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**Evidence-Based Series 12-11 Version 2**

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

# Patient Safety Issues: Key Components of Intravenous Systemic Cancer Therapy Labelling

*M. Trudeau, E. Green, R. Cosby, F. Charbonneau, T. Easty,*
*Y. Ko, P. Marchand, D.U, N. Berger, and S. Hertz*

**April 14, 2023**

**An assessment conducted in November 2025 deferred the review of Evidence-Based Series (EBS) 12-11 Version 2. This means that the document remains current until it is assessed again next year. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol)**

**EBS 12-11 Version 2 is comprised of 4 sections. You can access the summary and full report here:**
https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/1191

**Section 1: Recommendations**
**Section 2: Evidentiary Base**
**Section 3: EBS Development Methods and External Review Process**
**Section 4: Document Assessment and Review**

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## Guideline Report History

| GUIDELINE VERSION | SYSTEMATIC REVIEW | | PUBLICATIONS | NOTES AND KEY CHANGES |
|---|---|---|---|---|
| | Search Dates | Data | | |
| Original version<br>August 2009 | 1950 - 2009 | Full Report | Web publication<br>Journal publication | NA |
| Version 2<br>April 2023 | 2009-2022 | New data found in Section 4: Document Assessment and Review | Updated Web publication | 2009 recommendations are **ENDORSED** |

# Table of Contents

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**Evidence-Based Series 12-11: Section 1**

# Patient Safety Issues: Key Components of Intravenous Systemic Cancer Therapy Labelling: Guideline Recommendations

*M. Trudeau, E. Green, R. Cosby, F. Charbonneau, T. Easty, Y. Ko, P. Marchand, D.U, N. Berger, and S. Hertz*

A Quality Initiative of the Chemotherapy Labelling Panel
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

**Report Date: August 6, 2009**

The 2009 guideline recommendations have been ENDORSED, which means that the recommendations are still current and relevant for decision making. Please see Section 4: Document Assessment and Review for a summary of updated evidence published between 2009and 2022, and for details on how this guideline was ENDORSED.

## QUESTION

What are the necessary components and formatting of a chemotherapy label to maximize safe delivery and minimize errors? Chemotherapy labels associated with the delivery of a dose of intravenous chemotherapy are of particular interest.

## INTENDED USERS

The intended users of this guidance document are any health care professionals who prescribe, prepare, or administer intravenous chemotherapy, including medical oncologists, pharmacists, pharmacy technicians, and oncology nurses, as well as designers of prescription label software, patient safety directors in organizations, administrators of hospitals, and community access care organizations.

## RECOMMENDATIONS

The following recommendations are based on the expert opinion of the Chemotherapy Labelling Panel but informed by the currently available evidence (see Section 2). The evidentiary base is composed of three guidelines developed by expert groups, one systematic review, and 13 studies of varying design and sample size. These recommendations apply to the production of intravenous chemotherapy labels in a cancer setting. Although the production of labels for investigational cancer drugs was not specifically examined, the same principles apply

for all intravenous chemotherapy labels. Examples of labels using these recommendations are included at the end of this section.

**1. General Components for Medication Labels**

The following are general components of an optimal drug label for injectable dosage forms.

***(a) Identifying Information***

- Patient's name (first name, middle name or initial, and last name **OR** last name, first name, and middle name or initial such that it is consistent with the rest of the patient record) and unique identifier
- Drug name
- Amount of drug per container
- In those circumstances in which overfill is required, the overfill volume (in mL) should be printed on the label separately from the dose information
- If a product contains two or more active ingredients, they should all appear in the generic name field

***(b) Drug Information***

- Route of administration
- Amount of drug per dose (when the container holds more than one dose, e.g., multiple doses administered intermittently over a 24-hour time period)

***(c) Administration Information***

- Volume of fluid to be administered
- Duration of infusion
- Rate of administration expressed in mL/hour or as a duration in minutes in the case of medications given by IV push. There is a need to standardize pump technology within an institution or at least to use pumps with a common format. The use of pumps programmed in mL/hour is strongly recommended over the use of pumps programmed in mL/24 hour.
- Supplemental administration instructions (e.g., starting and completion dates/times, prohibitions about when medications are to be administered with respect to other medications, warnings about route of administration, handling and storage conditions)
- Numbering of the medication containers, when the drug is to be administered sequentially (e.g., bag 1 of 3)
- Relevant auxiliary information should be included on auxiliary labels. Examples of auxiliary labels include "AVOID EXTRAVASATION" and "FOR INTRAVENOUS USE ONLY – FATAL IF GIVEN BY OTHER ROUTES"

***(d) General Formatting***

- Allow for text wrap and continuation of information on another label. This is intended to allow for long names and enough space to ensure readability as well as eliminating the need to add in additional hand-written information.
- Use white labels: better visualization of text and bar codes (if used). Use black for bar codes.
- If a different colour label is required to draw attention to a specific class of high-alert drug, use yellow labels.

## 2. General Principles for Label Preparation

The following are general formatting principles to be considered when preparing a chemotherapy drug label for injectable dosage forms.

### *(a) Drug Name*

The following practices are recommended:

- Use the complete generic drug name rather than an abbreviated version.
  - cisplatin not CDDP
- Use lower case or mixed case lettering for generic drug names as appropriate
  - Use TALL man lettering to differentiate between look alike/sound alike drug names (examples can be found at http://www.ismp.org/tools/tallmanletters.pdf)
    - CISplatin to differentiate it from CARBOplatin
- List the brand name using uppercase letters.
  - HERCEPTIN

### *(b) Abbreviations and Dose Designations*

- The recommended practice is to follow Institute for Safe Medication Practices (ISMP) guidelines for abbreviations and dose expressions (examples are provided in Section 2, Table 6) and United States Pharmacopeia (USP) standards for dosage units and standard units for weight and measures (examples are provided in Section 2, Table 7). Alternative abbreviations and dose expressions should be avoided.

### *(c) Font, Font Size, and Formatting*

It is recommended that:

- Patient name, generic drug name and patient specific dose are bolded.
- 12-point Arial, Verdana or an equivalent proportionally spaced font is used for all text and numbers.
  - **Jane A. Smith** not Jane A. Smith
- When drug name, strength, dosage form, and dosage units appear together, provide a space between them
  - propranolol 20 mg ***not*** propranolol20 mg
- Laser printers that support all label formatting expectations be used.

### *(d) Order of Information*

- It is recommended that label information should be presented in the following order: generic name, brand name, patient dose, dosage units, and route of administration.
  - **ondansetron** (ZOFRAN) **4** mg IV Push
    Dose = 4 mg = 2 mL
    (2mg per mL)*

  *include this information only if needed by practitioners (e.g., to program infusion pump)
- The order of information on the label should match the user's workflow; that is the order in which information is programmed into the pump. This will vary depending on the type of pump used in an institution.

### *(e) Technology*

- While more evidence is required, the use of bar coding may be considered for use.
- The use of computerized physician order entry (CPOE) is recommended.

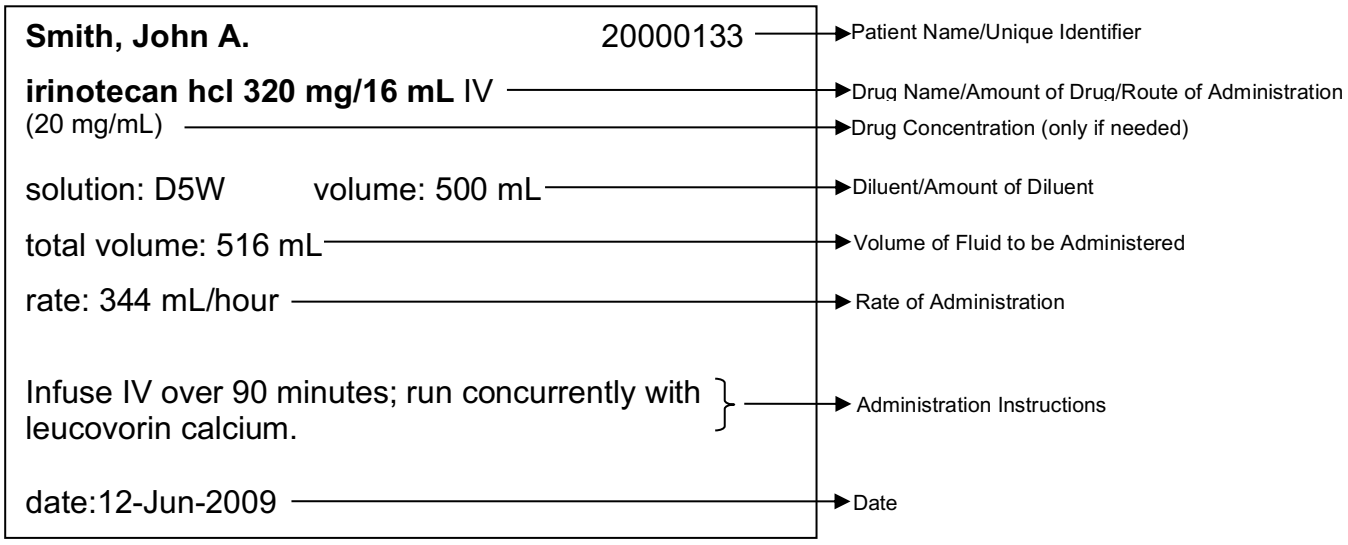
**KEY EVIDENCE**

- Guideline documents (1-3) provided a framework to identify domains that ought to be considered in an optimal label.
- Label generation should be guided by the overarching rule that medication labels not contain any unnecessary information (4).
- Communication of orders for infusions should be standardized such that "mL per hour" is used rather than "mL per 24 hour" (4).
- ISMP Canada (5) and ISMP United States [US] (6) provide sets of abbreviations, symbols and dose designations that should not be used, which the authors of this document endorse. Please see Tables 6 and 7 in Section 2 for examples.
- TALL man lettering has consistently been shown to reduce drug name identification errors (7-10).
- Larger font size and font weight results in fewer reading errors (11) and better knowledge acquisition (12).
- Proportionally spaced fonts result in better reading speed and accuracy (11).
- There are beginning studies on bar coding indicating that medication administration errors may be reduced with the use of this technology (13, 14). More research is needed before a recommendation regarding this technology can be made.
- CPOE has been demonstrated to reduce medication errors (15-19).
- There is limited evidence that laser printers are preferred over dot-matrix printers (20).

**Examples of Labels using the Recommendations in this Guidance Document**

The following examples are for illustrative purposes and do not account for overfill volumes which may require consideration.

**Example 1 – Intravenous Infusion**



**Example 2 – Intravenous Infusion**

**Smith, John A.** 20000133

**leucovorin calcium 360 mg/36 mL** IV
(10 mg/mL)

solution: D5W volume: 250 mL

total volume: 286 mL

rate: 191 mL/hour

Infuse IV over 90 minutes; run concurrently with irinotecan.

date:12-Jun-2009

**Example 3 – Continuous Intravenous Infusion**

**Smith, John A.** 20000133

**fluorouracil 4350 mg/87 mL** CIV
(50 mg/mL)

solution: D5W volume: 146 mL

total volume: 233 mL

rate: 5 mL/hour

IV continuous infusion over 46 hours.

*** INSERT INFUSOR REFERENCE NUMBER ***

date:12-Jun-2009

**Example 4 – Intravenous Push with Multiple Syringe and use of TALL man Lettering**

**Smith, Mary A.** 20000298

**EPIrubicin 166 mg/83 mL** IV
(2 mg/mL)

1 of 2 syringes.

Each syringe contains 83 mg/41.5 mL.

Infuse slowly IV at a rate of 5 mL/minute.

AVOID EXTRAVASATION → auxiliary label

date:12-Jun-2009

**Example 5 – Multiple Additives**

**Smith, John A.** 20000133

**calcium gluconate 1 g/10 mL** IV
(0.1 g/mL)

**magnesium sulfate 1 g/2 mL** IV
(0.5 g/mL)

solution: D5W volume: 250 mL

total volume: 262 mL

rate: 786 mL/hour

Infuse over 20 minutes prior to oxaliplatin.

date:12-Jun-2009

## FUTURE RESEARCH

More research is needed on the use and effectiveness of strategies to reduce medication administration errors. Specifically, more studies evaluating the effectiveness of bar coding to reduce medication errors and adverse events are needed. In addition, studies are needed to evaluate the best method(s) for patient identification to enhance the safe administration of chemotherapy. There are now a few institutions that generate two labels: one for pharmacy staff who fill the prescriptions and one for the nurses who administer the chemotherapy. Research is needed to determine if a system that makes use of two labels results in fewer medication errors than a system in which one label is used. The safe administration of chemotherapy is a complex process in which good labels are necessary but not a sole or sufficient strategy.

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**Evidence-Based Series 12-11: Section 2**

# Patient Safety Issues: Key Components of Intravenous Systemic Cancer Therapy Labelling: Evidentiary Base

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**Report Date: August 6, 2009**

## QUESTION

What are the necessary components and formatting of a chemotherapy label to maximize safe delivery and minimize errors? Chemotherapy labels associated with the delivery of a dose of intravenous chemotherapy are of particular interest.

