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What's in a Name? Proprietary Naming of Drugs

Amritha Kidiyoor, PhD
Senior Clinical Research Scientist

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Outline

- Types of drug names
- Generic names
  - USAN reserved stem names
- Proprietary names
  - Derivation of names
  - Consideration when naming
  - Why FDA scrutiny is important?
  - FDA guidance on what to avoid
  - FDA review process
  - Examples

PTO: Patent and Trademark Office
USAN: United States Adopted Names

How many names does a drug have?

- Chemical name
  - CAS Registry (American Chemical Society)

- Generic name
  - Also – Nonproprietary name, Established name
  - Assigned by health organizations such as the USAN Council (USAN names) and World Health Organization (International nonproprietary names – INN)
  - Applicant proposes a name (or names), but may be assigned something different
  - Established "stems" denoting pharmacological or chemical trait of a drug (details on next slide)
- Proprietary name
  - Also – Brand name, Trade name
  - Regulated by FDA (and the PTO)

Generic names

- USAN reserved stems

USAN Reserved Stems

Prefix	Infix	Suffix	Definition	Example
		-alol	combined alpha and beta blockers	labet***alol,*** medrox***alol***
		-azepam	antianxiety agents (diazepam type)	lor***azepam,*** clon***azepam***
	-barb-	-barb	barbituric acid derivatives	etero***barb,*** pheno***barb***ital
cef-			cephalosporins	***cef***azolin
		-ciclib	cyclin dependent kinase inhibitors	seli***ciclib,*** palbo***ciclib***
io-	-io-		iodine-containing contrast media	***io***damide, adip***io***done
	-kef-		enkephalin agonists (various indications)	caso***kef***amide
		-olol	beta-blockers (propranolol type)	tim***olol,*** aten***olol***
		-profen	anti-inflammatory/analgesic agents (ibuprofen type)	flurbi***profen,*** keto***profen***
sulfa-			antimicrobials (sulfonamides derivatives)	***sulfa***salazine
		-taxel	antineoplastics, taxane derivatives	pacli***taxel***
		-traline	selective serotonin reuptake inhibitors (SSRI)	ser***traline***

USAN Reserved Stems

Prefix	Infix	Suffix	Definition	Example
vir-	-vir-	-vir	antivirals	
		-amivir	neuraminidase inhibitors	zan***amivir***
		-asvir	nonstructural protein 5A (NS5A) inhibitors	daclat***asvir***
		-buvir	RNA polymerase (NS5B) inhibitors	nes***buvir***
		-cavir	carbocyclic nucleosides	lobu***cavir***
	-cyclovir, -ciclovir		antivirals (acyclovir type)	des***ciclovir,*** pen***ciclovir,*** fam***ciclovir,***
		-gosivir	glucosidase inhibitors	cel***gosivir***
		-navir	HIV protease inhibitors (saquinavir type)	droxi***navir,*** indi***navir,*** rito***navir***
		-previr	serine protease inhibitors	boce***previr,*** tela***previr***
		-sporivir	cyclosporine derivatives	ali***sporivir***
		-tegravir	integrase inhibitors	elvi***tegravir***
		-virimat	antiviral, disrupts viral maturation	be***virimat***

Example for reserved stem

- IONICCA™ (i-ON-ee-kah)
  - Name conveys the compound's mechanism of action, highlighting the restoration of ion transport via chloride channel activation (CCA).
  - Recognized risk of having *Io-* as the leading letters
    - Mitigated by the scientifically recognized *Ion-*
    - Positive market research findings
    - USAN reserves pre- and in-fix locations
- FDA Response
  - "The proposed proprietary name for <your> inhalation solution, Ionicca™, is unacceptable because the name contains the USAN stem *Io-* which is reserved for iodine containing contrast media."
- Moved on to HYCILIA™
  - Name derived from the compound's positive impact on airway hydration and ciliary function within the lung. It is a proprietary name that is functional and strong in tone.

