediatricians, gynecologists) or for each country.
- to build a relevant typology of physicians.
- to highlight the position of each sub-target according to the level of knowledge,…

Physicians are screened by telephone by interviewers on the following criteria:
- Representative of their universe at a local level (country level) based on quotas (age, male or female, region).
- Working full time.
- In active clinical practice since 5-25 years.
  ➢ 70% of the time is spent on patient care.
- Involved in vaccination (exclusion criteria: non vaccinating physicians).

There are three methodologies to interview physicians quantitatively: face to face, telephone or online.

- FACE TO FACE: this methodology is mainly used in countries where the incidence of Internet is low or where it is easier to get an appointment with physicians (such as Latin America). It is particularly convenient when we need to show them material, the questionnaire is a rather long one (more than 15 minutes).

- TELEPHONE: when the questionnaire is short (less than 15 minutes) and when nothing has to be shown to physicians.

- ONLINE: this is the best methodology to get at the same time homogeneous data across country and to get a clear cross country analysis. The on-line methodology is also particularly convenient to interview physicians, especially
when: we need to show material, the questionnaire is a rather long one (more than 15 minutes), and where the incidence of Internet is high enough (US, Canada, European countries,...)

Exemple of questions to be asked to physicians in a quantitative questionnaire

**Patient's level of interest**
Have some of your patients spontaneously asked you questions about vaccines against xxxx in the past month?
*Select one answer*
1. Yes
2. No

**Likelihood to prescribe**
Thinking of recommendations by National Health Authorities and the question of reimbursement, what is your attitude regarding the prescription of this new vaccine. Would you say...?
*Read out items – only one answer possible*
1. I have already prescribed the vaccine without waiting for the recommendations and the reimbursement
2. I intent to prescribe the vaccine without waiting for the recommendations and the reimbursement
3. I will prescribe the vaccine only if it is recommended by Health Authorities but not necessarily reimbursed
4. I will prescribe the vaccine only if it is both recommended by Health Authorities and reimbursed
5. I will not prescribe the vaccine
6. (DK – do not read out)

**Population breaks**
For each of the (age / gender / education level / at risk or not) breaks listed in the heading of the table below, please indicate what your attitude to this vaccine is?
1) You simply tell them about the vaccine without prescribing it or vaccinating them
2) You prescribe the vaccine without vaccinating them yourself
3) You vaccinate them yourself
4) You refer to another doctor without prescribing the vaccine or vaccinating them yourself
5) You do nothing
Example of questions to be asked to physicians in a qualitative interview or in a focus group

Today we’re going to talk about your opinion and attitude toward xxx vaccination.

We will more particularly talk about your motivations and barriers to xxx vaccination prescription. This is important. I will need your active participation. There is no question of self-censorship or censoring others.

⇒ General attitude of physicians regarding cervical cancer vaccination: motivations and barriers

**Physician’s motivations to propose xxx vaccination**
From your point of view, what are your 3 main motivations for you as a physician to prescribe [first vaccine quoted]? (Motivations linked to the product characteristics, to the profile of the patient...)

Why? What profile of patient would you prescribe this vaccine? Why?

Probe: and for [second vaccine quoted]

**Physician’s barriers to propose xxx vaccination**
From your point of view, what are the 3 most limiting elements for you as a physician to prescribe [first vaccine quoted]? (Barriers linked to the product characteristics, to the profile of the patient...)

For example: difficulties to initiate the discussion, time or doubts about vaccination benefits for some patient case, level of income of the patient...

Which of the following sentences, best describes your attitude to the vaccine against xxx?

1. Since a vaccine against xxx is available in your country, you have started to prescribe it systemically?
2. Since a vaccine against xxx is available in your country, you have started to prescribe it as often as you can?
3. You regularly prescribe vaccines against xxx, but you prefer to wait before prescribing it systematically?
4. You are still waiting to prescribe vaccines against xxx, because of the lack of hindsight

Do you talk about this vaccination systemically? Why? Why not?

⇒ Opportunities to speak and / or propose cervical cancer vaccination

Can you list me all opportunities, occasions during which you speak or propose this vaccination?

In front of the patient, in your daily practice what are the best opportunities to initiate discussion about cervical cancer vaccination?

Can you list me all situations when you will never initiate the discussion about cervical cancer vaccination?

What are the key medical criteria you investigate in front of your patient for which you decide to speak or not to speak about this vaccination?
Patients Drivers and barriers for this vaccination

Generally speaking what are the main motivations of your patients for asking questions about this vaccination?

And, according to you, what are their main motivations to accept to be vaccinated against this disease?

Have you already met patients who directly ask to be vaccinated against this disease?
Is this situation frequent?
How do you manage such a request? What do you say? Why?
And especially with patients out of your criteria you have mentioned previously?

What would you need to help you in this situation?
Have you already met patients who directly ask you advice, your opinion on this vaccination?
Is this situation frequent?
What do you answer to such a patient, what do you explain? Why?
And especially with patients out of your criteria you have mentioned previously?
What would you need to help you in this situation?

Patient profiles testing - Intention to prescribe the vaccination

Next I would like you to look at a series of adolescents, young women and mothers of adolescent’s descriptions.

[HAND PHYSICIAN THE PILE OF PATIENT PROFILES]

**SORTING EXERCISE**

First, I would like you to sort all those patients in different piles:

a) The first pile will be for the patients you would prescribe a cervical cancer vaccine

b) The second pile will be for the patients to whom you hesitate / may prescribe a cervical cancer vaccine

c) The last pile will be for the patients you would definitely not prescribe a vaccine against cervical cancer

Discuss for all the patients about the choice while the physician is sorting.
Advocacy Programmes to Support the Willingness to Vaccinate
John D. Grabenstein, Senior Director, Scientific Affairs – Medical Affairs & Policy
Merck Vaccines & Infectious Diseases, USA

Advocacy Programmes to Support Willingness to Vaccinate, main thoughts:
Even vaccines based on sound scientific evidence will not fulfill their potential, if not transformed into vaccination.
Vaccinations require professionals willing to vaccinate their patients.
Advocacy programmes prepare and support a cadre of professionals willing to vaccinate.
Advocacy programmes accelerate rate and magnitude of vaccination delivery.

Four components of Advocacy Programmes to Enhance Vaccination By Health-Care Providers
- Educate
  ➢ To increase awareness of disease burden
  ➢ To provide technical info, thus confidence
- Share “Best Practices”
  ➢ To simplify offering and delivering vaccination
  ➢ To ease the task of staying up-to-date
- Foster the “Standard of Care”
- Adopt “Quality Indicators”

The following is a web-Based & Selected Other Education Resources for reference
- US Centers for Disease Control & Prevention, www.cdc.gov/vaccines/ed
  - Immunization: You Call the Shots
  - Epidemiology & Prevention of Vaccine-Preventable Diseases
  - Various other topics via webcast, podcast, etc.
  - Immunization Practice Toolkit, www2.cdc.gov/nip/isd/immtoolkit/default.htm
  - Storage and Handling Toolkit, www2a.cdc.gov/nip/isd/shtoolkit/splash.html
- World Health Organization, IVB Document Centre,
  - www.who.int/vaccines-documents/DoxGen/H3DoxList.htm
- Teaching Immunization Delivery & Evaluation (TIDE), www.musc.edu/tide
- Teaching Immunization for Medical Education (TIME), www.aptrweb.org/education/TIME/time.html
- Merck Vaccine Network--Africa (MVN-A), www.merck.com/mvna,
  - Kenya, Mali, Uganda and Zambia

The Immunization University DoD was created in the USA. The university is a collection of training programs and resources to enhance the skills of professionals and paraprofessionals. “Imz U” offers training through distance learning and on-site classes. www.vaccines.mil/ImzU.
Provider Recommendation Can Overcome Negative Attitudes Among Patients
For instance: Vaccination Rates of influenza and PPV among High-Risk Patients with Negative Attitudes were importantly improved to up to 80% by the MD recommendations in an study performed by Nichol KL, MacDonald R, Hauge M. Factors associated with influenza and pneumococcal vaccination behavior among high-risk adults. *J Gen Intern Med* 1996;11:673-7.

The following are sources to find Share Best Practices
To simplify offering and delivering vaccination
- www.immunize.org
- www.cdc.gov/vaccines
- www.immunise.health.gov.au
- www.who.int/topics/immunization
- www.ecdc.europa.eu/health_topics/VI/VI.html

To ease the task of staying up-to-date
- CDC’s ImmuEd listserv, listserv@cdc.gov, “Subscribe ImmuEd <firstname lastname>”.
- https://service.govdelivery.com/service/multi_subscribe.html?code=USCDC&origin=
- FDA’s Center for Biologics Evaluation & Research, www.fda.gov/cber/pubinfo/elists.htm

Strategies for Increasing Adult Vaccination Rates
- Standing Orders
- Computerized Record Reminder
- Chart Reminder
- Performance Feedback
- Home Visits
- Mailed/Telephoned Reminders
- Expanding Access in Clinical Settings
  - “drop in” or “express lane”
- Patient Education
- Personal Health Records
Source: www.cdc.gov/vaccines/recs/rate-strategies/adultstrat.htm

This is a generic list but we can anticipate that some criteria might be more or less important depending of the type of population we are talking about. Whether is a pediatric or geriatric population and so on.
Foster the “Standard of Care”

**Recommended Adult Immunization Schedule**

*Note: These recommendations must be read with the limitations that follow.*

**Figure 1. Recommended adult immunization schedule, by vaccine and age group**

**United States, October 2007 – September 2008**

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>AGE GROUP</th>
<th>18–49 years</th>
<th>50–64 years</th>
<th>≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetanus, diphtheria, pertussis (Td/Tdap)*</td>
<td></td>
<td>1 dose Td booster every 10 yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus (HPV)*</td>
<td></td>
<td>2 doses (ages 11–12 yrs)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles, mumps, rubella (MMR)*</td>
<td></td>
<td>1 or 2 doses</td>
<td>1 dose</td>
<td></td>
</tr>
<tr>
<td>Varicella*</td>
<td></td>
<td>2 doses (0, 4–8 wks)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza*</td>
<td></td>
<td>1 dose annually</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal (polysaccharide)*</td>
<td></td>
<td>1–2 doses</td>
<td>1 dose</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A*</td>
<td></td>
<td>2 doses (0, 6–12 mos or 0, 6–18 mos)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B*</td>
<td></td>
<td>3 doses (0, 1–6 mos)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcus*</td>
<td></td>
<td>1 or more doses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zoster</td>
<td></td>
<td>1 dose</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Covered by the Vaccine Injury Compensation Program.

