Immunization safety in developing country vaccination programs

Philippe Duclos,
World Health Organization

Fifteenth Advanced Vaccinology Course

16th May 2014

Veyrier-du-lac, France

With thanks to WHO colleagues and particularly to Selma Khamassi, Denis Maire, and Sophie Boisson

Issues covered

1. Range of immunization safety issues

2. Real problems and challenges

3. Differences between developing and industrialized countries

4. What should be done to ensure immunization safety and related WHO's contribution

Immunization safety

"ensuring and monitoring the safety of all aspects of immunization, including:

- vaccine quality,
- transport, storage and handling,
- vaccine administration,
- and the disposal of sharps."

Examples of issues

- Egypt,1999: 3 deaths labelled post DPT encephalopathy due to methanol impregnated compresses
- Algeria, 2001: 7 infants died following measles vaccination. Use of selenium vials instead of proper diluent
- Guinea, 2002: 2 adults died after yellow-fever vaccination. Investigation points vial contamination
- Sri Lanka, 2008 Liquid pentavalent (DTwP-HepB-Hib) vaccine. Suspension 3 months after introduction following deaths: concern about a "new" reaction (hypotonic-hyporesponsive episodes)

Examples of issues

- Allegations of hormone contamination of vaccines in Nigeria, India and the Philippines (polio, TT)
- Kenya: Higher risk of HIV-1 seropositivity in women who received TT during pregnancy
  Int J STD AIDS 2006;17:749-52.
- Rotavirus vaccine: intussusception and porcine circovirus type 1
- France: hepatitis B vaccination and multiple sclerosis
- Brazil and Italy: MMR vaccine, increased risk of allergic reactions
- England and India: coincidental deaths following vaccination with HPV (series of more recent allegations in Israel and Japan)
- Increased risk of narcolepsy following use of Pandemrix in children

One death in 18 year old 13 hours after MR vaccination in context of mass vaccination campaign in Ukraine

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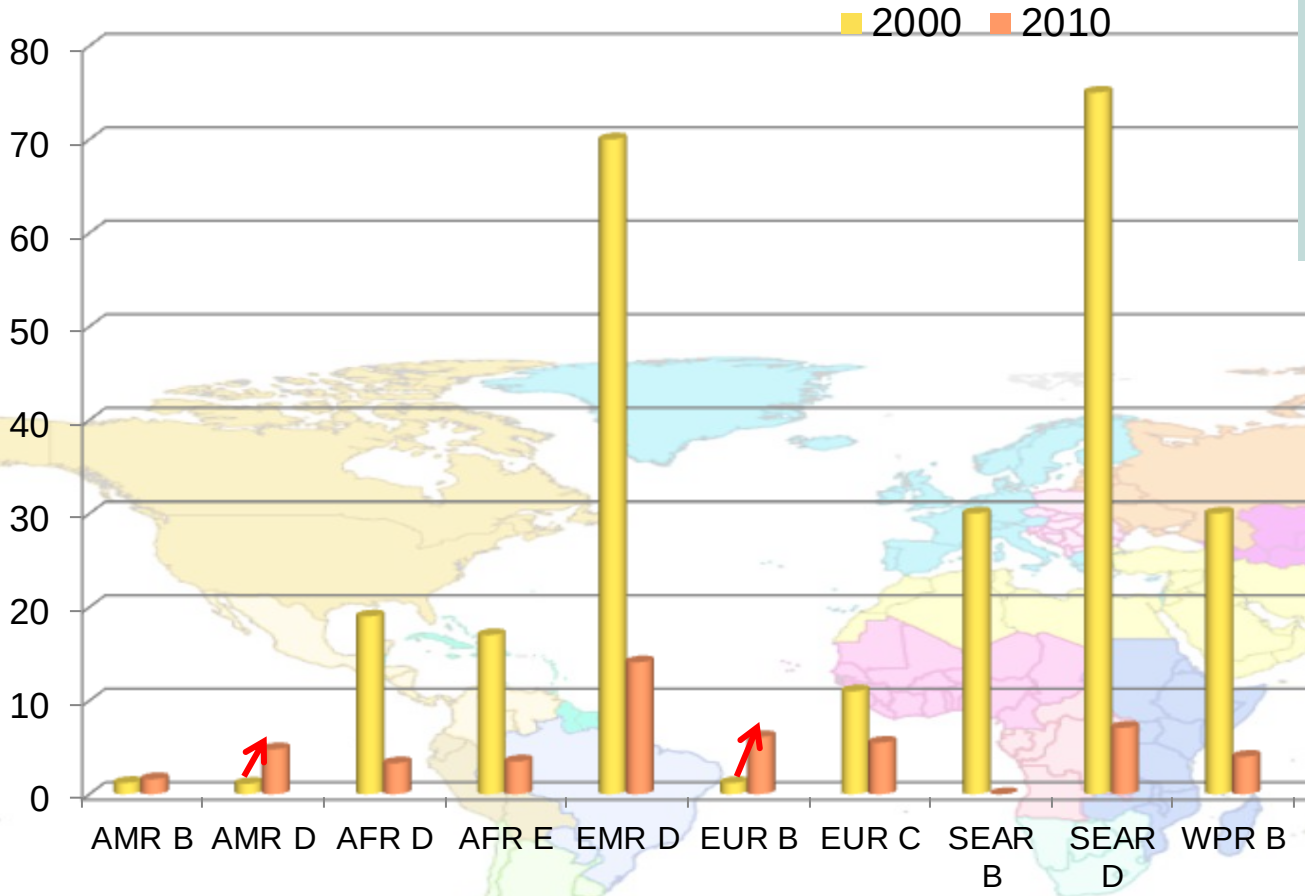
Global Burden of Unsafe Injections: Evolution in WHO Sub-Regions

Devices Reuse 2000 - 2010



Definitions of mortality strata used to define subregions

Mortality stratum	Child mortality	Adult mortality
A	Very low	Low
B	Low	Low
C	Low	High
D	High	High
E	High	Very high

www.who.int/whr/2003/en/member_states_182-184_en.pdf

AMR D: Bolivia, Ecuador, Guatemala, Haiti, Nicaragua, Peru

EUR B: Albania, Armenia, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Georgia, Kyrgyzstan, Poland, Romania, Slovakia, Tajikistan, Macedonia, Turkey, Turkmenistan, Uzbekistan, Yugoslavia

Between 2000 and 2010 global proportion of reuse of injection devices dropped from 39.8% to 5.5% and the average number of injections per person per year from 3.4 to 2.9.