## INTRODUCTION

Medication errors are deviations from the intended use of a medication. Delivery of the wrong medication, the wrong dosage, missed dose, wrong time and incorrect route are examples. These types of errors can occur anywhere along the path from medication ordering to medication administration and can compromise patient safety (1,2). It is estimated that medication errors accounted for 7000 deaths in the United States in 1993 alone (3). Medication errors in oncology can be particularly serious because of the narrow therapeutic ranges of antineoplastic drugs and their high toxicities (4,5). Even a moderate difference from the intended dose can have serious consequences. Over-dosing can result in considerably more toxicity than usual and under-dosing can result in an unfavourable therapeutic outcome (5).

The causes of medication error are numerous. However, the labelling and packaging of medications have been implicated as possible sources of medication error. Berman (1) estimates that 33% of medication errors are attributable to packaging and/or labelling confusion and another 25% are attributable to drug name confusion (either orthographic or phonologic similarities). Of the 1200 to 1500 reports of serious complications resulting from medications that the Institute for Safe Medication Practices (ISMP) receives each year, 25% result from name confusion and another 25% result from labelling and packaging issues. Given that the Institute for Safe Medication Practices (ISMP) estimates only 1 to 2% of events are reported to them each year, the magnitude of the problem is great (6). Several groups have attempted to provide systematic and standard approaches to preventing medication errors by improving chemotherapy labelling (5,7,8).

Confusion with respect to drug names on medication labels is one consistent source of medication error. Many drug names have similar spelling (orthographic similarity), or they sound alike (phonologic similarity). These are the so-called 'look-alike' and 'sound-alike' drug names. Several studies have demonstrated that drug name confusion increases as orthographic (9-11) and phonetic (10) similarity increases. In 1992, Davis et al. (12) were able to compile a list of 645 pairs of look-alike and sound-alike drug names. With each passing year as more and more drugs enter the market, this potential problem increases.

There are many other issues regarding the prevention of medication errors and medication labels. Font, font size, and the use of white space have become important as more and more information is included on labels (13,14). In addition, the use of bar codes in medication administration has been explored to ensure that the correct medication gets to the correct patient (15-18). The use of computerized physician order entry (CPOE) to avoid errors due to unintelligible handwriting is now becoming much more common (19-24). The purpose of this systematic review is to determine the components and formatting of an optimal label for a dose of intravenous chemotherapy such that it will contain all the necessary information and minimize delivery errors.

To this end, the following topics will be covered in this report: label content and design, drug name lettering, font and font size, bar coding, CPOE, and printers.

## METHODS

The evidence-based series (EBS) guidelines developed by Cancer Care Ontario's Program in Evidence-Based Care (PEBC) use the methods of the Practice Guidelines Development Cycle (25). For this project, the core methodologies used to develop the evidentiary base were the systematic review and environmental scan. Evidence was selected and reviewed by one methodologist (RC) on the guideline panel.

The systematic review is a convenient and up-to-date source of the best available evidence on the necessary components and formatting of a safe label for a dose of chemotherapy administered intravenously. The body of evidence in this review is primarily comprised of several guidelines that are either devoted to labelling or contain sections on the subject of labelling for injectable dosage forms. The information from these guidelines is supplemented by experimental evidence regarding various aspects of label design or by documents discovered in the environmental scan. This evidence forms the basis of the recommendations developed by the Chemotherapy Labelling Panel (Appendix 1) and published in Section 1 of this report. The systematic review and companion recommendations are intended to promote evidence-based practice in Ontario, Canada. The PEBC is supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

### Environmental Scan

The environmental scan included a search for published and unpublished sources relating to components and/or formatting of a chemotherapy label between March 5 and March 10, 2008. In addition to Canada, health care organizations in the United States (USA), United Kingdom (UK), Australia and New Zealand were searched. For a complete list of websites searched, please refer to Appendix 2.

### Literature Search Strategy

The MEDLINE (1950 through February [week two] 2008) and EMBASE (1980 through week 8 2008) databases were searched for relevant evidence. The search terms pertaining to drug labelling and medication errors were combined in the search strategies. Several key papers were catalogued quite differently, resulting in the need for several search strategies being

used. The full MEDLINE and EMBASE literature search strategies can be found in Appendices 3 and 4, respectively.

Relevant articles were selected and reviewed by one reviewer, and the reference lists from those sources were searched for additional trials.

Prior to the release of the final version of this document, the literature searches were updated for MEDLINE to April (week four) 2009 and for EMBASE to week 18 2009.

**Study Selection Criteria**

***Inclusion Criteria***

Articles were selected for inclusion in the systematic review if they were published English-language reports involving human participants of Phase II or III randomized controlled trials (RCTs), other comparative studies, single arm studies, practice guidelines, and systematic reviews, with or without meta-analyses, that related to the components or formatting of an optimal intravenous (IV) chemotherapy label.

***Exclusion Criteria***

Letters, editorials, notes, case-reports, commentaries and non-systematic reviews were not eligible.

**Synthesizing the Evidence**

Due to the heterogeneity of the outcomes reported on, the varying designs of located studies, and the lack of fully published RCTs, data were not pooled using meta-analytic techniques.

**Quality Appraisal of Systematic Review and Primary Studies**

Systematic review quality was assessed using the Assessment of Multiple Systematic Reviews (AMSTAR) tool. It began as a 37-item tool that combined the 10 items of the Overview Quality Assessment Questionnaire (OQAQ) (26), the 24 items of the Sacks et al (27) checklist, and three items judged to be methodologically important. Factor analysis identified 11 components from these 37 items, and one item from each component was chosen for the final 11-item AMSTAR instrument. The resulting instrument was deemed to have good face and content validity (28). Each item has a value of 1 point for a maximum total of 11 points. AMSTAR was recently validated externally (29).

All other studies were evaluated based on several study characteristics, if applicable to that particular study design. These included study design details, reporting of funding or support for the study, blinded assessment (if applicable), control details (if applicable), and power calculations.

**RESULTS**

**Environmental Scan Results**

The environmental scan yielded one guideline regarding the design of a medication label for injectable medications developed by the ISMP(US) (8).

**Literature Search Results**

The original MEDLINE search yielded 591 hits, of which 103 were potentially relevant and were ordered for full review (Table 1). Of those papers that were ordered for full review, eight were retained. The original EMBASE search yielded 40 hits of which 20 were potentially relevant, excluding duplicates from the MEDLINE search. None of the papers identified from the EMBASE search were retained. A search of the reference lists of included studies yielded 15 hits, and eight were retained.

One additional relevant study was identified when the literature search was updated just prior to the release of the final version of this guideline. Three additional relevant studies were identified during the external review process. Section 3 of this document contains the complete description of the external review process. A flow diagram illustrating the literature search results can be found in Appendix 5.

**Table 1. Literature search results.**

| Date | Database | Dates Searched | Hits | Ordered for full article review |
|---|---|---|---|---|
| February 29, 2008 | MEDLINE | 1950 - February (week 2 ) 2008 | 591 | 103 |
| February 29, 2008 | EMBASE | 1980 – Week 8 2008 | 40 | 20 |
| May 6, 2009 | MEDLINE | Updated to April (week 4) 2009 | 40 | 1 |
| May 6, 2009 | EMBASE | Updated to Week 18 2009 | 14 | 2 |

In total, 21 documents from the literature search, environmental scan, and external review met the eligibility criteria for this systematic review and are listed in Table 2.

**Table 2. Evidence included in this report by topic.**

| Topic | Number of Documents | Reference Numbers |
|---|---|---|
| Guidelines of Label Content and Design | 3 | (5,7,8) |
| Drug Name Lettering | 5 | (30-34) |
| Font and Font Size | 2 | (13,14) |
| Bar Coding | 4 | (15-18) |
| Computerized Physician Order Entry (CPOE) | 6 | (19-24) |
| Printers | 1 | (35) |

**Quality of Included Evidence**

A summary of the attributes used to assess the study quality as well as a brief description of the evidence included in this report can be found in Table 3.

**Table 3: Quality attributes of guidelines and studies used to inform each of the topics addressed in this report.**

| TYPE OF EVIDENCE | DOCUMENT | DESIGN | N | DESCRIPTION |
|---|---|---|---|---|
| **Guidelines** | Kohler et al. 1998 (5) | Guideline | NA | - specific to cancer treatment<br>- broad range of pharmacist expertise used to develop guideline<br>- compilation of recommendations supported by a majority of contributors |
| | ASHP Pharmacists, 2002 (7) | Guideline | NA | - specific to cancer medication errors<br>- not evidence-based; unknown if consensus based |
| | ISMP(US), 2008 (8) | Guideline | NA | - not oncology specific<br>- specific to the medication label design for injectable syringes<br>- recommendations based on an analysis of reported medication errors and a survey of pharmacy-generated labels |
| **Systematic Reviews of CPOE** | Kaushal et al. 2003 (19) | Systematic Review | NA | - scored 7 out of 11 AMSTAR points (details in Appendix 6) |
| | Shamliyan et al. 2008 (23) | Systematic Review | NA | - scored 8 out of 11 AMSTAR points (details in Appendix 6) |

| TYPE OF EVIDENCE | DOCUMENT | DESIGN | N | DESCRIPTION | | | |
|---|---|---|---|---|---|---|---|
| | Ammenwerth et al. 2008 (24) | Systematic Review | NA | - scored 8 out of 11 AMSTAR points (details in Appendix 6) | | | |
| **STUDIES BY TOPIC** | **DOCUMENT** | **DESIGN** | **N** | **FUNDING REPORTED** | **CONTROL DETAILS** | **BLINDED ASSESSMENT** | **POWER CALCULATIONS** |
| **Drug Name Lettering** | Filik et al. 2003a (30) | Series of Prospective Single Arm Studies | NR | No | NA | NR | No |
| | Filik et al. 2003b (31) | Series of Prospective Single Arm Studies | 40 (total in 2 studies) | No | NA | C | No |
| | Filik et al. 2004 (32) | Prospective Single Arm Study | 20 | No | NA | C | No |
| | Filik et al. 2006 (33) | Series of Prospective Single Arm Studies | 107 (total in 3 studies) | No | NA | C | No |
| | Gabriele, 2006 (34) | Exploratory Prospective Single Arm Study | 11 | No | NA | NR | No |
| **Font and Font Size** | Smither & Braun, 1994 (13) | Mixed Model Factorial Design | 34-39 per study | No | NA | NR | No |
| | Wogalter & Vigilante, 2003 (14) | Factorial Design | 210 | Yes | NA | Yes | No |
| **Bar Coding** | Patterson et al. 2002 (15) | Pre/Post Direct Observation Study | Pre = 10 medication passes Post = 23 medication passes | Yes | NA | No | No |
| | Paoletti et al. 2007 (16) | Pre/Post Direct Observation Study | Pre = 934 Post = 934 | No | NA | No | No |
| | Poon et al. 2006 (17) | Pre/Post Direct Observation Study | Pre = 115 000 Post = 250 000 | Yes | NA | No | No |
| | Koppell et al. 2008 (18) | Mixed Methods Design | Medication Administration Events = 307,698 | Yes | NA | NA | No |
| **CPOE** | Koppel et al. 2005 (20) | Mixed Method Design | >85% response rate | Yes | NA | NA | NA |
| | Kim et al. 2006 (21) | Pre/Post Implementation | Pre = 1259 Post = 1116 | Yes | NA | NP | No |
| | Huertas Fernandez et al. 2006 (22) | 2 arm trial | 60 | No | NR | NP | Yes |
| **Printers** | Luscombe et al. 1992 (35) | Survey | 55 | No | NA | No | No |

AMSTAR = assessment of multiple systematic reviews; C= computer based study in which outcomes recorded by automatically, no human assessment involved. CPOE = computerized physician order entry; NA = Not applicable; NP = not possible to blind a handwritten vs. computer generated prescription; NR = not reported

## Evidence Summary

### *(1) Guidelines for Label Content and Design*

### (a) General Components of a Medication Label

Kohler et al. (5) and the American Society of Health-System Pharmacists (ASHP) guidelines (7) provide some general information that should be on all medication labels for injectable dosage forms. The ISMP (US) (8) document also provides some general label components for label generation. The label components are summarized in Table 4. These guidelines helped inform the domains of a safe label reported in this document. All of this information needs to be guided by the overarching rule that medication labels should not contain any unnecessary information. This is one of the recommendations that emerged from a Root Cause Analysis that was conducted after a fatal error in the infusion of fluorouracil (36).

