

DISCOVERY

# Describing the Need: An Ontology End-user Case Study

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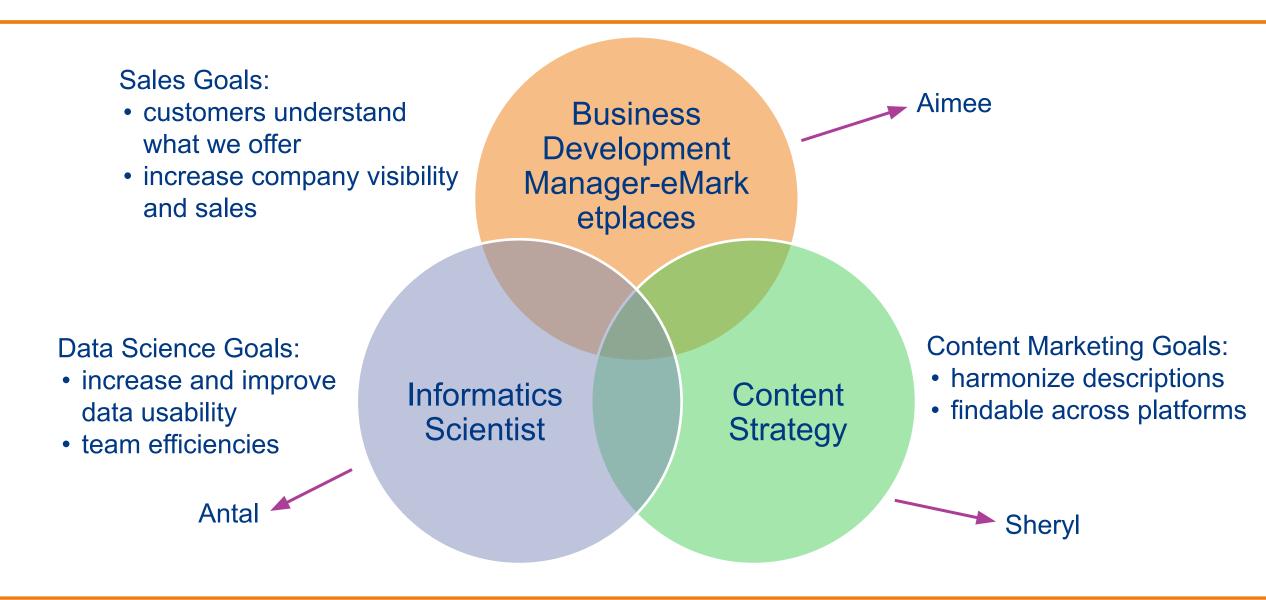
Workshop on Synergizing Biomedical Ontologies
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# Ontology Consumer: Life Sciences Products & Services CRO





## The Challenge of eMarketplaces



- ~1500 provided terms manually curated by 6 employee contributors (Product/Content Managers)
- Tedious effort resulted in a list of 523 terms

- A second, independent pool of 5K terms was provided
- How can we:
  - ✓ reduce manual labor in the curation effort
- obtain only highly relevant results
- not miss important terms

