

Using human factors and FMEA methods to evaluate labelling of injectables drugs

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The authors gratefully acknowledge the financial support of the Canadian Patient Safety Institute for this project.

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Main Messages

Poor labelling of injectable medications can be a contributing factor to medication errors leading to adverse drug events. We sought to address some of the issues with the labelling of ampoules and vials. The first phase of the project involved comparing a sample of existing labels on drug ampoules and vials with the 1999 Canadian Standards Association standard (CAN/CSA-Z264.2-99) and with the relevant Canadian Food and Drug Regulations (C.R.C., c.870). The adherence rate to the 23 mandatory requirements in the CSA Standard was 59%. The average proportion of the inner labels for ampoules and vials that did not adhere to one or more of the requirements in the Canadian Food and Drug Regulations was 35%, but a large portion of the non-adherence resulted from not including both the English and French versions of the word sterile and for not including the manufacturer address on the label. However, 1 % of the samples did not display the common name properly and 2% of the samples did not display the route(s) of administration. The second phase of the project involved conducting a Failure Mode and Effects Analysis (FMEA) with 7 healthcare professionals with previous experience with FMEA in order to identify the critical information needed on an ampoule or vial for safe medication use. Failure modes related to reading brand name, common name, concentration, total amount of drug ingredient(s) per total volume and route(s) of administration were rated with higher than the average criticality in the FMEA. The third phase of the project involved conducting a human factors experiment with a group of 24 nurses. This experiment demonstrated the superiority of black lettering on a white background over printing directly on ampoules. The findings in this report have implications for those involved in designing drug labels and for those involved in providing recommendations for the design of drug labels (i.e. Health Canada, the CSA, and ISMP Canada).

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Executive Summary

Poor labelling of injectable medications can be a contributing factor to medication errors leading to adverse drug events. We sought to address some of the issues with the labelling of ampoules and vials. The first phase of the project involved comparing a sample of existing labels on drug ampoules and vials with the 1999 Canadian Standards Association International standard (CAN/CSA-Z264.2-99) and with the relevant Canadian (Health Canada) Food and Drug Regulations (C.R.C., c.870). The adherence rate to the 23 mandatory requirements in the CSA Standard was 59%. The average proportion of the inner labels for ampoules and vials that did not adhere to one or more of the requirements in the Canadian Food and Drug Regulations was 35% but a large portion of the non-adherence resulted from not including both the English and French versions of the word sterile and for not including the manufacturer address on the label. However, 1 % of the samples did not display the common name properly and 2% of the samples did not display the route(s) of administration. In the cases of improperly displayed common name, it appears that there was preferential emphasis placed on the manufacturer's branding.

The second phase of the project involved conducting a Failure Mode and Effects Analysis (FMEA) with 7 healthcare professionals with previous experience with FMEA in order to identify the critical information needed on an ampoule or vial for safe medication use. Failure modes related to reading brand name, common name, concentration, total amount of drug ingredient(s) per total volume and route(s) of administration were rated with higher than the average criticality in the FMEA. The third phase of the project involved conducting a human factors experiment with a group of 24 nurses. This experiment demonstrated the superiority of black lettering on a white background over printing directly on ampoules (or on a clear substrate that is adhered to ampoules). The findings in this report have implications for those involved in

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designing drug labels and for those involved in providing recommendations for the design of drug labels (i.e. Health Canada, the Canadian Standards Association, and ISMP Canada).

The following diagram makes it clear why, in our experiment with 24 nurses, we found that the newly designed labels were read more quickly than the existing labels in current use.

Participants were given as much time as they liked to read the labels in a quiet room with no distractions. The improved performance with the new labels would likely be more exaggerated in a stressful workplace environment.



Existing labels (3 left) and the new labels (3 right).

Based on the results of this three-phased study, several suggestions are made regarding the improvement of guidelines, standards and recommendations related to drug labelling:

1. When the CSA standard and the government regulations are under review, consider
 - performing user testing regarding the interpretation of the guideline or regulations;

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- including an explanation (evidence) of the rationale for particular recommendations or requirements;
 - examining the failure modes (or errors) related to the brand name, common name, concentration, total amount of drug ingredient(s) and route of administration;
 - evaluating the necessity of the information required in regulations, such as “address of manufacturer,” which takes valuable space on the label.
2. Study the feasibility of using larger-sized ampoules and vials for small volumes to increase surface area for label information.
 3. Prohibit the use of printing directly on glass or a clear substrate in the labelling of ampoules or vials containing medications.

The following are recommended reading:

Cohen, M.R. (Ed.). 2007. *Medication Errors, 2nd Edition*. Washington, D.C.: American Pharmacists Association.

Institute of Medicine of the National Academies. 2007. *Preventing Medication Errors*, Quality Chasm Series. Washington, DC: The National Academies Press.