Proprietary names

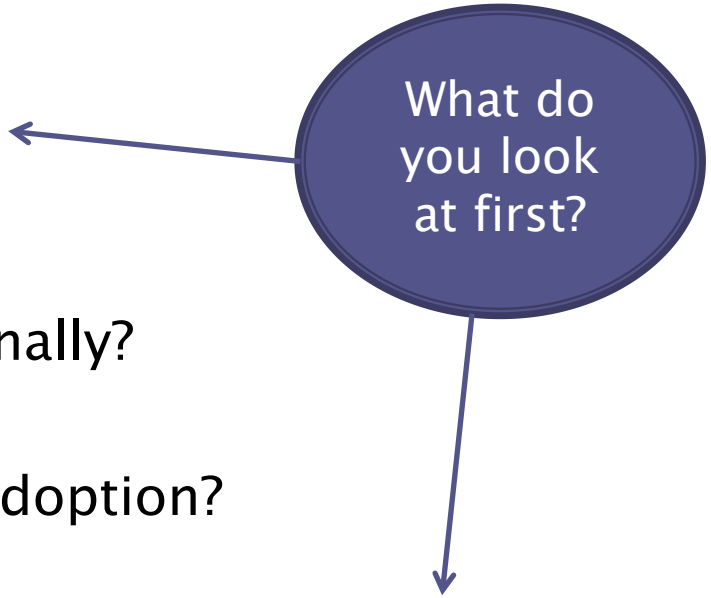
»

Derivation of Names

- Science-focused name
  - XELJANZ – targets a protein called Janus kinase. Works via a different cellular pathway from other arthritis drugs.
  - XALKORI – for anaplastic lymphoma kinase (ALK)-positive NSCLC
- Indication-focused name
  - NORTHERA – for neurogenic orthostatic hypotension
  - LAMICTAL – for epilepsy (middle phase of seizure is ictal phase)
- Inspirational/Aspirational
  - HORIZANT – for restless leg syndrome
  - VIAGRA – for ED
  - LUNESTA – for sleep
- Empty vessel
  - A collection of letters with no intended meaning
  - Get out the scrabble pieces and start throwing

Considerations

- Can the name be trademarked?
  - Critical factor
  - Legal review
- Can the name be used internationally?
  - Not essential, but nice to have
- Can the name enhance product adoption?
  - Inspire, captivate, intrigue, …
  - At least not hurt!
- Can the name be approved by the FDA (and other regulatory agencies as appropriate)?
  - Critical factor
  - Requires detailed, usually outsourced, testing, market research and analysis



IOM: Institute of Medicine

Why is FDA Scrutiny Important?

- End users may rely, in part, on the proprietary name to identify which product is intended for or used by a given patient
- Reports released by the IOM described medication errors as a significant public health concern that accounts for an estimated 7,000 deaths annually in the US
  - IOM recommended that FDA encourage Sponsor companies test their proposed proprietary names to identify and remedy potential sound-alike and look-alike confusion with existing drug names
  - IOM urged the FDA to apply the principles of cognitive and human factors engineering to the selection and evaluation of proprietary names

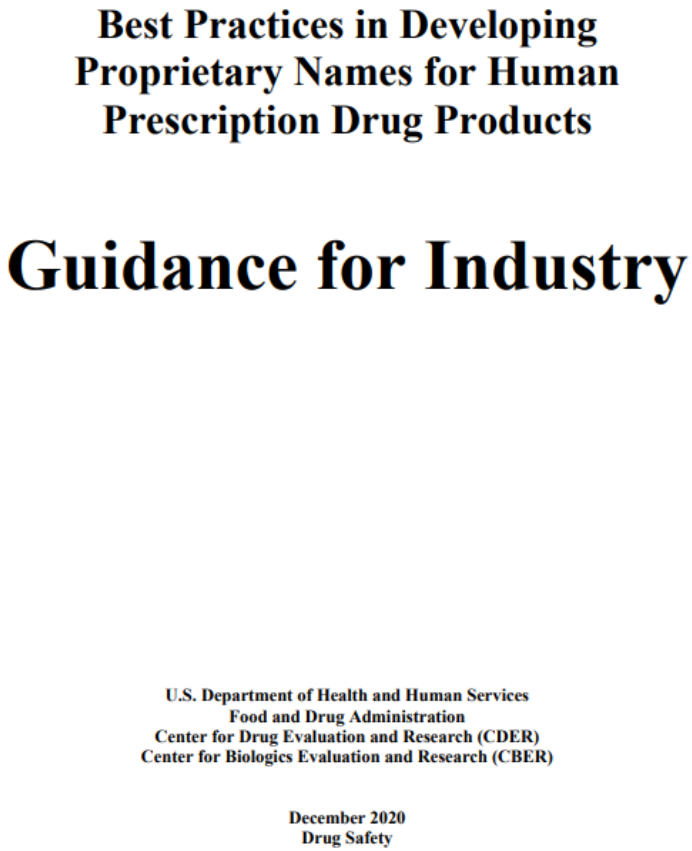
Drugs Associated with Medication Errors

Drug 1	Drug 2	Reason
Durezol	Durasal	Sound alike names
Flomax	Volmax	Look alike, sound alike names
Insulin	Heparin	Similar looking vials are often next to each other on a counter, drug cart, or under a pharmacy IV admixture hood. Both drugs are dosed in units.
Kaletra	Keppra	Sound alike names
Lanoxin	Levoxine	Sound alike names; Levoxine changed to Levoxyl
Reminyl	Amaryl	Sound alike names
Risperdal (risperidone)	Requip (ropinirole)	Similarities of both brand and generic names, as well as container/carton packaging
Zantac	Zyrtec	Look alike, sound alike names