**Table 4: General components for medication labels.**

| COMPONENT | Kohler et al. 1998 (5) | ASHP, 2002 (7) | ISMP (US), 2008 (8) |
|---|---|---|---|
| Patient's name and unique identifier | ✓ | ✓ | ✓ |
| Date of preparation (with or without the time) | ✓ | ✓ | |
| Date of expiry (with or without the time) | ✓ | ✓ | |
| Drug name | ✓ | ✓ | ✓ |
| Route of administration | ✓ | ✓ | ✓ |
| Amount of drug per dose (when the container holds more than one dose – e.g. multiple doses administered intermittently over a 24-hour time period and when excess drug product is added to a container to compensate for dead space in the administration set) | ✓ | ✓ | |
| Amount of drug per container (including how much additional drug is added to a container when overfill drug and fluid volumes are added) | ✓ | | |
| Name and amount (or concentration) of any drug additives in the formulation | ✓ | ✓ | |
| Diluent name | ✓ | ✓ | |
| Volume of fluid to be administered (especially when that amount is different from the total container volume) | ✓ | ✓ | |
| Duration of infusion and rate of administration | ✓ | ✓ | |
| Supplemental administration instructions (e.g. starting and completion dates/times, prohibitions about when medications are to be administered with respect to other medications, warnings about route of administration, handling and storage conditions) | ✓ | ✓ | |
| When it is necessary to prepare more than one medication that will be administered sequentially, the container labels should be numbered with the total number of containers included as well (e.g. bag 2 of 3) | | ✓ | |
| Warnings, as required, for hazardous-drug products | | ✓ | |
| Storage specifications | | ✓ | |
| Name of pharmacist who prepared medication | | ✓ | |
| Name of prescribing physician | | ✓ | |
| Frequency of the medication order if applicable and wanted using non-bolded 10-point font | | | ✓ |
| Allow for text wrap and continuation of information on another label (expandable label stock). This would provide room for long drug names, patient names and/or doses. Parameters would have to be set such that breaks in patient names or medications were clear and logical. | | | ✓ |
| Comments field should accommodate a minimum of 250 characters. Order comments must support carriage returns within the note to allow formatting of tabular type data including dose nomograms. A minimum of 10-point font should be used. | | | ✓ |
| Use white labels for better visualization of text and bar codes (if used). Use black for bar codes. If a different colour label is required to draw attention to certain classes of high-alert drugs use yellow labels. | | | ✓ |
| For combination products include the BRAND name. If a product contains two ingredients they should both appear in the generic name field. If a product contains more than two ingredients, name the two primary ingredients in the generic name field followed by the phrase "and others". | | | ✓ |

**(b) General Principles for Preparing and Formatting a Chemotherapy Label**

The two oncology specific guidelines (5,7) provide general formatting principles for prescribing antineoplastic medications, some of which are applicable to the production of any IV chemotherapy label. The ISMP(US) (8) document also provides some general formatting recommendations for label generation. Some examples are provided in Table 5.

**Table 5: General principles for medication label preparation.**

| PRINCIPLE | EXAMPLE | | Kohler et al. 1998 (5) | ASHP, 2002 (7) | ISMP (US), 2008 (8) |
|---|---|---|---|---|---|
| | RECOMMENDED | NOT RECOMMENDED | | | |
| Use complete generic drug name. Abbreviations can be misinterpreted. | cisplatin | CDDP | ✓ | ✓ | ✓ |
| Use lowercase letters for generic drug names (unless using TALL man lettering to help distinguish look-alike drug names). | **CISplatin** | Cisplatin or CISPLATIN | | | ✓ |
| Do not include the salt of the chemical when expressing a generic name unless there are multiple salts available (e.g. penicillin G potassium and penicillin G sodium). The salt should follow the drug name not precede it. | penicillin G potassium | potassium penicillin G | | | ✓ |
| If needed, list the brand name using uppercase letters. | HERCEPTIN | Herceptin | | | ✓ |
| Spell out 'units'. The letter 'U' can be mistaken for a zero resulting in a 10-fold overdose. | units | U | ✓ | | ✓ |
| Within a treatment protocol use consistent notation for units of quantity. | 1.2 g or 1200 mg | using both | ✓ | ✓ | |
| Never trail a whole number with a decimal point followed by a zero. The decimal can be missed resulting in a 10-fold overdose. | 3 mg | 3.0 mg | ✓ | ✓ | ✓ |
| A dosage of less than 1 measurement unit should always have a decimal point preceded by a zero. The decimal may be missed without the zero prefix. | 0.125 mg | .125 mg | ✓ | ✓ | ✓ |
| Bold patient name, generic drug name and patient specific dose. | **Jane A. Smith** | Jane A. Smith | | | ✓ |
| Use Arial, Verdana or an equivalent font for all text and numbers. | Jane A. Smith or Smith, Jane A. | Jane A. Smith or Smith, Jane A. | | | ✓ |
| Patient name, generic drug name and patient specific dose should be printed in 12-point font as a minimum. | Jane A. Smith or Smith, Jane A. | Jane A. Smith or Smith, Jane A. | | | ✓ |
| When drug name, strength, dosage form and dosage units appear together, provide a space between them (e.g. propranolol20 mg has been misread as 120 mg rather than 20 mg) | propranolol 20 mg | propranolol20 mg | | | ✓ |

| PRINCIPLE | EXAMPLE | | Kohler et al. 1998 (5) | ASHP, 2002 (7) | ISMP (US), 2008 (8) |
|---|---|---|---|---|---|
| | RECOMMENDED | NOT RECOMMENDED | | | |
| Provide adequate space in data fields for drug names, dosing units, routes of administration and frequencies thereby avoiding the use of potentially dangerous abbreviations. | | | | | ✓ |
| All applications and printers need to support uppercase, lowercase and characters that drop below the lower line. Mixed cases also need to be supported in order to use TALL man lettering. | | | | | ✓ |
| Give consideration to the role that certain symbols and letters may play in creating errors. Slash marks and hyphens have been mistaken for the number one, the symbols for less than and greater than (< and >) are frequently mixed up, the letter O can be mistaken for a zero (0), the letter z can be mistaken for the number 2, and a lower case L (l) can be mistaken as the number 1 or the letter i. | | | | | ✓ |
| When the drug name, patient dose, dosage units, and dosage form appear together, list them in the following order: generic name, brand name, patient dose, dosage units and route of administration. | Recommended Format<br><br>**ondansetron** (ZOFRAN) **4** mg IV Push<br>Dose = 4 mg = 2 mL<br>(2 mg per mL)*<br><br>*include the mg per mL only if needed by practitioner<br>(e.g. to program infusion pump) | | | | ✓ |

**(c) Use of Abbreviations and Dose Expressions**

ISMP(US) (8) recommends avoiding all potentially dangerous abbreviations, symbols, and dose designations. ISMP(US) (37) provide a list of error-prone abbreviations compiled from reports submitted to the United States Pharmacopeia-Institute for Safe Medication Practices (USP-ISMP) Medication Error Reporting Program and that are considered to be both frequently misunderstood and involved in harmful errors. ISMP Canada (38) has also published a "Do Not Use" list of abbreviations, symbols, and dose designations that they consider to be dangerous. Examples are shown in Table 6.

**Table 6: Examples of problematic symbols, abbreviations and dose designations that should be avoided and the proper method of expression.**

| Unacceptable Abbreviation, Symbol, or Letter | Problem | Solution |
|---|---|---|
| Slash marks (/ or \) and hyphens (-) | Mistaken for the number one (1). | Avoid using. |
| < or > | Mistaken for each other. | Use 'less than' or 'more than' |
| Letter 'O' | Mistaken for zero. | Avoid using. |
| Letter 'z' | Mistaken for the number two (2). | Avoid using. |
| Lowercase L (l) | Mistaken for the number one (1) or the letter 'i'. | Avoid using. |
| U | Mistaken for a zero resulting in a 10 fold overdose | Use 'units'. |
| IU | Mistaken for 'IV' (intravenous) or '10' (ten) | Use 'units'. |
| QD and QOD | Mistaken for each other | Use 'daily' and 'every other day' respectively |
| OD | Mistaken for 'oculus dexter' (right eye) | Use 'daily'. |
| cc | Mistaken for 'u' (units) | Use 'mL' or 'millilitre'. |
| @ | Mistaken for the number 2 or 5 | Use 'at'. |
| Trailing zero | Decimal is missed resulting in a 10-fold overdose | Use 3 mg ***not*** 3.0 mg |
| Lack of leading zero | With a dosage of less than one unit, the decimal may be missed without the leading zero resulting in a dose error | Use 0.125 mg ***not*** .125 mg |

**From**: ISMP(US), 2006 (http://www.ismp.org/Tools/errorproneabbreviations.pdf) (37) and ISMP Canada, 2006 (http://www.ismp-canada.org/download/ISMPCanadaListOfDangerousAbbreviations.pdf) (38)

In addition, the ISMP(US) (8) document recommends properly spaced commas for dose numbers that are in thousands, without resorting to the use of 'M' as an abbreviation for thousands (e.g., 5,000 units not 5 M units). For doses in the hundreds of thousands or millions, thousands and millions respectively should be used rather than excessive use of zeros and commas or spaces (e.g., 150 thousand units ***not*** 150,000 units; 1 million units ***not*** 1,000,000 units) that can be easily misread. This recommendation does differ from standard International System of Unit (SI) formatting.

ISMP(US) (8) also recommends the use of USP standard abbreviations for dosage units and standard units for weight and measures. Examples are shown in the Table 7.

**Table 7: Examples of standard ways of expressing weights, measures, and dosage units.**

| Abbreviation | Meaning |
|---|---|
| m | meter |
| kg | kilogram |
| g | gram |
| mg | milligram |
| mcg | microgram |
| mL | millilitre |
| L | litre |
| mEq | milliequivalent |
| mmol | millimole |

***(2) Drug Name Lettering***

There have been many studies done in an effort to mitigate the effect of look-alike and sound-alike drug name errors. Filik et al. (30-33) have extensively studied the use of 'TALL man' lettering in the perception and recognition of drug names. TALL man lettering consists of printing sections of the drug name in capital letters such that differences between similar names are emphasized. For example, it should be easier to distinguish 'vinCRIStine' and 'vinBLAStine' than it would be to distinguish 'vincristine' and 'vinblastine'. This group of researchers (30) conducted a same-different judgement task experiment. They found no difference in the reaction time for drug name pairs with or without TALL man letters unless participants were told that the TALL man letters were informative. This result has since been replicated among several groups of university staff and students (31,33). In a recognition memory task, accuracy was greater with TALL man lettering than with lowercase letters (30). Interestingly, TALL man lettering did not decrease the number of false positive errors. Filik et al. (30) conclude that TALL man lettering assists memory by increasing attention to drug names and not by making similar names less confusable.

Filik et al. (32) recorded participants' eye movements as they searched for a drug product among an array of 20 products on a shelf as quickly and accurately as possible. The array consisted of one distractor and 19 other drug products. Half the drug names were in lowercase letters and half in TALL man letters. Results demonstrated that there were significantly fewer errors for TALL man than for lower case letters ($p<0.005$). In addition, eye movement data indicated that significantly less time was spent fixating on the distractor when it contained TALL man letters rather than lowercase letters ($p<0.005$), and there were significantly fewer fixations on the distractor when it contained TALL man lettering than when it was presented in lowercase letters ($p<0.05$).

Filik et al. (33) have also studied the use of colour as a method of highlighting text within drug names. In one experiment, participants were asked to rate the confusability of seven methods of highlighting text. Ratings in increasing order of confusability were: colour, TALL man lettering, larger font, bolding, underlining, italicizing, and normal (control) print. There was a main effect for type of highlighting. Pair-wise comparisons demonstrated that the control or normal print was the most confusing (all $p<0.05$), whereas colour was the least confusing (all $p<0.05$). In a separate experiment using a recognition memory task, Filik et al. (3 used letter style and colour to determine the best conditions for identifying target drug names. With respect to the overall number of errors, there were main effects for letter style ($p<0.01$), with fewer errors with TALL man letters but not for colour.

Gabriele (34) examined ways to differentiate between similar drug names using formal typographic and graphic cues in an exploratory study. Participants were a small group of acute care hospital nurses. Three types of contrast used were: white characters on a black rectangle on the differentiating part of the name, boldface on the differentiating part of the name, and uppercase letters on the differentiating part of the name. Word recognition was better with uppercase letters as compared to boldface letters. Interestingly, word recognition was best with white characters on a black rectangle.

***(3) Font and Font Size***

Only two papers were found in the systematic review that pertained to issues around font and font size. Smither and Braun (13) designed factorial combinations of font, font size, and font weight for a total of 18 label conditions. Participants were younger (≤65 years) and older (>65 years) adults. They were asked to read 18 flat mounted labels to themselves as quickly and as accurately as possible, after which they were asked to read the labels out loud. Speed and accuracy were measured. Reading speed data showed significant main effects for

age ($p<0.01$), font ($p<0.01$), font weight ($p<0.01$), and font size ($p<0.05$). Specifically, older participants had slower reading speeds. In addition, non-proportionally spaced fonts, unbolded font, and smaller font size resulted in slower reading speed. Performance error data demonstrated a significant main effect for font weight ($p<0.05$) such that unbolded type weight resulted in more errors than did bolded type weight. The presence or absence of serifs was not a factor.

Wogalter and Vigilante (14) studied knowledge acquisition with respect to print size and amount of white space in simulated over-the-counter (OTC) labels in a group of older (>65 years) and a group of younger adults (mean = 21 years). Participants answered questions with either the label present (Information Search Task) or without the label present (Memory of Information Task). In addition, participants were asked to rank order a set of 12 labels by their perceived readability. Older adult's knowledge acquisition was significantly better in the medium and large print conditions than the small print conditions. Print size did not affect younger adults. White space had no effect on knowledge acquisition. However, in the perceived readability task, all participants, regardless of age, preferred the larger print sizes and the presence of white space. In terms of white space, line spacing was preferred over section spacing, and both of these were preferred over no spacing.

