

# Adverse Event Workshop, ICBO 2011

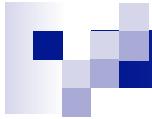
## AEO: a realism-based biomedical ontology for the representation of adverse events

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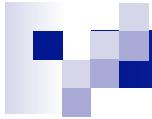
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# Adverse Event Representation Systems

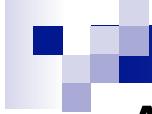
- COSTAR: (COding Symbols for Thesaurus of Adverse Reaction), later replaced by MedDRA
- MedDRA: Medical Dictionary for Regulatory Activities
- CTCAE: Common Terminology Criteria for Adverse Events, by USA National Cancer Institute (NCI)
- WHO-ART: WHO's Adverse Reaction Terminology
- All are controlled terminologies
- None of these is a biomedical ontology.



# AEO: Adverse Event Ontology

- Aim: Represent adverse events by following OBO foundry principles, with an aim to support automated reasoning
- Methods: a realism-based approach – based on reality instead of concepts
- OBO foundry principles, e.g.: openness, collaboration, shared syntax
- URL: <http://www.aeo-ontology.org>

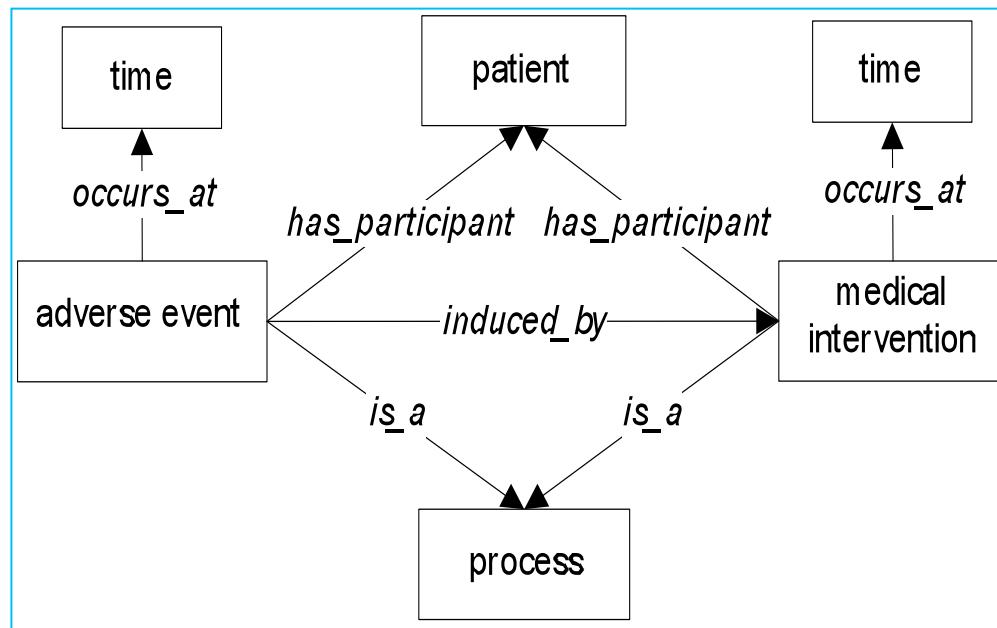
**Refs:** (1) Ceusters W, Smith B. A Realism-Based Approach to the Evolution of Biomedical Ontologies. URL: <http://ontology.buffalo.edu/bfo/Versioning.pdf>  
(2) Smith B, etc. The OBO Foundry: coordinated evolution of ontologies to support biomedical data integration. Nat Biotechnol. 2007 Nov;25(11):1251-5.



# Adverse Event (AE) Development Particulars

- Particulars in AE modeling:
  - #1: a medical intervention (e.g., vaccination, drug administration)
  - #2: a patient
  - t1: the time at which the medical intervention is given to the patient
  - #3: a clinically abnormal process (e.g., a fever process)
  - t2: the time at which the clinically abnormal process happens
- *adverse event* and *medical intervention* are subclasses of BFO *processual\_entity*
- *adverse event incubation time* =  $t2 - t1$

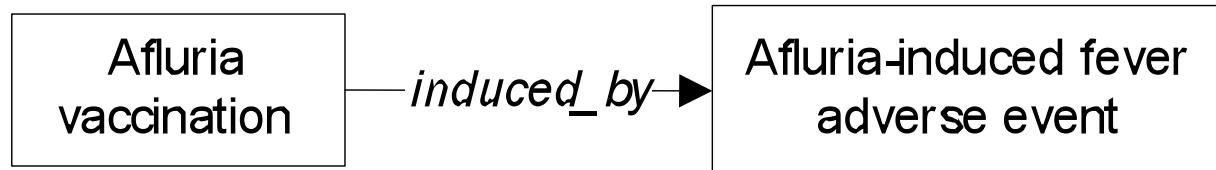
# Basic AEO Adverse Event Design Pattern

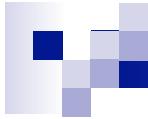


- OGMS *pathological bodily process*: A bodily process that is clinically abnormal.
- AEO defines an AE as “a pathological bodily process that is **induced** by a medical intervention”.

