OPMI - Clinical Trial Ontology (CTO) development notes:

LINKS:

- Clinicaltrials.gov term representation updates document: https://docs.google.com/document/d/1YGYx_gv9rNIeO7MkUGxr2T5bUKXY_2ijMhaRl5Ozh6o/edit
- https://prsinfo.clinicaltrials.gov/trainTrainer/WHO-ICMJE-ClinTrialsgov-Cross-Ref.pdf
- EU Clinical Trials Register: https://www.clinicaltrialsregister.eu/ctr-search/trial/2018-004285-34/GB https://www.clinicaltrialsregister.eu/
- Japan clinical trial example: https://rctportal.niph.go.jp/en/detail?trial_id=jRCTs021190009
- Chinese Clinical Trial Registry: http://www.chictr.org.cn/
- Germany: https://www.drks.de/drks_web/
- https://prsinfo.clinicaltrials.gov/definitions.html#FacilityContact
- ICMJE2clinicaltrial mapping (**revised april 2019**): https://prsinfo.clinicaltrials.gov/trainTrainer/WHO-ICMJE-ClinTrialsgov-Cross-Ref.pdf
- Terms used WHO for clinical trials: **https://www.who.int/ictrp/network/trds/en/**

Coronavirus related links:

- https://www.guidetopharmacology.org/coronavirus.jsp
- https://www.transparimed.org/single-post/2020/03/27/COVID-19-clinical-trials-information-sources

Title VIII of the Food and Drug Administration (FDA) Amendments Act of 2007 (FDAAA)

- https://www.govinfo.gov/content/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf

10/28/2021 9AM-9:20AM

Attendees: Meriam Essahi, Asiyah Lin, Leon Li

Asiyah will start working on the paper from next week.
Next step will be conducting a clinical trial meta-analysis. Besides the three drugs we investigated, other drugs could be Azithromycin. Asiyah will talk to her FDA colleagues about interesting drugs they want to investigate.

10/06/2021 9AM-10AM

Attendees: Meriam Essahi, Asiyah Lin, Leon Li

The team reviewed Meriam's statistics of included and excluded clinical trial related papers obtained from SCIView. The included papers are very low. Most of the papers are excluded:

Hydroxychloroquine: 84.4%(986/1168), Imatnib 76.7%(23/30) and Ivermectin (92.6%) are not in the final inclusion.
The team picked a few excluded papers to investigate. It is found that the clinical trial IDs are included in the discussion. Although the paper is relevant to COVID-19, the specific drug and the clinical trial, the actual content may not be as highly specific as reporting the results of a clinical trial or a protocol of a clinical trial.
The team concluded that the search results can be further narrowed down, and the search algorithm can be adjusted to search the clinical trial IDs included in the abstract which may help to narrow down the results. For epidemiological research purposes, further development of the search algorithm using machine learning, or analyzing the abstract text will be necessary to include.

Next step: writing. And sort out the non-clinical/excluded - which section is the registry ID number located?

09/22/2021 9AM-10AM

Attendees: Meriam Essahi, Asiyah Lin, Leon Li, Alpha Tom Kodamullil

Meriam and Asiyah have completed the screening of SCAIView output. Next step will be to generate a statistics table, and start a final review of the paper.
The group took a look at current edition for editing later. There is only 50% overlaps allowed between the conference paper and the journal paper.

Action item:

1. Asiyah will reach out Brian to set up a follow-up meeting with COKA.
2. Leon will check the PubChem portion of the paper writing.
3. Asiyah will discuss with Oliver the overall architecture part of the paper.
4. All members review the current version.

09/07/2021 9AM-10AM

Attendees: Meriam Essahi, Divya Gutala, Asiyah Lin, Leon Li, Alpha Tom Kodamullil

Meeting recording :
https://nih.zoomgov.com/rec/share/jQWO9fnWyetxAlm9DE0r-lZ5nk66174Sem1qxi4FXE5yHfSyGbecSD4Vvc1GsaLm.MpkDOEA_xFGwMNNT Passcode: +^Jn7e2Z

Meriam provided updates on her manual check on SCAIView output. The second check is needed. Divya and Meriam will work together on the second check.

Next step: provide a descriptive statistical analysis for the screening of SCIView output.
Then work on the paper writing. Target to send to editors: the end of September.

07/22/2021 9AM-10AM

Attendees: Asiyah Lin, Leon Li, Alpha Tom Kodamullil

Due to summer vacations, and work priorities, there is not much progress on analysis and paper writing. In August, we have two calls scheduled: Aug 5th, and Aug 25th. We may cancel these two calls if there are no updates, or if people will take vacations.
We will keep moving at a slow pace, and hopefully in September we will be back on track.

TODO for **Alpha**: follow-up the email with Brian regarding SCAIView presentation.

07/07/2021 9AM-10AM

Attendees: Asiyah Lin, Leon Li, Oliver He, Alpha Tom Kodamullil

Meeting recording:

Each member gave updates.

- Asiyah worked on the list from Alpha's group, and manually curated the article list. **Asiyah** still needs to work on the PMID list analysis part.
- **Asiyah** will connect with Alpha and Brian for SCAIView presentation.
- **Asiyah** will send Alpha the list of false positives identified by her manual curation.
- Leon has been working with Asiyah on modeling and adding properties into CTO ontology. He is working on the Pubchem RDF now.
- Alpha wanted the paper completion status. The paper is 70% done, and Asiyah's analysis should be added.
- The group also discussed the use of "investigational substance" vs. "investigational molecular entity". [https://github.com/ClinicalTrialOntology/CTO/issues/38] **Asiyah** will change the ontology and upload to CTO github.

06/17/2021 11AM-12PM [side meeting on investigational agent/substance/drug]

Attendees: Asiyah Lin, Leon Li, Rimma Belenkaya, Dmytry Dymshyts, Michael (Mik) Kallfelz, James liddil, Larry Callahan

Meeting recording:
https://nih.zoomgov.com/rec/share/b3kBOgwqy4GNQ-U91owst_EPbusUe0PqRInL5oFJmji6wVeWoBAYWZSd9AygZRPt.OHtGKL2Qm8f79noc Passcode: MFc&=wF5

The group discussed the current OHDSI vocabulary team and oncology WG team's proposal of creating a list of investigational drugs. Larry pointed out some useful resources such as GSRS (https://gsrs.ncats.nih.gov) and Inxight Drugs (https://drugs.ncats.io/) from NCATS and FDA.