.eukemia Models	Capillary Electrophoresi:	Human Immortalised Cell Ci	Ocular Permeability	Biosensor Assays	Histone Deacetylase (HDAC)
Thrombosis Models	Cell Free DNA Assay	Human iPSC's	Skin Permeability	Bone Resorption Assay	In Vitro Enzyme Activity Assay
Zucker Rat	Digital Polymerase Chai	Human Adult Stem Cells	Vaginal Permeability	Catecholamine Assay	Kinase Assays
Bone Metastases Models	DNA Pull Down Assay	Human MSC's	Cell Fractionation	Cell Based Assays Consultin	Methyl CpG Binding Domain (
Bone Models	DNA-lipid interaction an-	Human HSC's	Compound Distribution	Cell Membrane Lipidomics	Methyltransferase Assays
Cartilage Repair Models	DNase Footprinting Ass	Human DNA	Drug Distribution Studies	Chorioallantoic Membrane (0	Mutase Assays
n Vitro Bone Models	Electrophoretic Mobility		PharmacoScan - A Pharn	Chromium Release Assay	Nitric Oxide Synthase Assays
Osteoarthritis Models	Isothermal Amplification	Human Cell Lysates	Red Blood Cell (RBC) Pa	Ciliary Motility	Oxidase Assays
Osteoporosis Models	Linear DNA Amplificatio		Conjugate Detection	Co-cultivation Microscopy A	Oxygenase Assays
Artery On-A-Chip Platform	Plasmid Retention Assa		Glucuronyltransferase	Co-Culture Angiogenesis As	
Atrial Arrhythmias Models		Human Umbilical Cord Bloo		Coagulation	PDZ Domain Assays
Cardiovascular Metabolics Mod	aPCR Analusis	Human Serum	N Acetul Transferase	Cytokine Release Assay	Peroxidase Assays
Cardiovascular Models	Recombinant Nucleoso	Human Plasma	Sulfotransferase	Cutokines	Phosphatase Assaus
Coronary Artery Disease Models		Human RBC's	CYP Induction	Ecarin Clotting Time (ECT)	Phosphodiesterase Assays
xeGen® LDLR MiniSwine	Threshold DNA Detection	A SECRETARIA DE LA CONTRACTOR DE LA CONT	CYP Inhibition Assau	Factor X Assay	Phosphorylase Assays
	Tissue Microarray	Human PBMC's	CYP Isozyme Mapping	Fibrinogen Assays	Polymerase Assays
n Vitro Hypoxia Models	Whole Genome Amplific		Cutochrome P450s	Glucose Release Assau	Protease Assau
schemia Models	Amplicon - HLA Typing		Corning® HepatoCells	Glucose Uptake	Racemase Assays
Japanese White Rabbit	Amplicon 16s rRNA Seq		Drug Drug Interactions	Hairless Mouse	RNA Methylation Assays
Myocardial Infarction Models	ChIP-sequencing Profili		Phase I Metabolism	High Content Screening	Synthetase Assays
Dssabaw-ptFH3 Patient Model™			Phase II Metabolism	High Throughput Screening	Ubiquitin Ligase Assays
Pulmonary Hypertension Animal		Human amniotic fluid	GI Fluid Stability	Histamine Release Assay	UDP-glucuronosyltransferase
Restenosis Models	Metagenomic Sequencii		Metabolic Stability	In Vivo Angiogenesis Assay	Anaplastic lymphoma kinase j
SHR/NCrl Bat		Human Vitrious Humour	Metabolic Stability in Hep.		Angiopoietin-2 (Ang-2) Assay
					B-Cell Lymphoma 2 (BCL-2) A
/hite Rabbit		Human Sputum	Plasma Stability Assay		Carcinoembryonic Antigen (C
Zecardio		Human gastrointestinal fluid		Lipid Detection	CD134 (OX 40) Assays
Zucker Rat		Human Bone Marrow aspira		Lipid Disorder Screening	CD137 Assays
Acute Kidney Failure Models	TCR Repertoire Sequen			Lipid Kinase Assays	CD20 Assays
Acute Liver Failure Models	Whole Genome Bisulphi		Metabolite Quantification		CD252 (OX 40L) Assays
Acute Lung Injury Models		Human BronchoAlveolar La			CD79b Assays
Critical Care Models	ChIP-sequencing Profilir		Metabolite Synthesis		Checkpoint Kinase-1 (ChK-1) /
mesis Models		Human Bile	NMR Methods	Matrigel Plug Assay	Colony Stimulating Factor 1F
iver Disease Animal Models		Human Saliva	No Label Methods	Metabolomics	Cytotoxic T-Lymphocyte Anti
iver Fibrosis Models	Target Gene Expression		Non Isotopic Labeling		Extracellular signal Regulated
Sepsis Models		Human ceribral spinal fluid ((		Oxidative Burst	Fibroblast Growth Factor Red
lissue Rejection Models	Appropriate the second	Human TMA	Reactive Metabolite	Pathway Mapping	Human Double Minute 2 (HDI
Zucker Bat	Engineered Meganuclea		Reference Standards	Phenotype	Human Epidermal growth fact
Acne Models	THE RESIDENCE OF THE PARTY OF T	Human Brain	Equilibrium Dialysis	Phenotypic Assays	Human Organoids
Atopic Dermatitis Models	Recombinant AAV Med		Protein Aggregation	Platelet Function Testing	Hypoxia-Inducible Factor 1 (HI
Dermatology Models	Transcription Activator I		Protein Binding HPLC	Proteomics	Immuno-oncology Assays
Hair Growth Models	Zinc Finger Nuclease Ge			Reactive Species Assays	Indoleamine 2,3 Di-Oxygenase
Hairless Mouse	Allele Specific Oligonucl		1 Tokeni Dinang Oktanika	Serotonin Release Assay	Kallikrein (KLK)-related Serine
Hairless Rat	Amplified Fragment Len			Sprouting Assay	Killer cell Immunoglobulin-like
n Vitro Skin Models		Human Head and Neck Sam	nles	Stem Cell Differentation Micr	
upus Models		Human Lung	pies		Lymphocyte Activation Gene-
Pruritus (Itch)	Random Amplified Poly				Lysine Specific Demethylase-
Psoriasis Tissue Models	Restriction Fragment Le			Thrombophilia Screening	Mammalian Target of Rapam
Rosacea Models	Artificial Chromosomes				Mesothelin Assaus