***(4) Bar Coding***

Four studies on the use of bar coding to decrease medication administration errors were found (15-18). Direct observation was used in three of these studies to monitor medication errors pre- and post-implementation of a bar-coded-medication administration (BCMA) system. One study was identified (15) in which side effects from the introduction of BCMA were identified, with the hope of being able to recommend modifications to eliminate these side effects prior to the occurrence of an adverse event. One trained observer carried out all the observations. One hospital was observed pre-BCMA for 21 hours and 10 medication passes. Post-BCMA implementation, observations were made in three hospitals for 60 hours during 23 medication passes. Analysis of the data revealed five negative and unanticipated side effects following implementation of BCMA. They included (1) confusion on the part of nurses by the automated removal of medications by BMCA, (2) degraded coordination between nurses and physicians with respect to current, pending, and discontinued medication orders; (3) nurses dropping activities to reduce workload during busy periods, (4) increased prioritization of monitored activities (particularly timing of medication administration) during goal conflicts, and (5) decreased ability to deviate from routine sequences.

In the Paoletti et al. (16) study, four nurses trained as certified medication observers carried out the direct observations. Pre-implementation, all units were evaluated using a manual five-day medication administration record (MAR). During implementation, employee badges were affixed with bar codes for accessing the new bar-coded medication administration (BCMA) system as were patient wristbands. Nurses were trained in the use of the new system for medication administration. During the post-implementation evaluation, the control group continued to use the manual five-day MAR, and the intervention groups moved to the new BCMA system. Medication administration error rates were reduced by 54% ($p=0.045$) in a 30-bed medical-surgical unit compared to the control unit.

In the Poon et al. (17) study, a trained research pharmacist, in a 735-bed tertiary care academic medical centre, monitored all medications that had been dispensed by the pharmacy to look for dispensing errors. Over 115,000 and 250,000 doses were dispensed in the pre- and post-implementation periods, respectively. Three configurations of bar coding were tested, two of which required that all doses be scanned. These two methods resulted in a 93% to 96% relative reduction in target dispensing errors ($p<0.001$).

Koppel et al. (18) used a mixed method design to identify workarounds to BCMA systems at five hospitals. They analyzed over 300,000 medication administration events and found nurses overrode BCMA alerts for 4.2% of patients charted and 10.3% of medications charted. They identified 15 workarounds (e.g., affixing patient identification bar codes to the computer cart) and 31 causes for workarounds (e.g., unreadable or missing patient identification wristbands). These workarounds, which highlight suboptimal BCMA design and implementation, may increase medication errors. Identification of such issues should be used to improve the BCMA system in use.

***(5) Computerized Physician Order Entry (CPOE)***

Several papers, including three systematic reviews and three individual studies addressing the use of computerized physician order entry (CPOE), were found.

Three systematic reviews of the effects of CPOE on medication errors were found (19,23,24). Although there is some overlap in the individual studies included in these systematic reviews, they all demonstrated significant reductions in medication errors with the use of CPOE. Kaushal et al. (19) did not pool data, but all five of the included studies reported significant reductions in medication errors. Shamliyan et al. (23) pooled the data of 12 studies and reported that the use of CPOE resulted in a 66% reduction of medication errors in adults (OR=0.34, 95%CI: 0.22-0.52). The effect in children was similar but not statistically significant (OR=0.31, 95%CI: 0.09-1.02). Ammenworth et al. (24) calculated risk ratios for 25 studies of CPOE. Twenty three of these individual studies demonstrated a significant relative risk reduction in medication errors, ranging from 13% to 99%.

Koppel et al. (20) conducted a mixed methods study using qualitative and quantitative methods to evaluate CPOE in a major urban tertiary care teaching hospital. They conducted structured interviews, real-time observations, focus groups, and surveys and had participation rates in excess of 85% in all categories of employees, including house staff, pharmacists, nurses, nurse-practitioners, nurse-managers, attending physicians, and information technology managers. Twenty two sources of medication errors were identified and reported to be facilitated by the CPOE system in place. These authors note that the finding that CPOE facilitated certain types of medication errors was unexpected but that by identifying such errors, corrections to the system can be made.

Kim et al. (21) looked at the impact of CPOE in reducing ordering errors in pediatric chemotherapy using a pre/post implementation study. In the pre-CPOE setting, 1259 paper-based chemotherapy orders for 176 patients were analyzed for errors and in the post-CPOE setting, 1116 computer-based orders for 167 patients were analyzed. In the post-CPOE setting there were less dosing errors (relative risk [RR]=0.26, 95% confidence interval [CI]: – 0.11-0.61), less missing cumulative dose calculations (RR=0.32, 95%CI: 0.14-0.77), less incorrect dosing calculations (RR=0.09, 95% CI: 0.03-0.34), less incomplete nursing documentation (RR=0.51, 95%CI: 0.33-0.80), and more cases of not matching orders to treatment plans (RR=5.4, 95%CI: 3.1-9.5).

Finally, in 2006, Huertas-Fernandez et al. (22) compared manual (N=30) and computerized (N=30) prescriptions during one month in the medical oncology department of a university hospital. The chance of at least one error in a manual prescription was 100% compared to 13% in a computerized prescription ($p<0.001$). Median errors in manual versus [vs.] computerized prescriptions was 5 vs. 0 ($p<0.001$). The most common errors were errors of omission in manual compared to computerized prescriptions, including patient name ($p=0.0037$), age ($p=<0.001$), height ($p=0.0393$), physician name ($p=0.0037$), physician signature ($p<0.001$), diagnosis ($p<0.001$), administration frequency ($p<0.001$), and duration of infusion ($p<0.001$).

### *(6) Printer Style and Print Finish*

One study (35) was found that looked at the type of printer general pharmacy clients preferred (labels generated from dot-matrix vs. laser printers) as well as the print finish (matte vs. glossy) that was preferred. A survey was completed in which pharmacy patrons (N=55) were asked to rate four labels that all contained the same content but that differed on the type of print and label surface finish. There was no effect of age, but all groups preferred laser-generated labels over dot-matrix labels ($p<0.001$ for all groups). Matte surface was preferred over glossy surface by young females ($p<0.05$).

## DISCUSSION

The evidence base for this document consists of guidelines, a systematic review, experimental studies, and a survey. The three main guidance documents highlighted (5,7,8) collate the many approaches to and provide detailed guidance on how to prevent medication errors through better medication labels. They each cover unique components of a medication label as well as some common features. Collectively, they provide a comprehensive inventory of optimal label components and formatting that should minimize intravenous chemotherapy delivery errors. The primary studies found also cover various components of label design. This evidentiary base, however, consists mainly of small to moderate size studies of varying quality. This may limit the generalizability of their findings. As a result, the recommendations in this guideline are based on the expert opinion of the Panel but are informed by the currently available evidence.

Look-alike and sound-alike drug names have received a great deal of attention for the errors and potential errors they cause. The more orthographically or phonologically similar drug names are, the more likely it is that errors will occur (9-11). The fact that drug name confusion is estimated to contribute to 25% of medication errors (1,6) speaks to the need to ameliorate the effects of this identified problem. The use of TALL man lettering (30-33) or other typographic strategies (34) has been demonstrated to be effective when the totality of the evidence is considered. The evidence is consistent over several studies, though individual studies have a small number of participants. Another strategy would be to prevent potentially confusing new drug names from being approved at the outset. While manual methods of doing this would be overly onerous, computer programming advances would be a viable alternative (9).

Font and font size also play an important role in effectively and efficiently conveying information on a medication label. The experimental studies presented in this systematic review did not use chemotherapy labels or health care professionals as participants. However, there is no evidence to suggest that non-health professionals are any different from health professionals in their preferences for font or font size. The results of the study presented, which included younger and older adults from the general community, are likely generalizable to the community of health care professionals. Overall, everyone, regardless of age, preferred larger rather than smaller font sizes (14). Moreover, larger font sizes resulted in fewer performance errors as did fonts with proportional spacing rather than fixed-width spacing (13).

Bar coding is a relatively new approach in pharmacies, although the technology has been available for some time and has been used successfully in other sectors of society. In the United States, the number of hospitals, with 400 staffed beds or more, that had implemented a BCMA system increased from 3% in 2002 to 17.2% in 2005 (39). Two experimental studies of the use of bar coding both demonstrated significant reductions in medication errors following the implementation of a bar coding system (16,17). These results are encouraging, although more such studies would be welcomed.

CPOE is a computer software program that automates the medication ordering process and makes use of required fields to ensure standardized, legible, and complete physician orders

(18), in addition to providing clinical decision support at the time of prescribing. The use of CPOE has been generally found to significantly reduce medication errors (19,21-24). One study did demonstrate that CPOE actually facilitated certain types of medication errors. Although these findings were unexpected, the authors note that, by identifying these errors, the system can be corrected so that these types of errors are no longer made (20). CPOEs are not static systems. They can be adjusted and improved upon as potential sources of errors are identified.

Finally, one study looked at printer style and print finish of general pharmacy labels (35). Again, although this study was conducted on non-health care professionals, there is no evidence to suggest that it cannot be generalized to the health professional community. In this study all groups preferred laser-generated labels to dot-matrix printer labels. Matte surface was preferred to glossy finish but only by young females.

The Panel recognizes that it may be difficult for institutions to implement some of the recommendations provided in this guideline owing to the current limitations of the software and printers in their facilities. However, the Panel felt that it is important for these recommendations to be published not only so that health care institutions know what to look for when updating their systems, but also so that software developers are aware of the needs of their clients with respect to chemotherapy labelling. In this way, they will be able to develop and provide products that better meet the needs of their clients.

## CONCLUSIONS

Many components and principles are essential to creating a label for the safe administration of intravenous chemotherapy. The evidence found through this systematic review and the expert opinion of the Panel formed the basis for the following recommendations for the generation of labels that will influence the efficient, effective, and safe administration of intravenous chemotherapy. Good label design is just one feature of a complex process to increase the safety of chemotherapy administration.

### 1. General Components for Medication Labels

The following are general components of an optimal drug label for injectable dosage forms.

#### *(a) Identifying Information*

- Patient's name (first name, middle name or initial, and last name **OR** last name, first name, and middle name or initial such that it is consistent with the rest of the patient record) and unique identifier
- Drug name
- Amount of drug per container
- In those circumstances in which overfill is required, the overfill volume (in mL) should be printed on the label separately from the dose information
- If a product contains two or more active ingredients, they should all appear in the generic name field

#### *(b) Drug Information*

- Route of administration
- Amount of drug per dose (when the container holds more than one dose, e.g., multiple doses administered intermittently over a 24-hour time period)

#### *(c) Administration Information*

- Volume of fluid to be administered
- Duration of infusion

- Rate of administration expressed in mL/hour or as a duration in minutes in the case of medications given by IV push. There is a need to standardize pump technology within an institution or at least to use pumps with a common format. The use of pumps programmed in mL/hour is strongly recommended over the use of pumps programmed in mL/24 hour.
- Supplemental administration instructions (e.g., starting and completion dates/times, prohibitions about when medications are to be administered with respect to other medications, warnings about route of administration, handling and storage conditions)
- Numbering of the medication containers, when the drug is to be administered sequentially (e.g., bag 1 of 3)
- Relevant auxiliary information should be included on auxiliary labels. Examples of auxiliary labels include "AVOID EXTRAVASATION" and "FOR INTRAVENOUS USE ONLY – FATAL IF GIVEN BY OTHER ROUTES"

***(d) General Formatting***

- Allow for text wrap and continuation of information on another label. This is intended to allow for long names and enough space to ensure readability as well as eliminating the need to add in additional hand-written information.
- Use white labels: better visualization of text and bar codes (if used). Use black for bar codes.
- If a different colour label is required to draw attention to a specific class of high-alert drug, use yellow labels.

**2. General Principles for Label Preparation**

The following are general formatting principles to be considered when preparing a chemotherapy drug label for injectable dosage forms.

***(a) Drug Name***

The following practices are recommended:

- Use the complete generic drug name rather than an abbreviated version.
  - cisplatin not CDDP
- Use lower case or mixed case lettering for generic drug names as appropriate
  - Use TALL man lettering to differentiate between look alike/sound alike drug names (examples can be found at http://www.ismp.org/tools/tallmanletters.pdf)
    - CISplatin to differentiate it from CARBOplatin
- List the brand name using uppercase letters.
  - HERCEPTIN

***(b) Abbreviations and Dose Designations***

- The recommended practice is to follow Institute for Safe Medication Practices (ISMP) guidelines for abbreviations and dose expressions (examples are provided in Section 2, Table 6) and United States Pharmacopeia (USP) standards for dosage units and standard units for weight and measures (examples are provided in Section 2, Table 7). Alternative abbreviations and dose expressions should be avoided.

***(c) Font, Font Size, and Formatting***

It is recommended that:

- Patient name, generic drug name and patient specific dose are bolded.

- 12-point Arial, Verdana or an equivalent proportionally spaced font is used for all text and numbers.
  - **Jane A. Smith** not Jane A. Smith
- When drug name, strength, dosage form, and dosage units appear together, provide a space between them
  - propranolol 20 mg ***not*** propranolol20 mg
- Laser printers that support all label formatting expectations be used.

***(d) Order of Information***

- It is recommended that label information should be presented in the following order: generic name, brand name, patient dose, dosage units, and route of administration.
  - **ondansetron** (ZOFRAN) **4** mg IV Push
    Dose = 4 mg = 2 mL
    (2mg per mL)*

  *include this information only if needed by practitioners (e.g., to program infusion pump)
- The order of information on the label should match the user's workflow; that is the order in which information is programmed into the pump. This will vary depending on the type of pump used in an institution.