- RxNorm only captures all approved drugs.
- Drugbank is maintained by Canada University of Alberta. Sometimes the information may not be fully curated, but it is a good portal to use.
- Inxight includes approval indication (high level) and approval year with link the FDA drug approval portal. Although the information is not yet granular for detailed FDA level analysis, this information is good enough for a starting point.
- Rimma pointed out that often the regiment information is missing. Larry commented that the FDA does not approve regiments. Ontology for regiment has been built and incorporated into the OHDSI vocabulary (https://hemonc.org/wiki/Main_Page)
- Multiple investigational terms/concepts were mentioned: inverstigational medicinal products, investigational substance, investigational drug, investigational device, and etc.
- Gap/challenges at FDA is to capture the disease/phenotype/condition in a formalized way to make it computable.

The group also had vivid discussion on how an FDA approved drug related specifically with the indication and population. Off-label use and drug repurposing research needs to have those detailed information. However, there is no straightforward way to capture this.

Decision:

1. Mik will go ahead to add a new vocabulary for "investigational drug" in OHDSI vocabulary.
2. The group should work together on modeling drug approval, off-label use and regiment.

Next step:

1. Mik will send Asiyah the OHDSI poster submission for comments.
2. **Asiyah** will propose the hierarchy for the investigational entities.
3. **Asiyah** will continue working with the group and other ontologists to model the drug approval process and related concepts/terms, to provide a framework for representing off-label drug use and regiment.

06/10/2021, 06/17/2021

Attendees: Asiyah Lin, Leon Li

Asiyah and Leon worked on CTO github issues and added new relations that PubChem needed.
Next step:

1. Asiyah will continue working on the merge file, and GitHub Issues.
2. Leon will work on PubChem RDF next week. He will post any issue encountered with CTO on the GitHub issues for us to track.
3. Asiyah will submit a new term request to OBI to ask for a platform term.

06/03//2021
Attendees: Asiyah Lin, Leon Li, Oliver He

Meeting Recording:
https://nih.zoomgov.com/rec/share/CTwUMrSYff7RX6zEuS3U9nwSj5v-RsTVUTpqfmVql6gb0nXXJw2vHNZKfRdJTNhg.TLurjmTRjJNWIgnB (Access Passcode: SRm1j=M0)

- Status: Asiyah is parsing (programatically and manually) the SCAIView results by separating into : non_clinical trial, result, protocol, review and meta-analysis. - the result needs to feedback to SCAIView team.
    - Current result are viewable on Github : https://github.com/ClinicalTrialOntology/CTO/blob/master/CTO_SCAIView_analysis/output/results-unqie_PMIDs
- Compare the clinical trial list with the SCAIView result: Asiyah will provide a list of NCT ids to Leon, and Leon will provide the reference list from the ClinicalTrials.gov
- Another comparison is comparing among the three lists.
- Parsing the eligibility criteria is very difficult. A good and specific NLP tool is needed to do this work.
- Asiyah and Leon mapped the CT.gov XML tags to the new properties that pubchem requested to add to the CTO ontologies. (https://docs.google.com/spreadsheets/d/1zgVAraGxL_KKQkS1MTt2tQoQE9jp_k5GL9385KhXZqE)

TODO: **Asiyah** will add the terms into the ontology.

05/20//2021
Attendees: Asiyah Lin, Leon Li, Alpha Tom Kodamullil, Oliver He
Meeting recording:
https://nih.zoomgov.com/rec/share/WGQHt_D2CfgOAC2ewo31RynytLb0O4zJtHNuMSL4YjSOlWkBpMLmiQFjzUZQbaw1.d7pAawmstaCPJ8ce Passcode: =K?hD@@4

- Leon is getting the RDF ready, and he can provide the RESTful search. (RDF will not be published)
- Alpha is working on the editing.
- **TODO**: **Asiyah** will set up the call bi-weekly.
- Data exchange: PubChem and SCAIView. PubChem will only need three registries: CT.gov, WHO and Japan. Question to Alpha: will SCAIView have a function to select different clinical trial registries? (TODO: for next call)

04/28/2021

Attendees: Asiyah Lin, Leon Li, Alpha Tom Kodamullil, Oliver He
Meeting recording:
https://nih.zoomgov.com/rec/share/Z_qFA5m3ijuL5ymUDrtcPYrzVqqHuEN9Oz09UuXrGo5S8DqBo9TAn8C3OF3_vZ-o.9o-QVcqz4omu2Ql2 Access Passcode: 7$p10zCq

- We examined the literature list for three drugs given by Alpha's team.
    - Currently, there are 1078 for Imatnib, 8358 for Hydroxychloroquine, and 2159 for Ivermectin found in SCAIView. (received on April 26th)
    - Literature IDs are PubMed, CORDId , PMC and Europe PMC IDs. One clinical trial ID is cited in multiple publications.
    - As of April 28, there are 5502 COVID-19 clinical trials listed on CT.gov, WHO has 4068 clinical trials for COVID-19.
    - **Action item: Alpha's team** will provide an updated list for these three drugs.
    - **Action item: Asiyah** will use updated tables to perform some descriptive statistics and network visualization showing which trials have the most publications. If time allows, may look into those publications and clinical trials.
- Leon's data modeling was reviewed.
    - The team recognizes the need of relating an "investigation molecular entity" and medical intervention. OAE has a "medical intervention" and subclass "drug administration", however, in clinical trials setting the "investigational drug" but not the approved drug is used.
    - **Decision**: a CTO term of "investigational molecular entity administration" and subclasses "investigational drug administration", "investigational supplement administration" are created.
    - **Decision**: a RO relation "has agent" is used to link an investigational molecular entity and its administration process.
    - Leon and Asiyah modified the data modeling accordingly.
    - **Action item**:
        - **Asiyah** will add terms into the CTO.
        - **Leon** will update the data modeling figure in the shared folder.
- Paper progress:
    - We won't be able to make it by April 30th.
    - We should set up our deadline by **May 28th**. The first draft should be done by **May 14th**.
    - Leon's session will be presented as clinical trial centric data modeling guided by CTO.
    - **Action Item: Asiyah** will update the github with the modeling figures published from the CTO conference paper.
- Next meeting will be May 13th 9AM EST, Oliver won't be able to join.

04/22/2021 discussion between Leon and Asiyah

- The ivermectin has few synonyms on NCTI, which is included in the CT.gov backend

- The investigational molecular entity linking drugs and chemical compounds is a useful resource. -consider to share later
- Leon will finalize the modeling and send it back to Asiyah for review.