For all persons in this category who meet the age requirements and who lack evidence of immunity (i.e., task documentation of vaccination or lab test evidence of prior infection):

Recommended if any other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

Source: www.cdc.gov/vaccines/recs/schedules/adult-schedule.htm

**Adopt Quality Indicators**

Quality-improvement (QI) programs to enhance clinic operations and vaccination rates. The following are some of the sources from the USA.

- DoD Clinic Quality-Improvement Program (CQIP), www.vaccines.mil/CQIP.
- CDC Comprehensive Clinic Assessment Software Application (CoCASA), www.cdc.gov/vaccines/programs/cocasa.
- National Quality Forum: www.qualityforum.org
Immunization Standards
These are a way prototyping what expectation should be at the clinical level as part of a quality improvement program.

General themes regarding immunization standards:
1. Immunization availability
2. Information and education before immunization
3. Vaccine storage and handling
4. Indications and contraindications to immunization
5. Immunization record keeping
6. Training
7. Adverse events after immunization

References:

From where the sources of advocacy come from

- National or jurisdictional authorities
  - ACIP, NACI, ATAGI, STIKO, FACI, Oberster Sanitätsrat, MOHs, SAGE, others
- Professional societies
  - Professional membership associations
- Coalitions and nongovernmental organizations
  - Immunization Action Coalition, www.immunize.org
  - Regional (adult/pediatric) immunization coalitions
  - Cervical cancer task forces (prophylaxis, early detection)
- Patient, public groups
  - Influenza: www.FamiliesFightingFlu.org
  - Voices for Vaccines: www.voicesforvaccines.org
- Employers
  - Corporations
  - Military units (www.vaccines.mil)
Drivers or Barriers Leading Professionals to Support Vaccination Policies

- Preparedness of practice site (e.g., office, clinic, institution)
  - Training of staff (professional & paraprofessional)
    - Ongoing access to educational resources
  - Infrastructure (e.g., records, computers, cold chain)
  - Assessment, feedback on implementation of policies
  - Posters, handouts, stickers, screening forms to standardize messages and simplify processes
  - Systems to convey reminder and recall messages
- Routine screening processes and adopt correctly "standing orders"
- Information exchange of vaccination status (e.g., electronic registries)
- Financial circumstances, as billing and inventory cost.

The following is an example of standing orders:

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**Standing Orders for Administering Pneumococcal Vaccine to Adults**

**Purpose:** To reduce morbidity and mortality from pneumococcal disease by vaccinating all adults who meet the criteria established by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.

**Policy:** Under these standing orders, eligible nurses and other healthcare professionals (e.g., pharmacists), where allowed by state law, may vaccinate adults who meet any of the criteria below.

**Procedure**

1. Identify adults in need of vaccination with pneumococcal polysaccharide vaccine (PPV) based on the following criteria:
   a. Age 65 years or older with no or unknown history of prior receipt of PPV
   b. Age 64 years or younger with no or unknown history of prior receipt of PPV and any of the following conditions:
      i. chronic cardiovascular disease (e.g., congestive heart failure, cardiomyopathies)
      ii. chronic pulmonary disease (e.g., emphysema or chronic obstructive pulmonary disease [not asthmatic])
      iii. diabetes, alcoholism, chronic liver disease (cirrhosis), or cerebrospinal fluid leaks
      iv. functional or anatomic asplenia (e.g., sickle cell disease, splenectomy)
      v. immunocompromising condition (e.g., HIV infection, congenital immunodeficiency, hematologic and solid tumors)
      vi. immunosuppressive therapy (e.g., alkylating agents, antimetabolites, long-term systemic corticosteroids, radiation therapy)
      vii. organ or bone marrow transplantation
      viii. chronic renal failure or nephrotic syndrome
      ix. candidate for or recipient of cochlear implant

2. Identify adults in need of a second and final dose of PPV if five or more years have elapsed since the previous dose of PPV and the patient meets one of the following criteria:
   a. Age 65 years or older and received prior PPV vaccination before age 65 years
   b. At highest risk for serious pneumococcal infection or likely to have a rapid decline in pneumococcal antibody levels (i.e., categories iv.-viii. above)

---

See also: www.immunize.org/standingorders/
Factors that Affect Decisions on Accepting Vaccination

The physician needs to know what is going on in the patients mind to accept being vaccinated as the:

- Perceived susceptibility to the disease
- Perceived seriousness of the disease
- Perceived barriers (side effects, access)
- Perceived vaccine benefits
- Social influence of a respected person


The Role of Health Care Professionals in the Acceptability of Vaccination Programme

Adam Finn, Dept. Clinical Sciences at South Bristol – Head of Clinical Academic Training – Faculty of Medicine & Dentistry, University of Bristol, UK

The talk will overview some evidence illustrating the role and importance of front line healthcare workers as trusted advisers on immunizations and not as just deliverers of immunizations, and some hypotheses for further study.

Immunisations are administered by doctors, nurses and other healthcare professionals. Accordingly it is primarily to these individuals that vaccine recipients and their parents and carers turn for information and advice. Thus vaccination programmes depend on these front line individuals not only for effective logistical implementation, but also for effective communication. Several studies conducted in the UK and other European countries confirm the central importance of primary care professionals as trusted sources of advice about immunisation and their critical role in the decision making process for parents and young people considering immunization. Primary care staff need to be both expert in the practical aspects of administering immunisations and knowledgeable about the benefits and risks of the vaccines they administer and other matters that vaccine recipients commonly ask about. However their sources of information are diverse and their levels of knowledge about specific vaccines may be variable.

Accordingly designing and implementing effective ongoing education for these personnel about ongoing and new immunisation programmes is an essential component in the design of any programme. Information must be provided proactively in various formats but rapid, clear and accurate response-mode systems to address specific questions as they arise are also needed. Immunisation programmes are developing rapidly in both size and complexity. New public concerns around immunisation arise frequently. New information about existing vaccines and programmes emerges constantly. In order to retain the confidence of their patients, health care professionals need to ensure they are well and accurately informed. This aspect of communication concerning vaccines may be the single most important area to ensure their continued effective implementation.
Following some thoughts about what determines vaccine uptake:

- Perception of risks of disease whether personal or societal.
- Mandatory requirement to immunise.
- Perception of risks of vaccine.
- Fear of needles due to pain.
- Costs
- Inconvenience to go and get it done.
- Level of personal organization reliability.

An these factors seem to be relevant according to the countries, for instance in the USA what seems to make to make acceptability to vaccination is the Mandatory requirements; however in the UK this will reduce the acceptability to vaccination.

Thus, the effect of making immunization compulsory may increase overall uptake rates in some settings and populations but reduce it in others.

Most people will decide based largely or entirely on one or two issues, but not out of too many considerations. Many people will decide based on the opinion or advice of one or more others (Parents or other family members, peers, friends, medial sources as internet, publications, etc) Often times is not about what is said but when is said, there is an importance of timing.

Non acceptors to vaccination may be more likely to seek information than acceptors, whether they reach the right information or not. The sources people use for information are diversifying and changing, factors such as social class and age are likely to be important determinants.

The most trusted sources are not necessarily the most available or most used ones.

A survey done on about 5000 people across 5 countries in Europe to determine the percentage of respondents to chose which source is an important source of information on vaccines. The source that got the highest percentage was obtained by physicians (GPs, pediatricians, ) nurses, and in consecutive order by international Health Organizations, Govermente officials & Local authorities, Pharmacists, Friends & Relatives, Midwives & Kinderfarden staf, and last from information from vaccine companies.

Source: www.evm-vaccines.org

Professionals are being trusted and now the issue is whether professionals have the right knowledge: A study performed in Australia surveyed GPs, nurses and midwives, at N=434 with a return of 47%. 50% of GPs showed to be uncomfortable with 2 shots per visit, 33% expressed concerns about: Additives, immune system overload, and number of vaccines in schedule.


A systematic review of 39/553 studies to determine the factors that leads to low vaccination uptake, those found important were: Skepticism and doubts regarding provided medical information, inadequate support from healthcare providers, lack of available health structures, problems concerning transportation and accessibility to immunization clinics.
First line Health Care (HC) professionals may need to understand epidemiological and immunological principles behind immunization in order to reliably inform parents’ about immunizing their children.

Information regarding vaccines and vaccination must be well understood by the HC professionals and pick and given to the receivers and parents in an understandable manner, the information needs to be pitch at the right level to inform the patient and / or relatives. For instance an immunologist knows that vaccines administered at the same time will likely not overload the immune system, but this is a assumption that often physicians and patients have as an affirmation.

Nurses often are good at understanding what are the things that a parent knows best, at drawing the line between what mum knows best and what nurse knows best. Parents generally respect nurses opinions on what nurse knows best.

The parents are bombarded by all sorts of information as media, regional or national experts, internet, friends and family, and physicians doctors and nurses. Is difficult to determine whether information can be trusted especially when it comes from sources as the internet, thus is indeed an important matter to have a parent well informed with selective and trustable sources. This is the case of a local doctor or nurse however there is room for information accuracy.

Conclusions
We can’t preach that people must learn that immunization decisions are risk-benefit decisions (like many others in our risky lives) and also pretend that immunization is risk free. This is not the same as saying “vaccines are risky”!
If we do provide accurate information (or we have primary healthcare staff do it for us) we risk losing the trust they traditionally enjoy.

The Role of Health Care Professionals in the Acceptability of Vaccination Programme

Luc Hessel, (replacing Dr. Pecorelli), Sanofi Pasteur MSD, Lyon, France

The present talk will cover: The introduction of HPV vaccination in Europe, the key elements of supportive environment, the roles of experts and scientific societies in establishing recommendations, the roles of the medical community in the implementation of HPV vaccination programs and the challenges for the future.

The introduction of HPV vaccination was facilitated by what is called an existing supportive environment. A primary driving force behind willingness to vaccinate in scientific societies and expert groups, and the recommendations they issue. This supportive environment was present for HPV vaccination.
The long-term success of a vaccination program also depends upon key stakeholders responding effectively to challenges that may arise throughout the given programs’ lifetime.
The promise of a primary prevention for cervical cancer
There is a well recognized need for vaccination against HPV infection.

