What Did We Learn from the A/H1N1 Influenza Pandemic? The Swiss Experience

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What's been going on?
What did we plan to monitor?

- **A/H1N1 vaccines**
  - Online through Paniflow®, entries by HCP and MAH
- **Seasonal influenza vaccines**
  - Yellow forms processed by regional PV centres
- **Drugs used for treatment of influenza**
  - Neuraminidase inhibitors through yellow forms
  - Exposures in pregnancy monitored by Swiss Teratogen Information Service STIS (affiliated to regional PV centre)
  - Regular safety updates by MAH
What were we looking for?

A/H1N1 vaccines – reporting criteria (Switzerland):
- All serious or unexpected ADRs occurring within eight weeks of vaccination and necessitating a medical consultation and not otherwise explained
- Focus on: hypersensitivity reactions, autoimmune disease (or aggravation if preexisting), severe neurological symptoms, Guillain-Barré syndrome (GBS), fever > 39° C, severe local reactions (i.e. swelling extending over two joints or lasting > 6 days)

Neuraminidase inhibitors etc:
- All serious or unexpected ADRs especially in populations previously not or only seldom exposed (children, pregnant women)
- Lack of efficacy/potential drug resistance
Health Authorities in Switzerland

Responsibilities

• **Policy**: Federal Office of Public Health (FOPH)
• **Licensing and postmarketing surveillance**: Swissmedic
• **Immunization campaign**: coordinated by FOPH but carried out by cantonal authorities (n=26!)

→ bringing (and keeping!) everyone on board turned out to be…. 
...a major challenge
How did we plan to get organized?

- Direct data entry by primary reporters (HCP only, no consumer reporting) and the two MAHs involved; misdirected reports entered into Paniflow by regional PV centres
- Single case evaluation by hired CRO on a daily basis
- Exchange of daily line listings and teleconference CRO-PV Swissmedic
- Daily line listings to companies (own product only)
- Signal evaluation by PV Swissmedic
How did we plan to get organized?

• Daily communication to the public on Swissmedic (pandemic) website
  • Number of registered ADRs
  • Safety profile
  • Comments
• Long term evaluation of ADRs in pregnancy in collaboration with STIS
Goals and Worries

Our goal:

- To collect rapidly enough data to assess/verify the safety profile of the pandemic vaccines/drugs on a daily basis, in order to be able to take rapid risk-minimizing action as needed

Our worries:

- Safety issues such as hypersensitivity reactions, autoimmune disease, Guillain-Barré syndrome, other neurological ADRs, severe local reactions etc (adjuvant!) or lack of efficacy
- Insufficient reporting compliance
- Communication issues/failures
Challenges

• Electronic reporting with Paniflow ® had to go live without pilot phase

• Logistic plans changed from immunization in centres to immunization in GP rooms (→ repackaging)

• From „immunization for all“ to „populations at risk, health care and child care workers first“

• Dissatisfied public (and media!)
Start

Immunization campaign started November 6th 2009

- Paniflow® ready and online
- HCP informed
- Hotline and website up and running

and the first AEFI reports by HCP and companies were promptly entered in Paniflow®
Troubleshooting

• Bug in data evaluation tool
  • First evaluations done manually
• Primary reporters not to keen on precoded AEFI
  • AEFI reported as freetext thus needing more time for coding than planned
• Communication much more onerous than foreseen
  • Extra support needed
  • Schedule of public reports changed from daily to twice/week, then weekly
PaniFlow®

Welcome to PaniFlow!

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Als neuen Benutzer registrieren
Enregistrer un nouvel utilisateur

https://tools.who-umc.org/paniflow/
PaniFlow®

### Adverse event

Please select (with the “+”-symbol) all reactions that apply in section a) to c) and/or add other severe adverse events as free text in section d) below. By pointing on a ? details about the listed adverse event are shown. Any details, further explanations, and results (like lab values) should be added in the box in section d).