04/22/2021

Attendees: Asiyah Lin, Leon Li, Alpha Tom Kodamullil, Oliver He
Meeting recording:
https://nih.zoomgov.com/rec/share/X2gxqGP8gTmSjxCNEXejgLT3sPQBPNTVZxPociFXYfb67cns1kaiTl4stGRq2iZ_.E8vSSZ9np2F7AHWQ Passcode: !4HnLp@q

- Alpha showed the interface for covid.scaiview.com with search "Imatinib" example. The result does not provide the list of publications but only statistics. Alpha will resolve this technique issue.
- The team decided to add an analysis part for the three drugs: Ivermectin, Hydroxycloroquine, and imatinib.
    - Alpha will send the clinical trial list to Asiyah and Leon.
    - Asiyah and Leon will do a QC, as imatinib, imatinib mesylate and Gleenvec are often used interchangeably. The QC is to see if SCAIView can retrieve all clinical trials related with the three entities from clinicaltrials.gov
    - Asiyah will lead the analysis of the clinical trials' meta-data that will be collected from each clinical trial registries organized by CTO.
        - Two types of analysis can be done: study design and result comparison.
        - If the study design has limitations, then the results from biased or limited design are not reliable.

04/16/2021

Attendees: Asiyah Lin and Oliver He
Meeting recording :
https://nih.zoomgov.com/rec/share/6PxMCI-hsVpOa6Pp1n3aWJcqGr29X6a8hCZP_PYFn0hCXaTfhqHcGTaEvXDqBJCh Passcode: 6RXaAT

- Asiyah and Oliver discussed interoperability based on Asiyah's presentation on NCPI (NIH Cloud Platform Interoperability) effort.
- Oliver suggested Asiyah to develop an ontology for interoperability.

03/31/2021

Attendees: Asiyah Lin, Leon Li

- Create a list to include new terms needed to be added to the ontology
- The drug repurposing use case is too complicated to model. Mapping to DrugOn does not entail the drug is approved due to the vague use of the names of drugs in CT.gov. Consideration of drug repurposing need the approval

- Combinational therapy: the combinational drugs have to be used in the same arm. https://clinicaltrials.gov/ct2/show/NCT04359095

    - ClinicalTrial1 → Drug1
    - ClinicalTrial1 → Drug2
    - Drug1: DrugA → InvestigationalMolecularEntity1 (has-active-ingredient → ChemicalA)
    - Drug2: DrugB and DrugC → InvestigationalMolecularEntity2 (has-active-ingredient-> ChemicalB; has-active-ingredient-> ChemicalC);

03/25/2021

Meeting recording:
https://nih.zoomgov.com/rec/share/_5Erc4ne6m1Oep3G4275Y7QqELTeT6a8h3cc-fcNn0ZJDUxe8hJTOGBh51g-X76i Passcode: 5*rVejx9

Attendees: Asiyah Lin, Leon Li, Alpha Tom Kodamullil, Oliver He

- Alpha will present later when she is ready
- We discussed what drug names to give to Alpha for interop use case
    - Asiyah: Ivermectin
    - Leon: Imatnib - propose to use drug combination
    - Oliver: Hydroxychloroquine. - may have some drug names since he is working on COVID19 cocktail drugs
- We will connect with the COKA group, after Alpha searched the clinical trial studies, we could use his product to create the evidence for meta-analysis from those clinical trial studies.
- Next step, Alpha will not join the April 1st call. But the group will still meet.
- Asiyah will set up meetings April 8th onwards.
- Oliver proposed to use hydroxychloroquine as a use case to pull data out from PubChem RDF to add to CIDO ontology. He has 106 drugs candidates identified in his preprint paper:
  https://www.preprints.org/manuscript/202003.0413/v1
  https://www.nature.com/articles/s41597-021-00799-w.pdf
    - Asiyah proposed to search PubChem RDF for Oliver to pull into his ontology directly.
    - If possible, Oliver's student may help to scale up the one search example

Action item:

- Asiyah and Leon will meet next week separately to discuss data modeling and ontology editing.
- Asiyah and Leon will discuss how to pull hydroxychoroquine from PubChem for Oliver's use case.
- Alpha will prepare the SCAIView demo.

03/18/2021

Meeting recording:
https://nih.zoomgov.com/rec/share/uswpIa6urHlOHZ3P6mbNAox5BoLET6a81nMc-KYFmEZGh5c8zcjZ1CMEdUiHp4jf Passcode: jL5^VpBP

Attendees: Asiyah Lin, Leon Li, Alpha Tom Kodamullil, Oliver He

- Alpha will present a SCAIView Demo next week and publish to the Biomedical Ontology YouTube channel.
- Separating ontology modeling and data modeling for PubChem use cases is the direction for PubChem.
- Leon presented the data/annotation modeling part.
    - Future work: differentiate drugs used in different arms and cocktail drugs.
- Use case for Interoperability between PubChem and SCAIView: PubChem export to SCAIView on clinical trial related drug and compound, SCAIView will provide clinical trial associated literatures.
    - Imatinib as an example
- Oliver wants to see if there are interop opportunities for CIDO and CTO. Oliver can present the CIDO work to COVID19 ontology Harmonization WG.
- Asiyah updated the group on her call with Ida Sim. The need of making patient level clinical trial data open is there, although heavy lifting. Asiyah will talk to multiple personnel that Ida identified and find strategic partnership.However the CTO paper is the priority at the moment.

Action item:

1. Alpha to prepare the SCAIView presentation for next week if possible.
2. Alpha and Leon to prepare the Imatinib example for interoperability/data exchange use case between PubChem and SCAIView
3. Leon and Asiyah will continue discussing the ontology modelling and data modelling for PubChem.
4. Asiyah to follow-up with Ida's call.

03/12/2021

Attendees: Asiyah Lin, Leon Li

Leon and Asiyah discuss PubChem RDF modeling

- Create two diagrams: one for ontology modeling, the other for data/annotation modeling https://www.w3.org/TR/annotation-vocab/
- In the ontology modeling, the relation between an identifier and a clinical trial should be from identifier to clinical trial.
- Use case: finding the drug repurpose trials: if the compound is an entity from Drug Ontology or RxNorm, the clinical trial is a drug repurposing trial. However, the challenge is the timestamp of the clinical trials. If an investigational trial is being approved, the investigational entity will become a drug, and the clinical trial will become.
- Paper publication requirement: one XML file and a RDF example.

- For continuous development to production level on Github: we will document and provide convertion codes and examples for all use cases of the interventions: drug combination, procedure, drug and procedure, vaccine, behavioural, and many others.