Despite widespread implementation of screening, cervical cancer remains 2nd cause of cancer death in young women in EU
- 38,000 pa diagnosed with cervical cancer
- 17,000 pa will die

The combination of a primary (vaccination) and secondary (screening) prevention indeed represents a unique and exciting opportunity.

Rapid licensure and adoption of HPV vaccination

License, Recommendations and Funding processes are essentially country based. Interesting all these processes were accelerated for HPV vaccination:
- EU license was granted in 9 months for a quadrivalent vaccine a process that usually takes a period of 1-2 years.
- US license was granted in 6 months.

The green are the different countries and the timing since the license of the first vaccine in Europe. It is interesting that in many occasions funding was given even before recommendations, and overall the process was very rapid for this vaccine.
Regarding the topic of willingness to vaccinate, one can see that there are key elements of supportive environment for vaccine uptake.

As observed on the graph, the willingness to vaccinate intertwines many different aspects. It is based on clinical data to pass to all the other processes of registration, recommendations and through these processes the expert groups and scientific societies interact.

In terms of HPV, the recommendations from experts and scientific societies:
- Early support from these groups at both EU and national levels, and this reinforced recognition of public health need.
- Creation of expert committees to help with scientific assessment of files/drafting of recommendations.
  - This included professionals such as Health Economists, gynaecologists, oncologists, and not only vaccination experts.
- Scientific societies issued own recommendations.
  - Additional level of professional review accessible to policy makers
  - Driver of willingness to vaccinate
- (ECDC (European CDC) issue “Guidance for the introduction of HPV vaccines in EU countries”)

The recommendations from scientific societies and experts had an effect in mobilizing the issuing of national recommendations, impacted the willingness to vaccinate by health care workers; thus supported the establishment and implementation of policies.

**The medical community is the lynch pin of successful implementation of vaccination**
- HCPs are pivotal to influencing attitudes of vaccines: advocate and reassure.
- This community has an ensuring role in the success of implementation of a vaccine.
Role of HCP as source of information on HPV vaccination

As observed HCP is a critical source of information to parents and patient’s about vaccines and vaccination.

**Physicians reassure and educate**
Physicians are a primary source of information for parents on HPV vaccination.

- Data on parental/vaccinee attitudes to HPV vaccination highlight importance of safety and efficacy for acceptance of vaccination 1, 2, 3
- Mothers who trust doctors advice, or who believe their doctor would take their concerns seriously are more likely to accept HPV vaccination 4

Challenges for the future
A vaccination program for an adult cancer is particularly vulnerable to public tolerance of risk
“Success in public health relies on public trust” – Wynia (2007)
For HPV vaccination, public trust will be contingent upon continuing engagement of all stakeholders, particularly that of the health care professional
Session III: Understanding Willingness to be Vaccinated

Consumer Acceptance: A New Dimension in Vaccinology
Zoltan Bozoky, Department of Health, England

In the next 15 minutes the present talk will speak in terms of a policy maker about the England social research programme and how the data collected is used to better understand and frame programme strategy.

The talk will touch on some of the regular and extensive research with parents and will try to illustrate the power of research using a recent example from the planned introduction of the HPV programme (which is scheduled for rollout in England in September). The talk will conclude by summarising some lessons learnt, hoping that it will draw some parallels to be applied in other settings.

We regularly conduct research with parents to gain an insight about the attitudes, understanding about immunisation, their experience and how services are delivered.

In terms of talking to parents, the research study included the following criteria:

- 30 waves of research dating back to 1991
- over 1,000 personal interviews
- parents of 0-2 year olds
- attitudes towards immunisations and disease
- awareness of advertising and publicity

This research has been done since 1991 each year, in what is called waves; talk to over 1,000 parents. The sample is drawn by a random location method and stratified by SES.

Over 30 waves have been carried out, which represent around 30k respondent’s views. Immunisation is an emotive issue and often top of mind for parents, the national research agency goes out and talks face to face with parents.
During research is measured: The spontaneous awareness of immunizations
(see following graph)

Base: All primary care givers of 0-2s (W30 n = 1016)

It is also measured the Perceived Severity of the Disease

Base: All primary care givers of 0-2s (W30 n = 1016)
Moreover, the study try to gauge or better understand parents sense of trust about the information provided by health professionals and the government.

The data in the following graph compares the most recent wave to the previous year. The results tell us that parents are more likely to trust information from health professionals and the NHS, than the government. However, In comparison to the previous year there is an overall improvement in parents’ trust to government information.

For Health Visitors, and particularly GPs, there has been a shift since last wave from the proportion who strongly agrees that they trust the information, towards a ‘tend to agree’ viewpoint. Results for Practice Nurses and the NHS remain stable since last wave.

Noteworthy those who postponed or rejected MMR were less likely to trust information from any of the sources, and are particularly suspicious of information from the NHS or government.

Base: All primary care givers of 0 - 2s – Four-fifths sample
When taking a closer look at what parents take into account when weighting up the pros and cons of immunisation over the last few years the trends show interesting.

Consistently we see - specific mention of autism and – the risk of side effects (safety of immunisation) over and above the danger/risk of diseases that the child is being immunised against. The question is what drives these differences? Certainly, in part we can say that the advertising, information or publicity can play a role.

When observing over time at whether the things people saw actually may have persuaded them not to immunise; we can see in the following graph that this measure has been steadily decreasing over the past few years, now standing at 14% compared with the peak of 33% back in February 2002 (which coincided with the height of negative stories about the safety of MMR). Levels have since declined and are now at their lowest since 1998.
The data obtained on Perceived safety on immunisations

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Oct 03</th>
<th>Nov 04</th>
<th>May 05</th>
<th>Nov 06</th>
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</thead>
<tbody>
<tr>
<td>DTaP</td>
<td>80%</td>
<td>90%</td>
<td>80%</td>
<td>70%</td>
</tr>
<tr>
<td>Oral Polio</td>
<td>85%</td>
<td>90%</td>
<td>85%</td>
<td>80%</td>
</tr>
<tr>
<td>MMR</td>
<td>60%</td>
<td>65%</td>
<td>70%</td>
<td>75%</td>
</tr>
<tr>
<td>5 in 1 vaccine</td>
<td>70%</td>
<td>80%</td>
<td>85%</td>
<td>90%</td>
</tr>
<tr>
<td>Men</td>
<td>80%</td>
<td>90%</td>
<td>85%</td>
<td>90%</td>
</tr>
</tbody>
</table>

Base: All primary care givers of 0-2s (W30 n = 1016)
It is an interesting picture with the majority of parents considering that immunisations are completely safe or only present a slight risk and over time, perceived safety has remained stable or improved – such as for the 5 in 1 (or DTaP/IPV vaccines) where more than 4 in 5 parents consider them safe or just a slight risk.

The long term trend for MMR shows a steady increase in perceptions of safety from the low back in 2003.

As mentioned, the 5 in 1 has improved over the last few waves and we may well see a similar pattern for the pneumococcal vaccine, and we may see these results improve as the vaccine becomes more established.

Proportion who consider MMR a greater risk than the diseases it protects against

Base: All primary care givers of 0-2s (W30  n = 1016)

Turning to perceptions about risk and the proportion who consider vaccines present a greater risk than the disease it protects against here is the data about MMR, peaking during the height of the wakefield controversy. Perceptions of risks and addressing attitudes to risk is clearly important.

Following the licensure of the HPV vaccine in the UK, we spoke to potential recipients and discussed with them their views including risks in order to inform future planning

- 2005 – parents of 8-10 year old girls and boys
- 2007 – 11-12 year old girls, their parents and health professionals
- Pre-testing of leaflets
- Advertising creative development research
Over the course of 2 years we spoke to parents of 8 – 10 year old girls and boys, 11 – 12 year old girls, their parents and health professionals, pre-tested leaflets (because we wanted to determine and then test their preferences not our prejudices!) and put in place an advertising approach that was underpinned by quality evidence.

A strategic research was also carried out to underpin the communications strategy and approach to the use of media

**Overall communications strategy**

- primary role is to set the agenda and focus on cancer prevention -
- ‘HPV vaccine prevents cervical cancer and can save your daughters life’
- mothers and daughters will be encouraged to talk about the issue together
- information leaflet will be common to both daughters and mothers

A clear message from the research was that communications needed to ‘set the agenda and focus on the prevention of cancer’.

The following message was framed ‘HPV vaccine prevents cervical cancer and can save your daughters life’ and used this to help foster the sense of trust shared between mothers and daughters and to encourage that they talk together about the issues – that is why an information leaflet was produce that will be common to both.

A media strategy that was complementary to this approach was needed, where the messages were factual and directive, where supporting messages provided details about cervical cancers, issues such as safety in a way that felt relevant by our target audience.

**Media strategy - overview**

- primary messages will be factual and directive
- supporting messages will provide details on cervical cancer, safety of the vaccine and why it can’t be given later
- a range of media will be used to deliver these messages, offering a hierarchy of information content.
- Leaflets used as vehicle for getting consent form into the home
Sources of information consulted before immunisations were due (prompted)

<table>
<thead>
<tr>
<th>Source</th>
<th>Oct 03</th>
<th>Mar 04</th>
<th>May 04</th>
<th>Nov 04</th>
<th>May 05</th>
<th>Nov 05</th>
<th>Nov 06</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaflets</td>
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<td>20%</td>
<td>19%</td>
<td>19%</td>
<td>19%</td>
<td>23%</td>
<td>18%</td>
</tr>
<tr>
<td>Immunisation appointment card</td>
<td>25%</td>
<td>25%</td>
<td>25%</td>
<td>25%</td>
<td>25%</td>
<td>25%</td>
<td>25%</td>
</tr>
<tr>
<td>Healthcare/childcare magazines</td>
<td>23%</td>
<td>16%</td>
<td>14%</td>
<td>13%</td>
<td>13%</td>
<td>11%</td>
<td>9%</td>
</tr>
<tr>
<td>Childcare/parenting magazines</td>
<td>18%</td>
<td>16%</td>
<td>14%</td>
<td>13%</td>
<td>13%</td>
<td>11%</td>
<td>9%</td>
</tr>
<tr>
<td>Internet</td>
<td>18%</td>
<td>16%</td>
<td>14%</td>
<td>13%</td>
<td>13%</td>
<td>11%</td>
<td>9%</td>
</tr>
<tr>
<td>Books</td>
<td>16%</td>
<td>14%</td>
<td>13%</td>
<td>13%</td>
<td>13%</td>
<td>11%</td>
<td>9%</td>
</tr>
<tr>
<td>Television programmes</td>
<td>21%</td>
<td>16%</td>
<td>14%</td>
<td>13%</td>
<td>13%</td>
<td>11%</td>
<td>9%</td>
</tr>
<tr>
<td>Television adverts</td>
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<td>9%</td>
<td>7%</td>
<td>6%</td>
<td>6%</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Newspaper articles</td>
<td>9%</td>
<td>7%</td>
<td>5%</td>
<td>4%</td>
<td>4%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Women’s magazines</td>
<td>10%</td>
<td>8%</td>
<td>6%</td>
<td>5%</td>
<td>4%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Healthcare magazine articles</td>
<td>9%</td>
<td>7%</td>
<td>5%</td>
<td>4%</td>
<td>4%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>NHS Direct</td>
<td>7%</td>
<td>5%</td>
<td>3%</td>
<td>2%</td>
<td>2%</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>

Base: All primary care givers of 0-2s (W30 n = 1016)

Results show that leaflets continue to be the most used source, which remains around 7 in 10. Reference to the immunisation appointment card, TV programmes and newspaper articles has decreased since Nov 2005. Except for television programmes leaflets are really the written sources that continue to dominate. The reduced resource from TV programmes and newspaper articles reflects the lack of publicity around MMR. The internet continued to be used by around 1 in 5 parents.