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Context

Since the US Institute of Medicine report "To Err is Human"¹ and the subsequent IOM report 'Crossing the Quality Chasm'², there has been a greater public awareness of medication errors and their effect on patients. Adverse drug events, including in-hospital medication errors, are a well-documented worldwide problem.^{3,4,5,6,7,8,9,10} Poor labelling of injectable medications can be a contributing factor to medication errors leading to adverse drug events. In his comprehensive review, Cohen¹¹ discusses many of the issues and possible solutions to the design of drug labels.

In a survey of 687 Canadian anaesthesiologists, Orser, Chen and Yee¹² reported that misidentification of the label accounted for 46.8% of medication errors. Eighty-four percent of the anaesthesiologists agreed that improved standards for drug labels would reduce the incidence of error. In an analysis of medication errors reported to the United States Pharmacopoeia (USP) voluntary Medication Errors Reporting Program (MER), for a 1-year period between 1996 and 1997¹³, the USP found that 33% of the reports cited labelling or packaging as having contributed to the medication error. In nearly 30% of the fatalities reported, labelling or packaging was cited as a contributing factor to the medication error that led to the fatality. The following is a list cited in the USP report:

1. Lack of prominent placement of drug name and strength.
2. Small size and poor readability of printed information.
3. Insufficient prominence given to route of administration (e.g., nasal vs injection, intravenous vs. intramuscular).
4. Poorly designed or cluttered labels.
5. Lack of differentiation between drug products that have similar names.

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6. Similar-appearing labels or packages of different products.
7. Poor use or absence of color to differentiate products.
8. Prominence of company logos versus information that identifies the product.
9. Inadequate warnings about proper drug use.

In Berman's 2004 review ¹⁴ of efforts that have been made to date to reduce medication errors through naming, labelling and packaging, he points out that what used to work (the Identicode System first introduced by Eli Lilly in 1965 and mandated by the FDA in 1993), no longer works well with the current proliferation of manufacturers, medications, formulations, and doses.

Jensen et al. (2004) ¹⁵ performed a systematic review of strategies for preventing drug administration errors during anaesthesia. Based on the evidence (mainly from case reports and expert opinion), the following are strong recommendations from the authors:

- (1) The label on any drug ampoule or syringe should be carefully read before a drug is drawn up or injected.
- (2) Legibility and contents of labels on ampoules and syringes should be optimised according to agreed standards in respect of some or all of font, size, colour and the information included (NB: there may be some disagreement on the detail of how this should be achieved).
- (3) Syringes should be labelled (always or almost always).
- (4) Formal organisation of drug drawers, and workspace should be used with attention to: tidiness; position of ampoules and syringes; separation of similar or dangerous drugs; removal of dangerous drugs from the operating theatres.

Medication label design is an example of an area where the consideration of human factors principles is critical ¹⁶ and medication label design was the focus of this project.

Three questions regarding labelling of injectable drugs are addressed in this report:

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1. Do the ampoules and vials currently being used in Canadian healthcare facilities meet current standards and recommendations that exist for their design?
2. Is it possible to design a better label?
3. What contribution can human factors engineering methods contribute to help improve the standards and recommendations for the design of labels on ampoules and vials?

Other areas of concern regarding medication errors related to labelling of drugs where human factor methods have had and could continue to have an impact that were not addressed in this project include:

1. Look-alike / sound alike drugs.
2. Use of colour on drug labels.
3. Standardization of information content and location presented on inner labels versus that presented on outer labels.
4. Effectiveness of ambient lighting when preparing and administering drugs.
5. Effects of divided attention and distractions on the label-reading process.

Adherence of Existing Labels to the CSA standards and the Canadian Food and Drug Regulations

The original intent of this project was to compare existing labels on drug ampoules and vials with the 1999 Canadian Standards Association standard (CAN/CSA-Z264.2-99)¹⁷ for the labelling of drug ampoules, vials and pre-filled syringes. However, it was determined by the team that the value of the results of this project would be even greater if we were to compare the existing labels with the relevant Canadian (Health Canada) Food and Drug Regulations (C.R.C., c870)¹⁸ as well.

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The CSA standard focuses on ensuring the organization and the legibility of label content, especially for what it calls 'critical information': the drug product's common name(s) in English and French and the total amount of drug ingredient(s) as mg per total mL, followed by the concentration of drug ingredient(s) as mg per 1 mL. The standard's legibility section, which was adopted from NASA's Man-Systems Integration Standard¹⁹ defines typographical specifications for ensuring legibility of critical information. There is no legal requirement for pharmaceutical manufacturers to follow the CSA standard while there is a legal requirement for them to follow the Canadian Food and Drug Regulations. In addition, although some of the requirements set out in both the CSA standard and the NASA standard are based on previous research, there are many aspects of the CSA standard that are based on expert opinion. The objectives of the first phase in the current study were to answer the following two questions: (1) To what extent do the inner labels on ampoules and vials of injectable drugs currently being used in hospitals in Canada adhere to the CSA standard and (2) to what extent do they adhere to the Canadian Food and Drug Regulations?

