NTP
National Toxicology Program

Introducing OBI and CEBS

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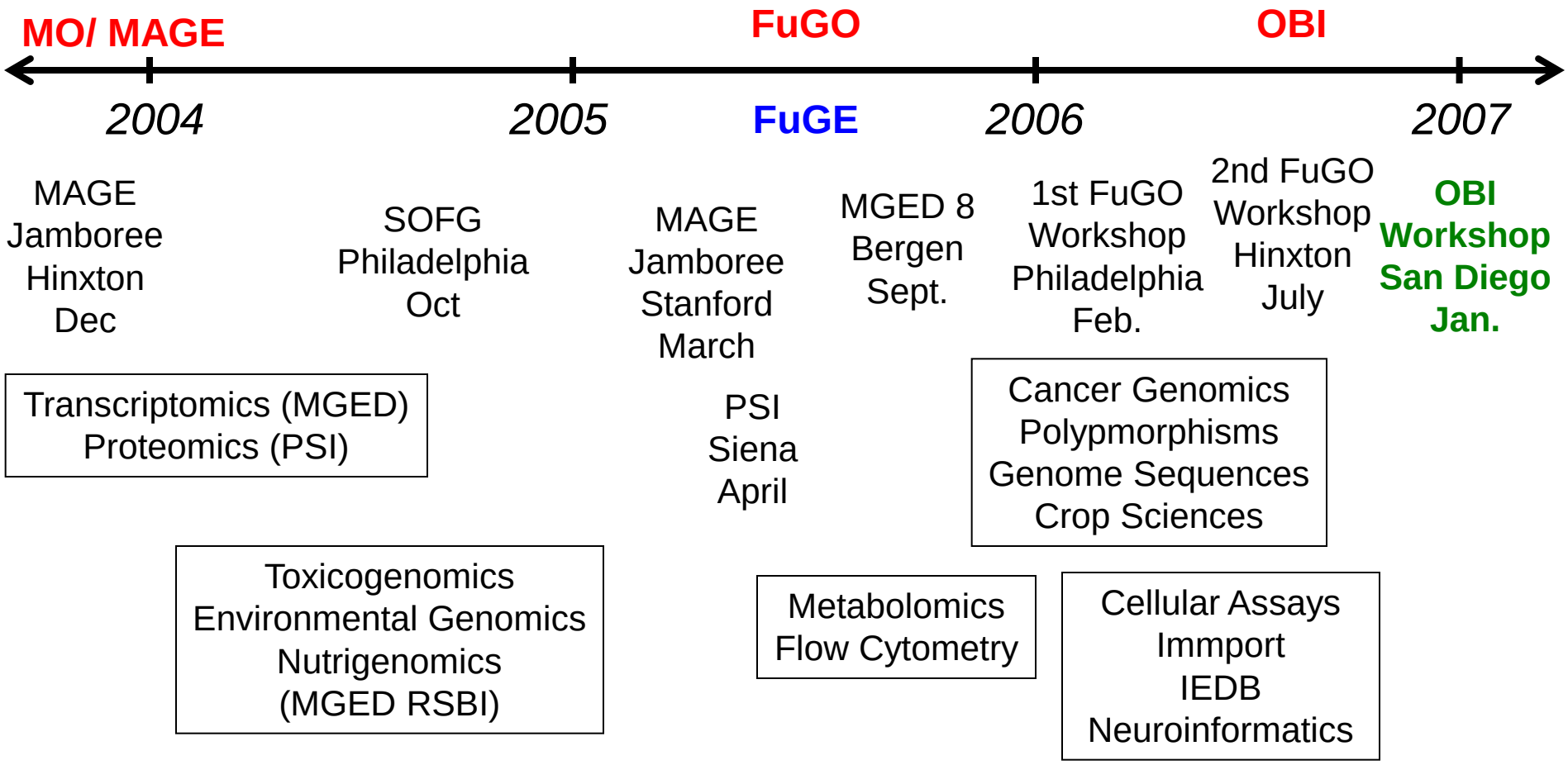
US National Toxicology Program
26 October 2011

OBI: The Ontology for Biomedical Investigations

- 19 communities that recognized they were trying to solve the same / related problems
- Members typically have one or more applications that drive OBI development
- 6 year effort, 1-2 phone calls per week, 1-2 meetings per year
- first stable release (Philly / 1.0) in Oct. 2009

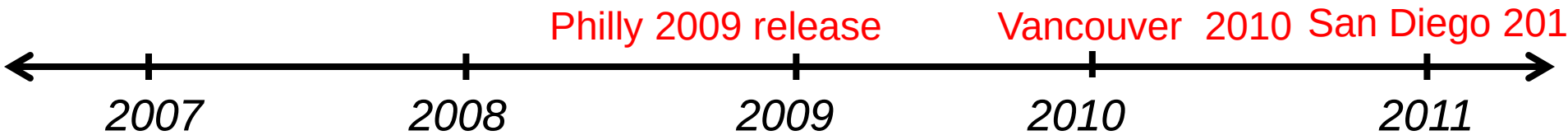
→ Open project with constant addition of new communities, please consider joining!

OBI Timeline



From Jan, 2007 OBI workshop in LIAI

OBI Timeline



Workshops: Bethesda Vancouver EBI EBI Philly Vancouver
San Diego

DENRIE -> IAO

OBO Foundry

MIREOT

J Biomed Sem.