*(e)* ***Technology***

- While more evidence is required, the use of bar coding may be considered for use.
- The use of computerized physician order entry (CPOE) is recommended.

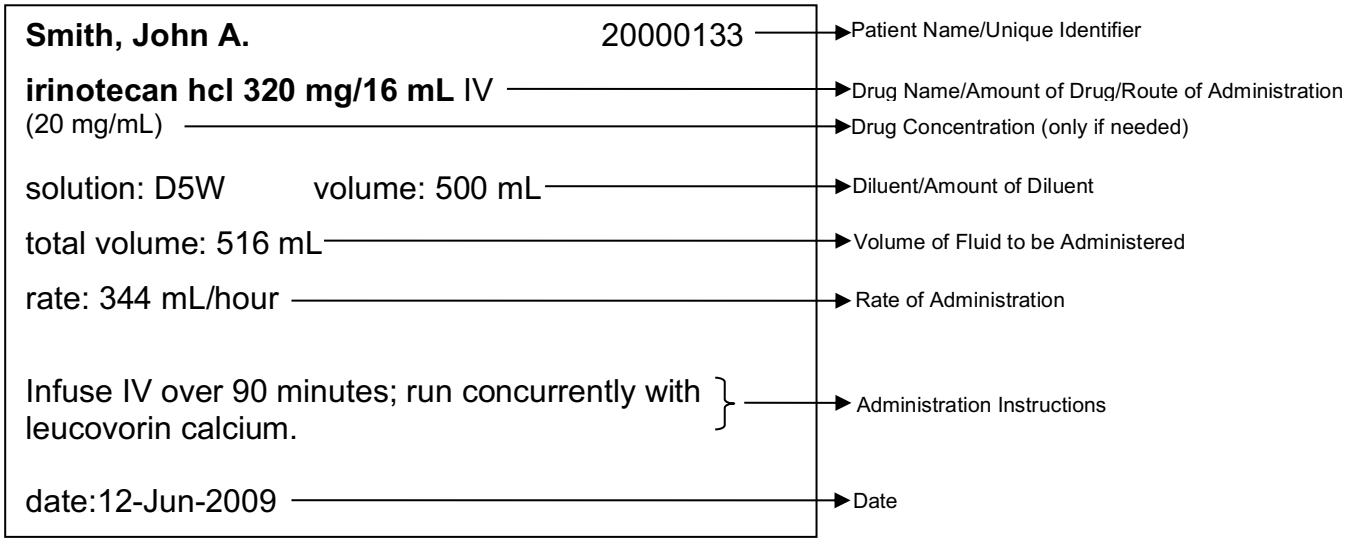
**KEY EVIDENCE**

- Guideline documents (5,7,8) provided a framework to identify domains that ought to be considered in an optimal label.
- Label generation should be guided by the overarching rule that medication labels not contain any unnecessary information (36).
- Communication of orders for infusions should be standardized such that "mL per hour" is used rather than "mL per 24 hour" (36).
- ISMP Canada (38) and ISMP United States [US] (37) provide sets of abbreviations, symbols and dose designations that should not be used, which the authors of this document endorse. Please see Tables 6 and 7 in Section 2 for examples.
- TALL man lettering has consistently been shown to reduce drug name identification errors (30-33).
- Larger font size and font weight results in fewer reading errors (13) and better knowledge acquisition (14).
- Proportionally spaced fonts result in better reading speed and accuracy (13).
- There are beginning studies on bar coding indicating that medication administration errors may be reduced with the use of this technology (16,17). More research is needed before a recommendation regarding this technology can be made.
- CPOE has been demonstrated to reduce medication errors (19,21-24).
- There is limited evidence that laser printers are preferred over dot-matrix printers (35).

**Examples of Labels using the Recommendations in this Guidance Document**

The following examples are for illustrative purposes and do not account for overfill volumes which may require consideration.

**Example 1 – Intravenous Infusion**




**Example 2 – Intravenous Infusion**

**Smith, John A.** 20000133

**leucovorin calcium 360 mg/36 mL** IV
(10 mg/mL)

solution: D5W volume: 250 mL

total volume: 286 mL

rate: 191 mL/hour

Infuse IV over 90 minutes; run concurrently with irinotecan.

date:12-Jun-2009

**Example 3 – Continuous Intravenous Infusion**

**Smith, John A.** 20000133

**fluorouracil 4350 mg/87 mL** CIV
(50 mg/mL)

solution: D5W volume: 146 mL

total volume: 233 mL

rate: 5 mL/hour

IV continuous infusion over 46 hours.

*** INSERT INFUSOR REFERENCE NUMBER ***

date:12-Jun-2009

**Example 4 – Intravenous Push with Multiple Syringe and use of TALL man Lettering**

**Smith, Mary A.** 20000298

**EPIrubicin 166 mg/83 mL** IV
(2 mg/mL)

1 of 2 syringes.

Each syringe contains 83 mg/41.5 mL.

Infuse slowly IV at a rate of 5 mL/minute.

AVOID EXTRAVASATION → auxiliary label

date:12-Jun-2009

**Example 5 – Multiple Additives**

| | |
|---|---|
| **Smith, John A.** | 20000133 |
| **calcium gluconate 1 g/10 mL** IV<br>(0.1 g/mL) | |
| **magnesium sulfate 1 g/2 mL** IV<br>(0.5 g/mL) | |
| solution: D5W | volume: 250 mL |
| total volume: 262 mL | |
| rate: 786 mL/hour | |
| Infuse over 20 minutes prior to oxaliplatin. | |
| date:12-Jun-2009 | |

## CONFLICT OF INTEREST

Six report authors (FC, RC, EG, PM, MT and DU) declared no conflict of interest. Two report authors report grant support. One author has support from the Canadian Patient Safety Institute (TE) and one author has support from Wyeth, Abraxis, Sanofi-Aventis, and Novartis (YK). One author (YK) also reports consultation/honoraria greater than $5000 annually from Sanofi-Aventis.

## JOURNAL REFERENCE

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- Trudeau M, Green E, Cosby R, Charbonneau F, Easty T, Ko Y, et al. Key components of intravenous chemotherapy labeling: a systematic review and practice guideline. J Oncol Pharm Pract. 2011 Dec;17(4):409-24. doi: 10.1177/1078155210385160. Epub 2010 Sep 27.


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*Disclaimer*

Care has been taken in the preparation of the information contained in this report. Nonetheless, any person seeking to apply or consult the report is expected to use independent medical judgement in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding the report content or use or application and disclaims any responsibility for its application or use in any way.

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**Appendix 1. Members of the Chemotherapy Labelling Working Panel.**

Co-Chairs:

| | |
|---|---|
| Esther Green | Nursing |
| Maureen Trudeau | Medical Oncologist |

Panel Members:

| | |
|---|---|
| Flay Charbonneau | Pharmacist |
| Roxanne Cosby | Methodologist |
| Tony Easty | Centre for Global eHealth & Innovation |
| Yooj Ko | Medical Oncologist |
| Patti Marchand | Clinical Nurse Specialist/Clinical Education Leader |
| David U | Institute for Safe Medication Practices Canada |

CCO Representatives:

| | |
|---|---|
| Nadia Berger | Provincial Planning |
| Sherrie Hertz | Systemic Treatment Program |

**Appendix 2: Environmental scan.**

**Canadian provincial cancer agencies:**
BC Cancer Agency
Alberta Cancer Board
Saskatchewan Cancer Agency
Cancer Care Manitoba
Cancer Care Nova Scotia

**National cancer agencies (UK, AUS, NZ):**
NZ Cancer control Strategy
NZ Cancer control Trust
Regional Cancer Centre, Waikato Hospital, Hamilton, NZ
Cancer Society of New Zealand
The Cancer Council Australia
National Cancer Control Initiative (AUS)
The Collaboration for Cancer Outcomes Research and Evaluation (AUS)
State Government of Victoria, Australia
Peter MacCallum Cancer Centre (Australia)
Medical Oncology Group of Australia
Clinical Oncology Society of Australia
Cancer UK
Cancer Services Collaborative, Avon Somerset and Wiltshire (UK)
Cancer Services Collaborative NHS Modernisation agency
NHS (UK)

**Other:**
Institute for Safe Medication Practices Canada (ISMP Canada)
Institute for Safe Medication Practices US (ISMP)
Canadian Society of Hospital Pharmacists
Canadian Association of Pharmacy in Oncology
International Society for Oncology Pharmacist Practitioners (ISOPP)
National Institute for Occupational Safety and Health (NIOSH)
Agency for Healthcare Research & Quality (AHRQ)
FDA's Manufacturer and User Device Experience (FDA MAUDE)
Emergency Care Research Institute (ECRI)
Human Factors Literature

**Appendix 3. MEDLINE search strategy.**

**Labelling**
1. exp *Drug Labeling/
2. exp *Medication Errors/
3. 1 and 2
4. Comment/
5. Editorial/
6. Letter/
7. News/
8. 4 or 5 or 6 or 7
9. 3 not 8
10. limit 9 to english language

**Labelling in Chemotherapy**
1. exp *Antineoplastic Agents/
2. exp *Medication Errors/
3. 1 and 2
4. Comment/
5. Editorial/
6. Letter/
7. News/
8. 4 or 5 or 6 or 7
9. 3 not 8
10. limit 9 to english language

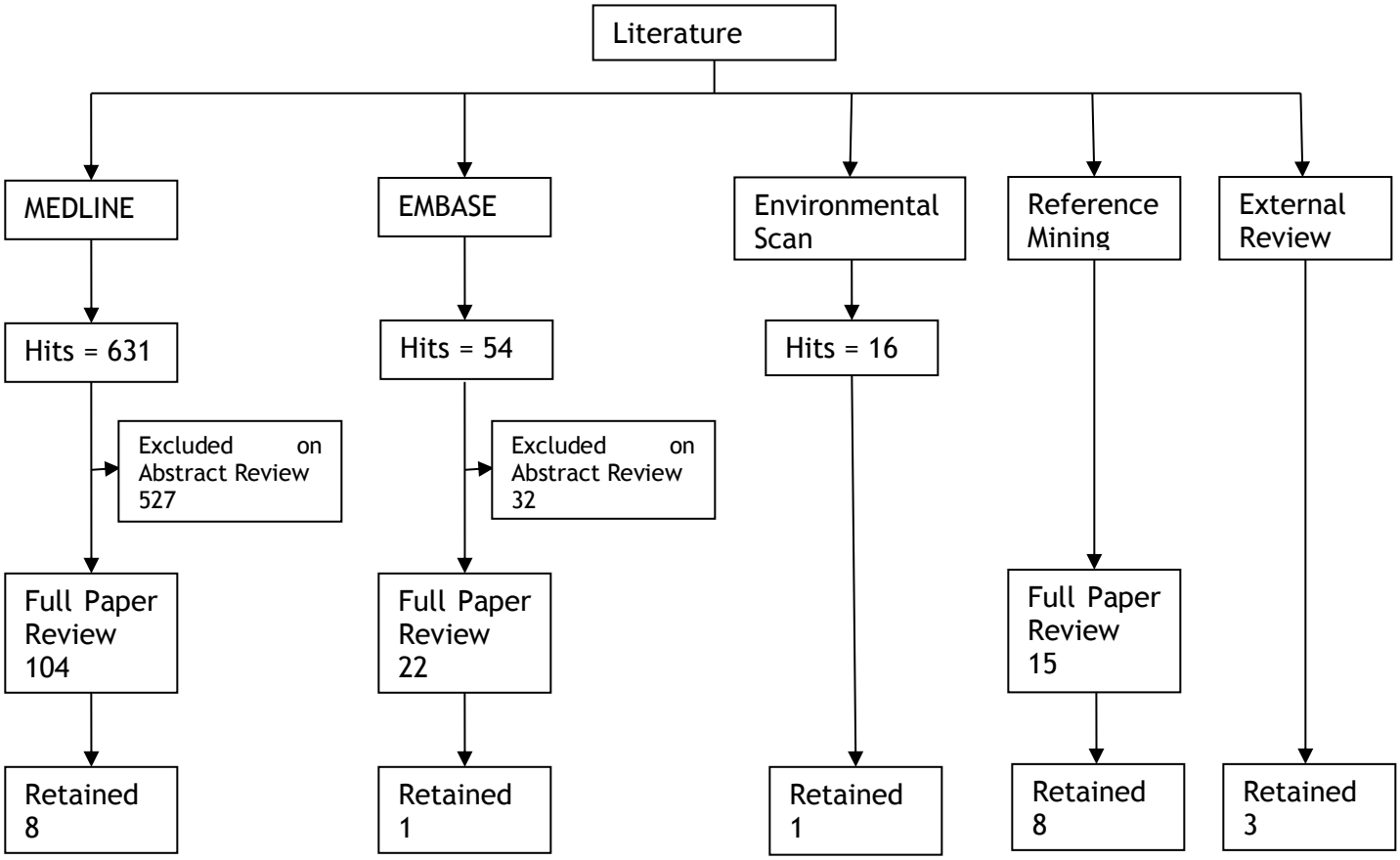
**Labelling Standards**
1. Drug labeling/st
2. Comment/
3. Editorial/
4. Letter/
5. News/
6. 2 or 3 or 4 or 5
7. 1 not 6
8. limit 7 to english language