FD&C Act: Federal Food, Drug, and Cosmetic Act

FDA guidance for developing proprietary names

- Helps sponsors develop proprietary names
- Describes best practices to minimize medication errors and avoid violations of FD&C Act
- Provides framework that FDA uses in evaluation of proposed proprietary names



Best Practices in Developing Proprietary Names for Human Prescription Drug Products

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

December 2020
Drug Safety

FDA's recommendations for Sponsor's assessment of proposed name

- FDA recommends that Sponsors:
  - do a medication error review for attributes that are likely to lead to medication errors
  - do a review focused on identifying if the proposed name overstates product efficacy or safety, expands product indications, suggests superiority without support
  - do comprehensive name simulation studies
  - get medication error data for existing proprietary/generic names
  - use a computational method to identify names with similar phonetics, spelling, or appearance

Best practices

- To minimize medication error and avoid violation of FD&C Act

Minimizing medication errors- prescreening with best practices

- Obvious similarities to other names (ex: Zantac and Zyrtec)
- Inclusion of reference to inert or inactive ingredients (ex: PEG)
- For combination drug products: avoid suggesting the name of one or more, but not all active ingredients
- Inclusion of a USAN stem
- Brand name extension- using the same name or same root name for a product that does not share at least 1 common active ingredient
- Reusing a proprietary name of a different discontinued drug product
- Unpronounceable as a word (ex: XWS778)

PRN: Pro re nata
API: active pharmaceutical ingredient

Minimizing medication errors- Additional best practices

- Inclusion of product-specific attributes (ex: Nametabs)
- Medical abbreviations (ex: PRN) used in prescription communication
  - Dose designations
  - Symbols
- Use of modifiers (ex: XR)
- Dual proprietary name (ex: same drug but for 2 indications)
- Drug names used outside the US (ex: drugs with different API marketed under the same/similar name in different countries)
- Use of numbers and symbols; use words
- Use of sponsor name in the proprietary name

NDA: New Drug Application
BLA: Biologics License Application

Avoiding violation of FD&C Act

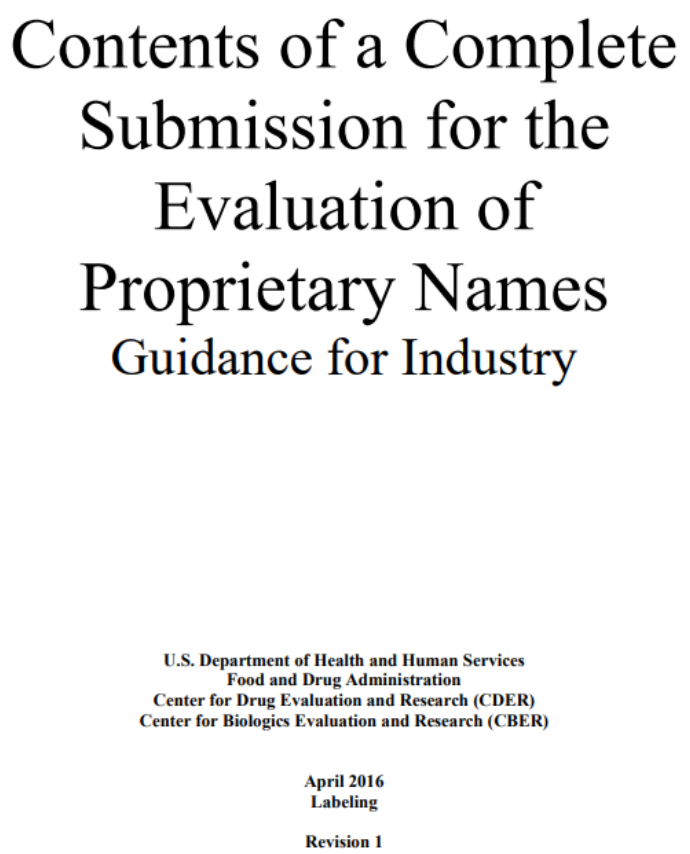
- Proprietary name is not misbranding (if its false or misleading)
  - Overstating the clinical benefit (ex: if it has the word ‘cure’ in it)
  - Suggesting superiority without substantiation
  - Proprietary name suggests that it be used under conditions for which it does not have an approved NDA/BLA

