

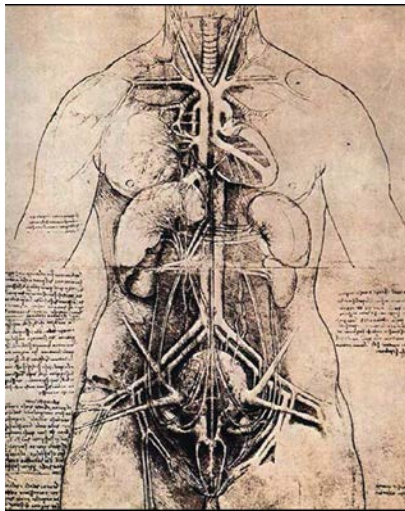
NIH Update

Warren Casey, PhD, DABT
Director, NICEATM

ICCVAM Public Forum
May 24, 2018

Microphysiological Systems Program “Tissue Chips for Drug Screening”

GOAL: Develop an *in vitro* platform that uses human tissues to evaluate the safety and toxicity of promising therapies.



•All 10 human physiological systems will be functionally represented by human tissue constructs:

- Circulatory
- Endocrine
- Gastrointestinal
- Immune
- Skin
- Musculoskeletal
- Nervous
- Reproductive
- Respiratory
- Urinary

•Physiologically relevant, genetically diverse, and pathologically meaningful

•Modular, reconfigurable platform

•Tissue viability for at least 4 weeks

•Community-wide access

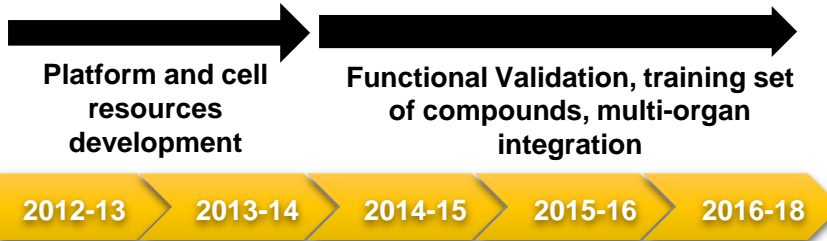
Microphysiological Systems Consortium 2012-2020 “Tissue Chips for Drug Screening”

AstraZeneca 



 GlaxoSmithKline


National Institutes
of Health




National Institutes
of Health

\$75 M over 5 years – cell source, platform development, validation and integration (NCATS, CF, NIBIB, NIEHS, NICHD, ORWH, NCI)



\$75 M over 5 years - development of 10-organ platforms



**FDA provides insight and expertise throughout the program



Publications: (as of Oct 2017; cited over 5600 times)
A total of 506 original and review articles published in top tier journals, including *Nature Medicine*, *Nature Communications*, *Nature Materials*, *PNAS*, *Science*, *Science Translational Medicine*, etc.



Tissues Typically Collected and Examined in a Pharma GLP Tox Study

- Adrenals
 - Aorta
 - Bone (femur)
 - Bone marrow (sternum)
 - Brain (at least 3 different levels)
 - Cecum
 - Colon
 - Corpus and cervix uteri
 - Duodenum
 - Epididymides
 - Esophagus
 - Eyes
 - Gall bladder (if present)
 - Harderian gland
 - Heart
 - Ileum
 - Gall bladder (if present)
 - Harderian gland
 - Heart
 - Ileum
 - Jejunum
 - Kidneys
 - Gall bladder (if present)
 - Harderian gland
 - Heart
 - Ileum
 - Jejunum
 - Kidneys
 - Liver
 - Lung (with main-stem bronchi)
 - Lymph nodes
 - Mammary glands
 - Nasal turbinates
 - Ovaries and fallopian tubes
 - Pancreas
 - Pituitary
 - Prostate
 - Rectum
 - Salivary gland
 - Sciatic nerve
 - Seminal vesicle (if present)
 - Skeletal muscle
 - Skin
 - Spinal cord (3 locations)
 - Spleen
 - Stomach
 - Testes
 - Thymus (if present)
 - Thyroid/parathyroid
 - Trachea
 - Urinary bladder
 - Vagina
 - Zymbal's gland
- Any other tissues showing abnormality