**Appendix 4: EMBASE search strategy.**

**Labelling**
1. exp *Drug Labeling/
2. exp *Drug Nomenclature/
3. 1 or 2
4. exp *Medication Error/
5. 3 and 4
6. Editorial/
7. Letter/
8. 6 or 7
9. 5 not 8
10. limit 9 to english language

**Labelling in Chemotherapy**
1. exp *Antineoplastic Agent/
2. exp *Medication Error/
3. 1 and 2
4. Editorial/
5. Letter/
6. 4 or 5
7. 3 not 6
8. limit 7 to english language

**Appendix 5. Flow diagram of literature search results.**



## Appendix 6: Evaluation of included systematic reviews using AMSTAR

| ITEM | Kaushal et al. 2003 (19) | Shamliyan et al. 2008 (23) | Ammenwerth et al. 2008 (24) |
|---|---|---|---|
| 1. Was an 'a priori' design provided? | Y | Y | Y |
| 2. Was there duplicate study selection and data extraction? | Y | N | Y |
| 3. Was a comprehensive literature search performed? | Y | Y | Y |
| 4. Was the status of publication (i.e. grey literature used as an inclusion criterion? | Y | Y | Y |
| 5. Was a list of studies (included and excluded) provided? | N | Y | N |
| 6. Were the characteristics of the included studies provided? | Y | Y | Y |
| 7. Was the scientific quality of the included studies assess and documented? | N | N | Y |
| 8. Was the scientific quality of the included studies used appropriately in formulating conclusions? | Y | Y | Y |
| 9. Were the methods used to combine the findings of studies appropriate? | NA | Y | Y |
| 10. Was the likelihood of publication bias assessed? | NA | Y | N |
| 11. Was the conflict of interest stated? | Y | N | N |

AMSTAR = assessment of multiple systematic reviews; N = no; NA = not applicable; Y = yes

Cancer Care Ontario
Action Cancer Ontario

**Evidence-Based Series 12-11: Section 3**

# Patient Safety Issues: Key Components of Intravenous Systemic Cancer Therapy Labelling: EBS Development Methods and External Review Process

*M. Trudeau, E. Green, R. Cosby, F. Charbonneau, T. Easty, Y. Ko, P. Marchand, D.U, N. Berger and S. Hertz*

A Quality Initiative of the Chemotherapy Labelling Panel
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

**Report Date: August 6, 2009**

## THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-based Care (PEBC) is an initiative of the Ontario provincial cancer system, Cancer Care Ontario (CCO) (1). The PEBC mandate is to improve the lives of Ontarians affected by cancer, through the development, dissemination, implementation, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer care.

The PEBC supports a network of disease-specific panels, termed Disease Site Groups (DSGs) and Guideline Development Groups (GDGs), as well as other groups or panels called together for a specific topic, all mandated to develop the PEBC products. These panels are comprised of clinicians, other health care providers and decision makers, methodologists, and community representatives from across the province.

The PEBC is well known for producing evidence-based guidelines, known as Evidence-based Series (EBS) reports, using the methods of the Practice Guidelines Development Cycle (1,2). The EBS report consists of an evidentiary base (typically a systematic review), an interpretation of and consensus agreement on that evidence by our Groups or Panels, the resulting recommendations, and an external review by Ontario clinicians and other stakeholders in the province for which the topic is relevant. The PEBC has a formal standardized process to ensure the currency of each document, through the periodic review and evaluation of the scientific literature and, where appropriate, the integration of that literature with the original guideline information.

**The Evidence-Based Series**

Each EBS is comprised of three sections:

- *Section 1: Guideline Recommendations*. Contains the clinical recommendations derived from a systematic review of the clinical and scientific literature and its interpretation by the Group or Panel involved and a formalized external review in Ontario by review participants.
- *Section 2: Evidentiary Base*. Presents the comprehensive evidentiary/systematic review of the clinical and scientific research on the topic and the conclusions reached by the Group or Panel.
- *Section 3: EBS Development Methods and External Review Process*. Summarizes the evidence-based series development process and the results of the formal external review of the draft version of Section 1: Guideline Recommendations and Section 2: Evidentiary Base.

**DEVELOPMENT OF THIS EVIDENCE-BASED SERIES**

**Development and Internal Review**

This EBS was developed by the Chemotherapy Labelling Panel of the CCO PEBC. The series is a convenient and up-to-date source of the best available evidence on the necessary components and formatting of a safe label for a dose of chemotherapy administered intravenously, developed through review of the evidentiary base, evidence synthesis, and input from external review participants. The Chemotherapy Labelling Panel consisted of medical oncologists, nurses, a pharmacist, a methodologist, patient safety specialists, and CCO representatives (see Appendix 1 of Section 2 for a complete list).

**Report Approval Panel**

Prior to the submission of this EBS draft report for external review, the report was reviewed and approved by the PEBC Report Approval Panel, which consists of two members, including an oncologist, with expertise in clinical and methodology issues. Key issues raised by the Report Approval Panel (RAP) and their resolution by the Chemotherapy Labelling Panel (italicized) included:

- There was a question about whether the recommendations made would apply to investigational drugs. *A statement was added to the recommendations section stating that, although we did not examine the production of labels for investigational drugs specifically, the same principles should apply for all intravenous chemotherapy labels.*
- It was suggested that the guideline question could be reworded to make it easier to read. *The question was reworded.*
- It was suggested that some of the evidentiary base was not specifically how to improve a label but described cognitive problems with reading a label and therefore should be included in the Introduction instead. *The information regarding look-alike and sound-alike drug names was moved to the Introduction.*
- Originally the evidence for a recommendation followed each recommendation. It was suggested that a 'key evidence' section at the end would be more appropriate. *A Key Evidence section was added.*
- It was suggested that the recommendations could be better grouped to make it more succinct and explicit. *These changes were made in the revised version.*
- Originally the Appraisal of Guidelines for Research & Evaluation (AGREE) instrument was used on two of the guidelines presented in the document. RAP felt that the AGREE

instrument was not appropriate for these guidelines. *This section was removed from the document*.

- It was suggested that Table 3 should include the number of studies for those described as a 'series' of studies. *This was added to Table 3*.
- It was observed that although there is an AMSTAR score in Table 3 for the one systematic review, no details are given. *Details of the scoring were added in Appendix 6*.
- It was suggested that the text summarizing Table 3 was not giving any new information. *This was removed from the document*.
- The reliability of the drug name lettering studies was questioned given the small size of these studies. *A statement was added to the Discussion indicating that, although the individual studies are small, the results are consistent, and thus the use of TALL man lettering was effective when looking at the totality of the evidence.*
- It was suggested that the presentation of the primary studies could be more succinct. *The description of the primary studies was edited.*
- It was suggested that the limitations and generalizability of the studies should be made more explicit in the discussion. *This was added to the first paragraph of the discussion.*

**External Review by Ontario Clinicians**

The PEBC external review process is two-pronged and includes a targeted peer review that is intended to obtain direct feedback on the draft report from a small number of specified content experts and a professional consultation that is intended to facilitate dissemination of the final guidance report to Ontario practitioners.

Following the review and discussion of Section 1: Recommendations and Section 2: Evidentiary Base of this EBS and review and approval of the report by the PEBC Report Approval Panel, the Chemotherapy Labelling Panel circulated Sections 1 and 2 to external review participants for review and feedback. Box 1 summarizes the draft recommendations and supporting evidence developed by the Chemotherapy Labelling Panel.

**BOX 1:**
DRAFT RECOMMENDATIONS (approved for external review January 21, 2009)

**QUESTION**

What are the necessary components and formatting of a chemotherapy label to maximize safe delivery and minimize errors? Chemotherapy labels associated with the delivery of a dose of intravenous chemotherapy are of particular interest.

**INTENDED USERS**

The intended users of this guidance document are any health care professionals who prescribe, prepare, or administer intravenous chemotherapy, including medical oncologists, pharmacists, pharmacy technicians, and oncology nurses, as well as designers of prescription label software, patient safety directors in organizations, administrators of hospitals, and community access care organizations.

**RECOMMENDATIONS**

The following recommendations are based on the expert opinion of the Chemotherapy Labelling Panel but informed by the currently available evidence (see Section 2). The evidentiary base is composed of three guidelines developed by expert groups, one systematic review, and 13 studies of varying design and sample size. These recommendations apply to the production of intravenous chemotherapy labels

in a cancer setting. Although the production of labels for investigational cancer drugs was not specifically examined, the same principles apply for all intravenous chemotherapy labels. Examples of labels using these recommendations are included at the end of this section.

**3. General Components for Medication Labels**

The following are general components of an optimal drug label for injectable dosage forms.

***(c) Identifying Information***

- Patient's name (first name, middle name or initial, and last name) and unique identifier
- Drug name
- Amount of drug per container (in those circumstances in which overfill is determined to be required, the overfill volume [in mL] should be printed on the label separately from the dose information)
- If a product contains two or more active ingredients, they should all appear in the generic name field

***(d) Drug Information***

- Route of administration
- Amount of drug per dose (when the container holds more than one dose, e.g., multiple doses administered intermittently over a 24-hour time period)

***(c) Administration Information***

- Volume of fluid to be administered
- Duration of infusion
- Rate of administration expressed in mL/hour or as a duration in minutes in the case of medications given by IV push. We strongly recommend against the use of pumps that are not programmed in mL/hr.
- Supplemental administration instructions (e.g., starting and completion dates/times, prohibitions about when medications are to be administered with respect to other medications, warnings about route of administration, handling and storage conditions)
- Numbering of the medication containers, when the drug is to be administered sequentially (e.g., bag 1 of 3)

***(d) General Formatting***

- Allow for text wrap and continuation of information on another label. This is intended to allow for long names and enough space to ensure readability as well as eliminating the need to add in additional hand-written information.
- Use white labels: better visualization of text and bar codes (if used). Use black for bar codes.
- If a different colour label is required to draw attention to a specific class of high-alert drug, use yellow labels.

**4. General Principles for Label Preparation**

The following are general formatting principles to be considered when preparing a chemotherapy drug label for injectable dosage forms.

*(f) Drug Name*

The following practices are recommended:

- Use the complete generic drug name rather than an abbreviated version.
  - cisplatin not CDDP
- Use lower case or mixed case lettering for generic drug names as appropriate
  - Use TALL man lettering to differentiate between look alike/sound alike drug names
    - CISplatin to differentiate it from CARBOplatin
- List the brand name using uppercase letters.
  - HERCEPTIN

*(g) Abbreviations and Dose Designations*

- The recommended practice is to follow Institute for Safe Medication Practices (ISMP) guidelines for abbreviations and dose expressions (examples are provided in Section 2, Table 6) and United States Pharmacopeia (USP) standards for dosage units and standard units for weight and measures (examples are provided in Section 2, Table 7). Alternative abbreviations and dose expressions should be avoided.

*(h) Font, Font Size, and Formatting*

It is recommended that:

- Patient name, generic drug name and patient specific dose be bolded.
- 12-point Arial, Verdana or an equivalent proportionally spaced font be used for all text and numbers.
  - **Jane A. Smith** not Jane A. Smith
- When drug name, strength, dosage form, and dosage units appear together, provide a space between them
  - propranolol 20 mg ***not*** propranolol20 mg
- Laser printers that support all label formatting expectations be used.

*(i) Order of Information*

- It is recommended that label information should be presented in the following order: generic name, brand name, patient dose, dosage units, and route of administration.
  - **ondansetron** (ZOFRAN) **4** mg IV Push
    Dose = 4 mg = 2 mL
    (2mg per mL)*

  *include this information only if needed by practitioners (e.g., to program infusion pump)

*(j) Technology*

- While more evidence is required, the use of bar coding may be considered for use.
- The use of computerized physician order entry (CPOE) is recommended.

**KEY EVIDENCE**

- Guideline documents (1-3) provided a framework to identify domains that ought to be considered in an optimal label.

- Label generation should be guided by the overarching rule that medication labels not contain any unnecessary information (4).
- Pumps programmed in 'ml per hour' reduce infusion rate errors (4).
- ISMP Canada (5) and ISMP United States [US] (6) provide sets of abbreviations, symbols and dose designations that should not be used, which the authors of this document endorse. Please see Tables 6 and 7 in Section 2 for examples.
- TALL man lettering has consistently been shown to reduce drug name identification errors (7-10).
- Larger font size and font weight results in fewer reading errors (11) and better knowledge acquisition (12).
- Proportionally spaced fonts result in better reading speed and accuracy (11).
- There are beginning studies on bar coding indicating that medication administration errors may be reduced with the use of this technology (13, 14). More research is needed before a recommendation regarding this technology can be made.
- CPOE has been demonstrated to reduce medication errors (15-17).
- There is limited evidence that laser printers are preferred over dot-matrix printers (18).

***Methods***

*Targeted Peer Review:* During the guideline development process, ten targeted peer reviewers from Ontario and Alberta considered to be clinical and/or methodological experts on the topic were identified by Chemotherapy Labelling Panel. Several weeks prior to completion of the draft report, the nominees were contacted by email and asked to serve as reviewers. Six reviewers agreed, and the draft report and a questionnaire were sent via email for their review. The questionnaire consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a guideline. Written comments were invited. The questionnaire and draft document were sent out on January 21, 2009. Follow-up reminders were sent at two weeks (email) and at four weeks (telephone call). The Chemotherapy Labelling Panel reviewed the results of the survey.