Method

A total of 78 samples (21 ampoules and 57 vials), were randomly collected from a pharmacy inventory in a large urban teaching hospital. This represents 18% of the 116 different ampoules and 22% of the 265 different vials carried by the hospital. The evaluation was conducted from May 2006 to July 2006. The first two-thirds of the samples were collected from used, or expired, ampoules and vials returned to the pharmacy. The remaining third were randomly collected from all areas of inventory to ensure refrigerated items and narcotic products were included in the sample. The final sample is thought to be representative of the available ampoules and vials currently in a hospital formulary in Canada.

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Typographical dimensions (i.e. the stroke width, character height, character width, etc.) were measured on the inner labels of the containers. A transparent plastic ruler in millimetres and a magnifying glass were used to make the measurements. The measurements are considered accurate to 0.5 millimetres.

Results

The CSA standard clauses are divided into three categories; clauses worded with 'shall' are proposed as mandatory requirements, clauses worded with 'should' are recommendations, and clauses worded with 'may' are suggestions. There are 25 'shall' clauses, 8 'should' clauses and 2 'may' clauses relevant to labelling of ampoules and vials. For the purposes of this study, 23 'shall' clauses and 6 'should' clauses were considered.

None of the samples adhered to all of the 'shall' and 'should' clauses of the CSA standard. Table 1 summarizes the average adherence score for 'shall' clauses and 'should' clauses. The adherence score was calculated by determining the ratio of the number of clauses to which a sample adhered to the total number of clauses.

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Category	Total no. of clauses	Average no. of clauses the samples adhered to (N = 78)	Average adherence score
Shall	23	14	59%
Should	6	5	80%

Table 1. Summary of CSA standard adherence scores for the samples

For the CSA standard clauses that had a non-adherence rate of 50% or more, the following table lists the ‘shall’ and ‘should’ clauses, and suggests findings/possible reasons for non-adherence.

Clause	% non-adherence	Brief description (paraphrased from the CSA standard)	Findings/possible reasons for non-adherence
Shall			
4.2.2	100	Common name printed immediately below the brand name and be legible according to requirements of 4.4.	Not all legibility requirements are clearly defined.
4.2.3	55	After common name, include: (i) the amount of drug ingredient(s) as mg per total mL followed by (ii) the concentration of drug ingredient(s) as mg per 1 mL. In some instances, the convention may be to express the amount of drug(s) in milliequivalents,	Findings: 1. The amount of drug ingredient(s) per total mL was displayed AFTER the concentrate per 1 mL. 2. The amount of drug ingredient(s) per total mL was missing.

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		millimoles, or international units.	3. The amount of drug ingredient(s) not expressed in the recommended units. The reasons for the above are likely to be varied.
4.2.8	99	Expiration date on the label in format CCYYMM. Example: EXP. 1999DE.	A variety of different formats were used.
4.4.11	63	A mixed character set shall be used.	Capital letters were often solely used. This may be due to a lack of awareness that mixed characters can increase legibility.
4.4.2	60	For critical information, character height on ampoules/vials: > 2 mL: 1.76 mm or more 2 mL or less: 1.5 mm or more	A combination of a large amount of text and a limited amount of space for labelling on small containers may have dictated the use of smaller type.
4.4.3	50	For critical information, specified width of letters (0.6 of the height with some exceptions).	
4.4.6	96	The critical information field shall be represented in black characters on a white background.	Awareness of this recommendation may be limited.
4.4.7	97	For critical information, height-to-	1. The absence of a description

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		stroke ratio of 6:1 to 7:1.	<p>for what the height-to-stroke ratio expresses.</p> <p>2. Difficult to measure small type accurately.</p> <p>3. Designers may not think of type in this way.</p>
Should			
4.2.9	54	Storage conditions should be clearly identified on the label.	<p>The joint USP-FDA Advisory Panel on Simplification and Improvement of Injection Labeling recommended eliminating storage requirements from injection labels when the product is to be stored at room temperature in normal light (USP, 1994).</p>

Table 2: Items of the CSA standard that had a non-adherence rate of 50% or greater.

Three samples were determined to be special access drugs that are not available for sale in Canada and were excluded from the analysis for evaluating adherence to Canadian Food and Drug Regulations. All three drugs failed one or more requirements of the regulations. Table 3 lists the non-adherence rate for the remaining 75 samples.

