Development of a Semi-Automated Study Quality Assessment Reporting and Evaluation (SQuARE) Tool and Framework for Evaluating Toxicological Datasets

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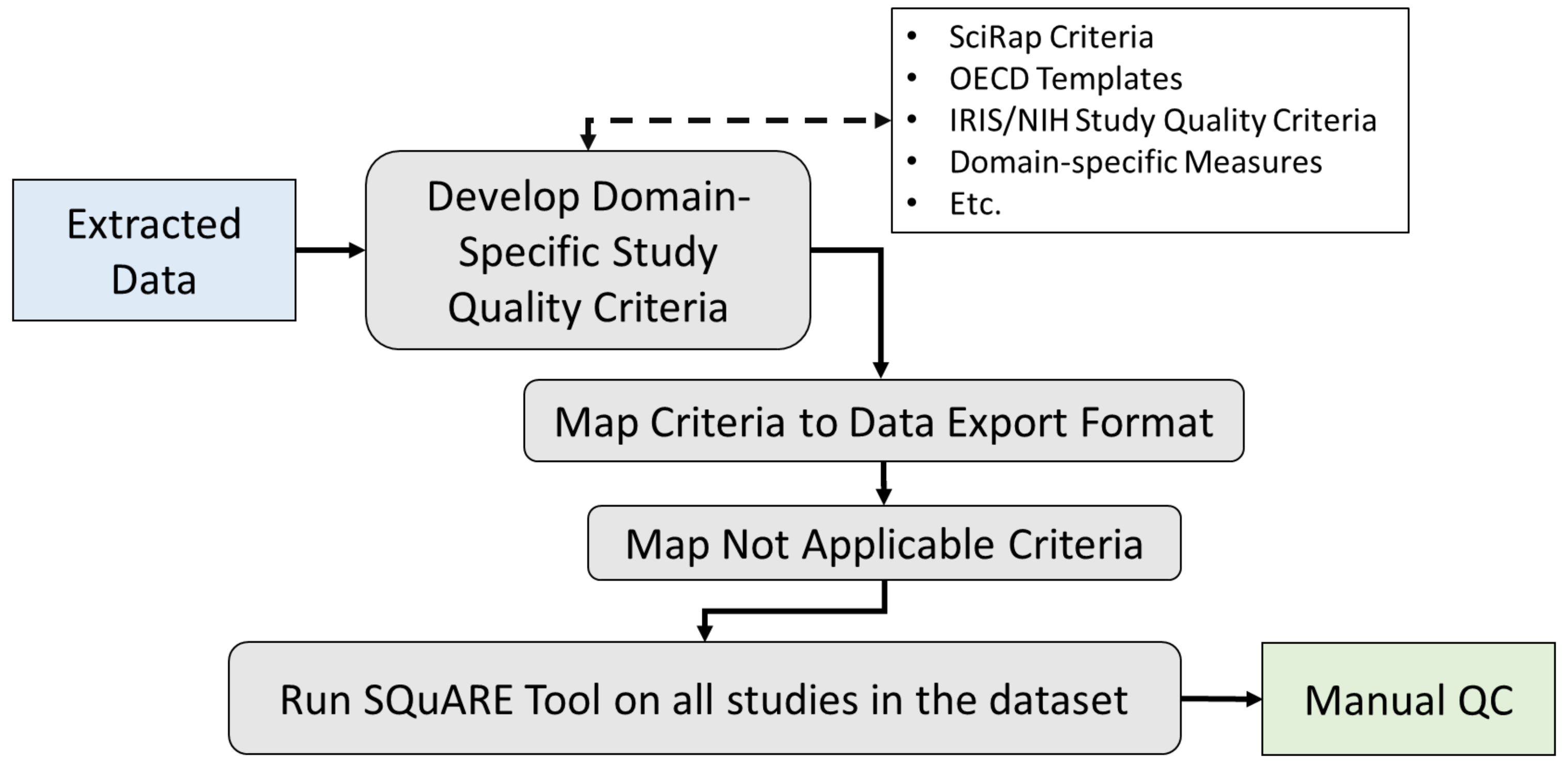
Introduction

- Evaluating individual study quality typically involves human experts assessing data against broad, variable reliability criteria and results in individual judgment calls that are highly specific and is one of the most time-intensive components of the systematic literature review process
- Because study quality evaluation often relies upon data which have been previously extracted, the opportunity exists to computationally assess study quality criteria when the data are properly integrated
- However, a key challenge to successful automation is the development of workflows that allow bench-level domain experts to identify and express the data criteria components necessary in a computer-readable format
- To this end, we present the Study Quality Assessment and Reporting Evaluation (SQuARE) Tool, a simplified, semi-automated framework to integrate extracted data and flexibly evaluate it against any quality criteria needed for a given project in a domain agnostic manner
- In addition to increased consistency across evaluations, the SQuARE tool has the potential to significantly reduce time and labor across fields engaging in systematic literature review, as well as those assessing the reporting quality of already- extracted datasets and databases