Pepin J. et al., Université de Sherbrooke, Canada

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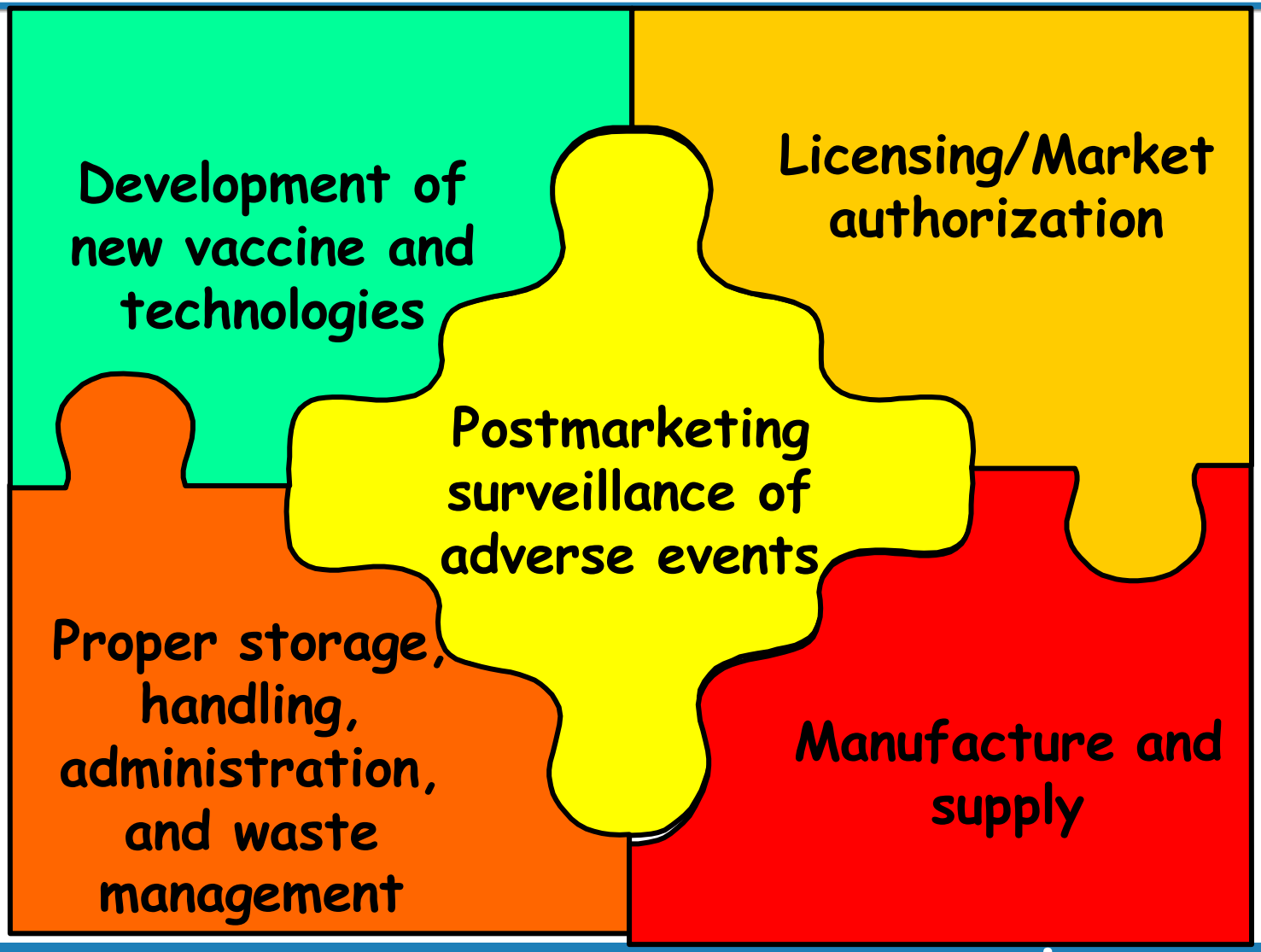
Unsafe injections and global disease burden: situation and progress

- In 2010, between 0.7% and 1.3% of the estimated 2.55 million new HIV infections (i.e. between 16,734 and 33,468) attributed to unsafe injections. For hepatitis C viral infections (HCV), the corresponding estimate is between 157,592 and 315,120 cases, and for hepatitis B viral infections (HBV) 1.68 million cases.
- Compared with 2000, in 2010:
  - unsafe injections decreased by 88%
  - reductions in unsafe therapeutic injection resulted respectively in 87%, 83%, and 91% decrease in HIV, HCV, and HBV infections acquired through unsafe injections
- In 2010 between 5.5 and 8.2 million DALYs saved due to reduction in incidence of injection related HIV, HBV, and HCV infections
- **In 2008, use of auto-disable syringes for immunization injections prevented and estimated:**
  - **5,457 HIV infections**
  - **217,900 HBV infections**
  - **50,234 HCV infections**
  - **86,103 infections with nosocomial bacteraemia**
  - **34,440 injection site abscesses**
- In 2008, hepatitis B vaccination prevented 1,548,678 infections from unsafe injections.

What makes a vaccination safe?



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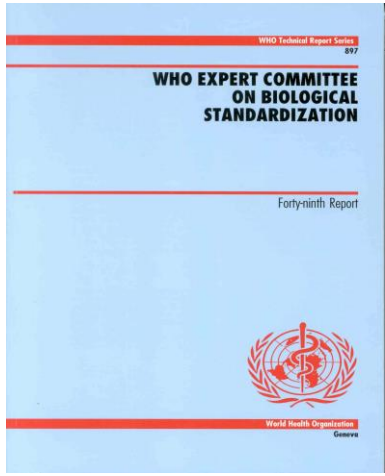
World Health Organization ‘s Goals

Ensure that **“100%”** of vaccines used in all national immunization programmes are of assured quality

Definition of “**Assured quality vaccines**”

- ✓ National Regulatory Authority (NRA) independent from vaccine manufacturer
- ✓ NRA fully functional *(system + 6 regulatory functions)*
- ✓ No unresolved reported problem with vaccine