Content of advertising, info or publicity that might have persuaded them not to immunise

Base: All who saw or heard something which might have persuaded them not to immunise (W30 n = 119)
Advertising is important it might just be the source parents will turn to for their information needs and which may drive them away from immunising.

A breakdown by content advertising or publicity ‘messages’ from our tracking shows that over time mentions of side effects in general have significantly decreased (to just 3%), and MMR and the danger of autism or Crohn’s remains stable.

**Supporting message channels**
- Press – ads, advertorials and feature stories in women’s and girls magazines carrying detailed facts and information
- Media briefings – series of events with key media editors before the vaccine introduction
- Digital – Signposting on teenage sites, virtual walking surgery, dedicated mini site on immunisation website

**Conclusions**
- Immunisation has the potential to ignite complex and emotive discussions
- to maintain the success and shape policy and future planning carry out regular and extensive research with parents
  - Assess likely take-up rates
  - Identify potential barriers
  - Identify information needs
Assessing Willingness to be Vaccinated: Social and Behavioral Aspects
Bonita Staton, Pediatrician in Chief, Caman and Ann Adams Department of Pediatrics, Children’s Hospital of Michigan, Wayne State University, School of Medicine, USA

This talk will explore three sets of issues regarding the socio cultural and behavioral aspects of assessing willingness to be vaccinated. Examples from the field will be presented to illustrate each point.

The talk will open with a brief exploration of the question: “Does assessing willingness to be vaccinated differ from actual willingness to be vaccinated?”

Next we will explore four operational aspects of assessing willingness to be vaccinated, specifically:
- Conceptual framework (e.g. theories of behavior and behavioral change);
- Data gathering approaches
- Data gathering formats
- Informant Perspective

To frame programme strategy, regular research can be focused around assessing likely take-up rates, examining potential barriers and identifying information needs.

What do we want to know when we assess willingness to be vaccinated?
How many/what proportion of eligible individuals will be vaccinated if a vaccine exists?
What factors would influence this number/proportion?

Issues to be addressed
- Relationship of assessed willingness to be vaccinated and actual willingness
- Considerations in approaching the question
  - Conceptual framework
  - Data gathering approach
  - Data gathering format
  - Informant Perspective
- Unintended changes

Relationship of assessed willingness to be vaccinated and actual willingness
Professed willingness and actual willingness to be vaccinated
- Assessing intention
- Intention is one of best predictors of subsequent behaviour
- Intention is an imperfect predictor of behaviour
- Samoff 2004: Among respondents at a STD clinic who had never been vaccinated against Hep B and were offered free vaccine and who said that day that they intended to be vaccinated (64% of eligible), only 56% did actually accept the vaccine when this one was offered to them immediately after the affirmative answer.

Professed willingness =? actual willingness to be vaccinated
- Seek to develop assessment tools in which the expression of desire/intention to be vaccinated are interchangeable AND
Able to identify those factors which would increase/decrease vaccine intention and ultimately vaccine acceptance.

The later differences are important because until intention to be vaccinated is nearly equivalent with actual vaccination behaviour, need to look at factors that might result in individuals not becoming vaccinated even if they say that they intend to do so—as we saw in the Samoff study.

**Considerations in approaching assessing willingness to be vaccinated**
- Conceptual framework
- Data gathering approach

**Conceptual Framework**

- **Grounded**: Observe and question before and ideally after decision is made.
- **Theory-based**: Guides the design of the assessment interview/tool and the intervention.

Both are used; typically grounded theory is used in the formative stages of the research although often even at this stage the questions presented in focus groups or individual interviews are in part guided by one or more models of behavior/behavioral change.

**Models of Behavior/Behavioral Change**

- Social Cognitive Theories including:
  - Health Belief Model
  - Protection Motivation Theory

**Health Belief Model (Liau 1999)**

Perceived: **Vulnerability, Severity, Benefits (Efficacy), Barrier**.

Developed scales to assess willingness to be vaccinated for HIV.

First three had one scale consisting of six items with adequate Cronbach’s alpha. Fourth (barriers) consisted of 4 subscales: 1. Pragmatic obstacles; 2. Conditional Non-membership in a Risk Group (i.e. if you are not doing risky things you do not need to be vaccinated); 3. Fear of the Vaccine; and 4. Fear of Needles not being Clean.

Acceptance of vaccine was assessed along 4 key dimensions corresponding to two of these Four constructs:
- **Efficacy** (90%, 70% or 50% efficacious)
- **Barriers**
  - Cost (free, $25 or $100);
  - Mode of administration (oral, 1 injection or 3 injections),
  - Type of vaccine (live, attenuated, whole killed, or viral fragment)

- Overall vaccine acceptability =53%
- Most acceptable was lowest cost, most efficacious, 1 injection, viral fragment=73% acceptance; least acceptable (most expensive, 50% efficacious, 1 injection, live attenuated)=32%
- **Factors associated with non-acceptance**: Perceived non-membership in HIV susceptible group and fear of vaccine.
Protection Motivation Theory
Self efficacy (I could get to the clinic) plus Response efficacy (the vaccine would prevent HPV) minus Response cost (the vaccine might cause disease) balanced by Intrinsic (my daughter is a good girl) and Extrinsic rewards (my friends think virgins should not be vaccinated) minus Severity (of the bad outcome) and Vulnerability (cancer is bad but I probably would not get it) yield Protection Motivation.

Questionnaires developed along dimensions of PMT to assess willingness to be vaccinated with shigella, cholera and typhoid vaccines among > 4000 residents of 5 Asian countries (geographic sampling frame). Included willingness to pay. Youlong 2004; Pack 2006; Chen 2006.

In contrast to the view of government health authorities discussed yesterday, they were the first line authority in China.

Perceived vulnerability of specific subgroups (odds ratios ranging from 1.6 to 8.1), knowing someone died of the disease (OR reached infinity) and response efficacy (satisfaction with past vaccination services) (OR reached infinity) consistently associated with perceived need for vaccines of specific subgroups.

Perceived need for a vaccine was positively associated with willingness to pay for the vaccine. Chen 2006

Other Models of Behavioral Change
- Related to Social Cognitive Theories
  - Theory of Reasoned Action
    - Theory of Interpersonal Behavior (Triandis)
  - Self-Determination Theory
- Transtheoretical Model (Stages of Change) (precontemplation, contemplation, preparation, action, and maintenance)
- Diffusion Theory (early adaptor, opinion leaders, laggards)

Data Gathering Format: Interviews
Participant Observation
Focus group
- Especially useful to gain full range of possibilities
  - Whose opinion might be influential
  - Perceptions of disease—severity, vulnerability
  - Perceptions of vaccines in general—vaccines in children---vaccines and STIs

Individual
Especially useful for understanding a specific phenomenon or perspective.
Less helpful to understand the possible range of certain opinions or popularity of specific views.
Individual interviews may be especially useful in debriefing individuals after they have been or have not been vaccinated—especially if their action differed from what they described their intention to be.
Data Gathering Approach: Vignettes and Case Scenarios
- Stories
- Descriptions of circumstances*
- Alterations of circumstances*
- Provision of basic facts*
- Free-listing (word association)
- Pile-sorting
- “Voting” (commitment, discussion of views)

Data Gathering Approach: Case scenario with changing component
Zimet 2005—HPV vaccine
Use of scenarios in which the mode of vaccination, severity of infection (curable, chronic, fatal), vaccine efficacy (50%, 70%, 90%) were varied;
Findings
- Age of recipient important: Providers and parents concerned about vaccinating children <12 for HPV;
- Endorsement by one or more professional society (AAP, AAFP or ACOG) important especially to providers

Vary disease, cost, age of vaccine recipient
Pack 2006; Youlong 2004; Chen 2006
- How much >3000 respondents willing to pay taken as a proxy for perceived need for Typhoid and Shigella vaccine in 5 Asian countries
- Much more enthusiasm for preschoolers to be vaccinated against dysentery and enteric fever (98% for both) compared to adults (66% and 60%); also varies by disease (77% thought elderly should get vaccine against shigella compared to 49% against enteric fever).

Combining variations in Approach and Format: Information scenarios and Likert
- Each item proceeded with a brief summary of facts about the disease (“A person usually gets GC through sex. GC can usually be cured with antibiotics. If untreated it can cause a painful pelvic infection that may affect a person’s ability to have children”) followed by questions assessing perceived physical and emotional severity of infection to the child, perceived vulnerability of the child to STI, and belief that vaccine would promote unsafe sex.
- 87% of parents accepted vaccines. With each 1 point higher perceived vulnerability, parent was >2 times more likely to accept vaccine and with each 1 point higher in severity scale, 1.6 fold more likely to accept.
- Adolescents whose parents were in the high acceptor model were threefold more likely to accept a vaccine.
- Zimet 2005b

Informant Perspective
- Three issues:
  - What does the informant (vacinnee) think?
  - What does the informant think other key individuals think do what do they actually think?)
  - Who, then, might be included as in willingness-to-be-vaccinated assessments and intervention efforts?
Informant Perspective: Vaccinee

What do you think?