Overview

- The SQuARE tool uses Python 3.6, Excel™, and extracted data (e.g., Excel Files) to provide a flexible, domain-agnostic platform for assessing the reporting quality of extracted datasets based on user-defined criteria



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Workflow

1. Develop Domain-Specific Study Quality Criteria

Source	Category	Criteria
SciRap	Test Compound	The chemical name or other identification, such as CAS-number, of the test compound was given.
SciRap	Test Organism(s)	The animal model (species, strain, age/life stage and, sex) was described
CRED	Exposure Conditions	The route of administration was stated
SciRap	Data Analysis	The statistical unit, e.g. the individual or the litter, was stated
CRED	Data Analysis	The statistical methods and software used were described
SciRap	Study Parameters	Any competing interests were disclosed or it was explicitly stated that the authors did not have any competing interests

2. Populating Tool Template

Answer Types	Boolean
num_entries	AND
string_match	OR
contains_string	

Data Output Level
One response per Study Design
One Response per Experiment

Answer Mappings
Fulfilled
Partially fulfilled
Not fulfilled
Not applicable

Category
Test Compound & Controls
Assay System & Dosing
Data Reporting
Test Organism

Data Columns: Experiment	Data Columns: Results/Outcomes
Study design short name	Experiment
Study location	Chemical Name
Test Organism Source	Sample subgroup
Organism Species	Data Categorization
Organism Sex	Effect
Strain	Endpoint Type (i.e. summary metric)
Exposure Type	Endpoint - Value
Exposure Media Type	Endpoint Unit
Habitat Description	Measurement Variability
Age at first dose	Variability Unit
Age Units	Response modifier
Exposure Duration	Effect Concentration
Units of exposure duration	Concentration Unit
Number of replicates per treatment	How many doses were tested?
Replicate Units	Timepoint
Number of treatment groups	Reported how?
Number of individuals in replicate	Where in the paper is this data found?
Dosing Frequency	Results Summary
Reviewer/Extractor Comments	Comments

- Specify criteria answer types, output parameters, and data output level (e.g., chemical-level criteria that may be answered multiple times)
- Specify headers in the extracted data file for the tool to reference

3. Map Criteria to Data Output Format

Category	Output Level	Evaluation Question	Answer mapping	Criteria 1				Criteria 2 Question				Criteria Combination
				Question	Answer Type	Answer Options	BOOLEAN	Question	Answer Type	Answer Options		
Assay System & Dosing	1- One response per Study Design	Study location was reported?	Fulfilled	Study location	num_entries	Is answered	-	-	-	-		Criteria 1
Test Compound & Controls	2- One Response per Experiment	Is the solubility of the test compound stated?	Fulfilled	Solubility	num_entries	Is answered	-	-	-	-		Criteria 1
Test Compound & Controls	2- One Response per Experiment	It was stated that a reference compound or positive control was included?	Fulfilled	Role in Experiment	string_match	Positive Control, Antagonist	OR	-	-	-		Criteria 1
Test Organism	1- One response per Study Design	The test species was described (species, strain, source)?	Fulfilled	Organism Species	num_entries	Is answered	-	Test Organism Source	num_entries	is answered	...	[Criteria 1] AND [Criteria 2]
Test Organism	1- One response per Study Design	The test species was described (species, strain, source)?	Partially fulfilled	Organism Species	num_entries	Is answered	-	Test Organism Source	num_entries	is answered	...	[Criteria 1] OR [Criteria 2]
Test Organism	1- One response per Study Design	The test species was described (species, strain, source)?	Not fulfilled	Organism Species	string_match	Not Reported	-	Test Organism Source	string_match	Not Reported	...	[Criteria 1] OR [Criteria 2]

Extracted Dataset

Refid	Study Design Short Name	Study location	Test Organism Source	Organism Species	Organism Sex	Exposure Type	Exposure Media Type
990552	fathead minnow 14d	Laboratory	Lab Colony	Fathead	Both	Aqueous	Lake Superior water
990552	fathead minnow 14d	Laboratory	Lab Colony	Fathead	Both	Aqueous	Lake Superior water
990552	fathead minnow 14d	Laboratory	Lab Colony	Fathead	Both	Aqueous	Lake Superior water
990552	fathead minnow 14d	Laboratory	Lab Colony	Fathead	Both	Aqueous	Lake Superior water
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990552	fathead minnow 14d	Laboratory	Lab Colony	Fathead	Both	Aqueous	Lake Superior water

- Complete the mapping process for all criteria (i.e., what answers are required in each data field to make each criteria "fulfilled" or "partially fulfilled" and where is it located in the data export?)
- Each question can be made up of up to 4 different data criteria, with different answer options
- Use the "Not Applicable Mapping" option to designate when questions become not applicable and therefore should not contribute to the quality score
- Following the mapping process, outputs are generated in a streamlined and reviewed process