03/11/2021

Attendees: Asiyah Lin, Leon Li, Alpha Tom Kodamullil, Stephan Gebel, Barry Smith
Meeting recording link:
https://nih.zoomgov.com/rec/share/5dFnD6Pp0jlLWdLf61j1Cos-Jan3T6a8hCUX_vNcz0YU5Vzs4pLd9P-lRuxQ8x-e Passcode: vf*vM7uv

- Leon presented the PubChem Clinical Trial RDF modeling
    - Barry comments: not all the clinical trials have the IDs
    - Barry: Medical intervention is a process, but not a ingredient - need to double check the shot relation
    - Barry's concern: Disease ontology box and pc:disease, literal box
    - SSSOM:lexical match and SKOS:close match needs more consideration.
    - Use case: finding the drug repurpose trials using Drug Ontology.
- Alpha can finalize the data analysis part by the end of March.
- Leon and Asiyah will target the PubChem Clinical Trial RDF modeling and writing by the end of March.
- Asiyah will update her involvement with OCRe, HL7 and FHIR for the 1st draft.
- Stephan will leave the SCAI officially next Monday. He will keep in touch
- Stephan showed the COVID19 SCAIView, which is awesome for potential use for the COKA working group and the COVID19 drug repurposing prediction.
- https://covid.scaiview.com/ needs promotion and funding opportunities.

03/04/2021

Attendees: Asiyah Lin, Leon Li, Alpha Tom Kodamullil, Barry Smith

- Alpha: most of the updates are done, and will be possibly finalize by next two weeks.
- Leon and Asiyah will meet on Friday to discuss PubChem use case and PubChem content updates.
- Asiyah will meet with Ida Sim to discuss collaborations with OCRe, Vivlly datasets.
- Barry suggested to check on Immport for the clinical trial data
- Alpha and Leon introduced themselves to Barry. Alpha is building some ontologies for mental diseases. She will send info to Leon and Barry.
- Asiyah updated her involvement on HL7BR&R group, and the group's work on FHIR resource ResearchStudy. Asiyah and Barry briefly discussed the FHIR. NIH has emphasized using FHIR for clinical research. Currently FHIR is in the early stage, and besides HPO, there is no coverage yet for biology data.

02/25/2021

Attendees: Asiyah Lin, Stephan Gebel, Leon Li, Barry Smith

- Leon: needs to add some property for the modeling.
- Barry Smith: We need to check with Ida Sim, who has the same ontology with the same acronym.
- Alpha: updated the document to JBMS format
- Stephan: waiting for data analysis updates.

02/18/2021

Attendees: Asiyah Lin, Stephan Gebel, Leon Li, Alpha Tom Kodamullil, Oliver He

- Paper preparation: Asiyah will send Alpha the JBMS example for her to format
- Alpha and Stephan will add some analysis
- Asiyah: more details will need to be modelled in the ontology, such as arms and selection criteria
- Asiyah: comparison with other ontologies and interoperability with other ontologies
- Asiyah: reach out to the OBI team to seek feedback.
- Oliver: address reviewer's comments.
- May change the title later.
- Current JBMS folder is here: https://drive.google.com/drive/folders/1kWwBPA8hcYyTO45TT29FECZjm0KDvbGN?usp=sharing

02/10/2021

Attendees: Asiyah Lin, Stephan Gebel, Leon Li, Alpha Tom Kodamullil

- Action item: Asiyah will contact the ICBO organizer to express the intention to publish JBMS paper.
- Paper submission:
    - Convert the current submission into new template
    - May need to extend the paper into 20+ pages (currently 11 pages)
    - Need to work on the ontology itself
    - Monthly meeting for CTO - last Wednesday 9AM-10AM EST.
    - Meet for paper, Feb 18th 9AM-10AM EST.

12/17/2020

Attendees: Asiyah Yu Lin, Stephan Gebel, Leon Li

- Asiyah: OMOP clinical trial WG; some people evaluated CTO, and determined that CTO is not yet useful for their use cases.
- Stephan: The CTO is not able to capture the measurement.
- Leon: For PubChem, missing relations and terms will be requested.
- We need to identify the gaps of CTO. - use case?
- COVID19 vaccine protocol modeling of CTO?
- GitHub (how to make changes): Record every change on the issue tracker, and members will follow-up with the issues. If no rejection, we could update and close the

issue. If there is a meeting needed to achieve consensus, we will convene a meeting to discuss the changes.

The proceeding paper published:
http://www.informatik.uni-leipzig.de/~loebe/tmp/ICBO2020/paperH.pdf

TODO:

- Check the missing relations and terms from the paper and add them to the issue tracker for adding them to the ontology.
- Leon and Asiyah will discuss the new pattern design for the new use case.
- Asiyah, Stephan and Leon will check on the issue tracker list, follow-up with the discussion on issue tracker.
- Stephan will discuss with Alpha about paper publishing in JBMS journal. Next meeting will be decided after the 18th of January, 2021.

09/29/2020

Attendees: Asiyah Yu Lin, Stephan Gebel, Leon Li, Oliver He

- Asiyah: Propose CTO implementation on COVID-19 vaccines currently in Phase III clinical trials: https://github.com/linikujp/ClinicalTrialParsingTool/tree/master/COVID19VaccineCT
    - Nature paper about: Covid19 related vaccines (Evolution of the COVID-19 vaccine development landscape)
    - https://github.com/linikujp/ClinicalTrialParsingTool/tree/master/COVID19VaccineCT
    - Modeling the phase III clinical trials and analyzing them, later mintor adverse events (AE).
    - Prepare a draft about the scope of the proposed work and send to everyone.
- Oliver:
    - Work on Vaccine presented in VDOS workshop.
    - Possible to get a student involved in this work.
- Skip next week's meeting.

TODO:

- Asiyah will send out an abstract to submit to WCO-2020 to the group

09/22/2020

Attendees: Asiyah Yu Lin, Stephan Gebel, Leon Li

- ICBO2020 feedbacks: Date as an ICE was asked. Asiyah answered it is unsolved. In CTO the implementation is as a data property.
- ICBO potential collaborators: Informed Consent Ontology and Behavioural Change Intervention Ontology - will follow up conversations with Marcy Harris and Janna Hasting

- Publish the video: Stephan will check if possible on Github. YouTube publication is better with ICBO2020 Channel.

09/15/2020

Attendees: Asiyah Yu Lin, Stephan Gebel, Leon Li, Oliver He

- ICBO2020 slides video recording has been uploaded.
- The group discussed the comments from Barry Smith: about the naming of “Japan Clinical Trial identifier”. Barry suggests to change to “Japanese”. We searched google, and found out that the naming of countries are used interchangeably for different countries, see wiki https://en.wikipedia.org/wiki/List_of_clinical_trial_registries . The Japan Clinical Trial means the clinical trial registry that is located in Japan. We will need to define better.