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



www.who.int/biologicals/expert_committee/en/

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National Regulatory Functions depend on vaccine source

Regulatory functions

- Regulatory system
- Licensing
- Surveillance AEFI
- Lot release
- Laboratory access
- GMP Inspections
- Clinical evaluation of safety & efficacy

Source of vaccines

UN agency	Procure	Produce
★	★	★
★	★	★
	★	★
	★	★
		★
		★

WHO prequalification

Objectives

- Provide UN purchasing agencies with an independent opinion/ advice on the quality, safety and efficacy of vaccines
- Ensure that candidate vaccines are suitable for target population and meet programme needs
- Ensure continuing compliance with specifications and established standards of quality

Principles

- Reliance on a "functional" NRA
- Production consistency ensured through good manufacturing practices
- Random testing for compliance with specifications
- Monitoring of complaints from field

Procedure recently revised

- Programmatic suitability

http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/

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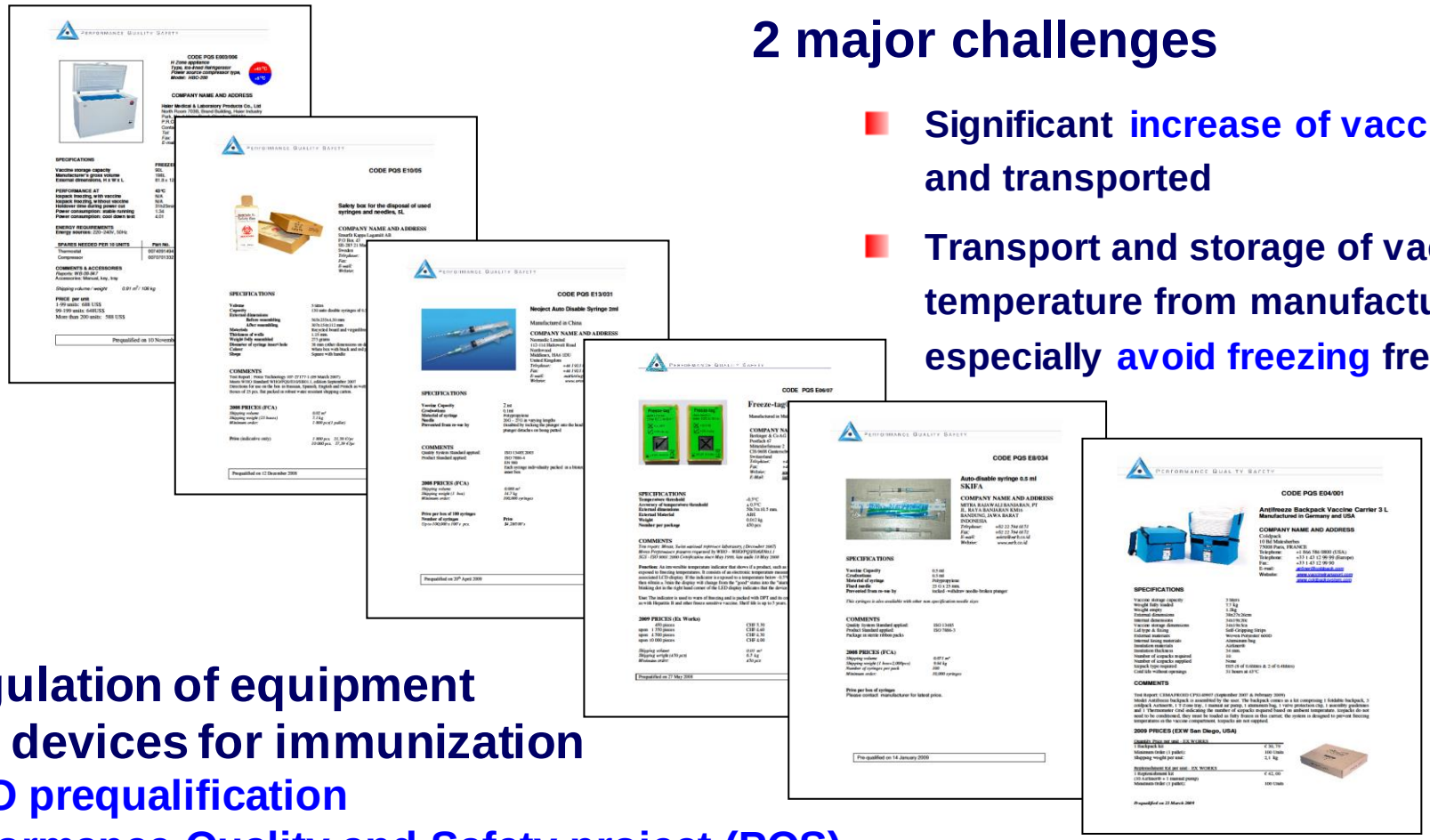
Injection and other immunization related equipment: regulations and prequalification



2 major challenges

- Significant **increase of vaccine volume** to be stored and transported
- Transport and storage of vaccines at correct temperature from manufacture down to end user, especially **avoid freezing** freeze-sensitive vaccines

Regulation of equipment and devices for immunization

WHO prequalification

Performance Quality and Safety project (PQS)

http://apps.who.int/immunization_standards/vaccine_quality/pqs_catalogue/

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A Safe Injection

- No harm to the recipient
- No harm to the health-care worker
- No harm to the community

Reuse of equipment

Unsafe collection

Unsafe disposal

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Drawing up diluent
UNICEF OPT/A. Battersby