Perceptions of individual to be vaccinated.

HPV adolescents: Researchers expected that adolescents would be concerned about relationship to STIs and fear that acceptance of vaccine would imply that they were “at risk”. Found that the adolescents were interested in what their pediatricians and parents recommended.

Parents in turn were interested in what their pediatricians recommended.

Informant Perspective: Provider

What do you think your provider thinks?

Fernandez 2007: Only 69% of ED HCW likely or very likely to be vaccinated this year (only 42% of nurses compared to 82% of physicians); HCW likely to be vaccinated more likely to support a ED vaccination plan for patients than those unlikely to be vaccinated (80% versus 55%).

Informant Perspective: Provider

Norwalk 2006: Using a 56-question questionnaire based on Triandis Theory, 85% of individuals whose physician recommended vaccination in fact did get vaccinated.

Daniels 2004: Focus group among 22 groups of African American adults, major factor for unwillingness to be vaccinated was providers who did not routinely discuss or recommend vaccination. In general lacked information about vaccines.

Zimet 2005: In three studies, one of 224 pediatric nurse practitioners, one of family practitioners and another of Fellows of the American College of OB-GYN, asked to rate 13 scenarios which varied by patient age (11, 14 or 17), infection prevented by the vaccine (herpes genitalis, mononucleosis, HIV), gender of the patient, and whether the vaccine had been endorsed by the professional society.

Across all of these categories, ratings highest when the vaccine endorsed by AAP, AAFP or ACOG.

Informant Perspective: Authorities

What do public health authorities think?

Youlong 2004: In China, in focus group discussions and then confirmed by cross-sectional data, public health authorities frequently cited as authoritative and respected figures in determining vaccine acceptance.

Similar findings in other Asian nations.

Informant Perspective: Family

What do my parents/family members think?

Family significant in vaccine decision-making in all cultures but role varies considerably.

Parents (mother, father or both) or grandparents decide on infant and child care.

In some societies immunization of women may be decided by themselves or husband but strong influences; in others women may be driver.

Immunization of the elderly by self or children or by providers.
Unintended Changes: Effect of questioning
Will/can questioning create concerns by reporting or raising false concerns – e.g. despite research finding that parents were not concerned about STIs, news media reported that they were and raised anxieties. Can we raise concerns when they did not exist by our research questions?

One study approach is to raise frequently asked questions (get response)---but then in the study provide the answer (in a fairly detailed fashion) *Gilbert 2003*

**Ensuring Willingness to be Vaccinated: The Content of Advocacy Programs**

*Walter Orenstein, Professor of Medicine and Pediatrics, Director Emory Vaccine Policy and Development, Associate Director Emory Vaccine Center, Emory Institute, USA*

Advocacy is critical for immunization program success. Goals of advocacy include obtaining resources to: 1) remove financial barriers to vaccination, 2) educate and promote vaccine recommendations to health professionals, who in turn become advocates to the public, and 3) educating and promoting vaccine to target populations.

**What do we advocate for?**
- Resources for vaccines
- Resources for vaccine implementation
  - Education/promotion
  - Monitoring and tracking
  - Disease surveillance
- Professional support
- Political support
- Public Acceptance

Critical partners include public health professionals, private physicians and other health providers, academic and other researchers, vaccine manufacturers, business, media and community leaders, politicians, and community organizations such as representatives of parent groups.

**Building Partnerships**
- Critical because government health authorities often cannot directly approach politicians
- Need to find common cause with other advocates
- Advocate for resources
  - Vaccine financing
  - Professional education and promotion
  - Public education and promotion

Partnerships are important because public health officials may be constrained with regard to reaching out to political leaders. Private organizations usually have no such constraints. Building partnerships involves finding common cause with other organizations. For example, in the United States, the immunization program established a relationship with the Children’s Defense Fund (CDF), a group which grew out of the civil rights movement, seeking to advocate for children including protecting them from disease. The group included major
public leaders including Hilary Clinton and Donna Shalala, who later became a Secretary for Health and Human Services in the Clinton Administration. The common cause was using immunization coverage rates to assess access to healthcare for poor children. Critical data needed for advocacy comprise disease burden (in addition to population burden, it is important to have illustrative clinical anecdotes), vaccine effectiveness and safety, cost-effectiveness, and immunization coverage levels. Extensive and frequent communications systems are required. This includes face-to-face meetings with partners, newsletters, websites, publications in the medical literature, press briefings and the support of coalitions of partners. Immunization mandates have played a critical role in sustained high coverage rates in the United States. Enforcement of school attendance immunization mandates became tolerable in the United States during the 1970s, when a resurgence of measles brought public health attention to large numbers of unvaccinated children in school sustaining transmission and leading to complications and deaths. School mandates have been documented to be associated with higher coverage for preschool children.

For instance the Interactions with Children’s Defense Fund (CDF)
- Invited them to speak at National Immunization Conference
- Established long-term relationship
- Hillary Clinton, then wife of Governor Clinton and Donna Shalala, later Secretary of Health and Human Services on the Board
- CDF had close relationship with key reporters

Other key actions:
- Establish and support coalitions of advocates.
- American Academy of Pediatrics, American Academy of Family Physicians, Association of State and Territorial Health Officials (ASTHO), Rotary, Kiwanis, and others.

Critical Data
- Cost-effectiveness
- Clinical burden
- Vaccine effectiveness
- Vaccine safety
- Immunization coverage levels
- Anecdotes and champions
- Focus on disease reduction rather than immunization rates

Communications
- Diagnostics
  - Focus groups
  - Surveys
  - Provider opinions
- Meetings
- Newsletters
- Websites
- Medical literature
- Press briefings
- Media Events
Mandates require strong medical consensus, broad-based public support, enforcement mechanisms, and an “opt-out” mechanism. They are most easily implemented when the voluntary system has failed and when herd immunity is an important consideration. Mandates are most effective at enhancing uptake among persons already supportive of immunization. They are not likely to be effective for persons with strongly held beliefs against vaccination and those with strong distrust of the government.

**What Can Immunization Laws Do?**
- Enhance vaccine uptake among supportive persons of immunization
- Improve immunization record keeping.
- Increase priority for immunization among parents and health care providers.
- Minimize barriers to access.

**What Problems Laws May Not Address?**
- People strongly opposed to immunization
- Persons with distrust of government and health care institutions

**What is Necessary for Mandates to be Considered and Effective?**
- Strong medical consensus
- Broad-based public support
- Need for some enforcement mechanisms
- Need for some “opt-out” mechanism
- Failure of voluntary system
- Contagious diseases and need for herd immunity
- Most indicated when spread of disease occurs in institution that would enforce the laws
- Helpful if laws do not need to be national. State and local laws allow precedents to be set, leaders to lead and others can follow
- Adequate vaccine supply
- No financial barriers to access
- No physical barriers to access
- Addressing compensation for those injured by vaccines

While persons with exemptions to mandates in the United States have been increasing recently, they constitute only a small proportion of the population in most communities, generally < 4% in any given state. However, statewide estimates may mask individual
communities or population groups where lack of immunization may be substantially greater. Nevertheless, despite continued disease in some of these groups, most vaccine-preventable diseases in the United States are at or near record lows.

**Summary**

Advocacy critical to:
1. Receive resources to vaccinate
2. Build consensus among professional groups
3. Reach out to key stakeholders
4. Convince the public to accept vaccination

Advocacy involves:
1. Critical partnerships
2. Extensive communication
3. Data on disease burden, vaccine effectiveness, vaccine safety, cost-effectiveness
4. Need to take advantage of common agendas with other groups
5. Mandates for solidifying support among persons not strongly opposed to vaccines
6. Mandates best started under circumstances of trying to control an outbreak

**Ensuring Parental Willingness for Vaccination: Implementation Practices**

Loretta Brabim, University of Manchester, UK

There are various approaches that could be used to improve vaccine delivery in order to increase vaccine coverage. Uptake of childhood vaccines is not uniform within populations and one suggestion is to use targeted strategies to improve uptake of subgroups with different characteristics. For example, both older, better educated parents, as well as those from socially disadvantaged and ethnic minority groups are under-immunised. Racial and socio-economic characteristics predict slower vaccine uptake and lower age-appropriated vaccination coverage. Well educated parents who decline vaccination usually do so consciously because of negative attitudes to immunisation. In the UK there is a higher level of trust in health advice and vaccine recommendations among Asian compared to Afro-Caribbean mothers. Groups that are partially immunized are not necessarily vaccine averse, but they may face barriers to completion of recommended vaccines if their children live in larger or single parent families and make less regular use of health services. Despite the attractiveness of focusing educational or other interventions on low uptake groups, it remains unclear how, in practice, these groups could be targeted, and whether this would yield benefits beyond generally improved access to health services.
Removing barriers to access of vaccines: a study from Middleton & Baker 2003

It is relevant to think of targeted interventions if certain segments of the population can be identified as having low vaccine uptake rates.

Socioeconomic status is consistently linked with vaccine uptake. M & B have shown, in an analysis of data from 60 health authorities in England that MMT coverage for under-twos was consistently higher in affluent authorities. Between 1991 and 1996 coverage increased more rapidly in DEPRIVED areas which reduced much of this inequality. This rise was associated with a decrease in the number of GPs over 65 and an increase in the number of practice nurses per 10,000 populations in these deprived areas— and this service improvement made a different to lower SES status groups but not to the more affluent

Making it easier for mothers to access vaccines is important, and it is probably most important for low SES mothers, although it may not of course, make any difference to mothers who have ideological reasons for not accepting vaccination.
Infant immunisation status with maternal factors
Sarnad et al, 2006

<table>
<thead>
<tr>
<th>MATERNAL FACTOR</th>
<th>Number</th>
<th>Partially v Fully Immunised OR (95% CI)</th>
<th>Unimmunised v Fully Immunised OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29 years</td>
<td>7,581</td>
<td>0.7 (0.6 to 0.8)</td>
<td>1.2 (0.9 to 1.6)</td>
</tr>
<tr>
<td>30-39</td>
<td>391</td>
<td>0.4 (0.2 to 0.8)</td>
<td>2.3 (1.3 to 4.0)</td>
</tr>
<tr>
<td>&gt;39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDUCATION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Ref No Qualifications)</td>
<td>2,903</td>
<td>0.9 (0.6 to 1.3)</td>
<td>1.9 (1.2 to 3.0)</td>
</tr>
<tr>
<td>Higher degree</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FAMILY SIZE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Ref 1 Child)</td>
<td>1,551</td>
<td>5.0 (3.8 to 6.4)</td>
<td>2.4 (1.4 to 3.9)</td>
</tr>
<tr>
<td>&gt;3 children</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WARD TYPE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Ref Advantaged)</td>
<td>8,807</td>
<td>1.3 (1.0 to 1.5)</td>
<td>2.1 (1.4 to 3.2)</td>
</tr>
<tr>
<td>Disadvantaged</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ETHNIC GROUP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Ref White)</td>
<td>891</td>
<td>1.2 (0.8 to 1.8)</td>
<td>0.5 (0.3 to 0.9)</td>
</tr>
<tr>
<td>Pakistani</td>
<td>264</td>
<td>1.2 (0.4 to 1.0)</td>
<td>2.4 (1.6 to 3.7)</td>
</tr>
</tbody>
</table>

Women from low SES backgrounds may be more likely not to complete their vaccine schedules.