09/08/2020

Attendees: Asiyah Yu Lin, Alpha Tom Kodamullil, Stephan Gebel, Leon Li, Oliver He

- The group discussed the slides talk for ICBO2020.
    - Stephan showed his slides.
    - Leon will finalize his part by tomorrow.
    - Stephan, Leon and Asiyah plan to set up a WebEx and work on the recording on Friday morning. The team will discuss the time offline.
- The group discussed the comments from Barry Smith. Asiyah will work on the manuscript by tonight and send it out to Barry as well as the ICBO 2020. It is unsure if the ICBO2020 will allow the uploading at this point. We will try.

09/01/2020

Attendees: Asiyah Yu Lin, Alpha Tom Kodamullil, Stephan Gebel, Leon Li, Johannes Darms, Oliver He

- The revision camera-ready version has uploaded to ICBO2020 easy chair. However, this version is currently under review at CDRH center level and Barry Smith. When those reviews are completed, we hope to upload a final version to ICBO2020.
- Prepare for the ICBO2020 virtual meeting:
    - Asiyah will provide the draft slides for 10 minutes’ talk by Thursday.
    - Tentatively 3 speakers: Asiyah, Stephan and Leon
    - Tentatively using WebEx or other meeting recording system to hold a three people’s meeting for recording.
    - Everyone who wants to participate should register. Alpha’s group will pay the 100 euro for publishing.
- Asiyah’s office is planning to use CTO for robotic devices analysis. We will need to prepare for next year’s face-to-face presentation.

08/25/2020

Attendees: Asiyah Yu Lin, Stephan Gebel, Leon Li, Johannes Darms, Oliver He

- Addressing the CTO ICBO2020 paper reviewer's comments. As the addressing comment portion is not needed for the camera-ready version, Asiyah will submit the camera-ready draft by the end of this week.
- Discussed the implementation of time ontology representing study start date and completion date in only xsd:date format
    - Leon and Asiyah implemented two solutions: 1) import the 'time instant' class and 'in XSD time' data property from time ontology; 2) directly define CTO's data property 'has start date' and 'has completion date' the range of "xsd:date"
    - The team discussed the options of importing time ontology's object property - has beginning and has end. -- this implementation requires a creation of the duration temporal region where a clinical trial process occupies. It is not the use case of PubChem at the present.
    - Oliver thinks both solutions are OK. Leon and Asiyah will continue to implement this and the team may continue to discuss.

08/18/2020

Attendees: Asiyah Yu Lin, Stephan Gebel, Leon Li, Johannes Darms

- Date format in the ontology: data property or annotation property? Use of Time ontology may be possible.https://raw.githubusercontent.com/w3c/sdw/gh-pages/time/rdf/time.ttl https://www.w3.org/TR/owl-time/#motivation
  Asiyah and Leon will continue looking into this issue.
- Manuscript review: Asiyah had multiple people at FDA to review and discussed the future possible use of CTO internally at FDA. FDA folks also suggest reaching out to ClinicalTrials.gov -- Barry Smith is unable to review the manuscript so far. Team addressed comments from FDA folks. -- Asiyah will work on revising the manuscript and aims to submit by the end of this week.
- Track issues: Stephan identified some terms from PubChem example, and Asiyah, Leon, and Oliver will follow up with the issue track.

08/11/2020

Attendees: Asiyah Yu Lin, Stephan Gebel, Leon Li, Johannes Darms, Oliver He

- Camera-ready version for ICBO2020 is due by the end of July. Will ask the committee to extend the deadline.
- Double checked the excel sheet for OPMI switch. Stephan will upload the excel sheet to the github/docs. Johannes will merge his branch to CTO.
- Moving forward: review the imported terms, submitting issues and addressing issues.

08/06/2020

Attendees: Asiyah Yu Lin, Stephan Gebel, Johannes Darms, Alpha Tom Kodamullil, Leon Li, Oliver He

- Johannes added the RO term to import
- Leon and Asiyah are implementing the CTO.

1. Issue with titles -- annotation property or an individual? There is no meaning to create individuals for titles.
2. We will keep the title classes
3. We keep implementing the PubChem use case, and we will find issues for CTO.
4. Keep few instances modelings in the CTO, but the whole clinical Trial RDF will be separate. -- once completed the ontology development, we could put an example file and implementation file/webpage.

- In the future, text mining use cases, applications for individual CTO RDFs, and reach out to ClinicalTrials.gov, or wikidata.

07/14/2020

Attendees: Asiyah Yu Lin, Stephan Gebel, Johannes Darms, Alpha Tom Kodamullil, Leon Li

- Discussed Stephan's excel sheet and assigned terms that should be clinical trial terms.

07/07/2020

Attendees: Asiyah Yu Lin, Stephan Gebel, Oliver He, Johannes Darms, Alpha Tom Kodamullil, Leon Li

- Johannes will work on the CTO namespace transformation, and then request the purl, and request the metadata to be listed.
- Some OPMI terms will be given CTO namespace: https://github.com/ClinicalTrialOntology/CTO/issues/10
    - maintain a excel sheet for OPMI - CTO terms conversion
    - Checking the completion of the excel sheet
    - After the completion check, OPMI will change the current OPMI URIs into CTO URIs.

06/29/2020

Attendees: Asiyah Yu Lin, Stephan Gebel, Oliver He, Alpha Tom Kodamullil

- CTO namespace is approved. So we will need to work on changing the URIs for all the CTO terms now.
- Schedule OBI meeting in the future.
- Future meetings will move to Tuesday 8:30AM to 9:30AM to accommodate other people's time.

06/23/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Johannes Darms, Oliver He, Alpha Tom Kodamullil

- Definition of clinical trial needs to get communities' buy-in. Maybe a survey or the delphi process is needed.