Recaping after drawing up diluent
UNICEF OPT/A. Battersby


Recaping after drawing up the vaccine
UNICEF OPT/A. Battersby

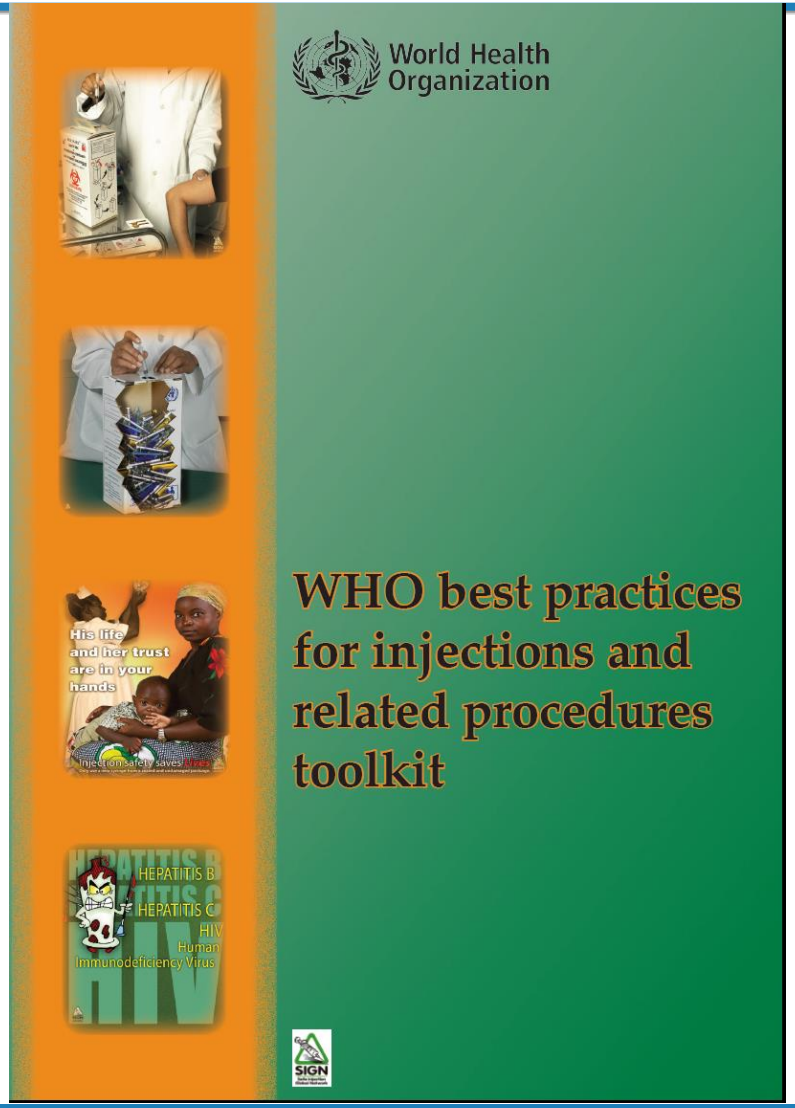

Preparing to inject


Injecting


Final recapping

Best infection control practices for skin piercing, intradermal, subcutaneous, and intramuscular needle injections

1. Using sterile injection equipment
2. *Preventing contamination of equipment and medication*
3. Preventing needle-sticks
4. *Preventing access to used needles*



Safe Injection Global Network (SIGN)
Mission: Ensuring universal access to safe injection devices and practices in all Member States

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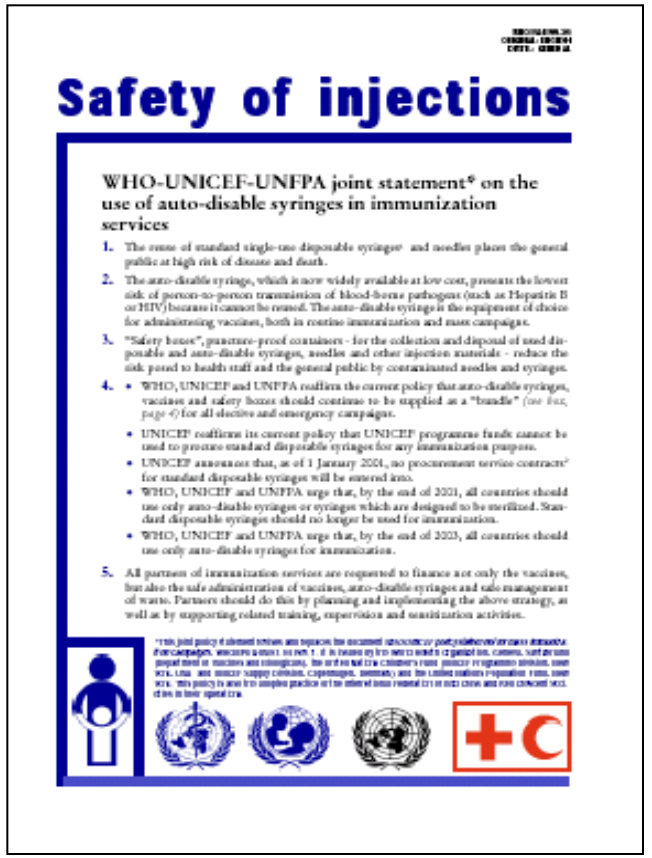
WHO/UNICEF/UNFPA joint statement on the use of AD syringes for immunization services

Policy on Injection Safety

All countries should use only Auto-Disable (AD) syringes for immunization injections (ISO 7886-3)
(*WHO & UNICEF in favor of AD mechanisms triggered at the start of injection)*



Safety of injections

WHO-UNICEF-UNFPA joint statement* on the use of auto-disable syringes in immunization services

1. The reuse of standard single-use disposable syringes and needles places the general public at high risk of disease and death.
2. The auto-disable syringe, which is now widely available at low cost, presents the lowest risk of person-to-person transmission of blood-borne pathogens (such as Hepatitis B or HIV) because it cannot be reused. The auto-disable syringe is the equipment of choice for administering vaccines, both in routine immunization and mass campaigns.
3. "Safety boxes", puncture-proof containers - for the collection and disposal of used disposable and auto-disable syringes, needles and other injection materials - reduce the risk posed to health staff and the general public by contaminated needles and syringes.
4. • WHO, UNICEF and UNFPA reaffirm the current policy that auto-disable syringes, vaccines and safety boxes should continue to be supplied as a "bundle" (see box, page 4) for all elective and emergency campaigns.
   • UNICEF reaffirms its current policy that UNICEF programme funds cannot be used to procure standard disposable syringes for any immunization purpose.
   • UNICEF announces that, as of 1 January 2004, no procurement service contracts for standard disposable syringes will be entered into.
   • WHO, UNICEF and UNFPA urge that, by the end of 2003, all countries should use only auto-disable syringes or syringes which are designed to be sterilized. Standard disposable syringes should no longer be used for immunization.
   • WHO, UNICEF and UNFPA urge that, by the end of 2003, all countries should use only auto-disable syringes for immunization.
5. All partners of immunization services are requested to finance not only the vaccines, but also the safe administration of vaccines, auto-disable syringes and safe management of waste. Partners should do this by planning and implementing the above strategy, as well as by supporting related training, supervision and sensitization activities.