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	Total No. of Samples (N = 75)	No. of samples that do not adhere to one or more of Canadian Food and Drug regulations	% Non-adherence
Ampoules	19	4	21
Vials	56	22	39
Total	75	26	35

Table 3: Percent non-adherence to Canadian Food and Drug regulations.

Failure Mode and Effects Analysis of the Label-reading Process

In order to investigate potential failures, causes and effects of the label-reading process, a failure mode and effects analysis (FMEA) was conducted with a group of seven healthcare professionals with previous FMEA training. ISMP Canada's FMEA framework was used as a basis for this study. The FMEA team consisted of a pharmacist, a nurse, a specialist in human factors engineering and a graduate student in human factors engineering. The FMEA procedure used for this study was as follows:

1. Define the process of interest.
2. Generate a flowchart of the process and their sub-processes.
3. Brainstorm for potential failure modes and their effects.
4. Identify causes of failure modes.
5. Rank each failure mode in terms of severity, frequency, and detectability.
6. Calculate Risk Priority Number (RPN) for each failure mode.

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7. Develop interventions to minimize the occurrences of the failure modes with high RPN values.

Frequency Rating	Frequency Description	Score
Remote	May happen some time in 3 to 5 years	1
Uncommon	May happen some time in 1 to 2 years	2
Occasional	May happen several times in a year	3
Frequent	May happen several times in a month	4
Very frequent	May happen several times in a day	5

Table 4. Frequency Rating Scale

For detectability, the 4-level scale of ISMP Canada's FMEA was adopted without modifications as shown in Table 5. Table 6 lists the 24 failure modes involved in the label-reading process identified by the FMEA.

Detectability Description	Score
Always	1
Likely	2
Unlikely	3
Never	4

Table 5. Detectability Rating Scale

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FM	Failure Mode Description	Potential Effect(s) of Failure	Potential Causes of Failure Mode
1	User cannot read the common name	Wrong drug error; Omission error	Unavailable information; Illegible typeface size and/or format; Information indicated at an unexpected location; Information covered by finger tips holding the container; Intagliated or silk-screened information
2	User does not read the common name.	Wrong drug error	Distractive colour and/or trade dress; Information lacks salience over other information; User under stress
3	User misperceives the brand name of a wrong drug as the common name of the correct drug.	Wrong drug error	Excessively salient brand name; Insufficient or no distinction from the look-alike/sound-alike brand name; Common name unavailable; User under stress
4	User misperceives a different common name as the correct common name.	Wrong drug error	Use of ambiguous acronyms; Insufficient or no distinction from other look-alike/sound-alike common names; Look-alike label design; User under stress; Container has to be rotated a lot to read the information
5	User does not read the brand name when the drug is available under different brand names.	Wrong drug error	User unaware of the need to read the information; User under stress
6	User cannot read the concentration or the total amount of the drug ingredient.	Wrong dose/quantity error; Omission error	Unavailable information; Illegible typeface format; Information indicated at an unexpected location; Information covered by finger tips holding the container

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7	User misperceives the concentration as the total amount of the drug ingredient or vice versa.	Wrong dose/quantity error	Only one of the two pieces of information available; Non-standard ordering of information; Lack of units; Non-standard units
8	User misperceives the values of the concentration/ total amount of the drug ingredient.	Wrong dose/quantity error	Location of the decimal point misperceived; Number of trailing zeros or zeros preceding a non-zero number miscounted; Non-standard units; Illegible typeface format; Intagliated or silk-screened information; Lack of units; User under stress; Container has to be rotated a lot to read the information
9	User does not read the route of administration.	Wrong route error	Distractive colour and/or trade dress; Information lacks salience over other information; ; User under stress
10	User cannot read the route of administration.	Wrong route error; Omission error	Illegible typeface size and/or format; Unavailable information; Information indicated at an unexpected location; Information covered by finger tips holding the container.
11	User cannot read the expiry date.	Expired product; Omission error	Unavailable information; Illegible typeface size and/or format; Information indicated at an unexpected location; Information covered by finger tips holding the container; Intagliated or silk-screened information
12	User misperceives the expiry date.	Expired product error;	Non-standard representation format; User under stress; Container has to be rotated a lot to read the information
13	User does not read the storage condition.	Deteriorated product error;	User under stress; Information lacks salience over other information
14	User cannot read the storage condition.	Deteriorated product error; Omission error	Unavailable information; Illegible typeface size and/or format; Information indicated at an unexpected location; Information covered by finger tips holding the container; Intagliated or silk-screened information