- OBO foundry name space: approach on wiki for decision at 4 weeks, or email. Alpha will lead and contact Oliver for questions. Cc everyone in the loop.
- Camera-ready revision by end of July.
- Address the comments:
    - Ontology for disease: reviewer suggested MONDO, PubChem has a repository for diseases, which can include MONDO.
    - Discussion OCRe and CDISC (reviewer 2)
    - OBI communications, to represent OBI and ask their input. (review 3)
    - Address review 3's questions: date, registry, use of "agent", "investigational"

06/16/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Johannes Darms, Oliver He

- Asiyah will add the relation terms in the CTO, and we need to add the definitions.
- Clinical trial definition:
    - A broader definition encompassing interventional study and observational study is CTO's goal.
        - a novel contribution to the community.
        - a consensus of the team.
    - What are the differences between clinical research and a clinical trial?
    - Differentiate the Interventional study and a clinical trial
    - Objective: generate data on safety and efficacy.
    - Clinical trial includes veterinary drugs - Asiyah will reach out to colleagues at FDA
    - Regulations?
    - Search "observational clinical trial" concept and read more to come up with a definition as CTO group.
    -
- Useful links:
    - https://www.ncbi.nlm.nih.gov/mesh/2009834
    - https://www.purdue.edu/vet/ctr/clinical-research/veterinary-clinical-trials.php
    - https://jbiomedsem.biomedcentral.com/articles/10.1186/2041-1480-5-29
    - https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

06/12/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Alpha Tom Kodamullil, Johannes Darms, Oliver He

- Time changing for next two weeks June 16th 8:30 to 9:30, June 23th 8:30 to 9:30.
- CTO discussion:
    - Study purpose -- OPMI clinical trial primary purpose specification-- is_a objective specification

    - We can add more subclasses for the purpose.
    - Clinical trial and study's difference -- to define the clinical trials to differentiate with studies
        - interventional study and observational study
        - Clinical trial relate to regulatory processes and registration requirement
        - CT.gov has study type list:
          <xs:simpleType name="study_type_enum">
          <xs:restriction base="xs:string">
          <xs:enumeration value="Expanded Access"/>
          <xs:enumeration value="Interventional"/>
          <xs:enumeration value="N/A"/>
          <!-- Redacted records only -->
          <xs:enumeration value="Observational"/>
          <xs:enumeration value="Observational [Patient Registry]"/>
          </xs:restriction>
          </xs:simpleType>

06/05/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Johannes Darms, Oliver He

- OBO foundry submission
    - Alpha already submitted the request for namespace on OBO foundry issue tracker: https://github.com/OBOFoundry/OBOFoundry.github.io/issues/1220
- CTO engineering:
    - Stephan will add or recheck CTO terms, add more terms on the issue track. https://github.com/ClinicalTrialOntology/CTO/issues/17
    - Then we will work on OPMI term to CTO term change (Oliver and Asiyah).
    - URL will need to change after the name space approval by OBO foundry (Alpha and Johannes).
- Leon will work on the RDF example for the paper, and notify Stephan on terms that are needed for the example. Stephan will prioritize the task.

05/22/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Sumit Madan, Oliver He

- Asiyah asked one or two examples of literature about clinical trial records.

results_annotated

count	conceptId	conceptName	synonym
26	CTI:NCT04252664	CTI:NCT04252664	NCT04252664
20	CTI:NCT04257656	CTI:NCT04257656	NCT04257656
17	CTI:ChiCTR2000029765	CTI:ChiCTR2000029765	ChiCTR2000029765
13	CTI:NCT04315948	CTI:NCT04315948	NCT04315948
13	CTI:ChiCTR2000029308	CTI:ChiCTR2000029308	ChiCTR2000029308
12	CTI:NCT02845843	CTI:NCT02845843	NCT02845843
9	CTI:NCT04287686	CTI:NCT04287686	NCT04287686
9	CTI:NCT04280705	CTI:NCT04280705	NCT04280705
8	CTI:NCT01304914	CTI:NCT01304914	NCT01304914
8	CTI:NCT04312009	CTI:NCT04312009	NCT04312009
8	CTI:NCT04283461	CTI:NCT04283461	NCT04283461
8	CTI:NCT02788188	CTI:NCT02788188	NCT02788188
8	CTI:NCT01610245	CTI:NCT01610245	NCT01610245

- NCT04280705 -- NIH remdesivir
  NCT04331808 -- Tocilizumab -- mentioned on NIH's treatment guideline
- Figure 2:
  - revised "Disease" to "Medical condition"
  - Deleted "healthy enrollee", because it doesn't apply to all clinical trials.
  - other changes, "human subject" etc.
- Japan clinical trial identifier is not a "real" identifier, but four individuals:
  - Japan Registry of Clinical Trials (jRCT),
  - The University Hospital Medical Information Network Center (UMIN-CTR),
  - The Japan Medical Association Center (JMACCT),
  - The Japan Pharmaceutical Information Center (JAPIC).

05/19/2020

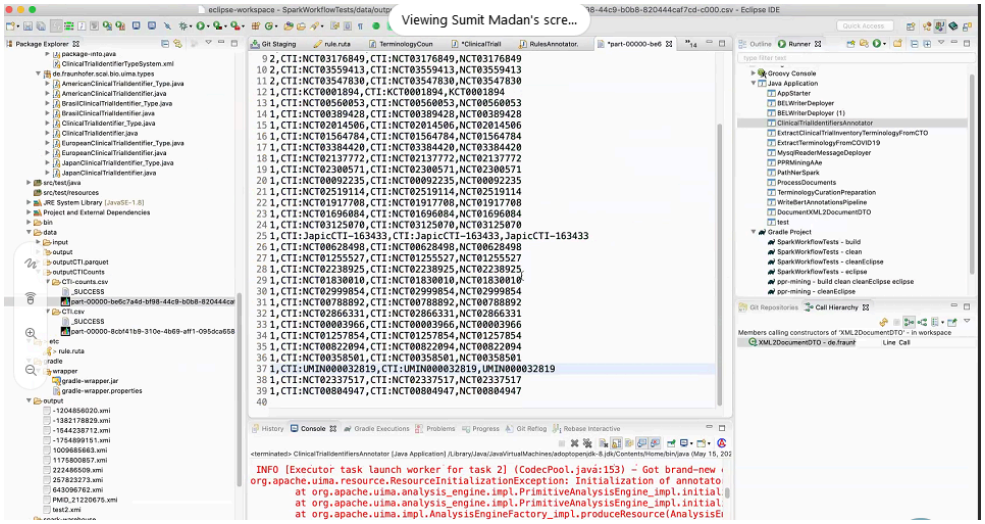
Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Sumit Madan, Alpha Tom Kodamullil