Bundling Policy

Ensure sufficient numbers of AD syringes, reuse prevention reconstitution syringes and Safety boxes for each vaccine dose

Reconstitution syringes

UNICEF supplies only syringes with re-use prevention features (ISO 7886-4)

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Over 30 WHO approved AD syringes (.05ml, .1ml, .25ml, . 5ml) including some with retractable features (Bangladesh, Belgium, China, Denmark, Hungary, India, Indonesia, Korea, Malaysia, Pakistan, Singapore, Spain, UAE, USA, Vietnam) and >50 WHO prequalified reuse prevention injection devices for therapeutic use including a large number with retractable features

Disposable syringes: ± 3 cents

AD & reuse prevention syringes: 4.5 to 6 cents per unit

Manual retractable syringes: 6 to 9 cents per unit; Automatic retractable syringes15 cents up

Retractable syringes: not all with AD features

Are ADs & reuse prevention injection devices an answer to all injections safety issues?

NO,

AD does not stand for

Auto Destructible or Auto Disposable syringe

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Are ADs & reuse prevention injection devices an answer to all injections safety issues?

NO,

AD does not stand for

Auto-Destructible or Auto-Disposable syringe

it is only

Auto-Disable syringe for fixed dose immunization

- **ADs & reuse prevention injection devices prevent reuse problems and do not protect the vaccinator nor the community**
- **WHO is in favour of syringes with safety-engineered protection mechanisms**

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Some good and some bad practices

Two-handed recapping is dangerous

Checking packages for breaks in integrity

The sharps box needs to be next to the patient care area

Needle left in the septum of a multi-dose diluent vial, Northern Asia

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Proper reconstitution?

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Reading labels?

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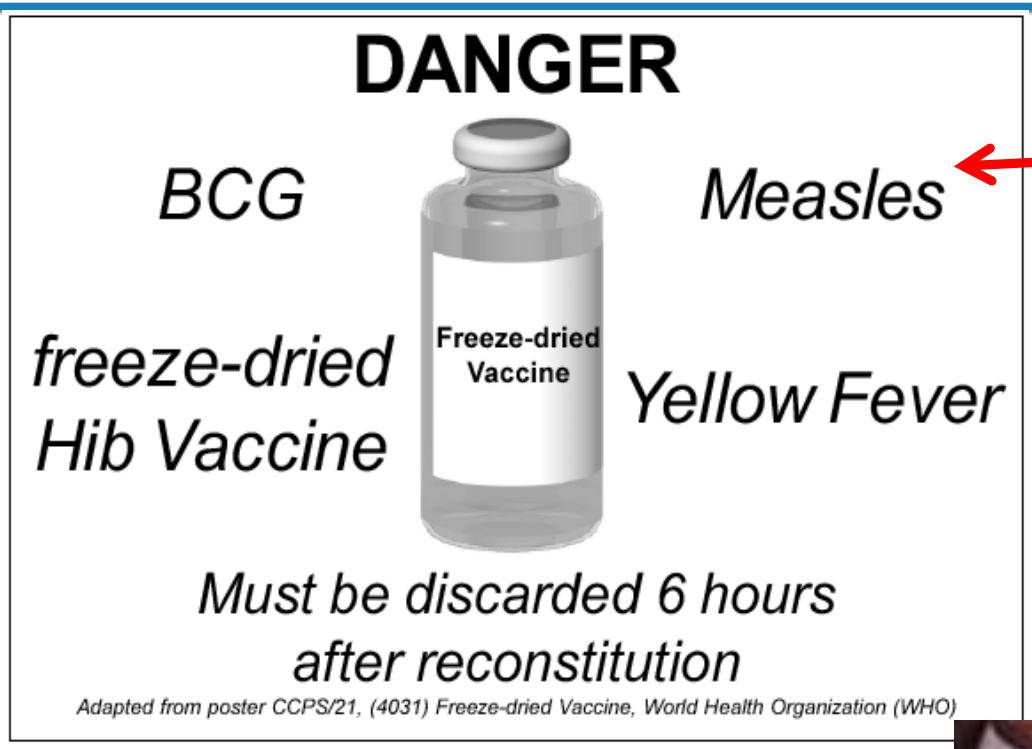
Following the open vial policy?



If Vaccine Vial Monitor (VVM) on cap discard after 6 hours

If VVM on vial you can keep vaccine for 28 days as per Multi Dose Vial Policy

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Using the proper technique?