This data taken form the Millenium Cohort study in the UK that followed children born between 2000 and 2002. This survey was undertaken when most infants were about 9 months old. This table shows how maternal factors were related to whether the child was under, partially or fully immunised at 2,3,4, months of age. Trained interviewers visited the home. Altogether, 3.3% were partially immunised and 1.1% were unimmunised.

Compared to the partially immunised the unimmunised mothers were likely to be older, better educated and Black Caribbean (adjusted for other factors in the table). Another study in Brent ascribed better compliance amongst Asian mothers to their higher level of trust in health advice, and being less aware of the MMR media debate than Afro Caribbean mothers.

Mothers with large families were more likely to be both partially and unimmunised, but had the highest risk of partial vaccination. These data again suggest that there is an excess risk due to service barriers among low SES whereas the unimmunised are more likely to have made an intentional decision that is unrelated to service delivery.

**Why are fewer pre-scholars vaccinated?**

Tickner et al, 2006

1. Intentional: Change of mind
2. Unintentional: Forgetting appointments; Time; Lack of awareness of boosters; Illness; Indifference.
3. Dissatisfaction with the service
Some of these problems increase after early infancy. This review asked why so few preschoolers were vaccinated, and looked at studies from a wide range of countries, finding common factors.

Change of mind – negative experiences. Parents have had more time to consider the implications of immunising.

Among the unintentional category identified factors such as the pressures on mothers who have returned to work, illness childcare commitments etc

Disaction: Know in UK there are differences between GP practices and PCTs in immunisation coverage rates. In Scotland, vaccine uptake lower in single handed practices. Parents are often unsatisfied with the information they received, or they feel rushed, or that vaccinators are unsympathetic
These parents miss or delay appointments.

In other words – lifestyles, as well as attitudes, impinge on vaccine coverage, but some of these disproportionately affect mother from low SES.

Infection-specific examples of under-vaccinated groups
-Increased risk of rubella in pregnant Oriental, Asian and black women (Tookey et al, 2002).
-Measles outbreaks in travellers and some religious communities (HPA 2007/8).
-Increased incidence of HBV infection in south Asians (Hahné et al, 2003).
-Deprived children/adolescents at higher risk of MenC before introduction of routine vaccination. (Heyderman et al, 2004)

Cochrane Review of Reminder and Recall systems
Characteristics of the review: Included interventions for immunising children birth to 18 years, any setting considered; 1966 - 2007
Interventions: Letters, postcards, autodialler, person to person reminders, single or repeated reminders, combinations with other interventions (eg. outreach).
Outcomes: Immunisation rates, proportion of target population up-to-date.

It is generally appreciated that reminder and recall systems are useful, but it is only very recently that a Cochrane review was conducted of the evidence.

Provider reminders includes such methods as computer generated lists of children to be seen at a clinic who are out of date, or stamping files by a receptionist to remind the health provider to vaccinate the next time the patient is seen.

The main limit in terms of method selection is computerisation and keeping accurate personal details. In the US CDC has developed software called CoCasa to address this. As yet their cost effectiveness has not been established, because the studies conducted so far have been in so many different settings, and types, that a comparison of costs would not be meaningful.
It would be meaningful to have data that showed that lower SE groups had better vaccine compliance.
Problems with patient reminders

- Providers overestimate their immunisation coverage
- Few providers operate a tracking system
- Lack of computerised technology for tracking vaccine status
- Opportunities for immunisation are missed

Pooled random effects odds ratios by type of vaccine for 47 eligible studies

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>1.57</th>
<th>1.41 to 1.75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine Childhood Immunisations</td>
<td>1.47</td>
<td>1.28 to 1.68</td>
<td></td>
</tr>
<tr>
<td>Childhood Influenza</td>
<td>2.87</td>
<td>1.65 to 4.98</td>
<td></td>
</tr>
<tr>
<td>Adult Pneumococcal, Tetanus and Hep B</td>
<td>2.19</td>
<td>1.12 to 3.99</td>
<td></td>
</tr>
<tr>
<td>Adult Influenza</td>
<td>1.66</td>
<td>1.31 to 2.09</td>
<td></td>
</tr>
<tr>
<td>Adolescent Hep B</td>
<td>1.14</td>
<td>0.98 to 1.98</td>
<td></td>
</tr>
</tbody>
</table>

Translates into a 5-20% increase in percentage points.

Patients receiving a reminder recall intervention were more likely to have been immunised or to be up to date. The exception was the adolescent hep B study. This fell done because it used an autodialler system, but the telephone numbers were unstable. Translated into impact on the % vaccine uptake, would seem to be quite substantial. The best improvements are for childhood flu vaccine, a serious infection that disrupts working parents schedules. And older patients – this is because they are easier track because they can be selected by age on the data base. Depending on the vaccine schedules, the creation of algorithms for younger patients can be complex. This analysis did not address the issue of which sub-groups most benefited from recall/reminder systems.

Adolescent HPV vaccine first dose uptake in two Primary Care Trusts (PCTs) in Manchester (UK) with different reminder systems

<table>
<thead>
<tr>
<th></th>
<th>PCT1 N=1178</th>
<th>PCT2 N=1639</th>
<th>PCT1 N=1178</th>
<th>PCT2 N=1639</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated</td>
<td>703 (59.7%)</td>
<td>1284 (78.3%)</td>
<td>645 (54.7%)</td>
<td>1020 (62.2%)</td>
</tr>
<tr>
<td>On scheduled visit</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Later *</td>
<td>58 (4.9%)</td>
<td>264 (16.1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Brabin et al, 2008)
I want to refer to the HPV adolescent vaccine study we conducted this year to pilot delivery of the bivalent vaccine to 12 year old girls in 36 schools in 2 PCTs in Manchester because it provides some preliminary evidence that reminders are most beneficial in increasing coverage in low SES groups.

2 PCTs offered the vaccine. PCT2 attained a much higher vaccine coverage than PCT1, which we attribute to differences in their reminder schedules. PCT1, school nurses sent two letters (initial plus one reminder) to parents, visited a school, and went back about 10 days later to vaccinate those who had been missed. PCT 2 sent the invitation letter, vaccinated and them sent a reminder. For parents who gave late consent, the children were accommodated either when the team was vaccinating at another school, or was picked up a month later when the second dose was given. As see from table, 21% of children vaccinated in PCT2 were picked up late.

**OR (95% CI) for response to health dialogue by school satisfaction, adjusted for sex and age group**

<table>
<thead>
<tr>
<th>Response</th>
<th>Medium Satisfaction</th>
<th>Low Satisfaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thought about the dialogue</td>
<td>0.85 (0.74 to 0.97)</td>
<td>0.68 (0.57 to 0.81)</td>
</tr>
<tr>
<td>Discussed with a parent</td>
<td>0.77 (0.67 to 0.88)</td>
<td>0.59 (0.49 to 0.70)</td>
</tr>
<tr>
<td>Complied with the school nurse’s advice</td>
<td>0.86 (0.75 to 0.99)</td>
<td>0.68 (0.59 to 0.81)</td>
</tr>
<tr>
<td>Did what he/she thought best</td>
<td>1.03 (0.90 to 1.18)</td>
<td>1.07 (0.89 to 1.28)</td>
</tr>
</tbody>
</table>

(Borup & Holstein 2006)

An interesting question is for adolescent vaccines is the extent to which the adolescent influences parental consent for vaccination.

There has been some discussion about vaccinating adolescents without parental consent if the provider considers them competent to make such a decision. This has been seen by some as a possible implementation strategy for increasing coverage. In principle, provided the vaccination could be kept confidentially, this could be done, and probably cause the same sort of consternation as a mandated adolescent vaccine, in that it erodes the parents right of consent. Would it work? It is difficult to know. However, a quite telling Danish study found that children who feel alienated from school or who have poor social relations with the school setting- who may not respond well to health advice. In this study the response of children aged 11-15 to a scheduled dialogue of talks by the school nurse, mirrored the level of school satisfaction. In this table, the Odds ratios for medium and low satisfaction rates are in comparison to children with high school satisfaction rates. I think the message here is that children who come from difficult background tend to have more problems in school and may themselves respond negatively to a health intervention, or may not seek to influence their parents because they don’t talk things over with their parents.
Mandated vaccination (Wilson et al 2005)
- Day care and school entry mandates associated with higher coverage beyond socio-demographic factors.
- When Adolescent Hep B vaccination was strictly enforced, as in California (by exclusions, school audits) coverage was better (Fogarty 2004).
- A link between school funding and student attendance decreases enforcement.
- The effect of the Hep B mandate on uptake of other recommended vaccines was mixed.
- Schools in urban areas did less well.

Whereas in UK we have relied on voluntary actions to increase vaccine coverage, in other health care systems there as been more used of legal mandates, which have, without doubt, increased vaccine coverage and have been justified as public health measures. According to this paper reviewing the success of adolescent hepatitis B vaccination, found that its success is relative to the degree of enforcement. But issues of funding may interfere with enforcement and this may be why schools in urban areas still do less well. The policy works for the vaccines that are mandated but does not seem be a catalyst for improving vaccination coverage for non-mandated vaccines.

For adolescent vaccines the picture is complicated because vaccine acceptance may be a joint decision, depending on the child’s age and maturity. Adolescent consent to vaccination in the event of parental disapproval or failure to give approval is controversial. There is presently little evidence of either positive or negative effects on vaccine coverage. Socio-demographic and cultural characteristics that shape parent attitudes also influence the adolescent. The responsibility for ensuring adolescent understanding of the pros and cons of vaccination would fall to health providers, and in school-based vaccine programmes, to school nurses. Yet a recent review found little evidence of their effectiveness in health promotion.