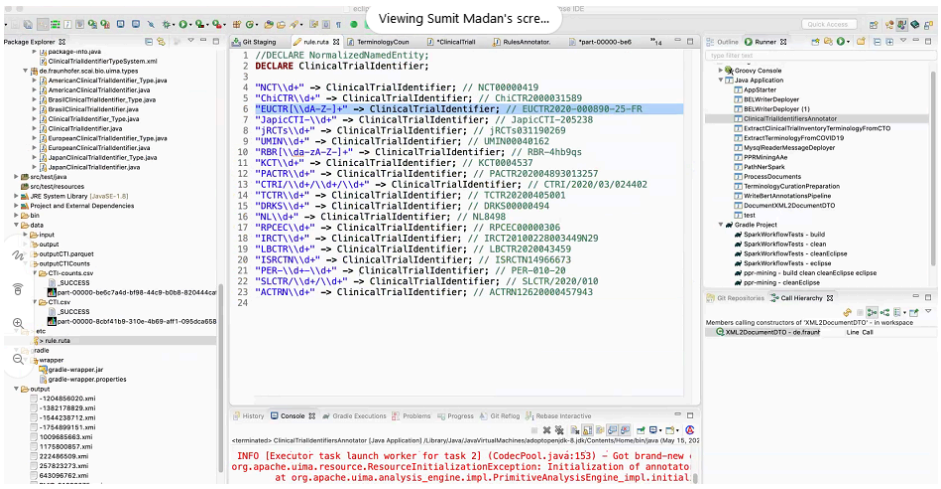
- Sumit will add the result for use case 2 today
- Asiyah will generate another document using the template, and share it with the group for finalizing by today.
- Asiyah suggests adding the Canada registry, but Stephan says the Canada registry is not in the WHO primary registries list, and use case 2 will only use the WHO primary. Leon mentioned that WHO registry network (https://www.who.int/ictrp/network/en/) include Primary Registries, Partner Registries, Data Providers, and Registries working with the ICTRP towards becoming Primary Registries. Ontology will include all the registries, but it's up to the application to choose to use the ontology.
- What is a clinical trial? Seems a combination of "clinical study" and "human subject study".

05/15/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Sumit Madan, Oliver He

- Sumit presented text mining results of identifying registry identifier in literature, however, the current rules do not include the chinese clinical trial registry identifier





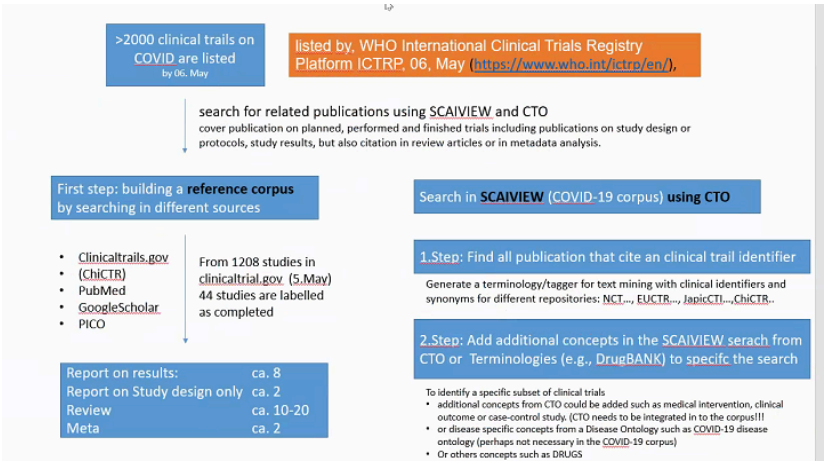
  - Oliver asks how the data shared among different registries. Leon said that some major data contributors(US, EU, and Japan) send data to WHO. How data interchange happens is unknown. It is unknown the data exchange in US ClinicalTrials.gov. Stephan said that WHO has a list of 2000 clinical trials from all over the world on COVID 19. The purpose of the text mining is to find the clinical trials identifier of the list from the literature. https://www.who.int/ictrp/network/en/
  - How ontology will address this? -- we should mention this in the paper.
  - Leon asks if there is license issue of using WHO clinical trial data. Per his example, he can download, but can not post it on the website or redistribute.
- Paper discussion:
  - Selection of the ontology to reuse: OPMI or ERO? Will use more OPMI, because ERO will phase out.
  - OPMI will donate the ‘clinical trial’ to CTO.
- Work on the ontology engineering part:

- Oliver and Asiyah will use branches to add new terms in CTO.Use pull requests to merge to CTO by Sumit or Johannes.
- Add everybody into the Github repo. -- should be done.
- Will focus on the terminologies used for the manuscript first, other issues will be left in the backlog for future development.

05/06/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Alpha Tom Kodamullil, Oliver He

- Stephan presented the text mining work:



- The SCAIVIEW is focused on finding studies research papers of clinical trials, such as the protocol, study results etc. that provide more detailed info but not the commentary papers. Besides, indexing is delayed in PubMed. Use free text search will be faster.
  - Alpha showed the platform covid.scaiview.com (publically available now but not publically announced)
  - We could work together on COVID 19 terminology (CIDO with Alpha's team for the backend of covid.scaiview) -- Alpha will get back to the group next week on this collaboration
- Oliver showed the WHO ICTRP site: https://www.who.int/ictrp/en/
  - COVID19 trials are downloaded in a csv file.
  - Stephan has explored this database and integrated with the text mining work.
  - How to use CTO to represent this as an example -- maybe a use case for the manuscript.
  - Stephan will take the lead on this use case investigation, and come back on the text mining results next week.
- The group agrees that we will put more efforts on the writing in order to meet the deadline for submitting the paper on time.

04/24/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Sumit Madan

- Next meeting will move to Thursday as May 1st is a holiday in Germany.
- Leon and Asiyah showed the use case model for PubChem
    - Key change: introduce experimental “drug” molecular entity
    - Sumit pointed out that one clinical trial may use multiple experimental “drug” molecular entity - which can be add into the PubChem figure in Github
    - Experimental molecular entity can be an repurpose approved drug for off-label indication
    - The different treatment group that uses an approved drug for comparison is not yet included in this model -- will be discussed as a limitation in the paper
- Stephan suggests to add subclasses under “clinical trial” - interventional clinical trial, observational clinical trial. (see 3/27 memo for other types)
    - ClinicalTrials.gov uses a broader concept of clinical trial--more close to any investigation using human subject.
    - The regulatory paradigm is changing to utilize the observational study for approval. -- a discussion point for the paper.
    - By defining different types of study, and investigational subjects, we can create a better interface to entering the clinical trials to see all different categories of the clinical trials.
- Oliver sent the figures for high level pattern but he couldn’t attend this meeting

04/17/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Oliver He, Alpha Tom Kodamullil, Sumit Madan

- Worked on the paper ICBO-2020: https://icbo2020.inf.unibz.it/call-for-papers/
- Sumit demonstrated the SCAIVIEW tool. -- use case discussion for ICBO paper.- not yet finalized.