Microphysiological Systems (MPS) for Disease Modeling and Efficacy Testing (2017-2022)

GOAL:

- Develop highly reproducible and translatable in vitro models for preclinical efficacy studies using MPS
 - discovery and validation of translatable biomarkers
 - development of standardized methods for preclinical efficacy testing and definitive efficacy testing of candidate therapeutics using best practices and rigorous study design
- 5-year UG3/UH3 program; \$75 M Funding partnerships between NCATS and other NIH ICs (NIAMS, NICHD, NIDCR, NIDDK, NIEHS, NINDS, NIBIB, NHLBI, ORWH)
- Non-funding partnerships with FDA and IQ Consortium



Kam Leong, Columbia U
Proteus Syndrome and DiGeorge Syndrome

Danielle Benoit, Lisa Delouise, Catherine Ovitt, U Rochester

Radiation-induced xerostomia

Kevin Kit Parker, William Pu, Harvard U
Barth syndrome, catecholaminergic polymorphic ventricular tachycardia, arrhythmogenic cardiomyopathy

Steven George, David Curiel, Stacey Rentschler, UC Davis and WashU **atrial fibrillation**

Joseph Vincent Bonventre, Luke Lee, Brigham and Women's **autosomal dominant/recessive models of polycystic kidney disease, Focal segmental glomerulosclerosis**

Christopher Hughes, UC Irvine
Hereditary hemorrhagic telangiectasia, Port Wine stain, Sturge-Weber syndrome

Rocky Tuan, U Pittsburgh
Osteoarthritis, inflammatory arthritis, adipose-mediated diabetic joint complications

Clive Svendsen, Cedars-Sinai
ALS; Parkinson's Disease

Aaron Bowman, Kevin Ess, John Wikswa, Vanderbilt U
tuberous sclerosis complex (TSC) epilepsy, DEPDC5-associated epilepsy, & associated cardiac dysfunction

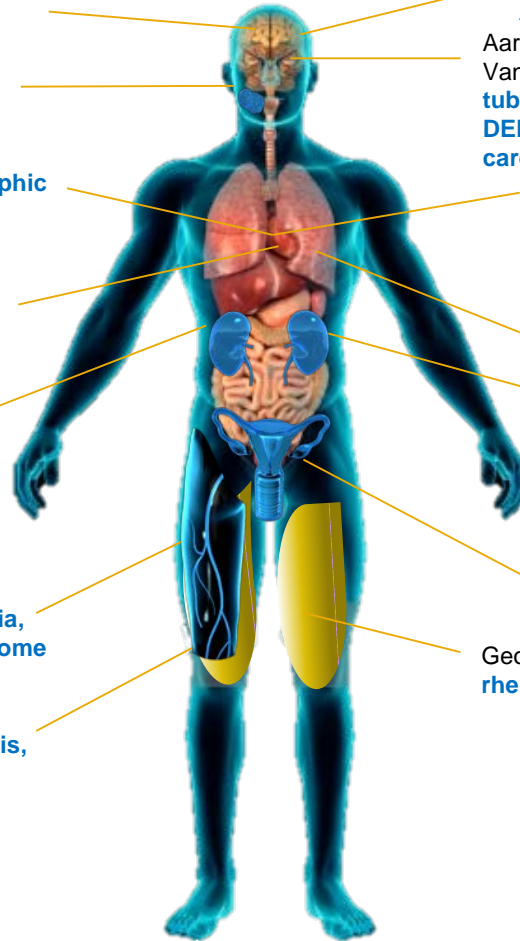
Gordana Vunjak-Novakovic, Columbia U
Dox induced cardiomyopathy; multi-system pathologies involving heart, liver, skin, bone and vasculature

Donald Ingber, Harvard U
influenza infection, COPD

Jonathan Himmelfarb, U Washington
apolipoprotein L1 mediated kidney disease, drug induced and host-pathogen interaction induced renal thrombotic microangiopathies

Teresa Woodruff, Northwestern U
Polycystic Ovarian Syndrome

George Truskey, Duke U
rheumatoid arthritis, atherosclerosis





Integrated Chemical Environment: ICE

- Uphold FAIR principles for ICCVAM Data
- Provide intuitive access to high quality (curated) data and tools to support:
 - chemical evaluations,
 - data integration, and
 - model development
- Enable wider community to engage in the use of alternative and computational approaches for assessing chemical safety





Latest Release: Formulations

Send the CASRNs to the Integrator

Run Search

Clear

Select Chemicals

- Acute Dermal Toxicity
- Acute Oral Toxicity
- Acute Inhalation Toxicity
- Primary Skin Irritation
- Primary Eye Irritation
- Dermal Sensitization

+ Select Reference Lists.

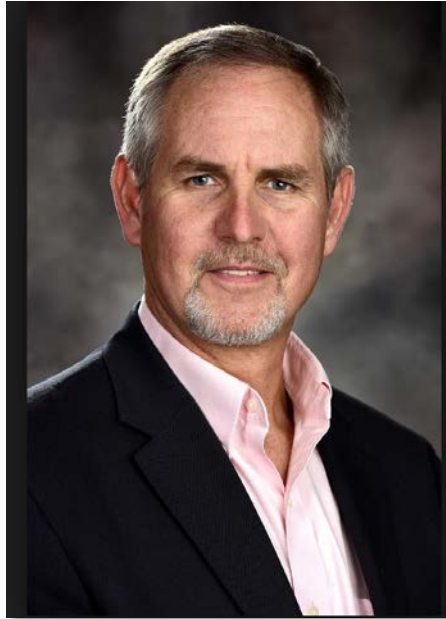
Enter one CASRN per line.

