



Design of (Safe) Drug Names

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Overview

- Safe systems vs. safe drug names
- Design as multi-objective optimization
- Identification of objectives
- Measurement of objectives
- Optimization Methods
- Limitations



Safe Systems vs. Safe Drug Names

- More distinct, less confusable drug names, alone, will not solve the problem
- Need integrated set of system improvements to make significant impact on name confusion
- Drug *products* get confused, not just drug *names*
- Need to focus on similarity in non-name attributes of drugs as well (e.g., strength, route, dosage form, and schedule)



Safer Systems for Ordering, Transcribing, Dispensing, and Administering Drugs

- CPOE
- Bar codes
- Restrictions on verbal orders and handwritten prescriptions
- Talk-back
- Mistake-proof formularies
- Better human factors in dispensing area (e.g., lighting, magnifiers, product storage)



Design as Multiple Objective Optimization

- Design involves the attempt to simultaneously optimize multiple objectives (i.e., design criteria)
- Difficult because objectives often trade-off against one another (e.g., horsepower and fuel efficiency) and because some product characteristics are not easily modified
- Need to be able to identify, weight, and objectively measure these objectives
- Need mathematical formula that yields a composite “objective function” that will be the target for optimization



Identification of Objectives

- Safety objectives/criteria
 - Minimize similarity to existing products
 - Name, strength, dosage form, route of administration, schedule, indication, shape, color, packaging, storage location, etc.
 - Minimize neighborhood frequency, density
 - Minimize severity of consequences of confusion
 - Harm=probability of error X opportunities for error X severity of each error



Identification of Objectives

- Scientific/Regulatory Objectives
 - Name should be informative to health professionals
 - USAN stem system
 - Generic names suggest pharmacologic category as well as other drug product characteristics



Examples of USAN Stems

Generic and Brand Names for Common USAN Council-Approved Stems

Stem	Definition	Generic Name	Brand Name (Examples)
-arabine	Antineoplastics (arabinofuranosyl derivatives)	Fludarabine	Fludara
-barb	Barbituric acid derivatives	Phenobarbital	Solfoton
-cillin	Penicillins	Amoxicillin	Augmentin
-cycline	Antibiotics (tetracycline derivatives)	Minocycline	Dynacin
-oxacin	Antibacterials (quinolone derivatives)	Ciprofloxacin	Cipro
-oxetine	Antidepressants	Fluoxetine hydrochloride	Prozac
-sartan	Angiotensin II receptor antagonists	Losartan potassium	Cozaar

Source: <http://www.acponline.org/journals/annals/15oct98/currtabl.htm>



Other Regulatory Constraints

- It is the policy of CBER that a proposed proprietary name will not be accepted if the name:
 - suggests greater safety or efficacy than supported by clinical data;
 - includes or suggests indications, dosage regimens, dosage forms or routes of administration other than those for which the product is labeled;
 - has the potential to contribute to medication errors or cause confusion in the market place because the spelling or pronunciation is similar to another product on the market.
 - includes or suggests an active component that is not part of the product e.g., use of a USAN stem in the stem position when the product does not have the therapeutic or pharmacological characteristic that the stem implies. However, if the USAN stem is used appropriately, is not used in the stem position, and enables differentiation between two or more potentially conflicting names, such use may be deemed appropriate.
 - Is a different name for an essentially identical product for a different indication. Practitioners and patients may not understand or realize that two products with different names may be the same. In such cases, a patient may be inadvertently overdosed. Additionally, use of different names for the same product may pose problems in the collection and management of adverse drug reaction reports.
- Source: <http://www.fda.gov/cber/regsopp/80014.htm>



Identification of Objectives

- Marketing Objectives
 - Able to register trademark globally
 - Name is short (2-3 syllables)
 - Name is aesthetically pleasing
 - Connotations consistent with marketing message
 - Rolls trippingly off the tongue
 - Memorable
 - Suggests indication or drug class
 - Minimize cost



Measurement of Objectives

- Safety objectives must be valid, i.e., must be demonstrably related to safety outcomes
- Measures of safety objectives must be objective, valid, transparent, reproducible, affordable, feasible