Reprinted with permission from *www.immunize.org*
Practice. WHO/EPI/TRAM/98.12

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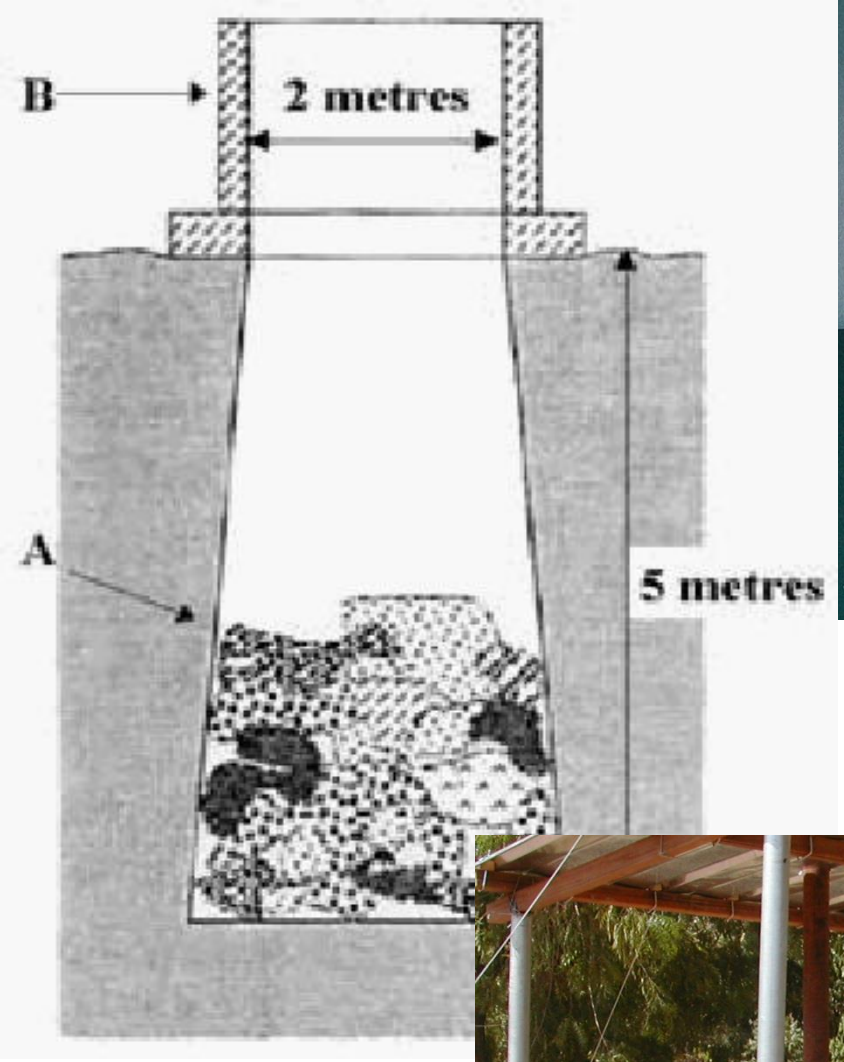
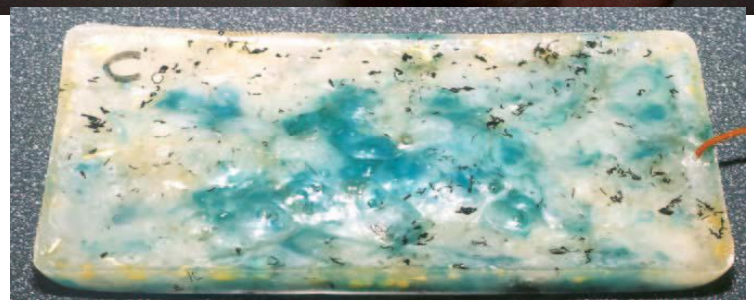
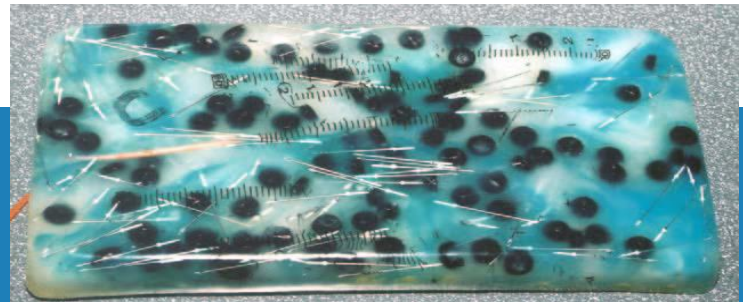
Waste Management

- No one-size-fits-all solution
- **Solutions do exist for many situations "non-availability" of technologies = "wrong problem" or not a technical one**
- Environmental concerns, pressure groups, Kyoto, bans on burning in some countries
- **Support Stockholm and Basel conventions**
- Strategies
  - Assessment and proper management
  - Identification and development of recycling options
  - All components same plastic, PVC free
  - Research and promotion of alternatives to small scale incineration
  - Small scale incineration acceptable if used appropriately


B
2 metres
A
5 metres





Non-Incineration Treatment Technologies: Examples

- Autoclave technologies
  - Small autoclave – health post
  - Medium-size autoclaves + shredders - hospitals
  - Large autoclave (5 tons/day) + compactor – central treatment facility

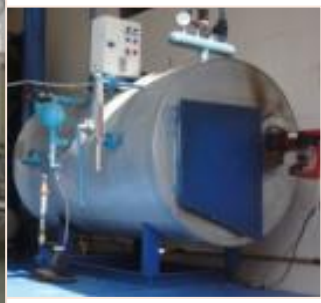
- Advanced hybrid autoclave systems – central treatment facilities
  - Rotating autoclave
  - Hybrid autoclave with internal shredding
  - Hybrid autoclave with fragmenting arm

- Microwave technologies - hospitals

- Alkaline hydrolysis for anatomical waste - hospitals





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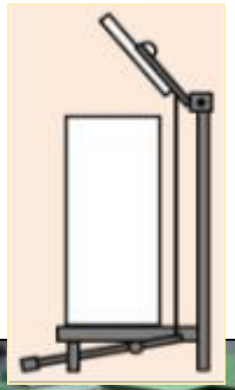
Low-cost Technology for Africa

(University of Dar es Salaam, College of Engineering & Technology, Tanzania)

- Low-cost autoclave (200 liters)
  - Horizontal, ergonomically designed
  - Compact, self-contained, modular
  - On-site or mobile (fits on pick-up truck)
  - Multiple energy options (electricity, bottled gas+solar, other fuels)
  - Gasket mold provided
- Autoclavable metal waste containers:
  - Leak-proof, color-coded, allows rapid steam penetration, durable to last for many years, stackable (35 & 20 liters)
- Autoclavable mechanical needle cutter & autoclavable sharps container
- Compactor +baler or shredder



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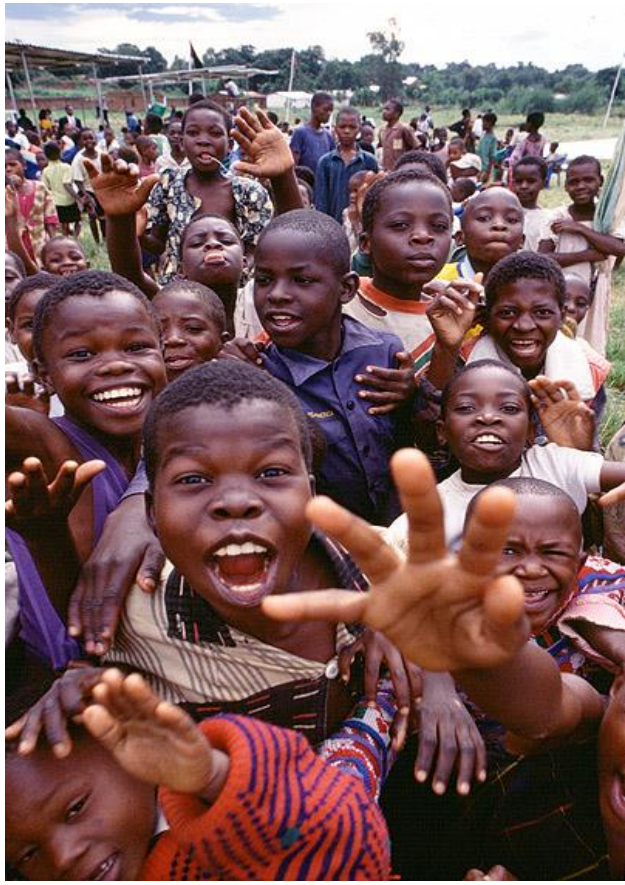
Lots of progress… but work is not finished yet !