172345-26-5
1928-43-4
1918-00-9
10007-85-9
120068-37-3
106-24-1
1071-83-6

Download

Query Integrator

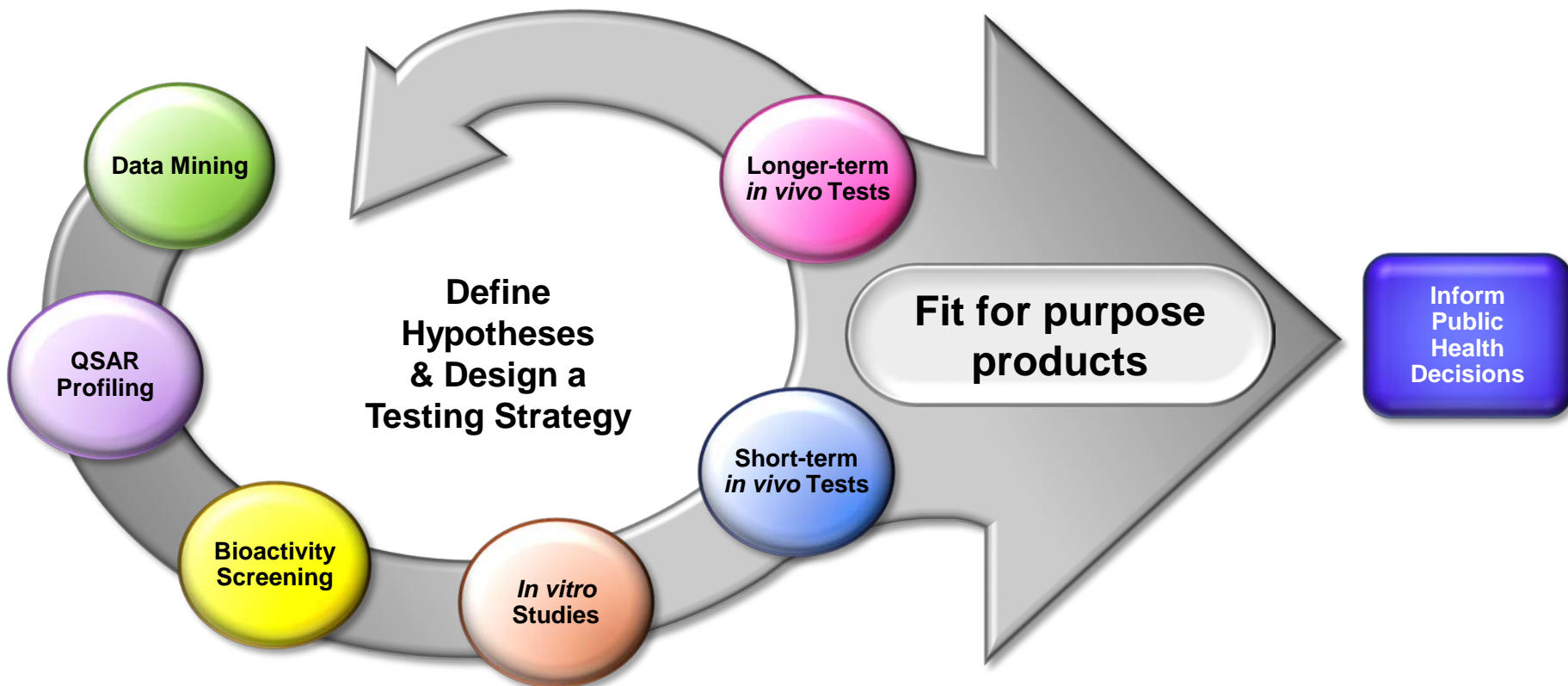
Formulation ID	Active Ingredient	CASRN	Percent AI
▶ Not Stated	-	ICE_42094346618	-
▶ Glyphosate	-	ICE_729956234	-
▶ Albaugh Glyphosphate Acid	-	ICE_1757011315	-
▶ Touchdown Diquat Home and Garden Concentrate	-	ICE_1433817882	-
▶ SYN 1219 Herbicide	-	ICE_1506463698	-
▶ Sharda Glyphosate	-	ICE_4646586107	-
▶ Celsius WG	-	ICE_1839890958	-
▶ M1750 Herbicide	-	ICE_41910034923	-
▶ Glyphosate Acid	-	ICE_1327297599	-
▶ Navigator 80WG Termicide/Insecticide	-	ICE_1010954240	-
▶ CSI Imidacloprid + Fipronil SC	-	ICE_1054278024	-
▶ Prodiamine/Diquat/Glyphosphate EW Ready to Use	-	ICE_4660223765	-
▶ NUP-07003 Herbicide	-	ICE_4509740805	-
▶ SM-9 Tergitol	-	ICE_42020205260	-
▶ Prodiamine/Diquat/Glyphosphate EW Manufacturing	-	ICE_1385261692	-
▶ Glyphosphate XG	-	ICE_1408275449	-
▶ Craze Herbicide	-	ICE_1119858598	-
▶ Certifect for Dogs	-	ICE_1932298155	-
▶ Tradename for Dogs	-	ICE_42117480911	-
▶ Prodiamine/Diquat/Glyphosphate EW Concentrate	-	ICE_19848904	-
▶ Regent 500TS Insecticide	-	ICE_41998701941	-
▶ Shooter Insecticide	-	ICE_41759811876	-
▶ Departure Herbicide	-	ICE_41502273265	-
▶ EH-1446 Herbicide	-	ICE_41541177964	-
▶ EH-1534 Herbicide	-	ICE_777883124	-
▶ UPL Glyphosphate	-	ICE_4510677064	-



Brian Berridge - NTP Associate Director



DNTP Translational Toxicology Pipeline Plan





NICEATM-ILS Staff