Measurement of Objectives

- Validated measures
 - Look-alike similarity
 - Sound-alike similarity
 - Neighborhood characteristics (density and frequency)
- Measures still needing validation
 - Severity/harm
 - Similarity of non-name attributes



Optimization Methods

- Methods for multiple-objective optimization (MOO) are well-developed in mechanical engineering
 - Weighted sum, deviation sum, constraint satisfaction, etc.
- Details of these techniques are beyond scope of this presentation, but literature is vast and easily accessible



Illustration: Weighted Sum

- Objectives
 - Spelling similarity
 - Dosage form similarity
 - Strength similarity
 - Route of administration similarity

File Search Initialize

Drug Name and Weight

ENBREL

Strength and Weight

25.0

Dose Form and Weight

POWDER FOR INJECTION

Route of Administration and Weight

SUBCUTANEOUS

MESSAGES:

You selected drug number 74337.
Brand name = OVIDREL
Similarity = 0.4173

- Spelling Search
- Phoneme Search

- Bigrams
- Trigrams

Space(s) Before Name
 Space(s) After Name

- Common Bigrams/Trigrams
- Consider Position
- Don't Consider Position

Threshold (>= 1):
 Similarity (0.0 - 1.0):

Brand name: OVIDREL
House name: CHORIOGONADOTROPIN ALPHA
Description: 250 MCG
Compared to: ENBREL
Similarity = 0.4173. Edit Distance = 0.5714

ATTRIBUTES

Strength: 250.0 MCG
Dose form: POWDER FOR INJECTION
Route of administration: SUBCUTANEOUS
NDC Code: 44087025001
Inner Pack Size: 1.0
Outer Pack Size: 0.0
OTC status: F
SERONO LABORATORIES INC
100 LONGWATER CIRCLE
NORWELL MA 02061

REMOVE REMOVE ALL

OVIDREL

[CLICK ME FOR SEARCH DATA](#)

[SPELLING SEARCH](#)

ENBREL

Place	No.	Drug Name	Similarity	Edit Distance	Strength	Dose Form	Admin. Route
1	39388	ENBREL	1.0	0.0	25.0 MG	POWDER FOR INJ...	SUBCUTANEOUS
2	74337	OVIDREL	0.485	0.5714	250.0 MCG	POWDER FOR INJ...	SUBCUTANEOUS
3	4048	ACTHREL	0.36	0.5714	100.0 MCG	POWDER FOR INJ...	INTRAVENOUS
4	41853	FACTREL	0.36	0.5714	0.1 MG	POWDER FOR INJ...	INTRAVENOUS
5	41854	FACTREL	0.36	0.5714	0.5 MG	POWDER FOR INJ...	INTRAVENOUS
6	72692	NOVAREL	0.36	0.5714	10000.0 U	POWDER FOR INJ...	INTRAMUSCULAR
7	4032	ACTHAR	0.35	1.0	25.0 U	POWDER FOR INJ...	INJECTABLE
8	20738	CARDIO GREEN KIT	0.35	0.875	25.0 MG	POWDER FOR INJ...	INJECTABLE
9	20787	CARDIZEM LYO-JECT	0.35	0.8824	25.0 MG	POWDER FOR INJ...	INTRAVENOUS
10	53634	IC-GREEN	0.35	0.75	25.0 MG	POWDER FOR INJ...	INJECTABLE
11	70462	NEUTREXIN	0.35	0.6667	25.0 MG	POWDER FOR INJ...	INTRAVENOUS
12	81212	PREMARIN INTRAVENOUS	0.35	0.8	25.0 MG	POWDER FOR INJ...	INTRAVENOUS
13	94339	THYMOGLOBULIN	0.35	0.9231	25.0 MG	POWDER FOR INJ...	INTRAVENOUS
14	39428	ENDEP	0.3346	0.5	25.0 MG	TABLET	ORAL
15	17845	BREVITAL SODIUM	0.3272	0.8667	2.5 G	POWDER FOR INJ...	INTRAVENOUS



Limitations

- Similarity-based searching only one part of the design process, and even this one part is full of challenges and open questions
 - Best similarity measures?
 - Similarity measures for non-name attributes?
 - Which reference database to search?
- Many objectives difficult to quantify
- Even quantifiable objectives need validation
- Weighting of objectives will be controversial
- Optimizing vs. satisficing