Bio-imaging,
Clinical Investigations,
Electrophysiology,
Structural Biology

Robot Scientists

Vaccines

Eagle-i

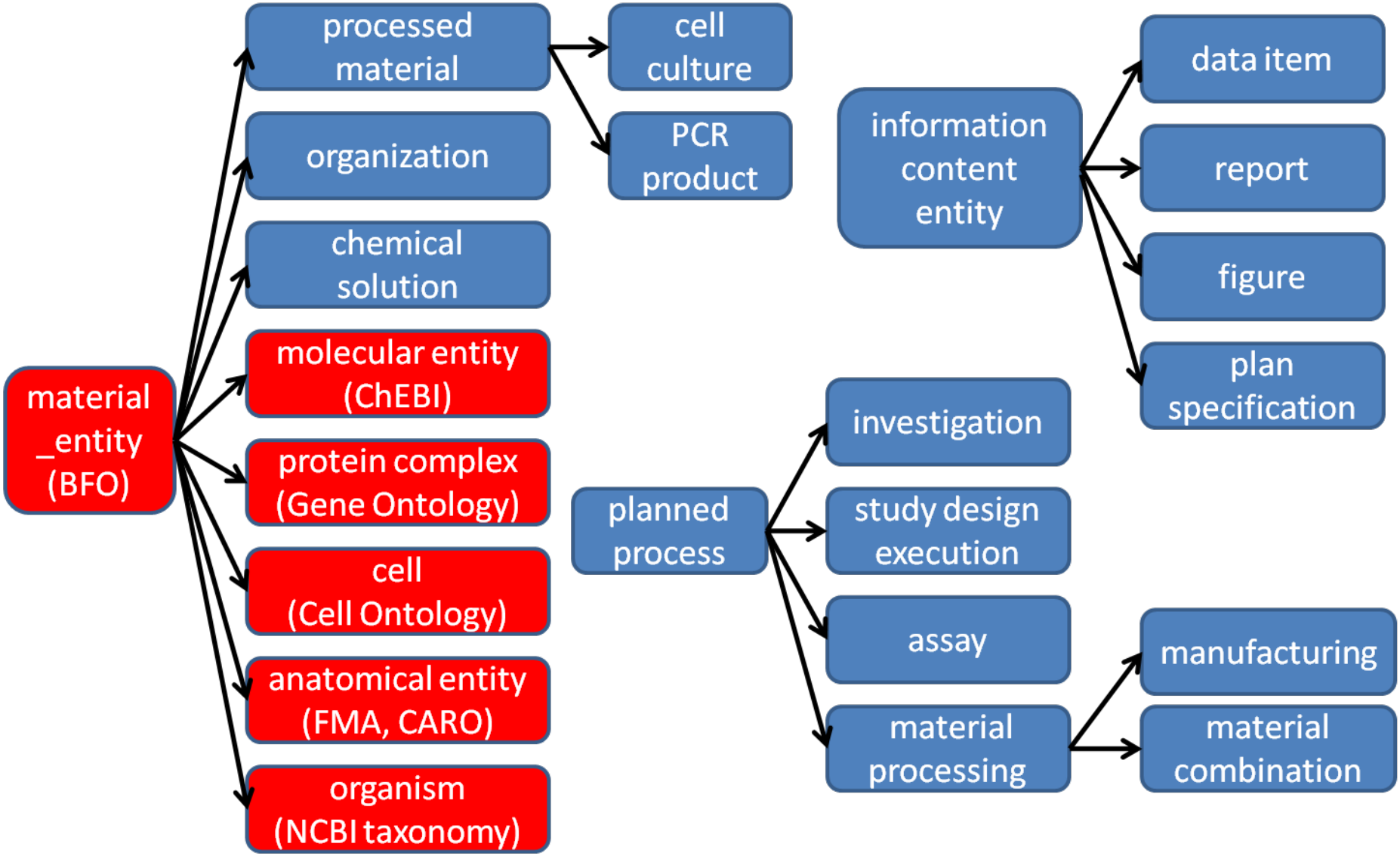
material entity

- merged bfo:object, object part, object aggregate
- import ‘natural biomaterials’ (MIREOT mechanism),
  e.g. organism (NCBI taxonomy), anatomical entity (FMA), molecular entity (ChEBI)

OBI’s primary scope

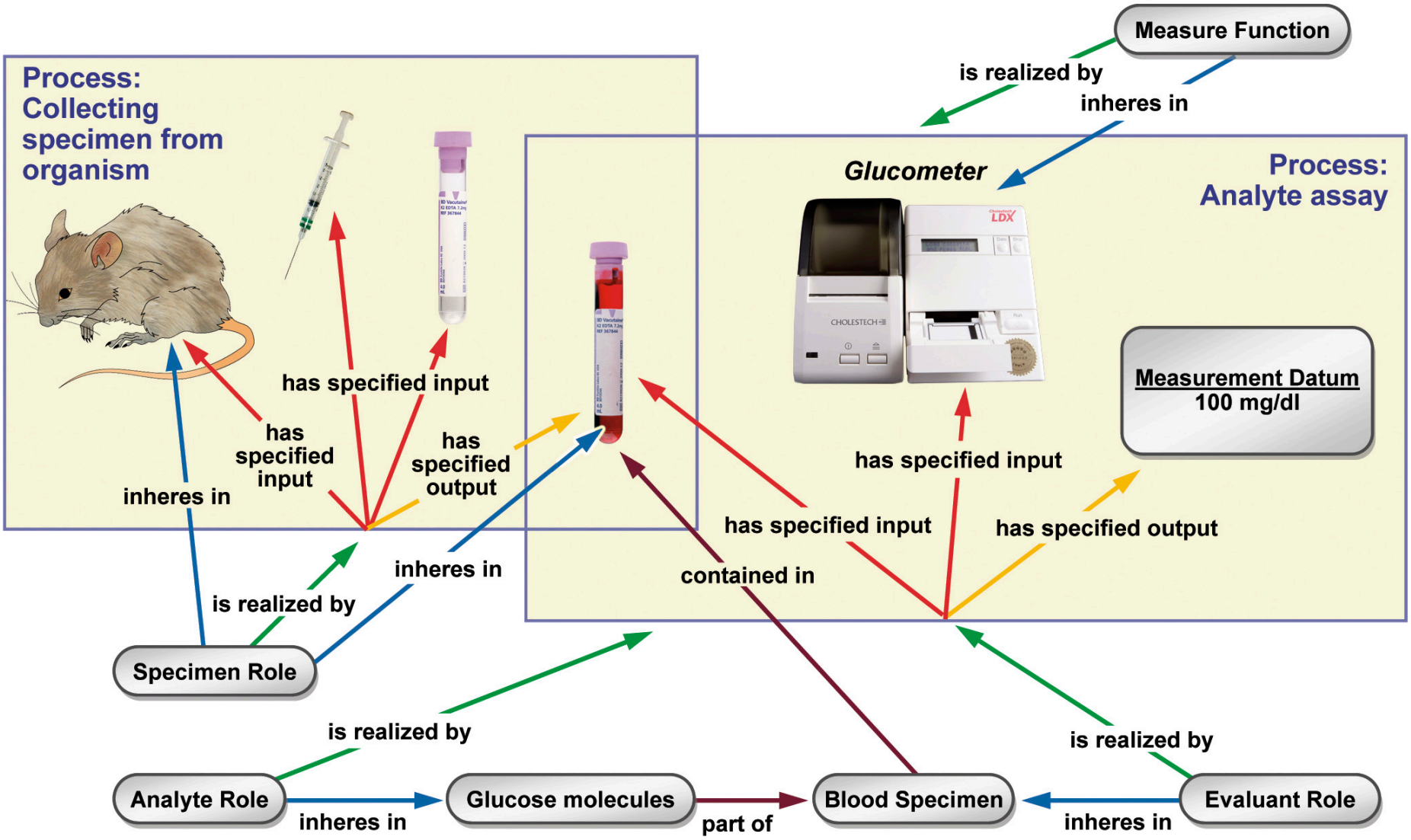
- ‘processed material entities’
  - output of a planned material transformation process
  - would not exist without intelligent life around
  - some ‘natural biomaterials’ can also be created (e.g. molecules)
    → no asserted disjoint
- specimen, study subject
  - material entities about which information is gathered during an investigation
  - may or may not be processed materials

High level class hierarchy (partial)