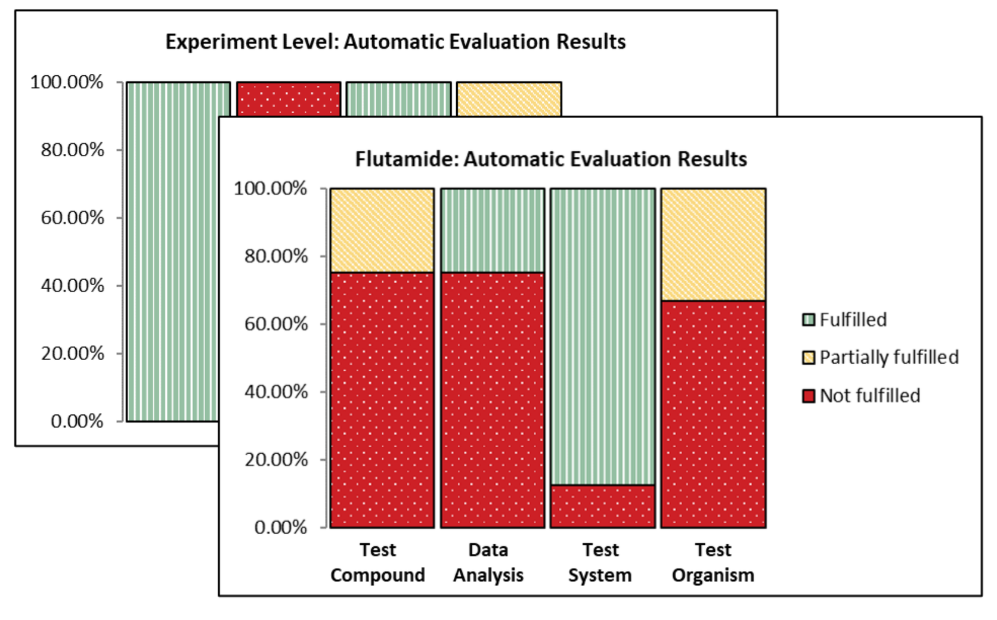
This question	is not applicable	if this question		is answered as...	
Data Export Column	Criteria Answer	Data Export Column	Answer Type	Answer Options	Boolean
Cell line	Not Applicable	In vitro test system type	contains_string	tissue, organ	OR
Type of genetic mutation	Not Applicable	native or mutated receptor?	contains_string	native receptor	

Reading Tool Outputs

(Level) Category	Evaluation Criteria	Evaluation Result
(1) Administration of test compound	Duration of treatment period was provided?Fulfilled: [Criteria	
	Fulfilled: Criteria 1: 3b_relevantexperimentsinventory - Q25.	
	Total	
(Level) Category	**Evaluation Criteria**	
(1) Funding and competing interests	Any competing interests were disclosed or it was explicitly stated tha	Not fulfilled
	Fulfilled: Criteria 1: 3b_relevantexperimentsinventory - Q30. compet	Not fulfilled
	The funding sources for the study were stated?Fulfilled: [Criteria 1]	Not fulfilled
	Fulfilled: Criteria 1: 3b_relevantexperimentsinventory - Q29. funding	Not fulfilled
	Total	0
(Level) Category	**Evaluation Criteria**	**Evaluation Result**
(1) Test System	Conditions (Inclubation temperature, humidity, CO2 concentration, e	Fulfilled
	Fulfilled: Criteria 1: cell experiments inventory subform - Q1. identifi	Fulfilled
	The androgen receptor source and characteristics(recombinant, nativ	Fulfilled
	Fulfilled: Criteria 1: 3b_relevantexperimentsinventory - Q17. invitro:	Fulfilled
	The tests and/or methods used were sufficiently described to allow f	Not fulfilled
	Fulfilled: Criteria 1: 3b_relevantexperimentsinventory - Q2. reportin	Not fulfilled
	Partially fulfilled: Criteria 2: 3b_relevantexperimentsinventory - Q3.	Partially fulfilled
	Total	7
(Level) Category	**Evaluation Criteria**	**Evaluation Result**
(1) Test compound and controls	Concentration of vehicle was provided?Fulfilled: [Criteria 1 AND Crite	Partially fulfilled
	Fulfilled: Criteria 1: experimental run information a - Q2. what role is	Not fulfilled
	Fulfilled: Criteria 2: experimental run information b - Q4. concentrati	Fulfilled
	Total	0.5

Refid: 1299720
Experiment: AR Fathead Minnow In Vitro Binding

Fulfilled	1
Partially fulfilled	0.5
Not fulfilled	0
Not applicable	



- Using data mapping and SciRap outputs as a model, the SQuARE tool automatically assesses all extracted studies, providing an overall quality summary and easily interpretable summary figures

Conclusions & Future Directions

- The SQuARE tool provides a semi-automated, user-friendly framework for assessing the quality of extracted studies in a consistent and time-effective manner
- This work represents a first step in the process of engineering features for automating the evaluation process using machine learning
- The domain-agnostic nature of the tool is amenable for potential utilization across numerous fields of study and efforts to apply the tool to diverse uses cases are underway
- Upon completion of tool development, it will be integrated to the extent possible within existing EPA databases and tools

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