04/09/2020

Attendees: Leon Li, Asiyah Yu Lin, Alpha Tom Kodamullil, Oliver He

- Alpha updated the text mining use case: mining the clinical trial literature from PubMed and Google Scholar, the goal is to better identify the clinical trial literatures than Google Scholar and PubMed.
    - Currently MERS and SARS are use cases. But not COVID-19, because no trials have been completed yet.
    - Next week Alpha and Sumit may present their work on text mining.
- Oliver: we should start writing.
    - **https://drive.google.com/open?id=12BdgrKi5afBrdrRgRc_GVN0ChaMHRG_eO6IfJXG2qFw**

04/03/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Sumit Madan and Oliver He

- Sumit gave updates on COVID-19 text mining activities - Kaggle Challenge.

- Oliver presented his two recently published and pre-print papers on COVID-19: Vaxgin-ML for vaccine design and Ontology based COVID-19 drug selection
    - https://www.preprints.org/manuscript/202003.0413/v1
    - https://www.biorxiv.org/content/10.1101/2020.03.20.000141v2
- ICBO Paper submission (due May 26) should be the priority.
    - PubChem use case 1
    - Discuss on 2nd use case
- Stephan will give an update on 2nd use case and date for next meeting (Friday is a Germany holiday)

03/27/2020

Attendees: Leon Li, Asiyah Yu Lin and Oliver He

- Oliver suggests classify clinical trials, drug clinical trials, vaccine clinical trials, etc.
    - https://clinicaltrials.gov/ct2/html/images/info/public.xsd
        - <xs:enumeration value="Behavioral"/>
        - <xs:enumeration value="Biological"/>
        - <xs:enumeration value="Combination Product"/>
        - <xs:enumeration value="Device"/>
        - <xs:enumeration value="Diagnostic Test"/>
        - <xs:enumeration value="Dietary Supplement"/>
        - <xs:enumeration value="Drug"/>
        - <xs:enumeration value="Genetic"/>
        - <xs:enumeration value="Procedure"/>
        -
        -
        - <xs:enumeration value="Other"/>
        - Vaccine
    - https://www.fda.gov/patients/clinical-trials-what-patients-need-know/what-are-different-types-clinical-research
        - **Treatment Research** generally involves an intervention such as medication, psychotherapy, new devices, or new approaches to surgery or radiation therapy.
        - **Prevention Research** looks for better ways to prevent disorders from developing or returning. Different kinds of prevention research may study medicines, vitamins, vaccines, minerals, or lifestyle changes.
        - **Diagnostic Research** refers to the practice of looking for better ways to identify a particular disorder or condition.

    - **Screening Research** aims to find the best ways to detect certain disorders or health conditions.
    - **Quality of Life Research** explores ways to improve comfort and the quality of life for individuals with a chronic illness.
    - **Genetic studies** aim to improve the prediction of disorders by identifying and understanding how genes and illnesses may be related. Research in this area may explore ways in which a person's genes make him or her more or less likely to develop a disorder. This may lead to development of tailor-made treatments based on a patient's genetic make-up.
    - **Epidemiological studies** seek to identify the patterns, causes, and control of disorders in groups of people.

- TODO
    - Split current design pattern into a very high level pattern
    - And then provide specific pattern for drug, vaccine, medical device, biologics etc.

03/20/2020

Attendees: Leon Li, Asiyah Yu Lin, Alpha Tom Kodamullil, Sumit Madan, Oliver He

- Pattern design has been uploaded to github:
    - https://github.com/ClinicalTrialOntology/CTO/tree/master/docs

- Leon and Asiyah presented the pattern design, below is the feedbacks from the group:
    - Added "investigates" to link "clinical trial" and "medical condition" as shortcut
    - Link "clinical trial" directly to a hypothetical class encompass "drug, vaccine, device, diet, or behavioural" -- still not decided yet
    - It's possible to add subclasses of clinical trials and link directly to the drug, vaccine or substances that "is the subject of investigation".
    - Adjust the link to show arrows

- Copy of the chat information:

from Sumit Madan to everyone:
RO has "Is used to study" which comes next to investigate
http://www.ontobee.org/ontology/RO?iri=http%3A%2F%2Fpurl.obolibrary.org%2Fobo%2FRO_0003301
from Yu Lin to everyone:
RO_0003301 is "has role in modeling"
from Yu Lin to everyone:
Sorry, "is used to study" is an alternative term.
from Sumit Madan to everyone:

yes, right.
from Sumit Madan to everyone:
what i wanted to say is, that we should create this new relationship.
from Sumit Madan to everyone:
@asiyah: for me "is used to study" and "has role in modeling" do not have exactly the same meaning..
from Sumit Madan to everyone:
probably change "investigate" to "investigateS" ..
from Yu Lin to everyone:
https://www.fda.gov/patients/clinical-trials-what-patients-need-know/what-are-different-types-clinical-research
from Sumit Madan to everyone:
[15:27:57] smadan@bond: /scratch/Clinical_trials > cat intervention_types.txt |sort | uniq -dc
37803 <intervention_type>Behavioral</intervention_type>
24275 <intervention_type>Biological</intervention_type>
917 <intervention_type>Combination Product</intervention_type>
42704 <intervention_type>Device</intervention_type>
5720 <intervention_type>Diagnostic Test</intervention_type>
13451 <intervention_type>Dietary Supplement</intervention_type>
219120 <intervention_type>Drug</intervention_type>
2344 <intervention_type>Genetic</intervention_type>
65783 <intervention_type>Other</intervention_type>
38810 <intervention_type>Procedure</intervention_type>
6715 <intervention_type>Radiation</intervention_type>
from Sumit Madan to everyone:
the numbers will change.

- Oliver suggested to link to vaccine ontology for certain types of clinical trials, such as COVID-19.
- Sumit re-sent invitation to grant maintain permission for github account .
- Sumit will present a text-mining use case next time.

03/13/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Johannes Darms, Oliver He

- Leon and Asiyah showed the modelling of clinical trial general terms and essential terms. Many relationships are missing for now.
- Oliver showed what is available in OPMI: modelling OMOP.
- Stephan showed the current CTO.
- Use “study design” instead of “study type”. Follow and align with OBI’s current example: http://www.ontobee.org/ontology/OBI?iri=http://purl.obolibrary.org/obo/OBI_0500000 (need to align with WHO and Clinical Trial’s terminologies)
  In OBI, a planning has a specific output that is a study design, and an investigation has part of this planning. We will need to investigate if a study design will need to directly link to a clinical trial per a use case.

TODO:

1. Leon and Asiyah will model one use case. Or model the clinical trial based on 03/06 discussion.
2. Leon will upload the VUE file onto Github site.

3. And Stephan will add terms and relations per our modelling.
    a. Add “outcome specification” as a subclass of “objective specification”
    b. Change “outcome measurement data” to “outcome measurement result”
    c. