NIH and CC Interactions with Pharma

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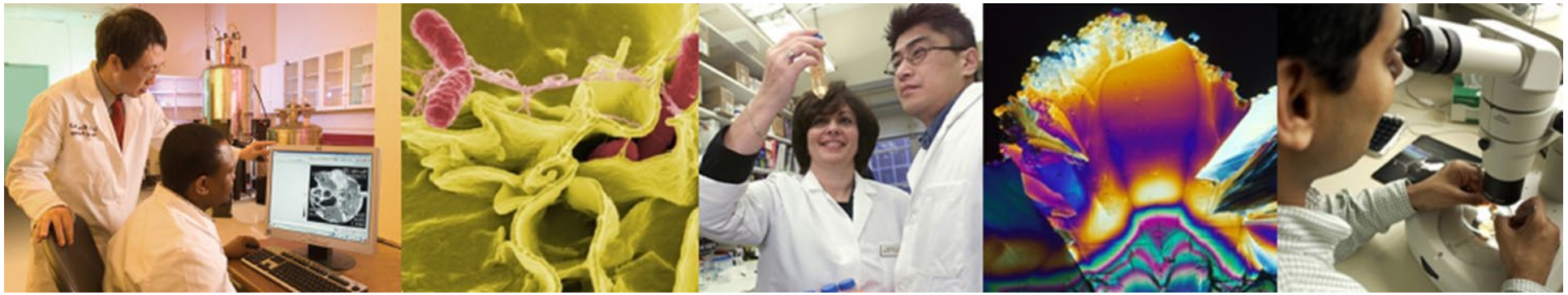
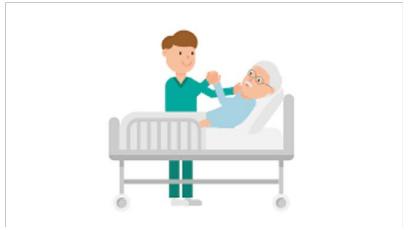


NIH and Pharma Interactions

- Many NIH researchers collaborate with industry
- Mutually beneficial collaborations
- Support development and testing of agents, procedures, interventions, etc. at NIH and the Clinical Center, especially through clinical trials

Pharma

NIH
National Institutes of Health



Mechanisms for NIH Clinical Investigators and Industry Collaborations

- Cooperative Research and Development Agreements (CRADAs)
- Clinical Trial Agreements (CTAs)
- Research Collaboration Agreements (RCAs)
- Material Transfer Agreements (MTAs)
- Conditional Gifts
- Direct Purchases for Standard of Care Drugs

Cooperative Research and Development Agreements (CRADAs)

- CRADA= an agreement between a federal laboratory and a non-federal party for conducting specified collaborative research or development.
- It is not a federal contract, grant or Cooperative Agreement

Cooperative Research and Development Agreements (CRADAs)

- >450 currently active of all types
- Allows collaborator to provide funds to support the Research Plan
  - Except for salary and benefits of government employees
- Can exchange personnel, materials, equipment, and expertise
- Unique in offering the collaborator an exclusive or non-exclusive license to NIH inventions that arise during the course of the research

Other Types of CRADAs

- **Clinical Trials CRADA**
  - Adds terms relevant to a clinical trial
- **Materials (M)- CRADA**
  - Tailored for receipt of proprietary materials from non-federal partner
  - Collaborator may also provide funds
  - No other collaboration

CRADA Restrictions and Policy

- Research must be collaborative, NOT fee for service
- Cannot substitute for an NIH purchase contract

More on CRADA policy can be found at: https://ott.nih.gov/policy/cradas

Examples of CRADA model agreements can be found at: https://ott.nih.gov/resources#MCRDA

Examples of NIH CRADAs

- **NHLBI: Rapid initiation of discovery of biological mechanisms and development of therapies against COVID-19**
  - CRADA with Inova and Rigel Pharmaceuticals to test first-in class treatment with highly promising in vitro and in vivo test results
  - Anticipated clinical trials at Inova and NIH Clinical Center as part of multicenter, randomized, double-blind, Phase I/II study of fostamatinib with current standard of care.
- **NCI: Clinical trial to evaluate Nivolumab, in combination with vancomycin and tadalafil, to treat liver cancer**
  - CRADA with Bristol-Myers Squibb for new Phase II Clinical trial at NIH CC
- **NCI: Approval of Avelumab to treat Merkel Cell Carcinoma (MCC)**
  - CRADA with EMD Serono, Inc to clinically develop Avelumab, an antibody that targets PD-L1, as the first FDA-approved treatment for MCC
- **NIAID: Pozelimab in Patients with CD55-deficiency**
  - CRADA with Regeneron to conduct an open-label efficacy and safety study (Phase II/III) of Pozelimab in patients with CHAPLE Disease, a genetic disorder caused by CD55 deficienc

Clinical Trial Agreement (CTA) and Research Collaboration Agreement (RCA)

- **Clinical Trial Agreement (CTA)**
  - Partnership between NIH and outside entity to conduct clinical trials to test new drugs, devices, procedures, and interventions on human subjects
- **RCA (Research Collaboration Agreement)**
  - Agreement between NIH and outside entity to conduct collaborative research (other than clinical trials)

Clinical Trial Agreement (CTA) and Research Collaboration Agreement (RCA)

- CTAs= one of the most common mechanisms used to receive drugs for clinical research at NIH
- Easier than CRADA to implement
- May be appropriate if:
  - Collaborator's contribution is small and license option may not be equitable
  - Collaborator does not require a license
- Collaborator may provide funds under which are accepted under agency gift acceptance authority
- Does not provide the option to license inventions arising from the research

Examples of NIH CTAs

- **NCI: Orphan Drug Zotiraciclib for treatment of Glioma**
  - CTA with Tragara Pharmaceuticals (now Adastra Pharmaceuticals) to evaluate agent TG02 in an NCI-sponsored phase I trial at NIH CC
- **NIAID: Development of COVID-19 Vaccines and Therapeutics**
  - 4 CTAs to develop COVID-19 vaccines
  - CTA with Gilead to test Remdesivir as COVID-19 treatment (ACTT, ACTIV)
- **NIAID: Anti-CD117 monoclonal antibody prior to transplant for chronic granulomatous disease (CGD)**
  - CTA with Jasper Therapeutics to conduct Phase I/II clinical trial to evaluate JSP191, the company's first-in-class anti-CD117 monoclonal antibody as targeted, non-toxic conditioning regimen prior to transplant

Material Transfer Agreement (MTA)

- Outside institution provides research materials only
- No research collaboration
- Neither a licensing option nor rights for commercial purposes may be granted

More on MTAs can be found at: https://www.ott.nih.gov/resources - MTACTA

Examples of NIH MTAs

- **NIAID: Rapid sharing of SARS-CoV-2 Prefusion Stabilized Spike Proteins to Develop COVID-19 Vaccines**
  - Signed MTAs with 75 entities to provide materials for research
- **NIAID: Developing Ebola treatments**
  - MTA to transfer mAB114 to treat Ebola patients in the DRC
- **NIAID: Controlling and preventing asthma progression and severity in children with omalizumab**
  - Clinical MTA with Kaleo, Inc to receive free Auvi-Q autoinjectors for use in a clinical trial testing omalizumab from Genentech, Inc.

Other Types of Interactions between NIH and Industry

- Conditional Gifts

- Direct Purchase for Standard of Care Drugs

Considerations for Human Subjects Research Collaborations

- Principles of the GDS Policy apply
  - Even when NIH funds do not support the genome sequencing and the industry partner performs it
- Certificates of Confidentiality requirement apply for exchange of materials and data

Recent NIH and Pharma Collaborations Leading to FDA Action

Status	Drug Name	Drug Type	Target	Investigator/s	Approval Date	Collaborator
Approved for marketing	Avelumab	Anti PD-L1 Antibody	Merkel Cell Carcinoma	Gulley/Schlom	March 2017	EMD Serono Inc/Pfizer
Approved for marketing	Yescarta	CD19 CAR T	B-Cell Lymphoma	Kochenderfer/ Rosenberg	October 2017	Kite Pharma
Approved for marketing	Lumoxiti	Anti CD22-toxin	Hairy Cell Leukemia	Pastan/Kreitman	September 2018	MedImmune/AstraZeneca
Approved for marketing	Selumetinib	MEK inhibitor	NF1	Widemann/Gross	April 2020	AstraZeneca
Approved for marketing	POMALYST	Immunomodulator	Kaposi Sarcoma	Yarchoan	May 2020	Celgene
Approved for marketing	Nivolumab and Cabozantinib	Checkpoint inhibitor plus tyrosine kinase inhibitor	Advanced Renal Cell Carcinoma	Apolo	January 2021	Bristol Myers Squibb
Approved for marketing	Idecabtagene vicleucel	CAR T-based gene therapy	Multiple Myeloma	Kochenderfer	March 2021	Bristol Myers Squibb
Approved for marketing	Belumosudil	Kinase inhibitor	Chronic graft-versus-host disease	Pavletic	July 2021	Kadmon Holdings
Approved for marketing	Belzutifan	Hypoxia-inducible factor inhibitor	Cancers associated with von Hippel-Lindau disease	Srinivasan	August, 2021	Merck
Breakthrough Therapy	LN-145	TIL therapy	Advanced Cervical Cancer	Surgery Branch	May 2019	Iovance Biotherapeutics
Breakthrough Therapy	MK-6482	Hypoxia-inducible factor-2 alpha inhibitor	von Hippel-Lindau disease-associated Renal Cell Carcinoma	Linehan/ Srinivasan	July 2020	Merck
Orphan Drug	Zotiraciclib	Kinase inhibitor	Glioma	Wu	December 2019	Adastra
Orphan Drug	PRGN-2012	Immunotherapy	Recurrent Respiratory Papillomatosis	Gulley/Schlom	March 2021	Precigen

To learn more, please contact the relevant IC Technology Development Coordinator (David Seager for CC):
https://ott.nih.gov/tdcs

Or read more at https://www.ott.nih.gov.