*Professional Consultation:* Feedback was obtained through a brief online survey of health care professionals who are the intended users of the guideline, namely medical oncologists, pharmacists, oncology nurses, and health care professionals with an interest in patient safety issues. Participants were asked to rate the overall quality of the guideline (Section 1) and whether they would use and/or recommend it. Written comments were invited. Participants were contacted by email and directed to the survey website where they were provided with access to the survey, the guideline recommendations (Section 1), and the evidentiary base (Section 2). The notification email was sent on January 21, 2009. The consultation period ended on February 28, 2009. The Chemotherapy Labelling Panel reviewed the results of the survey.

***Results***

*Targeted Peer Review:* Six responses were received from six reviewers. Key results of the feedback survey are summarized in Table 1.

**Table 1. Responses to nine items on the targeted peer reviewer questionnaire.**

| | **Reviewer Ratings (N=6)** | | | | | | |
|---|---|---|---|---|---|---|---|
| **Question** | Lowest Quality (1) | (2) | (3) | (4) | (5) | (6) | Highest Quality (7) |
| **1. Rate the guideline development methods.** | | | 1 | 2 | | 1 | 2 |
| **2. Rate the guideline presentation.** | | | | | 3 | 1 | 2 |
| **3. Rate the guideline recommendations.** | | 1 | 1 | | | 4 | |
| **4. Rate the completeness of reporting.** | | 1 | 1 | | 1 | 2 | 1 |
| **5. Does this document provide sufficient information to inform your decisions? If not, what areas are missing?** | | | 1 | 1 | | 3 | 1 |
| **6. Rate the overall quality of the guideline report.** | | | 1 | 2 | | 3 | |
| | Strongly Disagree (1) | (2) | (3) | (4) | (5) | (6) | Strongly Agree (7) |
| **7. I would make use of this guideline in my professional decisions.** | | | 2 | | | 2 | 2 |
| **8. I would recommend this guideline for use in practice.** | | 1 | | 1 | | 2 | 2 |

**9. What are the barriers or enablers to the implementation of this guideline report?**
Several reviewers commented that the main barrier to the implementation of the guideline would be the inability of end users to fully customize their labels to the recommendations made, because of the limitations of software and printers in their facilities.

***Summary of Written Comments***

The main points contained in the written comments were:

1. There was evidence missing.
2. A prescription number may be used in ambulatory clinics for reference to a hard copy.
3. The idea of using separate labels for preparation and administration of chemotherapy should be considered.
4. Sample labels should be titled.
5. Hospitals are migrating towards the use of smart pumps.
6. What should be done with respect to auxiliary labels?
7. "Prepared by" and "Checked by" are included on the labels; however, this is not included in the section that describes the general components for medication labels.
8. A few small editorial changes were suggested.

*Professional Consultation:* Ten responses were received. Key results of the feedback survey are summarized in Table 2.

**Table 2. Responses to four items on the professional consultation survey.**

| | **Number(%)*** | | | | | | |
|---|---|---|---|---|---|---|---|
| **General Questions: Overall Guideline Assessment** | Lowest Quality (1) | (2) | (3) | (4) | (5) | (6) | Highest Quality (7) |
| **1. Rate the overall quality of the guideline report.** | | | | | 1(10) | 5(50) | 2(20) |
| | Strongly Disagree (1) | (2) | (3) | (4) | (5) | (6) | Strongly Agree (7) |
| **2. I would make use of this guideline in my professional decisions.** | | | | | 1(10) | 5(50) | 2(20) |
| **3. I would recommend this guideline for use in practice.** | | | | | 1(10) | 5(50) | 2(20) |

*Percentages do not add up to 100 because two respondents only provided written comments and did not rate the questions.

4. **What are the barriers or enablers to the implementation of this guideline report?**
   The same barrier that was identified by the external reviewers was identified by those responding to the professional consultation survey. Specifically, it may be difficult to implement all the recommendations due to the current software and printers in a given facility.

***Summary of Written Comments***

The main points contained in the written comments were:

8. The report should be communicated with the chiefs of medical oncologists at each cancer clinic.
9. A much greater source of possible mistakes is chemotherapy given outside of a clinic. Community pharmacies dispense these medications often, and patients administer it themselves.

***Modifications/Actions***

1. Most of the evidence identified as missing by the targeted peer reviewers was either beyond the scope of this guideline, not evidence-based, or not in the public domain. Three of these papers, however, met the criteria for inclusion and were therefore added to the evidentiary base of this document. The addition of this evidence did not change any of the recommendations.
2. A prescription number is not an essential element in the current context. However, the Panel did note that provincial legislation for take-home medications may require additional elements such as a prescription number on the label.
3. The use of separate preparation and administration labels is mentioned in the Future Research section of the document.
4. Titles were added to the labels.
5. The recommendation regarding pumps was modified with respect to the needs for standardizing pump technology within an institution.

6. A recommendation regarding auxiliary information and auxiliary labels was added.
7. The Panel felt the "Prepared by" and "Checked by" were more a part of internal quality assurance processes and decided that these should be removed from the label examples.
8. The editorial changes suggested were made.
9. CCO carries out dissemination of guidelines.
10. The Panel recognizes that errors in chemotherapy administration outside of the clinic are a very important topic but beyond the scope of the current guideline.

**Literature Search Update**

Prior to the completion of the final version of this document, the literature searches were updated for MEDLINE to April (week four) 2009 and for EMBASE to week 18 2009. From these updated searches, one additional study met the criteria for inclusion and was therefore added to the evidentiary base of this document. The addition of this evidence did not change any of the recommendations.

**Conclusion**

This EBS report reflects the integration of feedback obtained through the external review process with final approval given by the Chemotherapy Labelling Panel and the Report Approval Panel of the PEBC. Updates of the report will be conducted as new evidence informing the question of interest emerges.

*Funding*

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**Evidence-Based Series 12-11 Version 2: Section 4**

# Patient Safety Issues: Key Components of Intravenous Systemic Cancer Therapy Labelling

## Document Assessment and Review

*K. Vu, R. Cosby, and Members of the Expert Panel on Key Components of Intravenous Systemic Cancer Therapy Labelling*

**April 14, 2023**

***The 2009 guideline recommendations are***

***ENDORSED***

***This means that the recommendations are still current and relevant for decision making***

**OVERVIEW**

The original version of this guidance document was released by Cancer Care Ontario's Program in Evidence-based Care in 2009 with the title 'Patient Safety Issues: Key Components of Chemotherapy Labelling'.

In November 2021, this document was assessed in accordance with the PEBC Document Assessment and Review Protocol and was determined to require a review. As part of the review, a PEBC methodologist (RC) conducted an updated search of the literature. A clinical expert (KV) reviewed and interpreted the new eligible evidence and proposed the existing recommendations could be endorsed. The Key Components of Intravenous Systemic Cancer Therapy Labelling Expert Panel endorsed the recommendations found in Section 1 (Clinical Practice Guideline) in April 2023.

DOCUMENT ASSESSMENT AND REVIEW RESULTS

Questions Considered

1. What are the necessary components and formatting of a chemotherapy label to maximize safe delivery and minimize errors? Chemotherapy labels associated with the delivery of a dose of intravenous chemotherapy are of particular interest.

Literature Search and New Evidence

The updated literature search (2009 to November 2022) yielded 7 studies, 2 systematic reviews and 1 report. The new environmental scan yielded 5 documents. Brief results of these publications are shown in the Document Summary and Review Tool.

Impact on the Guideline and Its Recommendations

The new data support existing recommendations. A small modification to the title of the guideline was recommended by the expert panel to be more inclusive of other treatments now available including biologic and targeted therapies. Therefore, it was decided to change the title of the guideline from 'Key Components of **Chemotherapy** Labelling' to 'Key Components of **Intravenous Systemic Cancer Therapy** Labelling'. Hence, the Key Components of Chemotherapy Labelling Expert Panel ENDORSED the 2009 recommendations.

Please note that the use of 'chemotherapy' throughout this guidance document is meant to include all intravenous systemic cancer therapy.

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# Document Review Tool

| | |
|---|---|
| **Number and Title of Document under Review** | 12-11 Patient Safety Issues: Key Components of Chemotherapy Labelling |
| **Original Report Date** | August 6, 2009 |
| **Date Assessed (by DSG or Clinical Program Chairs)** | November 10, 2021 |
| **Health Research Methodologist** | Roxanne Cosby |
| **Clinical Expert** | Kathy Vu |
| **Approval Date and Review Outcome (once completed)** | April 14, 2023<br>ENDORSE |

Original Question:

What are the necessary components and formatting of a chemotherapy label to maximize safe delivery and minimize errors? Chemotherapy labels associated with the delivery of a dose of intravenous chemotherapy are of particular interest.

Target Population:

The intended users of this guidance document are any health care professionals who prescribe, prepare, or administer intravenous chemotherapy, including medical oncologists, pharmacists, pharmacy technicians, and oncology nurses, as well as designers of prescription label software, patient safety directors in organizations, administrators of hospitals, and community access care organizations.

Study Selection Criteria:

**Environmental Scan** - The environmental scan included a search for published and unpublished sources relating to components and/or formatting of a chemotherapy label. In addition to Canada, health care organizations in the United States (USA), United Kingdom (UK), Australia and New Zealand were searched.

**Literature Search Strategy -** The MEDLINE and EMBASE databases were searched for relevant evidence. The search terms pertaining to drug labelling and medication errors were combined in the search strategies. Several key papers were catalogued quite differently, resulting in the need for several search strategies being used. The strategies can be found in Appendix 3 and 4 of the original guideline.
***Inclusion Criteria -*** Articles were selected for inclusion in the systematic review if they were published English-language reports involving human participants of Phase II or III randomized controlled trials (RCTs), other comparative studies, single arm studies, practice guidelines, and systematic reviews, with or without meta-analyses, that related to the components or formatting of an optimal intravenous (IV) chemotherapy label.

***Exclusion Criteria -*** Letters, editorials, notes, case-reports, commentaries and non-systematic reviews were not eligible.
Search Details:

- November 17 and 18, 2022 – Environmental Scan
- 2009 to November 23, 2022 (MEDLINE, EMBASE)

Summary of new evidence:

Environmental Scan yielded 31 documents of which 5 were retained.
Of the 662 total hits from MEDLINE and EMBASE 52 underwent a full text review and 9 were retained. One study was retained from reference mining.

| | |
|---|---|
| 1. Does any of the newly identified evidence contradict the current recommendations? (i.e., the current recommendations may cause harm or lead to unnecessary or improper treatment if followed) | No |
| 2. Does the newly identified evidence support the existing recommendations? | Yes |
| 3. Do the current recommendations cover all relevant subjects addressed by the evidence? (i.e., no new recommendations are necessary) | Yes |

| | |
|---|---|
| **Review Outcome as recommended by the Clinical Expert** | ENDORSE |
| ***If outcome is UPDATE, are you aware of trials now underway (not yet published) that could affect the recommendations?*** | |
| **DSG/Expert Panel Commentary** | One comment that was made by several reviewers was the use of the word 'chemotherapy'. So many non-chemotherapy drugs are now used. It was decided to change the title of the guideline from 'Key Components of **Chemotherapy** Labelling' to 'Key Components of **Intravenous Systemic Cancer Therapy** Labelling' to be more inclusive of other treatments now available including biologic and targeted therapies. |

| | |
|---|---|
| | There was a suggestion to include “Good Label and Package Practices Guide for Prescription Drugs” which is available on the Health Canada website. It was decided that this was unnecessary as it relates to manufacturer labels which require different information than that covered by this guideline.<br><br>There was a suggestion to include Lohmeyer et al. BMJ Qual Saf 2023 Jan;32(1):26-33 to support the use of Tall Man lettering. This reference was not included. It was outside date range for the guideline and there was already ample evidence to support the use of Tall Man lettering.<br><br>There was a suggestion to included Bryan et al. Br J Pharmacol 2021;87(2):386-94 regarding LASA names. This is a narrative review which we normally don’t include and there was already ample evidence regarding this issue using the types of evidence normally used by the PEBC evidence-based guidelines. |