## Use An Ontology! But Which One?



~900 ontologies related to biomedical sciences

Search repository <a href="https://bioportal.bioontology.org">https://bioportal.bioontology.org</a>

- cell-based assays
- phenotypic assays

HOW STANDARDS PROLIFERATE:
(SEE: A/C CHARGERS, CHARACTER ENCODINGS, INSTANT MESSAGING, ETC.)

14?! RIDICULOUS!

WE NEED TO DEVELOP

ONE UNIVERSAL STANDARD

SITUATION:

THAT CONTENT TO STANDARD

THERE ARE

14 COMPETING

STANDARDS.

THAT COVERS EVERYONE'S USE CASES.

YEAH!

SOON: SITUATION: THERE ARE 15 COMPETING STANDARDS.

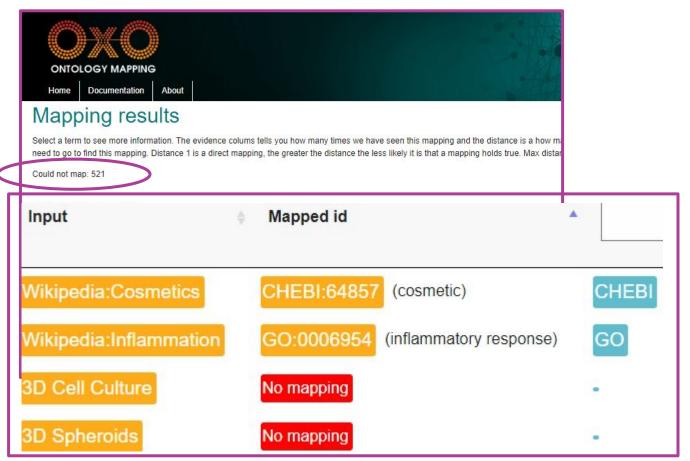
https://xkcd.com/927/

20-30 results, including BioAssay Ontology, SNOMEDCT, GO-PLUS

Where do we go from here?

## Let's Use A Mapping Tool!





- OxO finds cross-references between ontologies, vocabularies and coding standards
- Only 2 out of 523 terms were found: inflammatory response and cosmetic
  - Chemical Entities of Biological Interest (CHEBI)
  - Gene Ontology (GO)

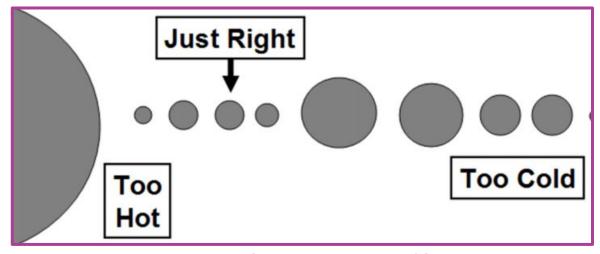
Finding and using the correct ontology is challenging for end users.

Our ultimate goal is to contribute assay data to an ontology that we find helpful.

#### Establish Our Own Search Criteria



- 1. Biology and Users
  - ✓ terms & classes (cell-based assays)
  - fit for commercial purposes
- 2. Complex
  - ✓ Large number of assay terms to cover breadth of offerings from Eurofins Discovery



Baum, Seth. (2013). Journal of Sustainability Education.

- 3. Maintenance
  - Currently active and maintained
  - Identified owners

Interesting, but minimally helpful in getting our work done.