planned process

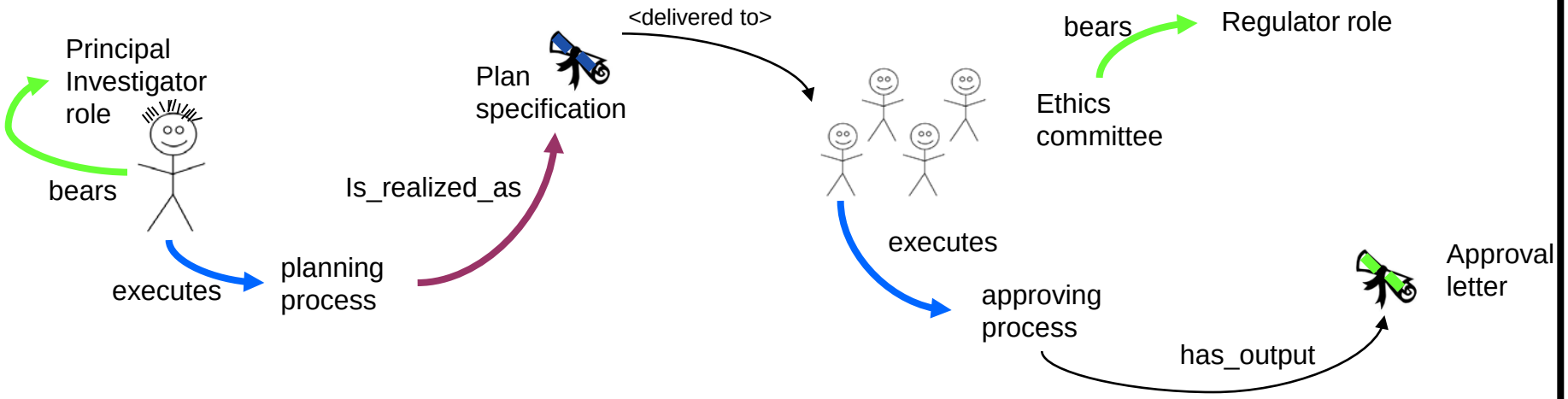
- realizes a ‘plan specification’ which includes an ‘objective specification’ (describing the desired endpoint)
- has specified inputs and outputs (=participants called out in the specification)
- high level classes:
  - material processing (input: material, output: material)
  - assay (input: material, output: data item)
  - data transformation (input:data item output:data item)


Measure Function
is realized by
inheres in
Process:
Collecting
specimen from
organism
Glucometer
Process:
Analyte assay
has specified input
has
specified
input
has
specified
output
inheres in
has specified input
has specified output
Measurement Datum
100 mg/dl
has specified input
has specified output
contained in
inheres in
is realized by
Specimen Role
is realized by
is realized by
Analyte Role
inheres in
Glucose molecules
part of
Blood Specimen
inheres in
Evaluant Role

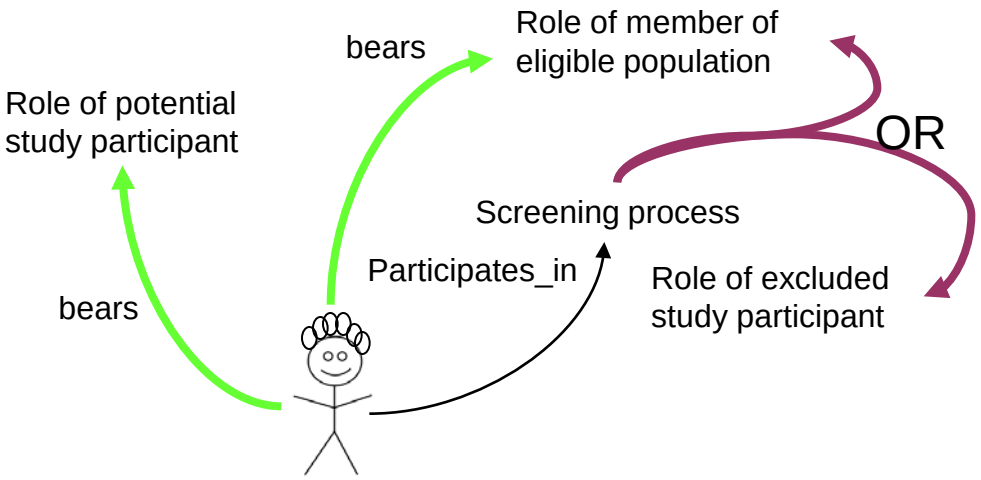
- Clinician studying aspirin / drug X / placebo effects on blood clotting measured by prothrombin time in human subjects.

- Secure approval from ethics committee
- Select balanced cohorts
- Collect materials; ensure that tablets appear similar
- Administer drug X, aspirin or placebo to one cohort
- Wait 2 hours
- Measure prothrombin time
- Analyze data

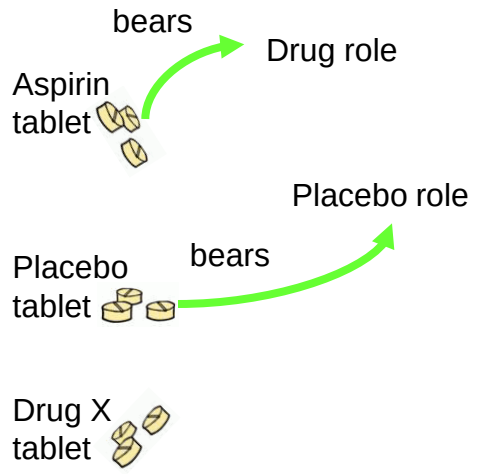
Plan and prepare for study



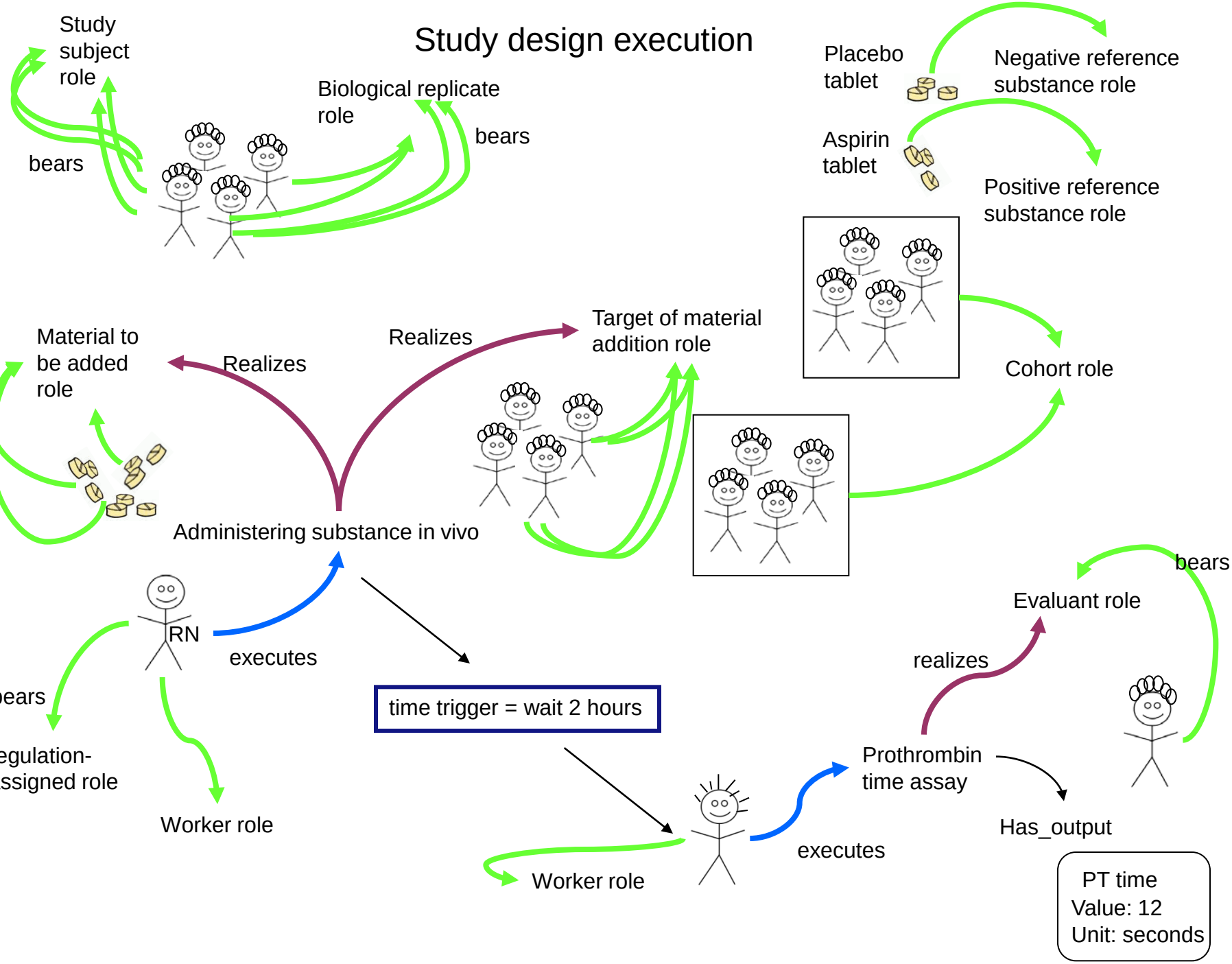
Identify study participants



Test substances:



Study design execution



CEBS = Chemical Effects in Biological Systems

- However, the CEBS database includes responses to chemicals **and**:
  - Studies of ***environmental agents*** such as ozone, hyperoxia
  - Studies of the responses of ***genetic changes*** such as knockouts
  - Studies of effects of ***physical agents*** such as magnetic fields

CEBS background

- Developed: Originally developed by NIEHS Division of Intramural Research (DIR)
- Purpose: To house data of interest to toxicologists and environmental health scientists
  - Data from DIR, Industry and Academic labs
- Result: CEBS has a flexible design, open to a variety of study types
- Advantage: CEBS captures data plus biological context
- CEBS moved to NTP in 2010 and now houses the public legacy NTP data

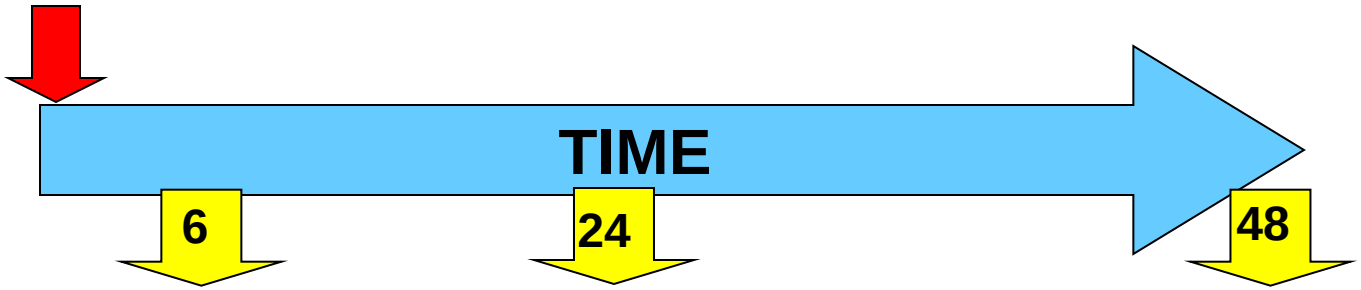
Biological context:

Care: feed, housing
time of day of dosing

Treatment:

0, 50, 150, 1500 mg/kg Acetaminophen by gavage
5 male Sprague-Dawley rats per group

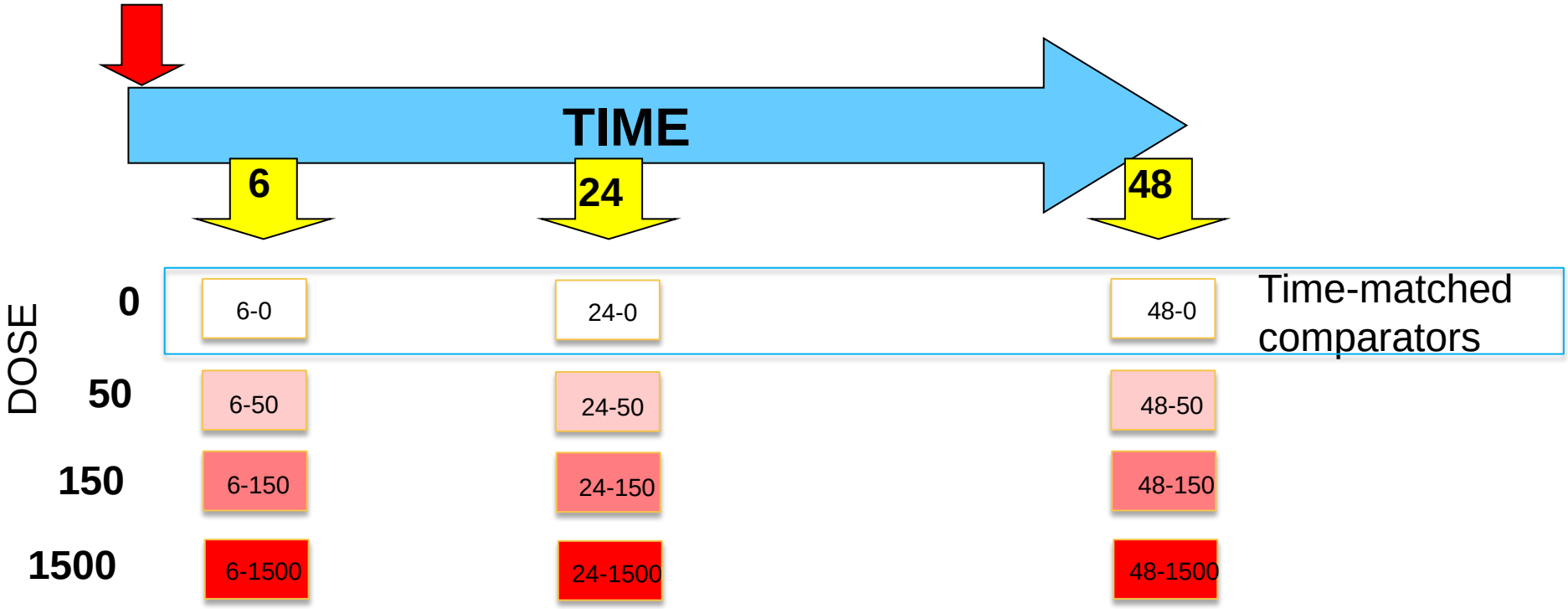
In life observations: in-cage morbidity, behavior



