

2015

POSITION STATEMENT

Safer design of vaccines packaging and labelling



POSITION STATEMENT

The International Medication Safety Network recommends the following steps as part of a comprehensive, worldwide solution to the problem of unsafe design of vaccines packaging and labelling.

1. Labelling of vaccines should: use larger fonts for better readability; adopt the WHO VPPAG expiration dates standard (MM-YYYY, meaning that the product expires at the end of the month); provide peel-off labels; and clearly differentiate pediatric and adult formulations.
2. Packaging of vaccines should minimize the need to prepare individual doses: provide unit dose according to the mode of administration (e.g., prefilled syringes for parenteral); if still used, redesign the vaccines packaged in vials to accommodate larger labels.
3. A particular attention should be paid to the packaging and the labelling of vaccines provided with diluents or of two component vaccines:
 - a. Packaging that forces proper mixing of the diluent intended to be used with the vaccine or of the two components of the vaccine should be preferred (i.e. dual chambered vial); if not feasible, the two vials of vaccine and diluent or of the two-component vaccine should be packaged together without prejudice of storage requirements.
 - b. All labels of vaccine products that require reconstitution prior to administration should provide clear instructions for mixing vaccine components. The directions for use and a warning to administer the contents of both vials together should be displayed on the front label of the carton, each vial and on the cap of the vial. A visual warning should appear on any diluent provided indicating that it is only a diluent, not the actual product. The Global Trade Item Number (GTIN) or national code numbers and barcodes should appear on each vaccine component and diluent.
4. Healthcare authorities and medicine regulators should promote safer labelling and packaging of vaccines and make available recommendations to healthcare providers for safer vaccination practices.

Manufacturers of vaccine products are strongly encouraged to revise the packaging and labelling of vaccine products as specified, with particular attention on vaccines and diluents or two-component vaccines. An international summit on vaccine safety should be held to discuss the feasibility of the IMSN recommendations.

BACKGROUND

Immunization is widely recognized as one of the most effective public health intervention ever introduced worldwide. According to the World Health Organization (WHO), immunization avoids between 2 and 3 million deaths per year from vaccine preventable diseases⁽¹⁾. However, errors with vaccines can result in an unintended and unrecognized source of vulnerability. While the immediate impact of a vaccine-related error on a patient may not be serious, errors such as an unsafe storage may render the vaccine ineffective or reduce its effectiveness, leaving patients unprotected against serious diseases.

The evidence of vaccination errors, specific medication errors related to the use of vaccines, is well established by national reporting programmes such as: the US Vaccine Adverse Event Reporting System (VAERS)⁽²⁻⁵⁾, jointly administered by the Centers for Disease Control and Prevention (CDC) and the US Food and Drug Administration (FDA); the ISMP National Vaccine Errors Reporting Program (ISMP VERP)^(6,7), in partnership with the California Department of Public Health; the Institute for Safe Medication Practices Canada (ISMP Canada)⁽⁸⁾; the UK Health Protection Agency (HPA)⁽⁹⁾; the England and Wales National Reporting and Learning System (NRLS)^(10,11). Most of these incidents are identified in countries with reporting programmes, but such errors can be expected in all countries.

If these various assessments were not sufficient to demonstrate the persistence of vaccine-related errors, the deaths in September, 2014 of 15 Syrian children among 75 vaccinated from a measles vaccine possibly reconstituted with atracurium instead of the diluent remind us that vaccine diluent mix-ups can be tragic, having a devastating effect on immunization and public health efforts⁽¹²⁾. The Institute for Safe Medication Practices (ISMP) have collated several similar incidents involving accidental reconstitution of vaccine with neuromuscular blockers that have previously been reported: in the United States of America (at least one death among several harmed patients); in Taiwan (a permanent injury and one death among 7 infants developing respiratory distress); in Mexico (one death among 14 patients presenting hypotonia, cyanosis, and dyspnea); in Kenya (6 infants exposed); in Lesotho (one death among 5 neonates)⁽¹³⁾. Similar mix-ups between vaccines or diluents and insulin have led to the deaths of 21 children in 1997 and continue to occur ^(1,14,15).

During its annual meeting held in Singapore on 20-21 October 2014, the International Medication Safety Network (IMSN) convened a workshop on vaccine errors, focusing on safer design of labelling and packaging of vaccines.