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15	User cannot read the multi-dose information.	Deteriorated product error; Omission error	Unavailable information; Illegible typeface size and/or format; Information indicated at an unexpected location; Information covered by finger tips holding the container; Intagliated or silk-screened information
16	User does not read the multi-dose information.	Deteriorated product error	User under stress; Information indicated at an unexpected location;
17	User does not read the formulation type.	Wrong dosage form error	User unaware that there are more than one formulation type for the drug; Information lacks salience over other information; User under stress
18	User cannot read the formulation type.	Wrong dosage form error; Omission error	Unavailable information; Illegible typeface size and/or format; Information indicated at an unexpected location; Information covered by finger tips holding the container; Intagliated or silk-screened information
19	User does not read NMI	Contraindicate; Drug allergy error	User under stress; User unaware of the need to read the information
20	User cannot read NMI	Omission error; Drug allergy error;	Unavailable information; Illegible typeface size and/or format; Information indicated at an unexpected location; Information covered by finger tips holding the container; Intagliated or silk-screened information
21	User misperceives an NMI	Contraindicate; Drug allergy error	Illegible typeface format; Use of ambiguous acronyms; Container has to be rotated a lot to read the label; User under stress; Container has to be rotated a lot to read the information
22	User misperceives a different identification number as DIN.	Wrong drug error	Numerals without text label; User under stress
23	User misperceives DIN.	Wrong drug error	Too many units of information to hold in memory; Container has to be rotated a lot to read the information; Illegible typeface format; User under stress

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24	User cannot read DIN.	Wrong drug error	Unavailable information; Illegible typeface size and/or format; Information indicated at an unexpected location; Information covered by finger tips holding the container; Intagliated or silk-screened information
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Table 6. The 24 failure modes involved in the label-reading process identified by the FMEA

The median value across participants for each of severity, frequency and detectability was calculated for each failure mode. The three median values were then multiplied to calculate a Risk Priority Number (RPN) for each failure mode as shown in Figure 1. By calculating the RPN values, it is possible to prioritize areas to concentrate improvement efforts.

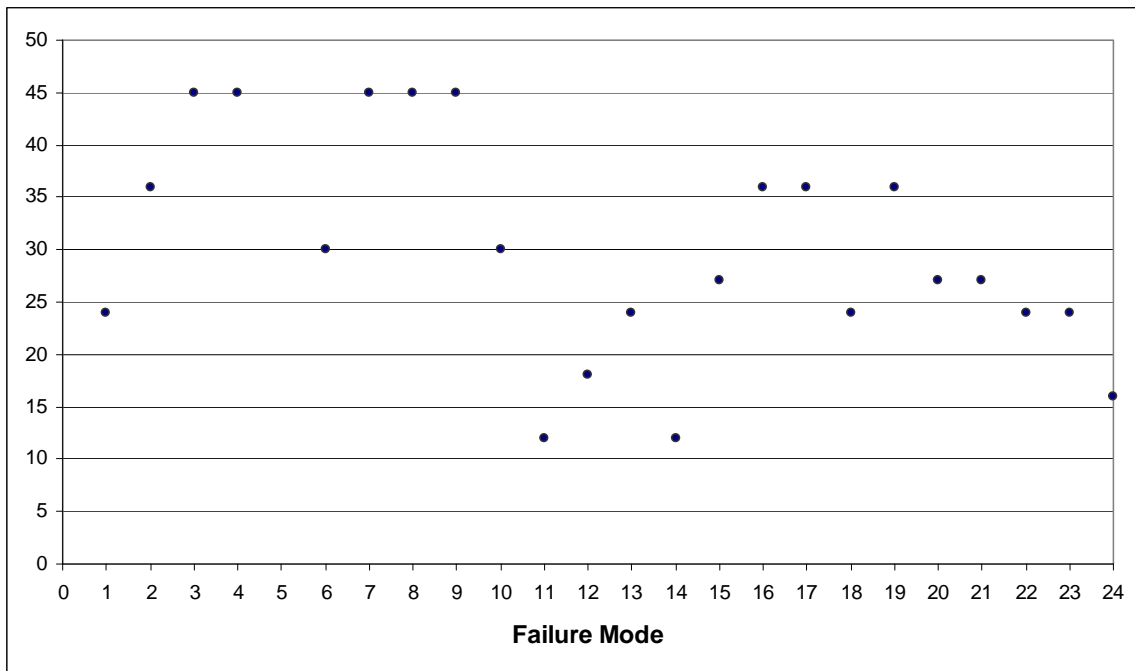


Figure 1. FMEA RPN Values

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The results of this FMEA revealed the components of the label on injectable drugs considered important by the end users for safe medication use. Failure modes (or errors) that are related to reading the brand name, common name, concentration, total amount of drug ingredient(s) and route of administration were rated as potentially severe modes of failure and therefore need to be carefully considered when designing labels. A full account of this FMEA is reported elsewhere (Jeon et al. 2007)²⁰.