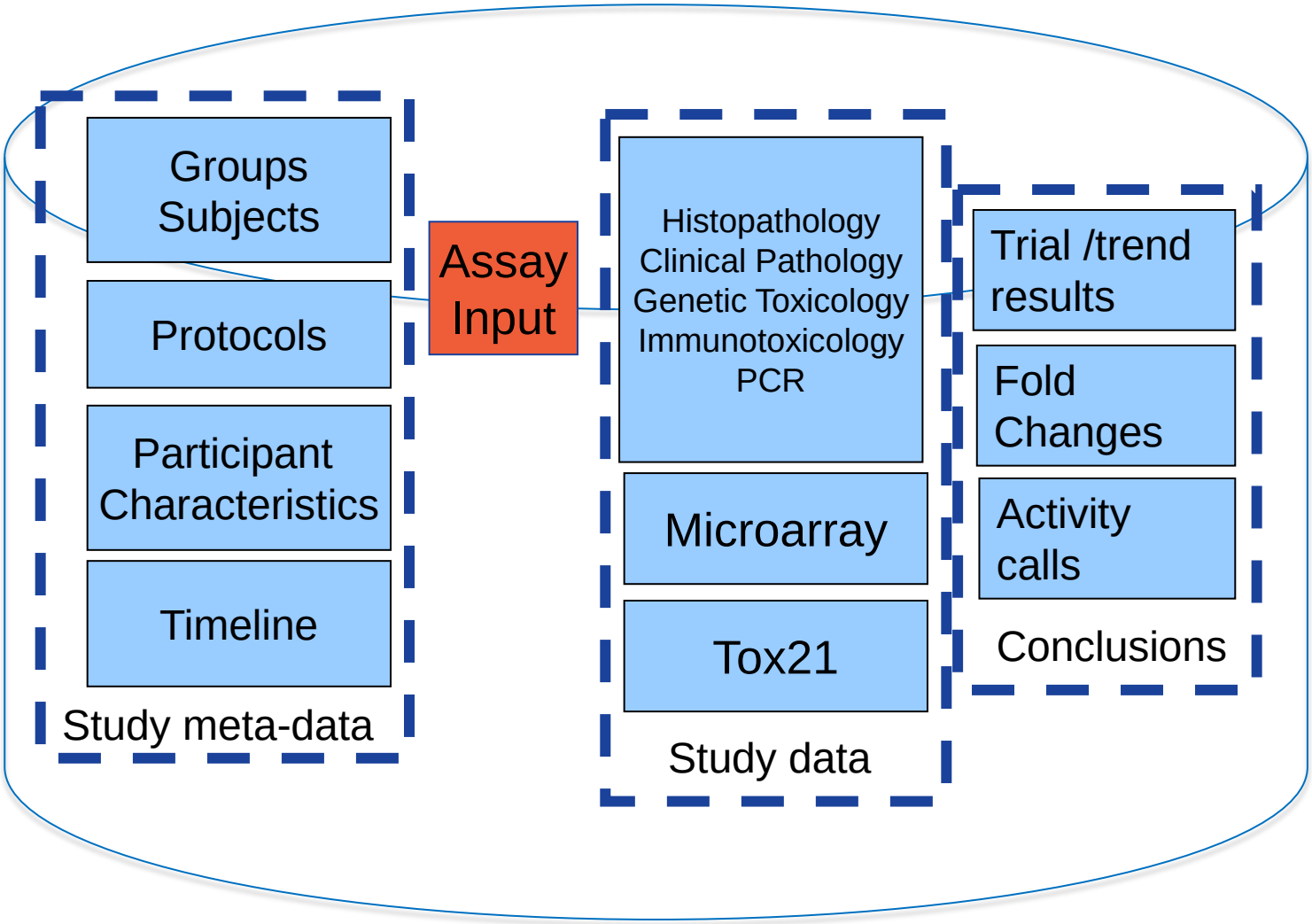
Sacrifice: using anesthesia, time of day

Take specimens: liver, blood, kidney,
for histopathology and microarray

Study design: groups, comparators, and study factors



CEBS database design



Original data
In file system

SIFT: Simple Investigation Formatted Text

- Standard format used to load studies into CEBS
- Based on SOFT (Simple Omnibus Formatted Test) from GEO (Gene Expression Omnibus)developed by the NCBI
- Study Sections
- Assay Sections
- Data Transformation Sections

SIFT Study sections

- STUDY
  - Title, Institution, PI, study factors, (stressor type, subject type, time type)
- GROUPS
  - Study factors and levels; comparators; characteristics
- SUBJECTS
  - Which subject belongs to particular group; subject characteristics
- PROTOCOLS
  - Care, In-life observations, Disposition, Specimen Preparation
  - Stressor Application (route, dose, frequency, stressor characteristics)
- TIMELINE
  - Link protocol group and time event

SIFT assay sections

- Identify data domain
  - clinical chemistry, histopathology, tissue level, microarray, PCR, …
- Identify assays
  - CEBS uses alias to link depositor name with CEBS name
  - Give the unit, instrument, other assay details
- Data spread sheet (in the SIFT file)
  - Subject ID, specimen prep protocol, (time and unit)
  - Assay name

SIFT data transformation section

- Input file
- Transformation protocol
- Output file

- Input can be group of study groups + group of assays

- Custom workflows (Tox21 statistics, for example)

NTP
National Toxicology Program

http://cebs.niehs.nih.gov

NIEHS
National Institute of Environmental Health Sciences – National Institutes of Health

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Chemical Effects in Biological Systems (CEBS)

A+ A-

The CEBS database houses data of interest to environmental health scientists. CEBS is a public resource, and has received depositions of data from academic, industrial and governmental laboratories. CEBS is designed to display data in the context of biology and study design, and to permit data integration across studies for novel meta analysis.

RELATED LINKS

» NIEHS Software and Online Tools Updates

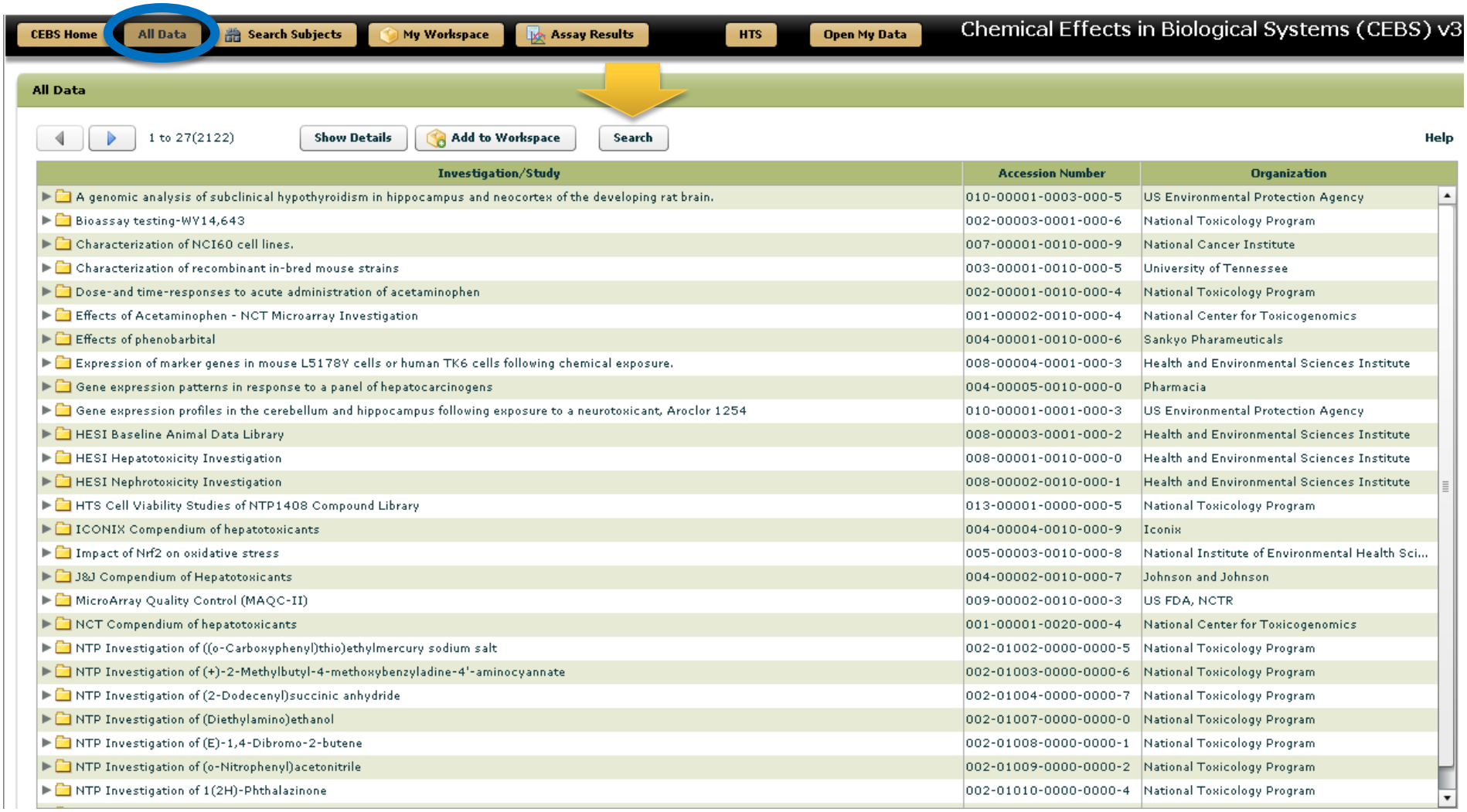
Note: *Users who are using JAWS as accessbility tool are advised to install scripts for using Adobe Flex applications with JAWS before using this application. These scripts have been developed by Adobe for Flex application. You can get the scripts from here (Get JAWS scripts for Flex). Once you have installed these scripts, press the insert key and q together to start the form mode in JAWS. There are number of sound hints available for alerts for opening of dialog boxes and data download. Use Tab key to navigate.*