FDA's evaluation

- Submission, FDA review

Proprietary Name Review Procedure

- Refer to 2016 guidance document *"Contents of a Complete Submission for the Evaluation of Proprietary Names"*
- During the IND phase, tentative acceptance or non-acceptance of a proposed name is provided to the sponsor within 180 days
- During the NDA/BLA phase, tentative acceptance or non-acceptance of a proposed name is provided to the sponsor within 90 days
- Requests to reconsider (with appropriate data), or submission of a new name for review, gets a new clock
- Two names can be submitted at a time, but FDA will only review one at a time


Contents of a Complete Submission for the Evaluation of Proprietary Names

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

April 2016
Labeling

Revision 1

Complete Submission

- General Information
  - Sponsor, application number, etc
- Proposed Proprietary Name
  - Primary and alternate proposed proprietary names
  - Intended pronunciation of the name
  - Derivation of the name
  - Intended meaning of proprietary name modifiers
  - Pharmacologic/therapeutic category
- Additional Information About the Product
  - Proposed labeling (if available)
  - Proposed container labels and labeling (if available)

  If labeling not available …
  - Established name
  - Prescription status
  - Dosage form(s)
  - Product strength(s)
  - Proposed indication(s) for use
  - Route(s) of administration
  - Dosage, frequency, interval, max dose
  - Dosing in specific populations
  - Instructions for use
  - Storage requirement
  - How supplied and packaging configuration
- Information About Product Dispensing & Delivery
  - Likely care environment(s) for dispensing and use
  - Delivery system
  - Measuring device
- Applicant's Assessment of Proprietary Name, Packaging, and/or Labeling

FDA Two-Prong Review

Office of Prescription Drug Promotion (OPDP)

Evaluates proposed proprietary names for promotional content.

Does the name contribute to:

- A misleading implication of unique effectiveness or composition
- Overstatement of product efficacy
- Minimization of risk
- Broadening of the product indication
- Unsubstantiated superiority claims

Division of Medication Error Prevention & Analysis (DMEPA)

Safety review.

Prospectively reviews proprietary names, labeling, packaging, and product design prior to drug approval to help prevent medication errors.

Does the name:

- Look or sound like an already approved drug
- Contribute in any other way to increasing risk of medication errors

LASA: look-alike, sound-alike

DMEPA LASA Review

- Look-alike names (orthographic appearance, spelling)
  - Verzali / Nizoral
- Sound-alike names (phonetic appearance, pronunciation)
  - “Fraud” / “Frog”
- Concerns heightened if there are overlapping product characteristics
  - Route of administration
  - Formulation
  - Dosage strength(s)
  - Dose
  - Regimen

Characteristic	Product 1	Product 2
Route	Oral	Oral
Formulation	Tablet	Capsule
Strengths	25, 50, 100 mg	100, 200, 400 mg
Dose	50–100 mg/day	100–400 mg/day
Regimen	BID	QD

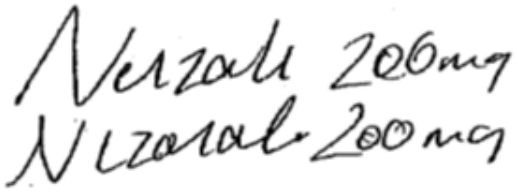
- Phonetic and Orthographic Computer Analysis (POCA) tool to determine the similarity between proposed proprietary name and names in drug references databases

DMEPA NSS Review

- Name simulation studies (NSS)
  - FDA's healthcare professionals simulate use of the proposed name
  - Full range and variety of tasks
    - Prescribing, Transcribing, Dispensing, Administration
  - Real-world conditions
    - Ruled and unruled paper/prescription pads, computer order entry, telephone orders
    - Background noise, handwriting styles, ink colors, voices/accents
    - Proprietary name with corresponding product characteristics (eg, strength, route, dosage, and frequency)

Example of real-world conditions

1. The proposed proprietary name Verzali is orthographically similar to and shares overlapping product characteristics with the currently marketed product, Nizoral. These similarities increase the risk of confusion between these products. The orthographic similarities between Verzali and Nizoral stem from the same length and shape of the names, similarly scripted letters in the beginning of the name ('Ve' vs. 'Ni'), same letter 'z' that appears in the middle of the name and identical 'al' ending of the name (see writing sample below).



In addition to the orthographic similarities, Verzali and Nizoral share identical product characteristics and settings of use that increase the likelihood of a medication error when used in the usual practice setting. These characteristics include strength (200 mg), dose (one tablet/capsule), route of administration (oral), frequency of administration (once daily), and setting of use (retail or hospital). Additionally, because Ketoconazole is a potent Cytochrome P450 3A4 inhibitor, the dispensing and administering of Ketoconazole instead of [redacted] could have serious consequences due to the drug interactions between Ketoconazole and other [redacted] medications.