# Get A "Simple" Task Done: Accurately Match Complex Concepts



#### Sample terms to match:

- affinity tag purification
- affinity binding assays
- inflammation assays
- assays for inflammation



- ~500 terms from one eMarketplace against ~5K terms from another
- ~2.5M pair-wise comparisons by eyeballing
- one pair/second...that's about 30 days non-stop

Needs a more analytical approach.

#### **Enter Data Science**



#### Approaches in increasing usefulness

- Eyeball
- Excel VLOOKUP
  - Exact match
  - Approximate match
- NLP
  - Levenshtein distance
  - Cosine similarity

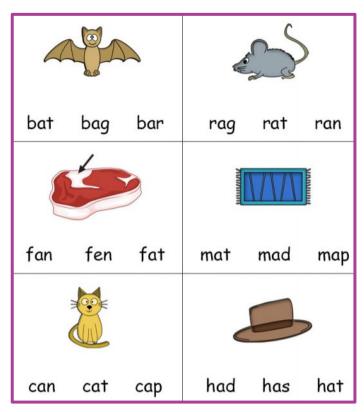
#### A Better Approach than Eyeballs?



#### **Excel VLOOKUP options**

- Exact match matches exact terms well
- Approximate match only looks at matching characters at the beginning of the words
  - catapult and caterpillar will be flagged as matches!

In cases where there are few exact matches, Excel doesn't help much. What about approximate matches?



https://www.myteachingstation.com/

# Approximate Matches Produced by Excel VLOOKUP



Search Term	Approximate Match
Basic Metabolic Profiling	Basic Metabolic Panel
Behavioral Testing Models	Behavioral Phenotyping
Bioequivalence Studies	Biodistribution Studies
BioMAP® Human Phenotypic Platform	Biology
Biomarker Services	Biomarker Discovery
Biomarker Services Consulting	Biomarker Discovery
Biosafety Services	Bioproduct Safety Testing
Biotin Protein Conjugation	Biostatistics & Bioinformatics
Biotin-Antibody Conjugation	Biostatistics & Bioinformatics
Bone Models	Bone Mineral Density Testing

## A Better Approach: Computational String Comparison

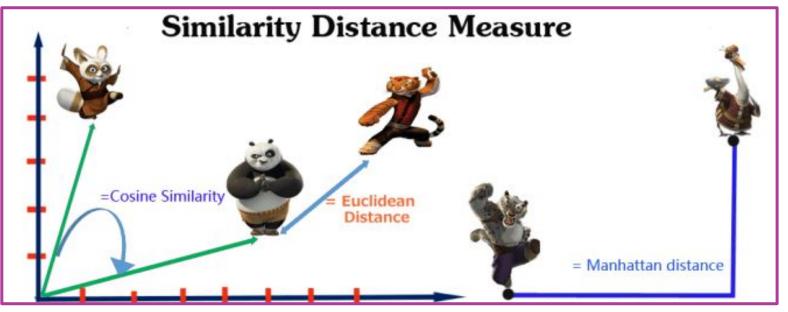


- Comparing words, phrases, terms collectively called strings is a non-trivial task
- Finding exact matches is easy, but finding a degree of similarity between strings is difficult
- A change in a single character can signal a small or a large difference in meaning:
  - Assay : assays similar meaning
  - 3d cell culture : 2d cell culture different meaning
  - Apparently different strings can carry the same meaning: human – homo sapiens

## **Comparison Metrics**



- Various metrics have been developed to measure similarity between terms
- We have used two similarity metrics and compared their usefulness
  - Levenshtein distance
  - Cosine similarity



https://dataaspirant.com/five-most-popular-similarity-measures-implementation-in-python/

#### First Metric: Levenshtein Distance



- The minimum number of single-character edits (insertions, deletions or substitutions)
   required to change one word into the other
- For example, the Levenshtein distance between "kitten" and "sitting" is 3:

- 1. kitten → sitten (substitute "s" for "k")
- 2. sitten  $\rightarrow$  sittin (substitute "i" for "e")
- 3. sittin  $\rightarrow$  sitting (insert "g")



https://en.wikipedia.org/wiki/Levenshtein\_distance





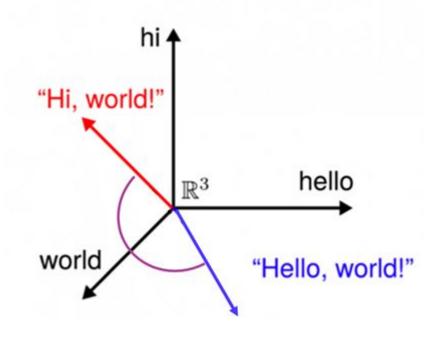
Query Term	Match_1	LSim_1
immunophenotyping	immunophenotyping	0
3d cell culture	2d cell culture	1
caco2 cell line	caco2 cell lines	1
caspase assay	caspase assays	1
cell based assays	cellbased assays	1
gene set enrichment analyses	gene set enrichment analysis	1
human buffy coat	human buffy coats	1
protease assay	protease assays	1
pulmonary hypertension animal m	odel pulmonary hypertension animal mode	ls 1
rna extraction	dna extraction	1
western blots	western blot	1
decarboxylase assays	carboxylase assays	2
facs	aas	2
vitro tme models	vitro eye models	2
sar assays	nab assays	2
aldolase assays	hydrolase assays	3
asthma	asapms	3
bone models	mouse models	3



## Second Metric: Cosine Similarity



- Cosine similarity is a measure of similarity between two non-zero vectors of an inner product space
- It is defined to be equal to the cosine of the angle between the vectors
- "S" is measured in the range 0 to 1
  - Exact match if S = 1
  - Approximate match if 1 > S ≥ 0.5
  - No match if S < 0.5</li>



https://medium.com/@adriensieg/text-similarities-da0 19229c894

## Natural Language Processing for String Similarity Search



- The Python Sklearn package contains algorithms for the necessary code-full
  - Vectorising
  - Natural Language Processing
  - Similarity calculation
  - Ranking
- String similarity was calculated in Python based on article by Dario Radečić

https://towardsdatascience.com/calculating-string-similarity-in-python-276e18a7d33a