# Causal relation in the AE definition in AEO

- AEO defines a causal relation between an adverse event and a medical intervention.
- New relation '*induced\_by*': a causal relation between the referents of two process terms.
- Example:





# AEO: Adverse Event Ontology

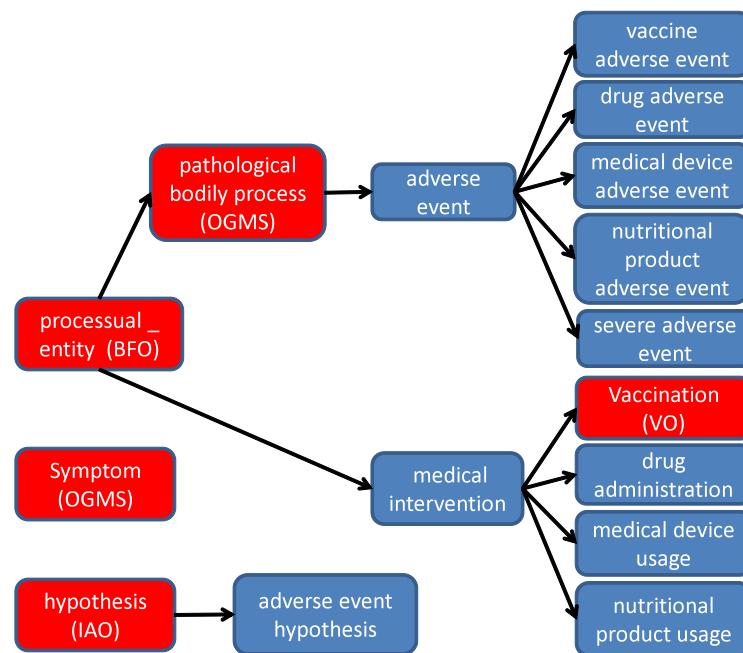
- Ontology terms in AEO or imported from existing ontologies:

Ontology Names	Classes	Object properties	Total
AEO (Adverse Event Ontology)	368	1	369
BFO (Basic Formal Ontology)	39	0	39
RO (Relation Ontology)	6	25	31
IAO (Information Artifact Ontology)	2	0	2
OBI (Ontology for Biomedical Investigations)	8	3	11
OGMS (Ontology for General Medical Science)	5	0	5
VO (Vaccine Ontology)	19	3	22
NCBITaxon (NCBI Taxonomy)	5	0	5
<b>Total</b>	<b>452</b>	<b>32</b>	<b>484</b>

- Importing external ontology terms using OntoFox:  
<http://ontofox.hegroup.org>