Evidence Tables

| STUDY | DESIGN | N | DESCRIPTION | FINDINGS |
|---|---|---|---|---|
| **Section 1: Guidelines for Label Content and Design** | | | | |
| **1a: General Components of a Medication Label** | | | | |
| Gupta et al. 2015 [1] | 2-arm trial | 108 | Evaluated contrast colour on an ampoule label.<br><br>Group A – read the original ampoule that did not have a label with a contrasting background.<br>Group B – read the modified ampoule with a label with white background and black lettering.<br><br>Outcomes<br>• time taken to read the label<br>• accuracy in reading the label<br>• difficulty in reading the label | Contrasting background on the ampoule label significantly:<br>• decreases reading time ($p<0.01$)<br>• decreases reading error ($p<0.05$)<br>• increases legibility (measured by the difficulty in reading score) ($p<0.05$) |
| Porat et al. 2009 [2] | Crossover within subjects study | 61 | Evaluated the use of colour-coded labels for IV high-risk medications to improve patient safety in the ICU.<br><br>A simulation that imitated an ICU.<br>• Intervention bed - used the colour-coded label (CCL) system.<br>• Control bed - used a standard white label with black print. | CCL method improved:<br>• Proper identification of IV bags ($p<0.0001$)<br>• Reduced time needed for description of overall drugs and lines ($p=0.04$)<br>• Improved identification of errors for drugs and lines ($p=0.03$)<br>• Reduced the performance time for overall tasks ($p<0.0001$). |
| NAPRA, 2018 [3] | Guidance Document | NA | Section 6.7 has some general guidance regarding the label and supplementary label. | The original guideline does not contradict anything in this document. Supplemental instructions should include any special precautions for disposal of the preparation. |
| ISMP Canada, 2013 [4] | NA | NA | Provides several methods for managing overfill during preparation and delivery of IV medications | Based on the information in this document, another example of Auxillary Information is "INFUSE ENTIRE CONTENTS FOR FULL DOSE" |
| **1b: General Principles and Formatting of a Chemotherapy Label** | | | | |
| None | | | | |
| **1c: Use of Abbreviations and Dose Expressions** | | | | |
| ISMP Canada, 2018 [5] | NA | NA | Reaffirms the "Do Not Use: Dangerous Abbreviations, Symbols and Dose Designations" List | Some new items have been added to the list. |
| ISMP US, 2021 [6] | NA | NA | ISMP List of Error-Prone Abbreviations, Symbols and Dose Designations | An updated list. |

| STUDY | DESIGN | N | DESCRIPTION | FINDINGS |
|---|---|---|---|---|
| **Section 2: Drug Name Lettering** | | | | |
| Larmené-Beld et al. 2018 [7] | Systematic Review | 11 studies TALL Man Letting | Note - 3 of the 11 studies were included in the original version of this guideline.<br><br>Various study designs and methods used in the included studies. Most common outcomes were error rate and response time. | Error Rate – 6 of 7 studies that reported this outcome demonstrated that TALL Man lettering resulted in significantly fewer errors compared to lowercase lettering.<br><br>Response Time - 3 of 9 studies that reported this outcome RT was significantly shorter for TALL man lettering compared to non-TALL man lettering. In 2 studies RT was longer. One study demonstrated that when participants did not know the purpose of TALL man lettering RT were similar for TALL man and lowercase but when participants were told about the purpose of TALL man, RTs were shorter for TALL man.<br><br>Other text enhancements (larger lowercase, boldface, and coloured lettering) all had lower error rates and shorter RTs compared to lowercase. Of these, boldface TALL man was the best. |
| Liu et al. 2019 [8] | 3-way counterbalanced repeated measures<br><br>3-way counterbalanced repeated measures<br><br>2-way repeated measures | Experiment 1 30 nursing students<br><br>Experiment 2 15 nurses<br><br>Experiment 3 15 nurses | Evaluated disfluency, enhanced text and increased exposure time<br>Outcomes – accuracy of visual differentiation and recognition memory<br><br>Independent Variables<br>• disfluency<br>• enhanced text<br>• increased exposure time.<br>Dependent Variables<br>• accuracy of visual<br>• differentiation<br><br>Independent Variables<br>• disfluency<br>• enhanced text<br>Dependent Variable<br>• recognition memory | Main Effects<br>Disfluency impaired visual differentiation accuracy.<br>Enhanced text significantly improved accuracy.<br>Increased exposure time significantly improved accuracy.<br><br>Disfluency did not improve visual differentiation accuracy.<br>Enhanced text significantly improved accuracy.<br>Increased exposure time significantly improved accuracy.<br><br>Disfluency did not improve recognition memory.<br>Enhanced text did not improve recognition memory. |
| **Section 3: Font and Font Size** | | | | |
| None | | | | |

| STUDY | DESIGN | N | DESCRIPTION | FINDINGS |
|---|---|---|---|---|
| **Section 4: Bar Coding** | | | | |
| ASHP, 2009 [9] | Report | NA | NA | Statement on Bar Code Enabled Medication Administration (BCMA) – they encourage the use of BCMA systems in all health systems in which medications are used. |
| Samaranayake et al. 2014 [10] | Pre/Post Direct Observation Study | Pre=1291 drug items<br>Post=471 (dispensing steps and time)<br><br>Pre=2828<br>Post=471<br>(PDEs) | Stand alone BCMA system (i.e., without the support of CPOE) introduced in one hospital ward.<br>Pre-implementation observation occurred one month prior to BCMA implementation.<br>Post-implementation observation occurred 8 months after BCMA implementation.<br><br>Outcomes<br>• Number of dispensing steps<br>• Dispensing timing<br>• Potential dispensing errors (PDEs) | Dispensing step increased from 5 to 8.<br>Dispensing time increased from 0.8(SD=0.09) to 1.5(SD=0.12) minutes.<br>Number of PDEs increased significantly after BCMA implementation ($p<0.001$).<br><br>The study highlighted weaknesses within the system. Nurses that were interviewed thought the BCMA could improve the drug administration process. Pharmacy staff that were interviewed thought the BCMA would work better if supported by CPOE. |
| Macias et al. 2018 [11] | Between Groups Pre/Post Direct Observation Study | Intervention = 627 patients<br>Control = 88 patients | BCMA implemented in a onco-hematology day unit for patients with solid tumours only. Observations were made starting one month prior to implementation and continued one month after implementation.<br><br>Intervention Group – Patients withy solid tumours<br>Control Group – Patients with hematologic malignancies<br><br>Outcomes<br>• Incidence of medication administration errors (MAEs)<br>• Type of MAEs<br>• Severity of MAEs<br>• Length of stay for treatment administration | Incidence of overall MAEs was significantly reduced in the intervention group ($p<0.001$) post-intervention but not in the control group ($p=0.3$).<br><br>Type of MAEs that were significantly reduced in the intervention group following BCMA implementation were:<br>• errors influenced by BCMA ($p<0.001$)<br>• pharmacy transcription errors ($p<0.001$)<br>• medication administration omission ($p=0.008$)<br>• wrong dose (higher) ($p=0.008$)<br>• wrong dose (lower) ($p=0.004$)<br>• wrong order ($p<0.001$)<br><br>Severity – errors of moderate ($p=0.038$) severity were significantly reduced in the intervention group following BCMA implementation, whereas errors of mild severity increased ($p=0.003$).<br><br>Length of stay for treatment administration – this outcome was not affected by BCMA implementation. |
| **STUDY** | **DESIGN** | **N** | **DESCRIPTION** | **FINDINGS** |

| | | | | |
|---|---|---|---|---|
| Huertas-Fernandez et al. 2017 [12] | Pre/Post Direct Observation Study | 500 patients (250 pre/ 250 post)<br><br>6584 treatment courses (3240 pre/ 3344 post) | Safeguards were implemented for using cytostatic agents in a hospital Oncology Outpatient Unit.<br><br>Safeguards Implemented<br>• staff training<br>• standardized procedures<br>• CPOE<br>• pharmaceutical validation<br>• bar codes<br>• new manual on drug interactions<br><br>Outcomes<br>• Overall Medication Errors (MEs)<br>• Types of MEs<br>• Severity of MEs | ME rates significantly reduced after safeguard implementation for:<br>• Overall MEs (4.4% vs. 2.8%, p<0.01).<br>• Prescription Stage (p<0.01)<br>• Preparation Stage (p<0.01)<br>• Dispensation Stage (p<0.01)<br><br>ME rates significantly increased after safeguard implantation for:<br>• Administration Stage (p<0.01)<br><br>Severity pre/post (no statistical analyses provided)<br>• B - Does not reach patient (83.3% vs. 93.7%)<br>• C - Reaches patient but does not cause harm (11.8% vs. 6.3%)<br>• D - Reaches patient, does not cause harm but required monitoring (4.2% vs 0.0%)<br>• F – Reaches patient, causes harm and requires hospitalization (0.7% vs. 0.0%) |
| Poon et al. 2010 [13] | Pre/Post Direct Observation Study | 14,041 medication administrations (6723 pre/ 7318 post) | Bar-code verification technology within an electronic medication-administration system (Bar-code eMAR) was implemented in a 35-unit tertiary academic medical centre<br><br>Outcomes<br>• Errors related to timing<br>• Errors unrelated to timing<br>• Severity | Non-timing errors significantly reduced with Bar-Code eMAR for:<br>• Overall errors – 11.5% vs 6.8%, p<0.01<br>• Oral vs. nasogastric-tube administration – p=0.003<br>• Other routes of administration p<0.001<br>• Administration documentation – p<0.001<br>• Dose – p<0.001<br>• Wrong medication – p<0.001<br>• Administration without order – p<0.001<br><br>Severity of non-timing errors significantly reduced with Bar-Code eMAR for:<br>• Clinically significant p<0.001<br>• Serious – p<0.001<br><br>Timing errors significantly reduced with Bar-Code eMAR for:<br>• Overall errors – 16.7% vs. 12.2%, p=0.001<br>• Early administration – p<0.001<br>• Late administration – p>0.001 |
| ISMP-Canada 2013 [14] | Resource Guide | NA | | Provides a large amount of information regarding BCMA particularly providing information regarding need for it in hospitals and nursing homes and information regarding implementation considerations.<br>Bar coding has become a standard of practice, therefore a recommendation regarding it is not necessary. |
| **STUDY** | **DESIGN** | **N** | **DESCRIPTION** | **FINDINGS** |

| | | | | |
|---|---|---|---|---|
| **Section 5: Computerized Physician Order Entry (CPOE)** | | | | |
| Srinivasamurthy et al. 2021 [15] | Systematic Review | 11 studies (8 studies used in the meta-analysis) | Note - 1 of the 11 studies were included in the original version of this guideline.<br><br>Evaluated the impact of CPOE on chemotherapy-related medication errors (CMEs)<br><br>Outcome - CMEs | CPOE lead to an 81% reduction in CMEs – RR=0.19, 95% CI: 0.08 to 0.44, $I^2$=99% (i.e., high heterogeneity) – but not surprising given the variability in many factors among these studies) |
| **Section 6: Printer Style and Print Finish** | | | | |
| None | | | | |

Abbreviations: ASHP, American Society of Health-System Pharmacists; BCMA, bar-code enabled medication administration; CCL, colour-coded label; CI, confidence interval; CME, chemotherapy-related medication errors; CPOE, computerized prescriber (or physician) order entry; eMAR, electronic medication-administration system; ICU, intensive care unit; ISMP, Institute for Safe Medication Practices; IV, intravenous; MAE, medication administration error; ME, medication error; NA, not applicable; NAPRA, National Association of Pharmacy Regulatory Authorities; PDE, potential dispensing errors; RR, risk ratio; RT, response time; SD, standard deviation; US, United States; vs., versus

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**Appendix 1. Members of the Expert Panel: Affiliations and Conflict of Interest Declarations**

| Name | Affiliation | Conflict of Interest Declaration |
|---|---|---|
| **Authors** | | |
| Kathy Vu | Clinical Lead – Safety Initiatives<br>Cancer Care Ontario | Ownership of RRSP stocks in Incyte Pharmaceuticals.<br>Within the past 5 years, I received an education grant (on behalf of the University of Toronto) from Pfizer to conduct a program evaluation on a Biosimilars education program that is being developed by the Leslie Dan Faculty of Pharmacy.<br>Provided advice or guidance regarding the objects of study in a public capacity:<br>Vu K, Hertz S, Green E, Kaizer L, Trudeau ME, Simanovski V, Lischka A. Chemotherapy safe handling and safe labeling guideline concordance evaluation: A Canadian experience. Journal of Clinical Oncology December 2012;30(34 Suppl):179. |
| Roxanne Cosby | Health Research Methodologist<br>Program in Evidence-Based Care | None declared |
| **Expert Panel** | | |
| Catherine Bond-Mills | Pharmacy<br>London Health Sciences Centre | Recently paid by AstraZeneca to moderate a talk on lung cancer. |
| Mario de Lemos | Pharmacy<br>BC Cancer Agency | None declared |
| Carolyn Hoffman | Nursing<br>ISMP Canada CEO | None declared |
| Allison Jocko | Nursing<br>Scarborough Health Network | None declared |
| Lorraine Martelli | Provincial Head – Cancer Nursing<br>Cancer Care Ontario | None declared |
| Silvana Spadafora | Medical Oncology<br>Sault Area Hospital | Advisory board for AstraZeneca-Novartis, Pfizer, Eli Lilly-Knight Therapeutics.<br>Ownership of Dr Silvana Spadafora Medicine Professional Corporation |

## DEFINITIONS OF REVIEW OUTCOMES

1. **ARCHIVE** – ARCHIVE means that a Clinical Expert and/or Expert Panel has reviewed new evidence pertaining to the guideline topic and determined that the guideline is out of date or has become less relevant. The document will no longer be tracked or updated but may still be useful for academic or other informational purposes. The document is moved to a separate section of our website and each page is watermarked with the words "ARCHIVE."

2. **ENDORSE** – ENDORSE means that a Clinical Expert and/or Expert Panel has reviewed new evidence pertaining to the guideline topic and determined that the guideline is still useful as guidance for clinical decision making. A document may be endorsed because the Expert Panel feels the current recommendations and evidence are sufficient, or it may be endorsed after a literature search uncovers no evidence that would alter the recommendations in any important way.

3. **UPDATE** – UPDATE means the Clinical Expert and/or Expert Panel recognizes that the new evidence pertaining to the guideline topic makes changes to the existing recommendations in the guideline necessary but these changes are more involved and significant than can be accomplished through the Document Assessment and Review process. The Expert Panel advises that an update of the document be initiated. Until that time, the document will still be available as its existing recommendations are still of some use in clinical decision making, unless the recommendations are considered harmful.