Case Study: Naming an Extended-Release Product

- Verzali
  - Needs a modifier
  - Confusion with written “Nizoral”
  - “Three options”
  - Vetted: Verzally, Vursalli, Vurzalli, Vurzally
- Verzally
  - Must have a modifier
  - Verzally is preliminarily acceptable, but you might get scooped
- Qucise SR … Qucise XR
  - Submitted with the NDA
  - Potential confusion with Orinase, Precose, and Gralise
- Udaxi XR
  - Orthographic similarity to Adoxa (doxycycline) with overlapping product characteristics
- [redacted] XR
  - Jovaday XR & Bantruza XR vetted as back-up
  - [redacted] XR finally accepted!

Case study

- Requip® (Ropinirol)
  v.
  Risperdal® (Risperidone)

FDA Drug Safety Communication: Medication errors resulting from confusion between risperidone (Risperdal) and ropinirole (Requip)

[06-13-2011] The U.S. Food and Drug Administration (FDA) is alerting the public to medication error reports in which patients were given risperidone (Risperdal) instead of ropinirole (Requip) and vice versa. In some cases, patients who took the wrong medication needed to be hospitalized.

The FDA determined that the factors contributing to the confusion between the two products include:

1. Similarities of both the brand (proprietary) and generic (established) names
2. Similarities of the container labels and carton packaging
3. Illegible handwriting on prescriptions
4. Overlapping product characteristics, such as the drug strengths, dosage forms, and dosing intervals.

Patients who take Requip, Risperdal, or their generic equivalents are reminded to take note of the name and appearance of their medication, know why they are taking it, and to ask questions when the medication appears different than what they expect.

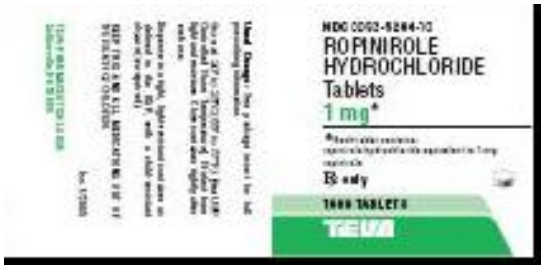
Healthcare Professionals are reminded to clearly print or spell out the medication name on prescriptions and make certain their patients know the name of their prescribed medication and their reason for taking it.

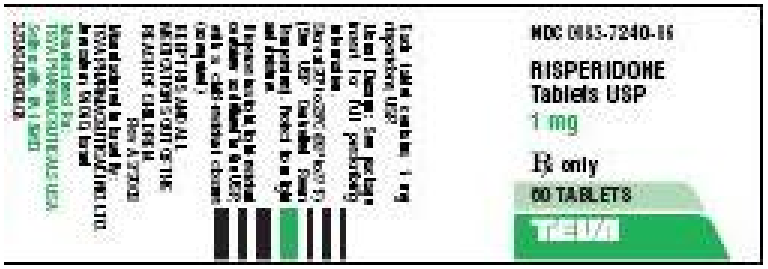
Facts about Risperidone and Ropinirole

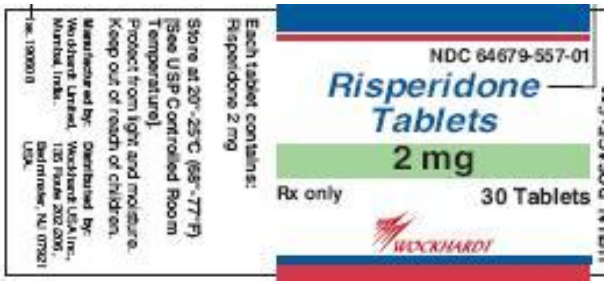
- Risperidone (Risperdal) is an antipsychotic medication used to treat mental illnesses including schizophrenia, bipolar disorder, and irritability associated with autistic disorder.
- Ropinirole (Requip) is a dopamine agonist used in the treatment of Parkinson's disease and Restless Legs Syndrome.

Overlapping Product Characteristics

Characteristic	Requip	Risperdal
Generic name	Ropinirole	Risperidone
Route	Oral	Oral
Dosage form	Tablet	Tablet
Strengths	0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg, 5 mg	0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg
Dose Range	1–24 mg/day	1–16 mg/day
Dosing intervals	QD, BID, or TID	QD or BID







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akidiyoor@impactpharma.com