# Cosine Similarity: NLP Workflow





https://en.wikipedia.org/wiki/Cosine\_similarity

# Matches Ranked by Term Similarity: Excel Output



Query Term	Match_1	CSim_1	Match_2	CSim_2	Match CSim	Match CSim_	Match CSim	Match CSim
Systemic lupus erythematosus (S	i Systemic Lupus Erythematosus (SLE) Hu	0.816	c Lupus Erythematosus (SLE) Hur	0.816	Systemic L 0.816	Systemic L 0.756	Systemic L 0.632	Lui Anin 0.289
Cancer Systems Biology	Systems Biology	0.816	ational S					v₂ 0.408
Thermal and Acoustic Imaging	Thermal Imaging	0.816	Imaging		Look a	cross		0.408
Thrombosis Models	Thrombosis Animal Models	0.816	odels		Look a	31 0 0 0		<b>⊿r</b> 0.5
Wistar Rat	Wistar Rat Model	0.816	KYOTO Rat Model	0.707	Rat Models 0.5	BDIX/Orlled 0.408	Custom Ra 0.408	KnIn F 0.408
Zucker Rat	Zucker Rat Model	0.816	lels	0.5	BDIX/Orlloc 0.408	Custom Ra 0.408	Knock-In F 0.408	Knockout F 0.408
Inflammatory Pain Models	Acute Inflammatory Pain Animal Models	0.775	Inflammatory Pain Animal Models	0.775	Custom Pa 0.577	Neuropathi 0.577	Nociceptive 0.577	Postoperat 0.577
In Vivo Whole Tissue and Animal I	Animal in vivo Imaging	0.775	/hole Brain Imaging	0.671	Animal Who 0.671	Small Anim 0.6	Animal Imag 0.516	Animal Tiss 0.516
Non GLP Large Molecule Bioana	Large Molecule Bioanalysis	0.775	olecule Bioanalysis	0.516	Bioanalysis 0.447	Bead-Base 0.316	GLP Auditii 0.316	Plasma Bio 0.316
Non GLP Small Molecule Bioanal	Small Molecule Bioanalysis	0.775	olecule Bioanalysis	0.516	Bioanalysis 0.447	Bead-Base 0.316	GLP Auditii 0.316	Plasma Bio 0.316
Amino Acid Analysis (AAA)	Amino Acid Substitution Analysis	0.75	ino Acid Analysis	0.75	Hydrolyzed 0.75	Bile Acid Ar 0.577	Fatty Acid / 0.577	Nucleic Ac 0.577
Copy Number Variant Analysis	Gene Copy Number Analysis	0.75	y Variant Analysis	0.577	Genetic Va 0.577	5-Batch Ar 0.354	Analysis of 0.354	Biomarker / 0.354
Gene Set Enrichment Analyses	Gene Set Enrichment Analysis	0.75	nnotation	0.354	Gene Char 0.354	Gene Fragi 0.354	Gene Knoc 0.354	Gene Syntl 0.354
Antibody Efficacy Testing In Vivo	In vivo Drug Efficacy Testing	0.75	y Testing	0.707	Ex vivo Dru: 0.671	Antimicrobi 0.577	In vivo Antit 0.577	In vivo Bios 0.577
LPS Lung Inflammation Models	Lung Inflammation Animal Models	0.75	flammation Models	0.577	Inflammatic 0.577	Acute Inflat 0.5	Chronic Infl 0.5	LPS-Induc 0.5
	Monoclonal Antibody (mAb) Developmen	0.75	y Development	0.707	Therapeuti 0.671	BiTE Antibo 0.577	Polyclonal 0.577	Monoclona 0.5
	Pulmonary Hypertension Animal Models	0.75	ne Animal Model	0.577	Diuresis An 0.577	Hypertensi 0.577	Animal Mod 0.5	Animal Moc 0.5
In Vivo Whole Tissue and Animal I		0.707	/hole Brain Imaging	0.612	Animal Who 0.612	Tissue Ana 0.577	Small Anim 0.548	AFM Imagir 0.471
Circulating Antibody Assay Devel		0.707	evelopment	0.707	Antibody S 0.577	Assay Deve 0.577	Biochemic 0.577	Biomarker / 0.577
Antibody and Protein Products H	I A SECULIA DE LA CONTRA DELIGIA DE LA CONTRA DELIGIA DE LA CONTRA DE	0.707	v Protein Sequencing	0.577	Membrane 0.5	Alginate Pr 0.354	Antibody C 0.354	Antibody C 0.354
Autoimmune disease	Autoimmune Disease Animal Models	0.707	Models of Disease	0.408	Celiac Dise 0.408	In vitro Dise 0.408	Infectious [ 0.408	Lyme Disea 0.408
Autoimmune Models	Autoimmune Disease Animal Models	0.707	ental Autoimmune Encephalomye	0.577	Experiment 0.577	Experiment 0.577	Avian Mode 0.5	Chicken Mc 0.5
BALB/c mouse	BALB/c Inbred Mouse Model	0.707	nu/nu Mouse Model	0.707	Mouse Mod 0.5	Mouse Phe 0.5	A/J Mouse 0.408	Agouti Mou 0.408
Sample Bioanalysis	Bioanalysis	0.707	ased Bioanalysis	0.5	Plasma Bio 0.5	Sample Pa 0.5	Sample Re 0.5	Clinical Sar 0.408
Chemokine Biomarkers	Biomarkers	0.707	Biomarkers	0.5	Serum Bior 0.5	Pharmacoc 0.408	1,25-Dihyd 0	10X Genori 0
Cytokine Biomarkers	Biomarkers	0.707	Biomarkers	0.5	Cytokine Ar 0.5	Serum Bior 0.5	Cytokine R 0.408	Cytokine St 0.408
Translational Biomarkers	Biomarkers	0.707	Biomarkers	0.5	Serum Bior 0.5	Pharmacoc 0.408	Translation 0.354	1,25-Dihyd 0
Metastasis Models	Bone Metastasis Animal Models	0.707	odels	0.5	Chicken Mc 0.5	Insect Mod 0.5	Invertebrati 0.5	Mammaliar 0.5
CRISPR	CRISPR Bioinformatics	0.707	Clonina	0.707	CRISPR Sc 0.707	CRISPR D∈ 0.577	CRISPR sg 0.577	Custom CR 0.577
Custom Antibodies	Custom Affinity Purification of Antibodies	0.707	Manufacturing	0.5	Custom Mic 0.5	Custom Prc 0.5	Llama Antit 0.5	Custom An 0.408
Model Development	Custom Cell Model Development	0.707	ic Animal Model Development	0.707	Algorithm C 0.5	Antibody D 0.5	App Develo 0.5	Assay Deve 0.5
Pain Models	Custom Pain Animal Models	0.707	Ne pathic Pain Animal Models	0.707	Nociceptive 0.707	Postoperat 0.707	Visceral Pa 0.707	Acute Inflar 0.632
Cutotoxicitu	Cytotoxicity Assays	0.707	Real-Time Cytotoxicity Assay	0.577	Medical De 0.5	Natural Kille 0.447	1,25-Dihyd 0	10X Genorr 0
Electroporation Transfection	Electroporation	0.707	Transfection	0.707	Chemical T 0.5	In utero Ele 0.5	Microinject 0.5	Neuronal E 0.5
Endocrine Models	Endocrine Disease Animal Models	0.707	Avian Models	0.5	Chicken Mc 0.5	Insect Mod 0.5	Invertebrati 0.5	Mammaliar 0.5