- Injection safety is NOT only about devices and national plans alone do not provide the answer but are important steps forward
- Training, advocacy and information, education and communication are essential and require continued attention and resources (money and people) at all levels!

Mass vaccination campaigns - special issues



- Apparent increase in adverse events
  - many doses over short period of time
  - more vigilance/awareness
- Real rise from programmatic errors
  - pressure and fatigue result in normal safe injection practices not observed
  - new staff lack specific training and expertise
- Increased risk of negative impact of rumours
- Adverse events generate criticism of campaign
- Different age groups

Global capacity building and harmonized tools

- WHO and partners Global Vaccine Safety Initiative
- Brighton Collaboration
- CIOMS/WHO working group

Global analysis and response

- GACVS
- Other global or regional advisory bodies

National AEFI surveillance, investigation and response

- Immunization programme
- Regulatory authority
- AEFI review committee
- Other support groups

Global signal detection and evaluation

- Uppsala Monitoring Centre
- Global vaccine safety data link
- Global Network for Postmarketing Surveillance of Prequalified Vaccines *
- Other partners

Product monitoring

- Vaccine manufacturers
- Licensing authorities in countries of manufacture
- Procurement agencies

* Senegal, Uganda, Brazil, Mexico, Iran, Tunisia, Albania, Kazakhstan, India (1 State), Sri Lanka, Vietnam

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Global Advisory Committee on Vaccine Safety (GACVS)


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Health topics | Data | Media centre | Publications | Countries | Programmes | About WHO

Global Vaccine Safety

- Global Vaccine Safety
- Global Vaccine Safety Initiative
- Global Advisory Committee on Vaccine Safety
  - Topics
  - Committee reports
- Reference documents and publications
- Related links

The Global Advisory Committee on Vaccine Safety

The Global Advisory Committee on Vaccine Safety (GACVS) was established in 1999 to respond promptly, efficiently, and with scientific rigour to vaccine safety issues of potential global importance.

The Committee provides independent, authoritative, scientific advice to WHO on vaccine safety issues of global or regional concern with the potential to affect in the short or long term national immunization programmes.

GACVS_ToRs.pdf
pdf, 51kb

– Topics

Contact us
Essential Medic
World Health Or
20 avenue Appia
1211 Geneva 27
Switzerland
E-mail: gvsi@wh

GACVS areas

Members

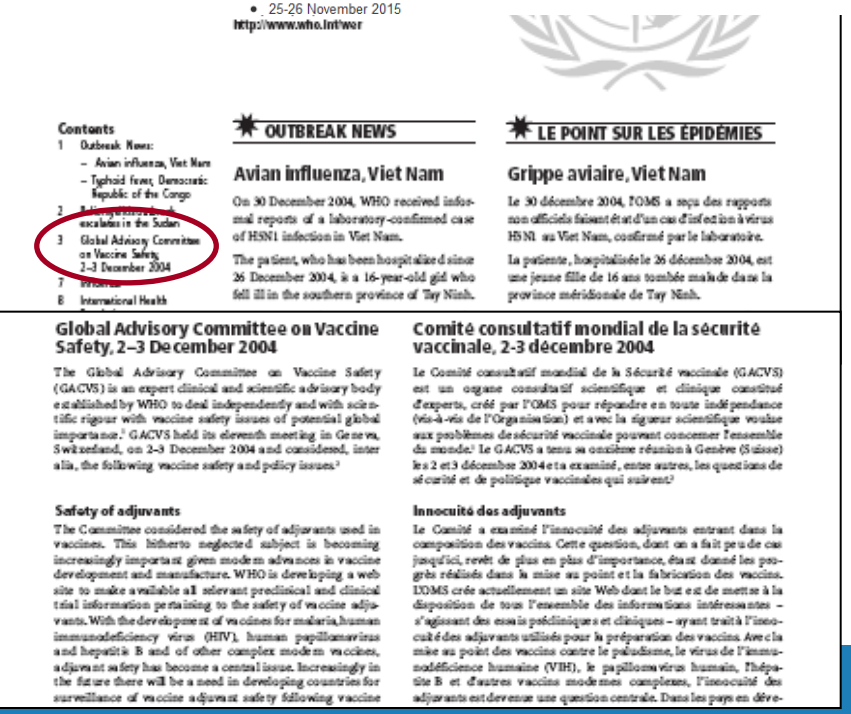
Working mechanisms

Next meetings

The next meetings of the Committee will be held on:

- 11-12 June 2014
- 26-27 November 2014
- 10-11 June 2015
- 25-26 November 2015

http://www.who.int/wer


Contents

1 Outbreak News:
– Avian influenza, Viet Nam
– Typhoid fever, Democratic Republic of the Congo
2 [illegible] escalation in the Sudan
3 Global Advisory Committee on Vaccine Safety, 2–3 December 2004
7 [illegible]
8 International Health

OUTBREAK NEWS

Avian influenza, Viet Nam

On 30 December 2004, WHO received informal reports of a laboratory-confirmed case of H5N1 infection in Viet Nam.

The patient, who has been hospitalized since 26 December 2004, is a 16-year-old girl who fell ill in the southern province of Tay Ninh.

LE POINT SUR LES ÉPIDÉMIES

Grippe aviaire, Viet Nam

Le 30 décembre 2004, l'OMS a reçu des rapports non officiels faisant état d'un cas d'infection à virus H5N1 au Viet Nam, confirmé par le laboratoire.

La patiente, hospitalisée le 26 décembre 2004, est une jeune fille de 16 ans tombée malade dans la province méridionale de Tay Ninh.