Open CEBS **Download Data**

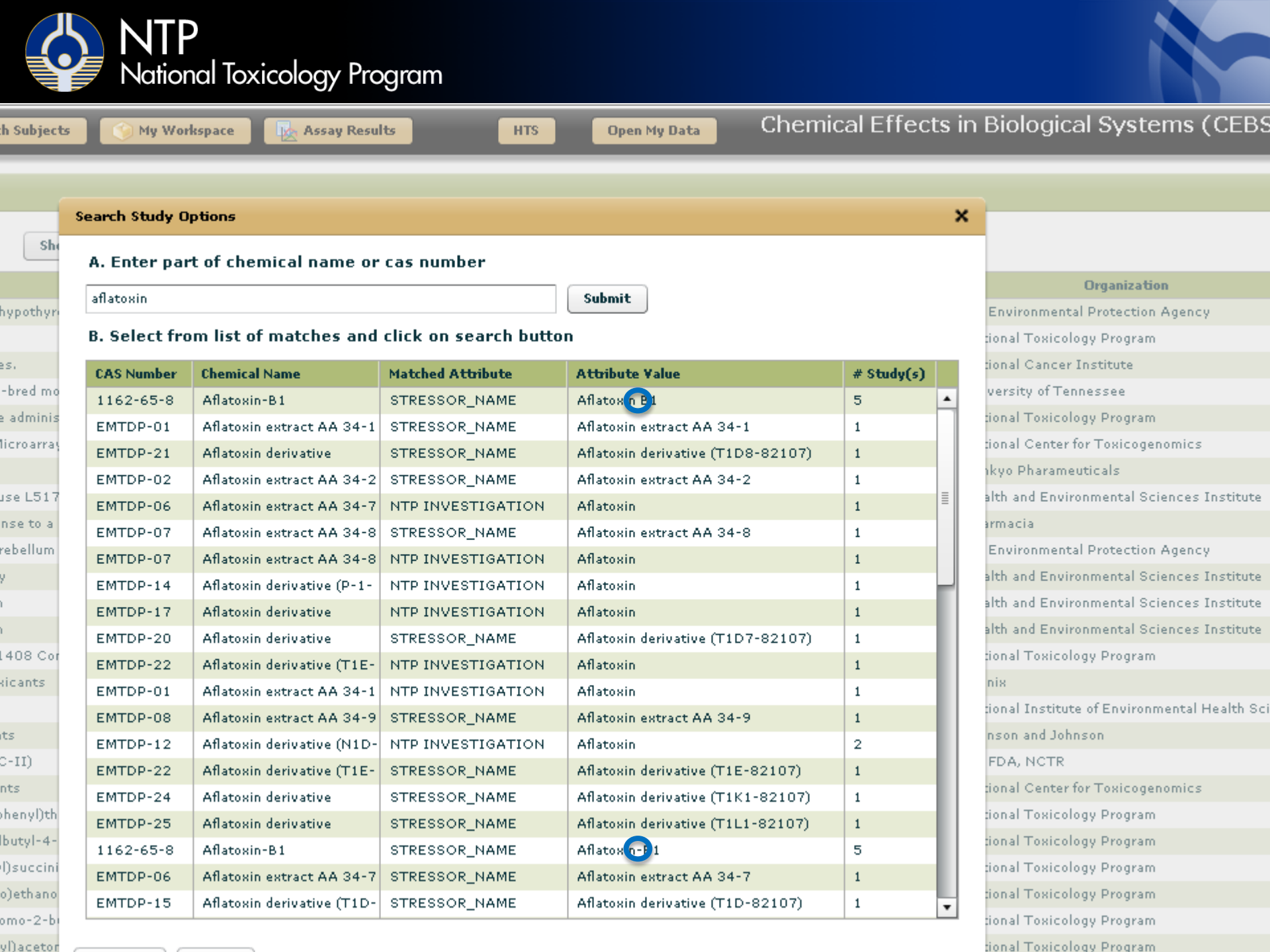
Contact CEBS

CEBS Scientific Administrator
E-mail: cebsfeedback@list.niehs.nih.gov

CEBS “All Data” page



Investigation/Study	Accession Number	Organization
A genomic analysis of subclinical hypothyroidism in hippocampus and neocortex of the developing rat brain.	010-00001-0003-000-5	US Environmental Protection Agency
Bioassay testing-WY14,643	002-00003-0001-000-6	National Toxicology Program
Characterization of NCI60 cell lines.	007-00001-0010-000-9	National Cancer Institute
Characterization of recombinant in-bred mouse strains	003-00001-0010-000-5	University of Tennessee
Dose-and time-responses to acute administration of acetaminophen	002-00001-0010-000-4	National Toxicology Program
Effects of Acetaminophen - NCT Microarray Investigation	001-00002-0010-000-4	National Center for Toxicogenomics
Effects of phenobarbital	004-00001-0010-000-6	Sankyo Pharameuticals
Expression of marker genes in mouse L5178Y cells or human TK6 cells following chemical exposure.	008-00004-0001-000-3	Health and Environmental Sciences Institute
Gene expression patterns in response to a panel of hepatocarcinogens	004-00005-0010-000-0	Pharmacia
Gene expression profiles in the cerebellum and hippocampus following exposure to a neurotoxicant, Aroclor 1254	010-00001-0001-000-3	US Environmental Protection Agency
HESI Baseline Animal Data Library	008-00003-0001-000-2	Health and Environmental Sciences Institute
HESI Hepatotoxicity Investigation	008-00001-0010-000-0	Health and Environmental Sciences Institute
HESI Nephrotoxicity Investigation	008-00002-0010-000-1	Health and Environmental Sciences Institute
HTS Cell Viability Studies of NTP1408 Compound Library	013-00001-0000-000-5	National Toxicology Program
ICONIX Compendium of hepatotoxicants	004-00004-0010-000-9	Iconix
Impact of Nrf2 on oxidative stress	005-00003-0010-000-8	National Institute of Environmental Health Sci...
J&J Compendium of Hepatotoxicants	004-00002-0010-000-7	Johnson and Johnson
MicroArray Quality Control (MAQC-II)	009-00002-0010-000-3	US FDA, NCTR
NCT Compendium of hepatotoxicants	001-00001-0020-000-4	National Center for Toxicogenomics
NTP Investigation of ((o-Carboxyphenyl)thio)ethylmercury sodium salt	002-01002-0000-0000-5	National Toxicology Program
NTP Investigation of (+)-2-Methylbutyl-4-methoxybenzyladine-4'-aminocyannate	002-01003-0000-0000-6	National Toxicology Program
NTP Investigation of (2-Dodecenyl)succinic anhydride	002-01004-0000-0000-7	National Toxicology Program
NTP Investigation of (Diethylamino)ethanol	002-01007-0000-0000-0	National Toxicology Program
NTP Investigation of (E)-1,4-Dibromo-2-butene	002-01008-0000-0000-1	National Toxicology Program
NTP Investigation of (o-Nitrophenyl)acetonitrile	002-01009-0000-0000-2	National Toxicology Program
NTP Investigation of 1(2H)-Phthalazinone	002-01010-0000-0000-4	National Toxicology Program