More generally, a systematic review found good evidence to recommend reminder and recall systems to improve immunization rates in all settings, though only one (ineffective) study in adolescents had been conducted. In the US, where the vaccine schedule has become increasingly complex and moving home or changing health provider disrupts this schedule, reminder systems, could be critical as mis-timed vaccinations could reduce vaccine immunity. Finally, some countries mandate vaccination. In the US school entry rules have greatly increased vaccine coverage of some vaccines, and in Belgium, parents who do not immunize against polio face fines and imprisonment.

It can be concluded that there are a range of strategies that might be employed either to encourage or compel parents to vaccinate their children but evidence for some strategies is currently lacking.

Conclusions
- Some evidence that socio-demographic factors can be mitigated by vaccine implementation practice and policies to increase uptake.
- Very little systematic research on interventions.
- Need to investigate issues specific to adolescent vaccine programmes.
Much of the research on SES was done in the late 80s and 90s and then with high vaccine coverage, those studies seemed less relevant. Now vaccine coverage is decreased, and with the advent of new adolescent vaccines, it is perhaps timely to return to the question of social disadvantage, in addition to our focus on attitudes and culture.

**Case Study: Zoster Vaccination**

**Robert Johnson, Vaccine and Infectious Disease Institute, Fred Hutchinson Research Center, Washington, USA**

Herpes zoster results in significant suffering and cost both to patients and healthcare providers. As prevention and management of its main complication, postherpetic neuralgia, by other means are less than satisfactory, an effective and safe vaccine seems highly desirable. Much work is being undertaken to assess the cost effectiveness of this strategy and it seems likely that the cost would be acceptable. A recent study from the USA indicates that the zoster vaccine at a cost of $150 is likely to be cost effective for immunocompetent U.S. vaccine recipients aged =60 years using commonly cited thresholds for judging cost-effectiveness. This holds good over a broad range of scenarios (Pellissier JM, Brisson M, Levin MJ. *Vaccine* 25 (2007) 8326-8337).

Killed vaccines are not very effective for enhancing cell mediated immunity (CMI) of prolonged duration. Michiaki Takahashi developed the live attenuated Oka strain of VZV which is now incorporated in vaccines for both varicella and herpes zoster. The attenuated virus was developed from a three year old boy with varicella whose family name was Oka. This strain, when attenuated, appears not to stimulate tumour growth and not to result in serious breakthrough disease or clinically significant herpes zoster from reactivation. Older adults exhibit a significantly reduced immune response to vaccines compared with children: thus a considerably stronger (higher titer) preparation of the vaccine is required for protection against HZ than is used for childhood protection against varicella.

The Merck herpes zoster vaccine, Zostavax, is licensed in the USA, Europe and other regions. The Shingles Prevention Study was reported in the New England Journal of Medicine in 2005. In approximately 38,500 adults of 60 years of age and greater, the vaccine reduced the incidence of HZ by 51.3% compared with placebo and of PHN by 66.5%. Burden of illness (BOI) – the area under the curve of incidence, severity and duration of pain associated with HZ – was reduced by 61.1%. It is anticipated that protection will be long lasting but the precise duration of such protection will require long term surveillance studies. Apart from mild to moderate sore arms related to the injection site, there was no significant difference in adverse effects in the vaccine group and the placebo group.

Maintenance of adequate zoster-specific CMI through adulthood to prevent HZ is believed to rely on two factors. Firstly, endogenous boosting resulting from intermittent sub-clinical reactivations of persistent virus and secondly from exogenous boosting as a result of contact with children with varicella. Mathematical modelling raises the hypothetical possibility that reduced exogenous boosting, resulting from a reduced pool of children with varicella which occurs in a population utilizing childhood vaccination (not the U.K. at this time), might lead to an increased incidence of HZ in seropositive adults. To date there is no evidence that this actually happens. If it did, it would be expected to last about 20 or 30 years until the pool of seropositive adults declines as a result of varicella vaccination.
In summary, the burden of herpes zoster and PHN can be greatly reduced by the use of live attenuated VZV vaccines. Long term surveillance will answer remaining questions regarding their effects on epidemiology of HZ and PHN. The current vaccine is not appropriate for use in significantly immunocompromised individuals and a heavy burden of herpes zoster falls upon this group of patients.

4. Session IV: How to Assess the Acceptability of Vaccination by the Vaccinees: The Concept of Patient Related Outcomes

Benoit Arnould, Mapi Values, Lyon – France

Vaccinology is joining other areas of health care in considering the subject as having an important role in vaccination decisions. The concepts of “acceptability”, “willingness to vaccinate”, or “willingness to be vaccinated” have recently become key considerations in vaccinology. These concepts are in line with the growing interest in the individual’s perspective in health. After the first measurements of Quality of Life in the 70s, the measurement of the patient’s perspective with appropriate self-completed questionnaires developed consistently with a central role given to the subject in western societies. In the mean time, relations between patients and their doctors have dramatically changed, evolving from a paternalistic model to a consumer-provider model. The change we observe in vaccinology regarding subjects’ participation in the decision and evaluation of the service received is both a revolution and a normalisation. It is a revolution because it has major and durable impacts on many aspects of vaccinology, including the roles of the parties involved, and a normalisation because the same change has already begun in many other fields of health care.

Subjectivity is a natural consequence of an individualisation of decisions
The individualisation of a decision means that the subject is placed at the centre of multiple interactions between four main distinct aspects: culture, environment, personality and cognition. First, subjects have to position themselves in one of several roles: consumer (when actively choosing protection), obeying subject (when receiving imposed protection), or responsible citizen (when participating in collective protection). Second, they receive information from and are influenced by relatives or parents, professional societies, advocacy programs. Third, the way they participate in and make their decision is dependent upon their personality traits (risk-aversion, perceived vulnerability, locus of control) and specific history (previous experiences, family history, etc). Fourth, the way patients receive and treat information, and the way they make their decision, becomes an important factor for effective vaccination. Clinical researchers, professional associations, and health authorities think about vaccination as a balance between advantages and risks or harms, but do subjects think about it in the same way, and what does “acceptability” mean in the subject’s mind?

The need for adapted and specific scales developed and validated following appropriate methodology
Because of all the factors that influence whether or not a subject will ask for or accept to receive a certain vaccine, there is a new need for descriptions, explanations and evaluations;
describing attitudes, beliefs and behaviours; explaining what drives them and how they interact; and evaluating the impact of programmes, campaigns, and quality of care. Therefore, there is a great necessity in the science of vaccinology for measurement instruments to address these needs.

We know - thanks to the research work conducted in psychosocial sciences and its adaptation to the field of health in the past decades – how to measure subjectivity. Measurement means assessment in a valid, reliable, and sensitive way. Today, the consensus in the medical and scientific community is strong about the appropriate methodology to manage subjective information with regards to its quantitative aspects (psychometrics), its cultural aspects (linguistic validation), as well as its cognitive aspects (qualitative research methods). Moreover, the regulation authorities in Europe as well as in North America have acknowledged the importance of these measures - today termed “Patient-Reported Outcomes” - and have made explicit how they can contribute to registration decisions.

**Patient-Reported Outcomes and vaccinology: a potential still to be exploited**

Patient-Reported Outcomes have become an important part in clinical evaluation, leading to an extraordinarily rich development of new questionnaires used as specific measurement instruments. They cover an amazing variety of concepts (such as Health-Related Quality of Life, Satisfaction, Well-Being, Pain and symptoms, and also Functional Status) in an impressive number of specific diseases or conditions.

However, the development and use of these measures is still an exception in vaccinology. This is likely to change in the near future, as the subject’s perspective becomes critical in the process of somebody receiving a vaccine. This perspective includes various components related to beliefs, attitudes and perceptions such as disease awareness, risk perception, the feeling of vulnerability, acceptance / denial, locus of control, attitude toward medical expertise, confidence in health care system or constraints and harms linked to vaccine administration.

**A key for the success of vaccine strategy**

To properly understand and manage all psycho-social aspects that need to be taken into account, existing questionnaires can be validated in the populations of interest, and new ones should be specifically developed. A full set of specific, well-validated measures will be essential for all stakeholders to make decisions: regulators for market authorisation, professional associations for recommendations, healthcare professionals for prescription, parents or legal guardians and subjects themselves for requesting or accepting vaccination.

**Appropriate Measurement of Subjective Factors: A New Key for the Science of Vaccinology – Applications of Patient Reported Outcomes to Vaccinology**

**Carla Dias Barbosa, Mapi Values, Lyon – France**

The acceptability of both vaccine and vaccination programmes by the individual and by healthcare professionals are two key elements contributing to the success of vaccination policies and their public health impact. These elements are all the more important to consider 1) with the vaccines targeting new diseases that are perceived less life-threatening, 2) with the rise of the patient as an active consumer of healthcare services rather than merely a passive recipient of these services and 3) with the vaccination policies on new vaccines that are less and less mandatory and rely exclusively on voluntary compliance of individuals and healthcare professionals with public health recommendations.
These major changes in vaccine environment enhance the need for public awareness about the severity and burden of the diseases to be prevented with the new vaccines, and also underline the importance of changing individuals’ behaviour and their perceptions regarding new vaccines through educational campaigns and public information. Based on these changes it becomes important to assess the individual perceptions of vaccines and vaccine programmes and to 1) identify the environmental variables that would trigger health care professionals’ and/or individuals’ decision to adhere to recommendations 2) identify the important health state descriptors that would influence the decision to vaccinate or to be vaccinated 3) explore the perceived value of the new vaccines and how this translates into “willingness to vaccinate” for healthcare professionals and “willingness to be vaccinated” for individuals.

Systematic measurement of the patient perspective with adequate instruments can contribute to decision-making in several ways:

1) **Disease awareness.** Development of disease models based on literature review of epidemiological and clinical data describing the burden of disease (i.e. morbidity, mortality, costs of treatment, and loss of productivity). The measurement of patient perception, beyond clinically observable events, is essential to adequately document the severity of symptoms, the impact of the disease on daily functions and the resulting impairment of all aspects of Quality of Life.