<table>
<thead>
<tr>
<th>Date of first reaction</th>
<th>Interval between last administration of vaccine and onset</th>
<th>Duration</th>
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<tbody>
<tr>
<td>(dd mm yyyy)</td>
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#### a) Application site and general disorders

- Adenopathy
- High fever (>39 degrees C)
- Severe skin reaction: Stevens Johnson
- Severe skin reaction: Lyell syndrome
- Uricaria
- Erythema
- Angio oedema / face swelling
- Dyspnea
- Larynx oedema
- Bronchospasm
- Anaphylaxis with hypotension / shock
- Arthritis, joint swelling: new onset
- Arthritis, joint swelling: exacerbation
- Vasculitis
- Seroitis
- Serum sickness syndrome
- Oculo-respiratory syndrome
- Other allergic reaction

#### b) Hypersensitivity reactions (allergy)

- Convulsion, with fever
- Guillain-Barre Syndrome or related syndromes
- Parasis, including Bell’s palsy
- Neuropathy
- Encephalitis / Encephalopathy
- Meningitis
- Multiple sclerosis: new diagnosis
- Optic neuritis: new onset
- Optic neuritis: exacerbation

#### c) Nervous system disorders

- Diabetes: new onset
- Diabetes: exacerbation

Describe reactions / add details

Information about symptoms, other details and explanations, histology and lab values
Safety issues

• Death following immunization: 18 reports, unlikely
• Fetal loss: 10 reports, 6 unlikely, 4 not assessable
• GBS: 4 reports, 2 possibly related
• Herpes zoster: 13 reports, possibly related
• MS: 5 reports, 4 unlikely
• Severe allergic reactions IT: (grade III 15, grade IV 5)
• Severe skin reactions: 3 reports (erythema multiforme, vasculitis, exfoliation), possibly related

• For the public:
  • Severe local reactions, myalgia
Communication

„Words are, of course, the most powerful drug used by mankind“

R. Kipling
Communication issues

- Reports to be published simultaneously in four languages
- Coordination with FOPH
- Division of responsibilities between different health care authorities not clear to the public
- Three different hotlines running (campaign, reporting, medical aspects of AEFIs)
- Causality: AEFIs reported automatically assumed by public to be also causally related
Harvest

- 557 AEFI reports with 1566 reactions entered in Paniflow between November 6th 2009 and March 31st 2010 (usual reporting of AEFI: 250 reports/yr on ALL vaccines)
- Safety profile of the vaccines under surveillance +/- confirmed
- Nine safety reports published in four languages
- Final report reviewed by Vaccines Safety Experts Committee published end of July 2010
- Many complaints (HCP/public/media) about immunization campaign but none on the safety surveillance performed
International activities

• WHO NC Meeting 2007: joint presentation on Paniflow® (H5N1 scenario) by Swissmedic (R. Stoller) and WHO-IVB (D. Pfeifer)
• ICDRA 2008: real time PV for hypothetical H5N1 pandemic discussed (presentation Paniflow®)
• No communication on common/coordinated PV activities until October 2009 (UMC asks Swissmedic for access to Paniflow®, UMC Website set up right after NC Meeting)
• From November 2009 on regular teleconferences on safety of H1N1 vaccines for DRAs organized by WHO-IVB (confidential information)
• Initiatives at national/regional level (national PV Centres, regular reports by EMA)
Lessons learned

- Coordination issues between different players in public health and their communication needs to be worked on
- Leadership in international collaboration on safety surveillance is needed
- Data entry/evaluation at one focal point within the PV network worldwide facilitates international coordination
- More generous data release to the public
More lessons learned

• Direct electronic reporting was well received by HCP → consider for everyday life

• HCPs like to tell a story → allow enough space for freetext in reporting tool

• Proactive, regular, updated information on safety was appreciated by all stakeholders
...and last but not least

• Trust and credibility are precious items
Thank you for your attention