NTP
National Toxicology Program
My Workspace
Assay Results
HTS
Open My Data
Chemical Effects in Biological Systems (CEBS
Search Study Options
A. Enter part of chemical name or cas number
aflatoxin
Submit
B. Select from list of matches and click on search button
CAS Number | Chemical Name | Matched Attribute | Attribute Value | # Study(s)
1162-65-8 | Aflatoxin-B1 | STRESSOR_NAME | Aflatoxin B1 | 5
EMTDP-01 | Aflatoxin extract AA 34-1 | STRESSOR_NAME | Aflatoxin extract AA 34-1 | 1
EMTDP-21 | Aflatoxin derivative | STRESSOR_NAME | Aflatoxin derivative (T1D8-82107) | 1
EMTDP-02 | Aflatoxin extract AA 34-2 | STRESSOR_NAME | Aflatoxin extract AA 34-2 | 1
EMTDP-06 | Aflatoxin extract AA 34-7 | NTP INVESTIGATION | Aflatoxin | 1
EMTDP-07 | Aflatoxin extract AA 34-8 | STRESSOR_NAME | Aflatoxin extract AA 34-8 | 1
EMTDP-07 | Aflatoxin extract AA 34-8 | NTP INVESTIGATION | Aflatoxin | 1
EMTDP-14 | Aflatoxin derivative (P-1- | NTP INVESTIGATION | Aflatoxin | 1
EMTDP-17 | Aflatoxin derivative | NTP INVESTIGATION | Aflatoxin | 1
EMTDP-20 | Aflatoxin derivative | STRESSOR_NAME | Aflatoxin derivative (T1D7-82107) | 1
EMTDP-22 | Aflatoxin derivative (T1E- | NTP INVESTIGATION | Aflatoxin | 1
EMTDP-01 | Aflatoxin extract AA 34-1 | NTP INVESTIGATION | Aflatoxin | 1
EMTDP-08 | Aflatoxin extract AA 34-9 | STRESSOR_NAME | Aflatoxin extract AA 34-9 | 1
EMTDP-12 | Aflatoxin derivative (N1D- | NTP INVESTIGATION | Aflatoxin | 2
EMTDP-22 | Aflatoxin derivative (T1E- | STRESSOR_NAME | Aflatoxin derivative (T1E-82107) | 1
EMTDP-24 | Aflatoxin derivative | STRESSOR_NAME | Aflatoxin derivative (T1K1-82107) | 1
EMTDP-25 | Aflatoxin derivative | STRESSOR_NAME | Aflatoxin derivative (T1L1-82107) | 1
1162-65-8 | Aflatoxin-B1 | STRESSOR_NAME | Aflatoxin B1 | 5
EMTDP-06 | Aflatoxin extract AA 34-7 | STRESSOR_NAME | Aflatoxin extract AA 34-7 | 1
EMTDP-15 | Aflatoxin derivative (T1D- | STRESSOR_NAME | Aflatoxin derivative (T1D-82107) | 1
Organization
Environmental Protection Agency
National Toxicology Program
National Cancer Institute
University of Tennessee
National Toxicology Program
National Center for Toxicogenomics
Takeda Pharmaceuticals
National Institute of Environmental Health Sciences
Pharmacia
Environmental Protection Agency
National Institute of Environmental Health Sciences
National Institute of Environmental Health Sciences
National Institute of Environmental Health Sciences
National Toxicology Program
Johnson
National Institute of Environmental Health Sci
Johnson and Johnson
FDA, NCTR
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National Toxicology Program

CEBS Home | All Data | Search Subjects | My Workspace | Assay Results | HTS | Open My Data | Chemical Effects i

All Data

1 to 3(3) | Show Details | Add to Workspace | Search

Investigation/Study	Accession Number
ICONIX Compendium of hepatotoxicants	004-00004-0010-000-9
NTP Investigation of Aflatoxin	002-01615-0000-0000-5
Prediction of hepatocarcinogenic potential of alkylbenzene flavoring agents using transcriptomics and machine learning.	002-00100-0001-000-4
Toxicogenomic Evaluation of Rat Liver Carcinogens and Non-carcinogens in Male Fischer 344 Rats	002-00100-0003-000-6

Three investigations containing studies of Aflatoxin.
Open the investigation to show studies.

Double-click to see investigation details:

Investigation Details - Prediction of hepatocarcinogenic potential of alky...

Characteristics	Characteristic Values
Accession Number	002-00100-0001-000-4
Investigation Title	Prediction of hepatocarcinogenic potential of alkylbenzene flavoring agents using transcrip
Organization	National Toxicology Program
Organization Abbr.	NTP
PI	Rick Irwin

Close | Show Raw Files

and to access raw data files

Toxi nic Evaluation of Rat Liver Carcinogens and Non-carcinogens in Male Fischer 344 Rats

Characteristics | Design | Timeline | Data

Study Conclusion:

Stressor Name: 1-Amino-2,4-dibromoanthraquinone

More

Press More button to see other study stressors

Study Variables: TIME|COMPOUND

Characteristic	Characteristic Value
ACCLIMATION_DURATIOI	12
ACCLIMATION_DURATIOI	day
DURATION	150
DURATION_UNIT	day
INSTITUTION	NTP
START_DATE	January 19, 2006

Publications:

Title	PubMed Id	Year
Predicting the hepatocarcinogenic potential of alkenylbenzene flavoring agents using toxicogenomics and machine learning	20004213	

Close | Add to workspace

Toxicogenomic Ev[illegible] Rat Liver Carcinogens and Non-carcinogens in Male Fischer 344 Rats