Vaccine related errors may occur at all stages of the medication use process: prescribing, dispensing, preparing, administering, follow-up and planning with a particular emphasis to scheduling and documenting the patient held record (PHR):

- ❖ Wrong patient, especially sibling confusion
- ❖ Wrong time: omissions, too early, delay, extra dose
- ❖ Wrong vaccine: incorrect vaccine administration
- ❖ Wrong preparation: wrong diluent, component omitted in a multicomponent vaccine
- ❖ Wrong dose: incorrect dose (under dose, overdose), extra dose
- ❖ Wrong dosage form
- ❖ Wrong storage: expired vaccine, thermally damaged or deteriorated vaccine
- ❖ Wrong administration technique
- ❖ Wrong route of administration

Many causes of errors and contributing factors are increasing in the context of an increasing number of vaccines, more complex vaccines (combinations of multiple components and valences), ever changing vaccination recommendations and schedules, and vaccine shortages that disrupt immunization plans:

- ❖ Confusion due to unclear brand names; similar names; unclear or similar abbreviations
- ❖ Confusion due to similar and ambiguous packaging: insufficient differentiation among products from one manufacturer, lack of consistency of packaging
- ❖ Confusion due to similar and ambiguous labelling: illegible labels due to small font and label sizes; on curved items such as vials or ampoules, full pieces of information cannot be seen in one view; use of difficult to see colors for text; use of multi-language on packaging; information placement; multidose not stating the number of doses available nor the volume per dose
- ❖ Confusion between multi-dose and single dose vaccines
- ❖ Age-related contributing factors: age-dependent formulations of the same vaccine; confusion between pediatric and adult formulations; unfamiliarity with dosing and timing of vaccines based on the patient's age; failure to verify the patient's age prior to administration
- ❖ Combined or multicomponent vaccines: lack of identification and use of the appropriate diluent; misunderstanding of the reconstitution of a vial with a prefilled syringe; giving just one component instead of the intended combination vaccine; use of an unintended diluent instead of the specific diluent
- ❖ Complex vaccination schedules and frequently changing vaccination recommendations
- ❖ Vaccine shortages leading to the use of different combined vaccines than intended and modification of the vaccination schedules
- ❖ Storage conditions: temperature lower or higher than recommended; products stored near each other (not only vaccines, but also neuromuscular blocking agents, insulin, etc.); unclear expression of expiry date; water damage (from freeze packs) degrading labels
- ❖ Overcrowded leaflets: hidden information related to the validity of reconstituted vaccines

Safer packaging and labelling of vaccines

Immunization experts, pharmaceutical companies, technology vendors, professional organizations, and regulatory/standard-setting organizations, can help improve vaccine safety and efficacy by taking actions to vastly reduce the risk of vaccine-related errors.

Globally, several WHO recommendations already exist, addressing in particular:

- ❖ Reporting and learning from adverse events following immunizations (AEFI) under the guidance of the WHO Global Advisory Committee on Vaccine Safety (GACVS): the AEFI surveillance system encompasses reporting, investigation, causality assessment and classification of cause-specific AEFI, including immunization error-related reactions defined as AEFI that are caused by inappropriate vaccine handling, prescribing or administration and thus, by their nature, are preventable^(1,16);
- ❖ Presentation and packaging of new vaccines for use by public-sector programmes in developing countries, recommendations for vaccine producers and developers generated by the WHO Vaccine Presentation and Packaging Advisory Group (VPPAG)⁽¹⁷⁾.

Taking into account these global recommendations, IMSN welcome some progress in vaccine safety but wishes to go further in order to foster safer design of vaccines packaging and labelling. IMSN prepared recommendations on the basis of the work previously done by members, especially the ISMP⁽¹⁸⁾. The following IMSN recommendations were submitted for discussion and adopted during its meeting held in Cartagena on 30 September - 1 October 2015.

IMSN Recommendations for the packaging and labelling of vaccines

The International Medication Safety Network recommends the following steps as part of a comprehensive, worldwide solution to the problem of unsafe design of vaccines packaging and labelling:

- a. Package vaccines in unit dose, prefilled syringes appropriate to the mode of administration (e.g., needleless parenteral vs. oral) to minimize the need to prepare individual doses.
 - Redesign the vaccine package in vials that will accommodate larger labels to reduce label crowding and allow larger fonts.
 - Whenever feasible, consider packaging that forces proper mixing of a diluent or two component vaccines (i.e. dual chambered vial or syringe).
 - Storage requirements should not hinder packaging together the 2 vials of vaccines and diluents or two-component vaccines in a way that facilitates selection of both vials at the same time but allows separation if necessary to prepare the vaccine for administration.
- b. Improve the labelling of vaccines by:
 - displaying expiration dates in a standard, straight-forward way that can be understood by all, i.e MM-YYYY meaning that the product expires at the end of the month.
 - clearly differentiating pediatric and adult formulations.
 - using larger fonts to make labels more readable, considering a minimum 12 fontsize.
 - making peel-off labels available to promote immediate labelling of prepared syringes and accurate documentation of administration.
 - providing clear instructions for mixing vaccine components on all labels of vaccine products that require reconstitution prior to administration: directions for use and warnings to administer the contents of both vials together on the front carton label and vials—eventually on the vial caps.
The diluent, if provided, should include a bold statement indicating that it is only a diluent, not the actual product.
 - providing unique Global Trade Item Number (GTIN) or national code numbers and barcodes on each vaccine component and diluent.
- c. Conduct usability testing with vaccine users to test labels, packages and preparation process for safety, convenience, clarity and effectiveness.

International Medication Safety Network

The International Medication Safety Network (IMSN) is an international network of safe medication practice centers established with the aim of improving patient safety. This is achieved by operating medication error reporting programmes and producing guidance to minimize preventable harms from medicine use in practice. IMSN promotes safer medication practice to improve patient safety internationally.

For more information

www.intmedsafe.net/contents/AboutIMSN.aspx

References

1. World Health Organization "Global manual on surveillance of adverse events following immunization" 2014; 128 pages.
2. Varrichio F "Medication errors reported to the vaccine adverse event reporting system (VAERS)" *Vaccine* 2002 ; **20** (25-26) : 3049-3051.
3. Varrichio F et Reed J "Follow-up study of medication errors reported to the vaccine adverse event reporting system (VAERS)" *South Med J* 2006 ; **99** (5) : 486-489.
4. Chang S et coll. "Preventable mix-ups of tuberculin and vaccines: reports to the US Vaccine and Drug Safety Reporting Systems" *Drug Saf* 2008 ; **31** (11) : 1027-1033.
5. Hibbs BF et coll. "Vaccination errors reported to the Vaccine Adverse Event Reporting System, (VAERS) United States, 2000-2013" *Vaccine* 2015 ; **33** (28) : 3171-3178.
6. Institute for Safe Medication Practices (ISMP) "First annual review of data submitted to the ISMP National Vaccine Errors Reporting Program (VERP)" *ISMP Medication Safety Alert! Acute Care* 2013; **18** (24): 1-5.
7. Institute for Safe Medication Practices (ISMP) "Confusion abounds! 2-year summary of the ISMP National Vaccine Errors Reporting Program (Part I)" *ISMP Medication Safety Alert! Acute Care* 2014; **19** (24): 1-6.
8. Institute for Safe Medication Practices Canada (ISMP Canada) "Administration of Product-Specific Diluent without Medication" *ISMP Canada Safety Bulletin* 2010; **10** (7): 1-3.
9. Craig L et coll. "Pragmatic management of programmatic vaccination errors--lessons learnt from incidents in London" *Vaccine* 2010 ; **29** (1) : 65-69.
10. Rees P et coll. "Safety incidents in the primary care office setting" *Pediatrics* 2015; **135** (6) : 1027-1035.
11. Rees P et coll. "Pediatric immunization-related safety incidents in primary care: A mixed methods analysis of a national database" *Vaccine* 2015; **33** (32) : 3873-3880.
12. Cousins S "Contaminated vaccine deaths a serious setback for Syria" *Lancet* 2014 ; **384** (9949) : 1172.
13. Institute for Safe Medication Practices (ISMP) "Tragic vaccine diluent mix-ups in Syria have also happened here." *ISMP Medication Safety Alert! Acute Care* 2014; **19** (19): 1-3.
14. Institute for Safe Medication Practices (ISMP) "What else is stored in a refrigerator with influenza vaccine?" *ISMP Medication Safety Alert! Acute Care* 2014; **19** (24): 1.
15. Shanks L et coll. "Learning without Borders: A Review of the Implementation of Medical Error Reporting in Medecins Sans Frontieres" *PLoS One* 2015; 10 (9): e0137158.
16. World Health Organization "Causality assessment of adverse event following immunization (AEFI): user manual for the revised WHO classification." WHO/HIS/EMP/QSS. March 2013; 56 pages.
17. WHO Vaccine Presentation and Packaging Advisory Group (VPPAG) "Generic Preferred Product Profile for Vaccines. Version 2.1 Recommendations" 31 March 2015; 31 pages.
18. Institute for Safe Medication Practices (ISMP) "Recommendations for practitioners and manufacturers to address system-based causes of vaccine errors" *ISMP Medication Safety Alert! Acute Care* 2014; **19** (5): 1-5.