# AEO: Adverse Event Ontology

## ■ Key representational units in AEO.



\* Red boxes contain imported terms, and blue boxes are AEO-specific terms

## ■ AEO currently includes four different types of AEs based on four different medical interventions.

# AEO Aims to serve as an AE Knowledgebase

## ■ Example: Flu vaccine Afluria-induced AEs:

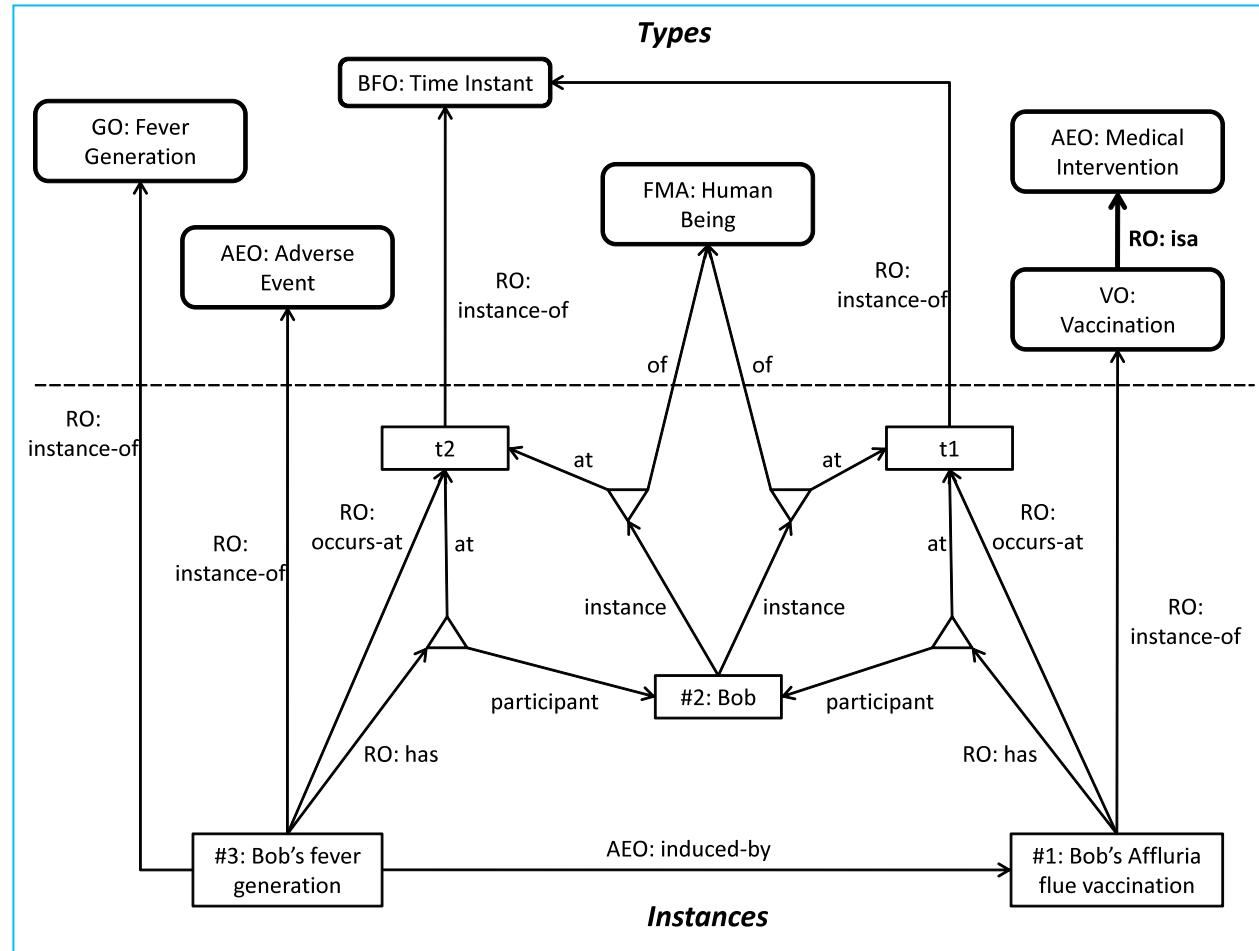
### -----ADVERSE REACTIONS-----

- In adults, the most common ( $\geq 10\%$ ) local (injection-site) adverse reactions were tenderness, pain, redness, and swelling. The most common ( $\geq 10\%$ ) systemic adverse reactions were headache, malaise, and muscle aches. (6)
- In children, the most common ( $\geq 10\%$ ) local (injection-site) adverse reactions were pain, redness, and swelling. The most common ( $\geq 10\%$ ) systemic adverse reactions were irritability, rhinitis, fever, cough, loss of appetite, vomiting/diarrhea, headache, muscle aches and sore throat. (6)
- Administration of CSL's 2010 Southern Hemisphere influenza vaccine has been associated with increased postmarketing reports of fever and febrile seizures in children predominantly below the age of 5 years as compared to previous years. (6)