Human Factors Experiment: One Problem Identified with Existing Labels

Although Cohen¹¹ argues against printing directly on ampoules because the lack of contrast between the print and the background renders the text illegible, this concern related to print is not adequately addressed in the CSA standard, and is not addressed in the Canadian Food and Drug Regulations. We therefore designed an experiment to test the speed and accuracy of identifying information on ampoules with type printed directly on the glass container, or on a clear substrate that is adhered to the glass, and compared the result to the same label design printed with black ink on an opaque, white substrate adhered to a container.

Method

Participants

Twenty-four registered nurses (2 males and 22 females) from an acute care hospital were recruited for the experiment. They ranged in age from 33 to 60 (mean of 44), and had 8 to 37 years of practice experience (mean of 21.4 years). Participants were allowed to wear their glasses or contact lenses. All participants were tested for visual acuity and colour vision.

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Stimuli

Three ampoules with type printed directly on the glass or a clear substrate (existing labels) that are currently available in Canada, and identical ampoules with label information printed with black ink on an opaque, white substrate were presented to the participants (i.e. a total of 6 different labels). The details of the existing drugs used are summarized in Table 8.

Drug No.	Generic Name	Brand Name	Concentration	Route of administration	Volume
D1	Desmopressin	DDAVP	4 µg/mL	IV, IM, SC	1 mL
D2	Epinephrine	N/A	1 mg/mL	IM, IV, SC	1 mL
D3	Paraldehyde	N/A	1 mg/mL	IM, IV	5 mL

Table 7: Injectable products with label information printed directly on glass or clear substrate.



Figure 2: The three on the left are existing labels for desmopressin (D1), epinephrine (D2) and paraldehyde (D3); the three on the right are the newly-generated labels for D1, D2 and D3 in the same order.

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The labels designed for this experiment were identical to the existing labels except for the use of black lettering on a white paper substrate (see Figure 2 above).

Procedure

For each of the six ampoules, participants were asked three different questions and the rate of response was timed:

1. What is the concentration?
2. What is the generic name?
3. What are the routes of administration?

The experiment was conducted in two rooms with similar lighting conditions. The sessions were video recorded with a camera positioned behind and diagonally from the participants such that their faces were not shown in the recordings. A set of six ampoules were placed upright in a single row on top of a flat table surface covered by a white foam cup until the participant was ready. The participant read a question displayed on a computer monitor and then picked up the ampoule to answer the question. Time to read the information being asked and accuracy of the response was recorded. Each 40-minute session consisted of 6 practice trials preceding 18 actual trials divided into 3 blocks of 6 trials.

Results

Since the participants were allotted as much time as they needed to identify the generic name, concentration and routes of administration of the drug, the accuracy rate for reading the existing labels and the new labels was similar with the exception of the generic name for D1 and the route of administration for D3. These results are presented in Table 6. The only statistically

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significant difference ($p < .05$) between the accuracy of responses for the existing and the new labels was for D3 route of administration.

Drug Type	Concentration		Generic Name		Route of Administration	
	Existing	New	Existing	New	Existing	New
D1	91.7%	91.7%	56.5%	47.8%	100.0%	100.0%
D2	100.0%	95.8%	100.0%	95.8%	100.0%	100.0%
D3	95.8%	83.3%	95.8%	100.0%	50.0%	79.2%

Table 8: Accuracy of responses

The amount of time that it took to identify the information on the existing labels that were printed directly on glass or a clear substrate, versus the experimental labels printed with black ink on an opaque, white substrate, was statistically significantly longer ($p < .0001$). For instance, the mean correct reaction time for each of the 3 questions asked for epinephrine (D2) is presented in Figure 3.

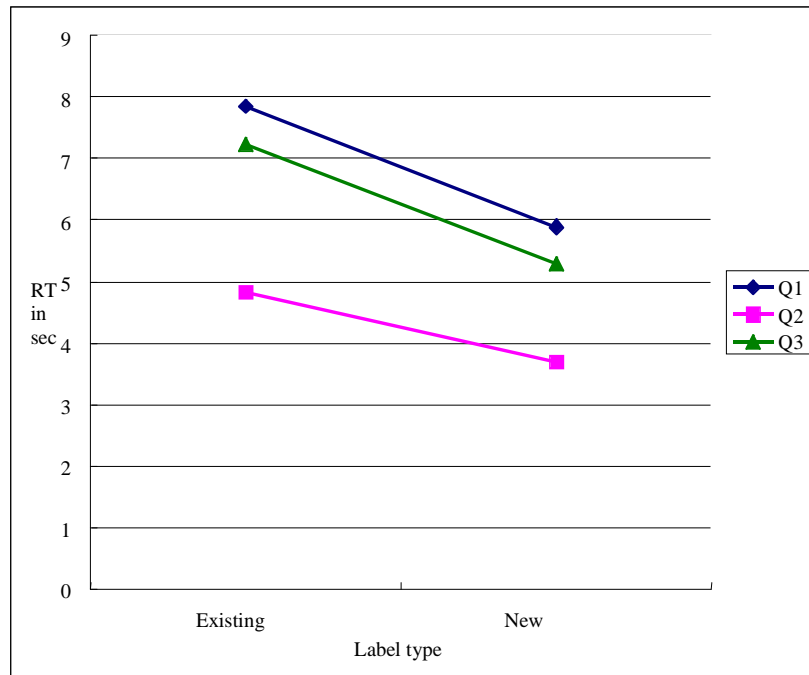


Figure 3. Mean reaction time to correctly identify essential information for the original epinephrine printing and the new black and white labels.

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(Q1: Drug concentration, Q2: generic name, Q3: routes of administration)

Discussion

Two approaches which have not been extensively employed to help decrease medication errors and which have been reported in this paper are (1) routine examination of the adherence of drug labels to standards and regulations and (2) experimentation to support existing and future recommendations.

In the first phase of this study, 78 sample vials and ampoules collected from a hospital pharmacy inventory were evaluated against the current Canadian Standards Association recommendations that define minimum design requirements for labels on ampoules and vials. The vials and ampoules were also evaluated for adherence to the Canadian Food and Drug Regulations for labelling.

Some of the statements in the CSA standard and in the Canadian Food and Drug Regulations are worded in a way that requires interpretation. For example, the Food and Drug Regulations C.01.004. (3) states: "Where the container of a drug is too small to accommodate an inner label that conforms to the requirements of these Regulations, ...", and it is not clear how small a container can be considered too small to accommodate an inner label as required in the Regulations. For the purposes of this study, a container capacity of 5 mL or less was considered to be 'too small' as is the case in the CSA standard. As per the CSA standard, it specifies the minimum space between characters for displaying critical information in Clause 4.4.8. However, the use of the word 'space' between characters is not clearly defined in the Standard. For the purposes of this study, the space was interpreted as the space between two straight-sided characters such as 'H' and 'L' as defined in the NASA's Man-Systems Integration Standard, from which the legibility section of the Standard was derived.

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The adherence rate to the 23 mandatory requirements in the CSA standard was 59%. The average proportion of the inner labels for ampoules and vials that did not adhere to one or more of the requirements in the Canadian Food and Drug Regulations was 35%. Although the percentage of drugs that did not meet one or more of the Canadian Food and Drug Regulation requirements was 35%, a large portion of the non-adherence resulted from not including both the English and French versions of the word sterile (24% of the total samples) and for not including the manufacturer address on the label (9.3% of the total samples). Health Canada does allow exceptions to the labelling information requirements through a policy for labelling of "special containers". The policy applies to containers that are too small to accommodate a full label and containers whose design causes their label to be destroyed during use. Health Canada is in the process of developing new labelling guidelines. Therefore, the non-adherence rate found in this study might change if the new labelling guideline or the special container policy were to be taken into consideration. Health Canada has recently initiated a Progressive Licensing Project that aims to improve the drug regulatory system and will include a review of current drug regulations and labelling requirements.

Of concern is that 1 % of the samples did not display the common name properly and 2% of the samples did not display the route(s) of administration. In the cases of improperly displayed common name, it appears that there was preferential emphasis placed on the manufacturer's branding. There may be instances where explaining the rationale for specific recommendations in a document might improve adherence. For example; an explanation of why a mixed set of characters is preferable to all capital characters (lower case characters have more variation in character design and thus the visual cues provided by a combination of capitals and lowercase

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characters renders type more legible than if it is set in all capital characters) conveys the importance of the choice of a mixed character set.

The second phase of the project involved performing a Failure Mode and Effects Analysis (FMEA) with 7 healthcare professionals with previous experience with FMEA in order to identify the critical information needed on an ampoule or vial for safe medication use. Failure modes related to reading brand name, common name, concentration, total amount of drug ingredient(s) per total volume and route(s) of administration were rated with higher than the average criticality in the FMEA.

The third phase of the project involved conducting a human factors experiment with a group of 24 nurses. This experiment demonstrated the superiority of black lettering on a white background over printing directly on ampoules (or on a clear substrate that is adhered to ampoules).

A human factors engineering approach has been taken toward the evaluation of drug labels which have resulted in the recommendations found in this report. Other studies, have similarly taken a human factors approach and some of these are summarized in the table below.