## Cosine Similarity Approximate Matches Work Fairly Well



Query Term	Match_1		CSim_1	Match_2	CSim_2	
Acetyltransferase Assays	Acetyltransferase Assays		1	Histone Acetyltransferase (HAT) Assays	0.707	
Activity Prediction	Activity Prediction		1	Animal Antiplasmin Activity	0.408	
Acute Kidney Failure Models	Acute Kidney Failure M	odels	1	Acute Liver Failure Animal Models	0.671	
wound healing	In vitro Wound Healing	ealing Assay 0.707	0.707	Wound Healing Animal Models		
In Vivo Efficacy	In vivo Drug Efficacy Testing		0.707	Ex vivo Drug Efficacy Testing	0.632	
LCMS Analysis		LC-MS	LC-MS			
Multidrug Resistance		Multidrug Resistance (MDR) Testing			.707	
DNA Mutagenesis		Mutagenesis			.707	
Membrane Permeab	ility (PAMPA)	Parallel A	Artificial N	Membrane Permeability A:	.707	
Respiratory Models	Respiratory Disease An	imal Models	0.707	Avian Models	0.5	
Cardiovascular Toxicology	Toxicology		0.707	Computational Toxicology	0.5	
Cell Transfection	Transfection		0.707	B Cell Count	0.5	
RNA Interference	Vector Based RNA Interference		0.707	Human RNA	0.5	
Human Primary Cell Disease Model Human Primary Cell Isol		lation	0.671	Animal Models of Disease	0.516	
Small Cell Lung Cancer Models	Lung Cancer Animal Models		0.671	Lung Small Cell Xenograft	0.671	
Adherent Cell Culture	2D Cell Culture		0.667	Actinomycete Cell Culture	0.667	
Method Development and Validation	Analytical Method Deve	elopment	0.667	Analytical Method Validation	0.667	
Disseminated Disease Models	Animal Models of Disease		0.667	In vitro Disease Models	0.667	
Annexin V Apoptisis Assay	Annexin V Staining Assay		0.667	1,25-Dihydroxyvitamin D Assay	0.408	
Basic Metabolic Profiling	Basic Metabolic Panel		0.667	Compound Profiling	0.408	
Brain Tumor Mouse	Brain Tumor Models		0.667	Brain Xenograft	0.408	
	Caco-2 Cell Line Caco-2 Cell Lines					

In the best match column (Match\_1)

Out of 523 terms:

- ~20% exact matches
- ~60% approximate matches
- ~20% unresolved

with this particular contributor group

#### Where Are We Now, As Users?



Finding and using the correct ontology is challenging.

Our ultimate goal is to contribute assay data to an ontology that we find helpful.

- Many biomedical ontologies relevant for cellular assays exist
- Excel is excellent for matching exact terms but poorly matches anything beyond that
- Cosine similarity for string matching works well for approximate matches
- People are still needed for curation
  - A key term, phenotypic screening, missing from the list of 5K terms was added
  - Irrelevant terms (12 %) included by the similarity scoring method were removed

## Could We Have Used A Different Ontology Mapping Tool?



- Short time frame and resources to complete the project
- We have little expertise with ontologies
- Although there are free ontology mapping tools online...
  - ...the terms we worked with we think were not encompassed by any ontology





#### What If...



- Categories & terms were equally understood / meant the same thing to contributors of diverse backgrounds?
- eMarketplaces were educated about ontologies & established adherence to controlled ontologies?
- Terms were harmonized across content platforms beyond eMarketplaces?
  - assay descriptions
  - web content
  - file properties and keyword tags