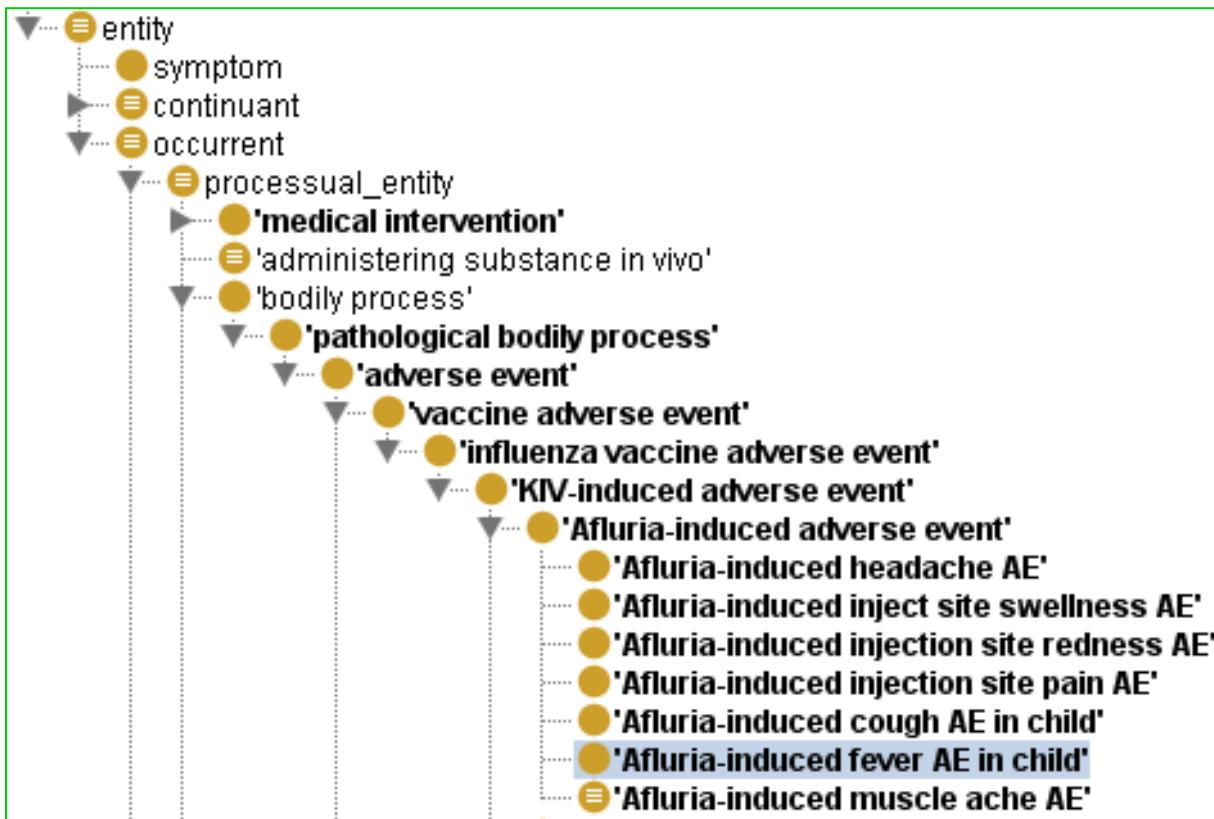
**Refs:** FDA Afluria Product Information

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM220730.pdf>

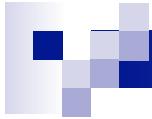
# Example: Modeling of Afluria vaccination-induced fever adverse event in AEO



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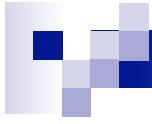
The knowledge of Afluria vaccination-induced fever adverse event is now stored in AEO



# Logical definition of AE in AEO

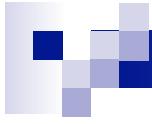
- Medical intervention: a process in which independent continuants (e.g., anatomical parts of human body) participate in.
- After intervention, bodily processes go on with at least one continuant involved in intervention.
- 'induced' indicates existence of a causal chain.
  - P1: C1, C2, C3
  - P2: C2, C4, C5
  - P3: C5, C6, ...

where Px means a process, and Cx is an independent continuant
- Likely intermediate steps, and processes that do not 'share' at least one continuant.
- So mere temporal precedence is not enough.



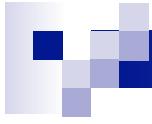
# AEO and AERO (AE Reporting Ontology)

- Three major differences:
- In AERO, no causal relation is assigned.
- In AERO, AE is a child term of *ogms:sign*: "A *quality* of a patient, a *material entity* that is part of a patient, or a *processual entity* that a patient participates in, any one of which is observed in a physical examination and is deemed by the clinician to be of clinical significance."
  - too broad since all AEs are processes
  - too narrow because not all AEs are observed.
- AERO focuses on AE reporting → not an AE knowledgebase. AEO is a AE knowledgebase



## AE vs. AE Hypotheses

- AEO's requirement of a causal relation between an adverse event and a medical intervention is an important and novel point which removes a lot of ambiguity.
- The causal requirement is the major aspect in which AEO differs from others, e.g., AERO.
- Data in an AE reporting system is used to generate hypotheses on causal effects.
- Such a hypothesis is represented in AEO as an *adverse event hypothesis*



# Acknowledgements

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AEO website:  
<http://www.aeo-ontology.org>