2) **Value demonstration.** Development of specific tools assessing individual perception of the value of being vaccinated and vaccination acceptability (e.g. acceptability of local site reactions, pain at injection site, and the vaccine in general)

3) **Communication strategy.** Development of educational materials based on qualitative research e.g. focus groups or face-to-face interviews with individuals and clinicians aiming to identify major drivers and barriers that:
   a. Lead health care professionals to actively support vaccination policies: the “willingness to vaccinate”
   b. Drive the acceptability of vaccination programmes in the targeted population: the “willingness to be vaccinated

Two case studies will be briefly presented as an illustration:

1) **Zoster vaccination:**
   Development of a disease model to demonstrate the importance of the negative impact that Herpes Zoster and Post Herpetic Neuralgia have on lives and the consequent value of prevention.

2) **Influenza vaccination:**
   Development of a PRO questionnaire assessing subjects’ level of acceptance and perception of influenza vaccination, the level of subjects’ anxiety before and after vaccination and their willingness to be vaccinated the following year.
Evaluating the Acceptability of Vaccine and Vaccination Programmes: An Individual and Public Health Perspective

Lyon, June 20, 2008 - Fondation Mérieux welcomes vaccinology experts and private & public organizations to “Les Pensieres” Conference Center in Veyrier du Lac – France to address during the three day forum several aspects that are impacting the use of vaccines due to vaccine acceptability issues.

Public health prevention strategies are importantly based on vaccination programs, despite serious research & development for the improvement of more effective and safe existing vaccines and the creation of novel ones to address new pathologies, the acceptability and use of certain vaccines still very limited. This is importantly observed in the older age patients group. The concept of vaccine acceptability still abstractly managed among the different players in the vaccinology arena, main roles in this process are indeed taken by health care providers and the patients themselves; however, industry, regulatory agencies and governmental institutions, among other, due have a relevant roll in the utilization of vaccines, thus in the process of vaccine acceptability and its impact in public health strategies.

Many questions will likely be accessed as to:
• What are the barriers for health care workers and / or patients for the acceptability of vaccines?
  Are those barriers related intrinsically to the vaccine (vaccine collateral effects, components, etc), due to vaccine misconceptions, and / or due to logistical matters such as costs or lack of vaccine accessibility in a given population?
• How can new regulations and policies intervene to improve acceptability & access to vaccines?
  How can the different players work together through patient / health care workers education, among other strategies, to enhance vaccine acceptability?
• Can certain vaccines become mandatory to the population? How can this be done by also enhancing population vaccine acceptability?

The forum in congruency with the foundation’s mission promotes knowledge sharing by disseminating novel information, and fostering new approaches to access this topic.

Fondation Mérieux

Fondation Mérieux was created in 1967 by Doctor Charles Mérieux and was granted charity status in 1976. Presided by Alain Mérieux, the Foundation’s mission is to fight infectious diseases affecting developing countries. The Foundation works to develop and make available new and affordable approaches based on biotechnologies, in the field of prevention, diagnostics and therapeutics.

To achieve its goal, Fondation Mérieux plays a catalyst role in Research and Development by mobilizing a network of excellence that gathers the foremost international experts working in the scientific world today. The Foundation fosters the dissemination of scientific information and innovation through international seminars and conferences, like the Santiago symposium. The Foundation also provides high-level, practical scientific training for health practitioners in the developing world. Finally, Fondation Mérieux works directly in the field by strengthening and building local health infrastructures to enable long-term sustainable development. It is present in Africa, Asia and in Haiti.
### Meeting Program

#### Monday, July 7, 2008

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>17h30-18h30</td>
<td>Registration</td>
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<tr>
<td>18h30-18h45</td>
<td>Welcome Address</td>
<td>Benoit MIRIBEL</td>
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<tr>
<td>18h45-19h15</td>
<td>Keynote lecture</td>
<td>David SALISBURY</td>
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<td></td>
<td>The principles of vaccine adoption</td>
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<td>19h45</td>
<td>Welcome Dinner</td>
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Based on the experience of the recent introduction of several vaccines in the UK, the speaker will review and analyse the key elements that have made the vaccination programmes successfully adopted (key success factors) and the pitfalls health authorities are facing when introducing a new vaccine (reality check).

#### Tuesday, July 8, 2008

**SESSION I**

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Presenter</th>
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<tbody>
<tr>
<td>08h30-08h50</td>
<td>The medical needs</td>
<td>Paolo BONANNI</td>
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<tr>
<td>08h50-09h10</td>
<td>Discussion</td>
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<tr>
<td>09h10-09h30</td>
<td>The regulatory process</td>
<td>Nora DELLEPIANE</td>
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This session will review in more details some of the elements analysed in the keynote lecture, illustrated by practical examples:

- **Medical needs**: how to make sure that they are identified and properly addressed upfront as part of the development programme of a new vaccine. This includes addressing the epidemiology of the disease and the elements that will have a critical importance in the design of the vaccine (e.g. vaccine strains, formulation...), what will be the meaningful clinical and/or immunological endpoints, and the relevant outcomes to assess early impact of the vaccination programme;

- **Regulatory process**: regulators have the critical role of assessing the quality, safety and efficacy of new vaccines to register them. More and more frequently regulators request the input of expert groups (e.g. Vaccine Working Party at EMEA) and are expected to provide advice that could go beyond the strict technical assessment of a given vaccine and influence the speed of introduction of a vaccine (e.g. risk management plan);

- **The recommendation process**: a more and more transparent evidence-based process for which the role of health technology assessment (HTA) is growing. It is important to understand how health-economics data can be balanced by other parameters like social and ethical values. How the policy-making process is influenced by other stakeholders would also be appropriate to identify.

- **The financing process**: easy access to vaccine is an important factor of the success of a vaccination programme and its acceptability by the population (example of seasonal flu). Reviewing the vaccine financing sources, existing gaps in funding, understanding the different options to fund vaccination programmes would help defining the optimal financing process for a new vaccine and possible alternative approaches.

- **Health infrastructures**: another critical element of the successful implementation of vaccination programmes relates to its “feasibility”. This especially includes several issues: will vaccine supply be appropriate? Is or can the new vaccine be administered as part of existing vaccination programmes? Is the health care infrastructure appropriate for running the programme? Will the target population have an easy access to the vaccine?
Anticipating successful vaccine adoption: the Willingness to Vaccinate

Chair: Roger Glass

Recommendations and funding of vaccination programmes as well as the appropriate infrastructure to ensure access and delivery of the vaccine to the end users are not sufficient to ensure its successful implementation. Acceptance, or better “adoption” of the policy and of the vaccine by those in charge of advising the target population and/or administering the vaccine is essential. This “willingness to vaccinate” is critical when one knows that health care professionals are the most trusted adviser by the patients.

The session will:
- analyse the elements that will influence the health care provider in her/his willingness to vaccinate;
- review the methodological approaches to evaluate this behavioral aspect;
- analyse the key components of successful advocacy programmes aimed at ensuring the acceptability of vaccination programmes by health care providers;
- and address the role of scientific and professional societies in supporting vaccination policies and providing guidance to their health care professionals.

These aspects of the successful adoption of vaccination programmes will be illustrated by the recent introduction of HPV vaccination.
### SESSION III

**Anticipating successful vaccine adoption: the Willingness to be Vaccinated**

*Chaired by: S. L. ROSENTHAL, Daniel SALMON*

Recommendations and funding of vaccination programmes as well as the infrastructure to ensure access and delivery of the vaccine to the end users are not sufficient to ensure its successful implementation. Acceptance, or better, "adoption" of the policy and of the vaccine by the target population is essential. This rather new dimension in vaccinology needs to be understood and properly addressed by those in charge of conducting vaccination policies.

The session will:
- analyse the elements that will influence the consumer acceptance and result in the willingness to be vaccinated;
- review the methodological approaches to evaluate this social or personal behavioural aspects;
- analyse the key components of successful advocacy programmes, i.e. that the vaccination is the right answer to a given situation.
- address whether vaccine implementation practices may reduce barriers that deter parents from vaccination.

These aspects will be illustrated by the recent introduction of zoster vaccination.

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<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Chair</th>
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<tbody>
<tr>
<td>08h30-08h50</td>
<td>Consumer acceptance: a new dimension in vaccinology</td>
<td>Joanne YARWOOD</td>
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<tr>
<td>08h50-09h10</td>
<td><strong>Discussion</strong></td>
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<td>09h10-09h30</td>
<td>Assessing the Willingness to be vaccinated: social and behavioural aspects</td>
<td>Bonita STANTON</td>
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<td>09h30-09h50</td>
<td><strong>Discussion</strong></td>
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<td>09h50-10h20</td>
<td><strong>Coffee Break</strong></td>
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<tr>
<td>10h20-10h40</td>
<td>Ensuring Willingness to be vaccinated: the content of advocacy programmes</td>
<td>W. ORENSTEIN</td>
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<td>10h40-11h00</td>
<td><strong>Discussion</strong></td>
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<tr>
<td>11h00-11h20</td>
<td>Ensuring Parental Willingness to be vaccinated: Implementation Practices</td>
<td>Loretta BRABIN</td>
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<td>11h20-11h40</td>
<td><strong>Discussion</strong></td>
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<td>11h40-12:00</td>
<td><strong>Case study: Zoster vaccination</strong></td>
<td>Robert JOHNSON</td>
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<td>12h00-12h20</td>
<td><strong>Discussion</strong></td>
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<tr>
<td>12h20-14h00</td>
<td><strong>Lunch</strong></td>
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This session will first address the concept of “patient-related outcomes” (PRO), defined as the impact a given event will have on the acceptability or rejection of the vaccine by the patient. This includes the perception of adverse events, or injection techniques that could paradoxically be better accepted than expected based on their usual assessment of severity or intensity.

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<tr>
<th>Time</th>
<th>Session Title</th>
<th>Speaker</th>
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<tbody>
<tr>
<td>14h00-14h20</td>
<td>The concept of patient related outcomes (PRO) and its measurements</td>
<td>Benoit ARNOULD</td>
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<td>14h20-14h40</td>
<td>Discussion</td>
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<tr>
<td>15h00-15h20</td>
<td>Role of PRO in vaccination process</td>
<td>Carla DIAS BARBOSA</td>
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<td>15h20-15h40</td>
<td>Discussion</td>
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<td>15h40-16h15</td>
<td>Concluding Remarks</td>
<td>Luc HESSEL</td>
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<td>16h15</td>
<td>End of the meeting</td>
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