Global Advisory Committee on Vaccine Safety, 2–3 December 2004

The Global Advisory Committee on Vaccine Safety (GACVS) is an expert clinical and scientific advisory body established by WHO to deal independently and with scientific rigour with vaccine safety issues of potential global importance.[1] GACVS held its eleventh meeting in Geneva, Switzerland, on 2–3 December 2004 and considered, inter alia, the following vaccine safety and policy issues.[2]

Safety of adjuvants

The Committee considered the safety of adjuvants used in vaccines. This hitherto neglected subject is becoming increasingly important given modern advances in vaccine development and manufacture. WHO is developing a web site to make available all relevant preclinical and clinical trial information pertaining to the safety of vaccine adjuvants. With the development of vaccines for malaria, human immunodeficiency virus (HIV), human papillomavirus and hepatitis B and of other complex modern vaccines, adjuvant safety has become a central issue. Increasingly in the future there will be a need in developing countries for surveillance of vaccine adjuvant safety following vaccine

Comité consultatif mondial de la sécurité vaccinale, 2-3 décembre 2004

Le Comité consultatif mondial de la Sécurité vaccinale (GACVS) est un organe consultatif scientifique et clinique constitué d'experts, créé par l'OMS pour répondre en toute indépendance (vis-à-vis de l'Organisation) et avec la rigueur scientifique voulue aux problèmes de sécurité vaccinale pouvant concerner l'ensemble du monde.[1] Le GACVS a tenu sa onzième réunion à Genève (Suisse) les 2 et 3 décembre 2004 et a examiné, entre autres, les questions de sécurité et de politique vaccinales qui suivent:[2]

Innocuité des adjuvants

Le Comité a examiné l'innocuité des adjuvants entrant dans la composition des vaccins. Cette question, dont on a fait peu de cas jusqu'ici, revêt de plus en plus d'importance, étant donné les progrès réalisés dans la mise au point et la fabrication des vaccins. L'OMS crée actuellement un site Web dont le but est de mettre à la disposition de tous l'ensemble des informations intéressantes – s'agissant des essais précliniques et cliniques – ayant trait à l'innocuité des adjuvants utilisés pour la préparation des vaccins. Avec la mise au point des vaccins contre le paludisme, le virus de l'immunodéficience humaine (VIH), le papillomavirus humain, l'hépatite B et d'autres vaccins modernes complexes, l'innocuité des adjuvants est devenue une question centrale. Dans les pays en déve-

- Advisory body to WHO
- Response to vaccine safety issues of potential global importance
- Broad expertise & Independence
- Decisions and recommendations based on best available evidence
- Issues discussed include: reviews of safety profile/issues, alegations of global dimension, safety of new vaccines/vaccines under development, proactive review of safety of non active ingredients
- http://www.who.int/vaccine_safety/committee/en/

Folb et al .A global perspective on vaccine safety and public health : the Global Advisory committee on Vaccine Safety. American Journal of Public Health 2004;94: 1926-31.

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Vaccine Safety Net

- **GACVS endorsed criteria for evaluating websites**
  - **Credibility (essential criteria)**
  - **Content (important criteria)**
  - **Accessibility (practical criteria)**
  - **Design (desired criteria)**
- **Web sites evaluations**
- **Sites meeting credibility and content criteria listed with brief description** (over 38 sites as of 9 May 2014 – Dutch, English, French, German, Hungarian, Italian, Polish, Spanish, Swedish)
- **Networking**

Immunization safety

WHO > Programmes and projects > Immunization safety > Vaccine safety and quality

printable version

Vaccine Safety Net

Websites providing information on vaccine safety which adhere to good information practices

The World Wide Web is a mine of useful information on various topics, but also contains websites of dubious quality. While many quality web sites offer science-based information about vaccine safety, other sites provide unbalanced and misleading information. This can lead to undue fears, particularly among parents and patients.

:: WHO Note for the media - May 2005 (English)

:: WHO Note for the media - May 2005 (French)

To assist readers in identifying web sites providing information on vaccine safety that comply with good information practices, the Global Advisory Committee on Vaccine Safety has recommended a list of criteria that sites providing information on vaccine safety should adhere to.

D. Pfeifer

The recommended criteria fall into four categories:

- Essential criteria i.e. with respect to credibility
- Important criteria i.e. with respect to content
- Practical criteria i.e. with respect to accessibility
- Desired criteria i.e with respect to design

WHO has reviewed a number of sites for adherence to the credibility and content criteria noted above.

Asociación Española de Pediatría (AEP). Portal de Vacunas. Vacunas - sí!

:: http://www.vacunasaep.org

Language: Spanish

Audience: Spanish-speaking health-care professionals, parents, interested members of the public the media

This is the official site of the Spanish Association of Paediatrics Advisory Committee on Vaccines (ACV), which consists of a panel of immunization and vaccine-preventable disease experts.

Information on the site, which has full free access, is structured by target group (health-care professionals, the general public and the media). There are sections on immunization schedules, vaccine-preventable diseases and vaccine safety. Parents can activate personal calendar alerts fo their children. Both the public and professionals can interact with the ACV through an interactive question and answer section. The site provides links to original sources wherever possible.

The AEP, founded in 1949, is the largest paediatric organization in Spain, with more than nine thousand paediatricians and paediatric surgeons.

The site is systematically updated on a monthly basis. The news area is updated as and when required.

Date of primary evaluation: March 2009

www.who.int/vaccine_safety/initiative/communication/network/approved_vaccine_safety_website/en/

Immunization safety: What is needed?

- Exclusive use of vaccine of ensured quality
- Prevent reuse of needles/syringes (AD syringes)
- Proper disposal of immunization waste
- Appropriate waste management

YOUR ADVOCACY

- Training of staff and monitoring
- Effective AEFI monitoring and management (background rates)
- Appropriate handling of safety issues and rumours
- GACVS = independent process to review safety issues
- Global collaboration

Additional web resources resources

- http://www.who.int/vaccine_safety/en/
- www.healthcarewaste.org/en/115_o/verview.html
- WHO Protecting health workers – preventing needle stick injuries tool kit www.who.int/occupational_health/activities/pnitoolkit/en/
- www.who.int/injection_safety/en/index.html
- www.who.int/patientsafety/en/
- www.who-umc.org/
- www.cioms.ch/

With thanks to WHO colleagues and particularly to Selma Khamassi, Denis Maire, and Sophie Boisson