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Author	Title	Problem Addressed	Method	Findings / recommendations
Wheeler et al. (2008) ²¹	The effect of drug concentration expression on epinephrine dosing errors	Expression of drug concentration as a ratio.	Randomized simulation trial of a child with a peanut allergy in anaphylaxis, requiring epinephrine. Speed and accuracy of epinephrine dosage delivered measured. N = 28 physicians unfamiliar with pediatric dosages.	Reduced accuracy and increased number of errors when the concentration was expressed as a ratio (1 mL of 1:1000) compared with mass concentration (1 mg in 1 mL) Recommend elimination of expressing drug concentrations as ratios or percentages, which the authors argue, were useful when drug dosages were expressed in imperial units but this is no longer the case.
Garnerin P et al (2007) ²²	Drug selection errors in relation to medication labels: a simulation study	Varying methods of presenting drug strength information on labels and in a location that is not predictable.	Time-limited, randomized trial using computer-based task where drug strength information varied and was in either a random or a fixed location. N = 75 (15 each of ward nurses, intensive care nurses, nurse anesthetists, ward physicians, anesthetists). Number of tasks per participant = 72.	Standardization of drug strength information in - mg.ml ⁻¹ - amount - volume all displayed in standard, fixed locations.

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<p>Filik et al. (2006)²³</p>	<p>Labeling of medicines and patient safety: Evaluating methods of reducing drug name confusion</p>	<p>Labels of look alike drugs</p>	<p>Three experiments, computer-based. Experiments 1 and 2: Participants (20 different university staff and students for each) were timed as they decided whether similar name pairs were the same name or two different names comparing Tallman lettering with no Tallman lettering. Experiment 3: Participants were 28 university staff and students. The task was a recognition memory task using Tallman lettering or colour.</p>	<p>Some support for the use of Tallman lettering of drug names on labels.</p>
<p>Gabriele (2006)²⁴</p>	<p>The role of typography in differentiating look-alike/sound alike drug names</p>	<p>Visual cues for differentiating look-alike/sound alike drug names.</p>	<p>Recall task on a stimulus list of look-alike/sound alike names. N = 11 acute care hospital nurses.</p>	<p>Participants recognized more names with the use of uppercase characters than with boldface characters. White letters on a black rectangle were the most helpful in differentiating names.</p>
<p>Wogalter & Vigilante (2003)²⁵</p>	<p>Effects of label format on knowledge acquisition and perceived readability by younger and older adults.</p>	<p>Effects of smaller font sizes, less white space and label design on knowledge acquisition and perceived readability.</p>	<p>One recognition task and one recall task with 101 older adults (mean age 78 years and 109 younger adults (mean age 21 years).</p>	<p>Older adults' performance was significantly better in the medium and large print conditions than in the small print conditions--with the latter conditions not differing from the</p>

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				control condition. Younger adults showed no performance differences among the different print-size conditions. No substantial effects on knowledge acquisition performance from the white space manipulations were found. However, the perceived readability ranks showed that both groups preferred larger print size and white space.
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Table 9. Other notable experiments addressing various issues with labeling of drugs using ‘human factors engineering’ methods.

Implications

The findings in this report have implications for those involved in designing drug labels (i.e. the manufacturers) and for those involved in providing recommendations for the design of drug labels (i.e. Health Canada, the Canadian Standards Association International, and the Institute for Safe Medication Practices (ISMP Canada)). There is an opportunity to work collaboratively to improve the design of drug labels in order to decrease medication errors while at the same time protecting the interests of pharmaceutical companies.

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Recommendations

Overall, there is a need for a standardization of objective and subjective measures of drug labels in order to easily identify which ones not only do not comply with existing recommendations and regulations, but in order to provide manufacturers with information on how to improve the label design before the drug goes on the market. The current project identified where CSA standards and Health Canada Food and Drug regulations are not being adhered to as well as areas where the standards and guidelines could be improved to be better understood by manufacturers. This project also utilized the FMEA process to identify particular parts of drug labels that are most likely to lead to medication errors, and a human factors experiment was designed to point out a poor label design.

Based on the results of this three-phased study, several suggestions are made regarding the improvement of guidelines, standards and recommendations related to drug labelling:

1. When the CSA standard and the government regulations are under review, consider
 - performing user testing regarding the interpretation of the guideline or regulations;
 - including an explanation (evidence) of the rationale for particular recommendations or requirements;
 - examining the failure modes (or errors) related to the brand name, common name, concentration, total amount of drug ingredient(s) and route of administration;
 - evaluating the necessity of the information required in regulations, such as “address of manufacturer,” which takes valuable space on the label.
2. Study the feasibility of using larger-sized ampoules and vials for small volumes to increase surface area for label information.

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3. Prohibit the use of printing directly on glass or a clear substrate in the labelling of ampoules or vials containing medications.

The authors gratefully acknowledge the financial support of the Canadian Patient Safety Institute for this project.

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