Characteristics | Design | Timeline | Data

GROUP	time	compound
DW control 150-day	90-day stop	DW control
N-Nitrosodimethylamine 91-day	90 day	N-Nitrosodimethylamine
N-Nitrosodimethylamine 3-day	3-day	N-Nitrosodimethylamine
N-Nitrosodimethylamine 150-day	90-day stop	N-Nitrosodimethylamine
Acetaminophen 3-day	3-day	Acetaminophen
Methyleugenol 150-day	90-day stop	Methyleugenol
L-tryptophan 3-day	3-day	L-tryptophan
L-tryptophan 15-day	15-day	L-tryptophan
Dibromoanthraquinone 150-day	90-day stop	Dibromoanthraquinone
Acetaminophen 91-day	90 day	Acetaminophen
Acetaminophen 150-day	90-day stop	Acetaminophen
Gavage control 150-day	90-day stop	Gavage control
Gavage control 3-day	3-day	Gavage control
Methyleugenol 91-day	90 day	Methyleugenol
Methyleugenol 15-day	15-day	Methyleugenol
DFD control 15-day	15-day	DFD control
Ascorbic acid 15-day	15-day	Ascorbic acid
L-tryptophan 91-day	90 day	L-tryptophan
Aflatoxin B1 91-day	90 day	Aflatoxin B1
Gavage control 91-day	90 day	Gavage control
DW control 3-day	3-day	DW control
DW control 15-day	15-day	DW control

GROUP Details

GROUP

- N-Nitrosodimethylamine_91-day

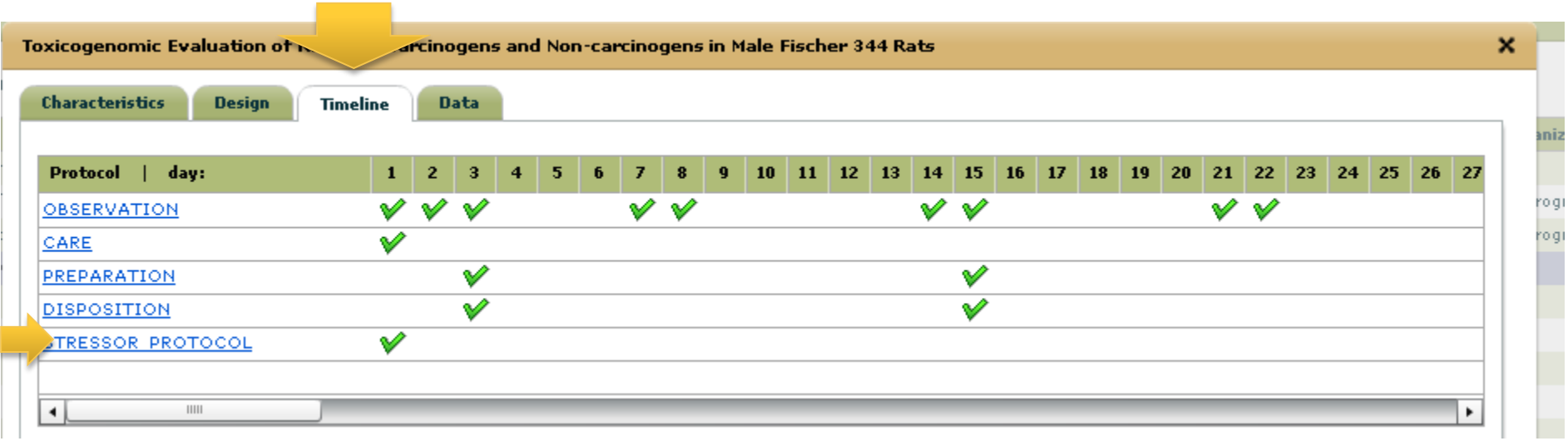
GROUP Characteristics

Help

Characteristic	Characteristic Value
DEPOSITOR NAME	N-Nitrosodimethylamine_91-day
COMPARITOR NAME	DW control_91-day
AGE RANGE FIRST DOSE	35 to 41
AGE RANGE SACRIFICE	123-129
AGE UNIT	day
BODYWEIGHT START LOW	67.7
BODYWEIGHT START UPPI	89
BODYWEIGHT UNIT	g
CHEM STRESSOR CLASS	C
COMPOUND	N-Nitrosodimethylamine
DOSE	5
DOSE DURATION	90
DOSE DURATION UNIT	day
DOSE UNIT	ppm
GENUS	Rattus
SEX	Male
SPECIES	norvegicus
SPECIES COMMON NAME	Rat

Close

Add to workspace


Toxicogenomic Evaluation of
arcinogens and Non-carcinogens in Male Fischer 344 Rats
Characteristics
Design
Timeline
Data
Protocol | day:
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27
OBSERVATION
CARE
PREPARATION
DISPOSITION
TRESSOR PROTOCOL

ol | day: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24

Study Protocol Details (STRESSOR_PROTOCOL)

Hel

Protocol Type/Name/Attributes	Value
CHEM_STRESSOR_PROTOCOL	
AFA	
LOT	015K4060
DOSE PER ADMIN	1
DOSE PER ADMIN UNIT	ppm
ROUTE ADMIN	Dosed feed
DOSE FREQUENCY DESC	Continuous
CHEM SUPPLIER	RTI
PURITY PERCENTAGE	101.3
STRESSOR NAME	Aflatoxin-B1
STORAGE TEMP	5
STORAGE TEMP UNIT	degrees C

Close

Toxicogenomic Evaluation of Rat Liver Can ns and Non

Characteristics | Design | Timeline | Data

A. Available Data

IN_LIFE_OBSERVATIONS

MICROARRAY

B. View Options

CEBS View

xicogenomic Evaluation of Rat Liver Carcinogens and Non-carcinogens in Male Fischer 344 Rats

Characteristics | Design | Timeline | Data

IN LIFE OBSERVATIONS

Group	S...	Collection Time (day)	Study Factors					
			COMPOUND	TIME	BW (g)	BW_RATIO (%)	FC (g)	W (g)
Acetaminophen_15-day		7	Acetaminophen	15-day	119.7	97.7	16.5	
Acetaminophen_15-day		15	Acetaminophen	15-day	161			
Acetaminophen_15-day		14	Acetaminophen	15-day	154.7	98.3	17.4	
Acetaminophen_15-day		1	Acetaminophen	15-day	93.1	98.3		
Acetaminophen_150-day		119	Acetaminophen	90-day stop	393.9	102.7		
Acetaminophen_150-day		77	Acetaminophen	90-day stop	331.9	99.5	20.3	
Acetaminophen_150-day		14	Acetaminophen	90-day stop	154.7	98.3	17.4	
Acetaminophen_150-day		21	Acetaminophen	90-day stop	194.8	99.7	19.3	
Acetaminophen_150-day		56	Acetaminophen	90-day stop	298.2	99.4	20	
Acetaminophen_150-day		63	Acetaminophen	90-day stop	312.9	100.1	19.4	
Acetaminophen_150-day		147	Acetaminophen	90-day stop	415.7	103.7		
Acetaminophen_150-day		35	Acetaminophen	90-day stop	247	98.7	20.2	
Acetaminophen_150-day		133	Acetaminophen	90-day stop	406.1	104.2		
Acetaminophen_150-day		1	Acetaminophen	90-day stop	93.1	98.3		

Back | Download

CEBS and OBI

- CEBS now – relational database, SQL queries
- OBI now – ontology with classes, terms, relationships
- Uniting the two:
  - Replace CEBS CV with OBI terms
    - Consistent definitions
    - Avoid duplications
    - Enhance searching
  - Export CEBS conclusions into triple store
    - Enable Sparql queries, interoperability
  - Integrate rules-based validation system

Acknowledgements:

- Bjoern Peters and OBI consortium
- DNTP and
  - Asif Rashid, Hui Gong, Anand Paleja, Laura Hall (CEBS)

- Questions?
- Contact: fostel@niehs.nih.gov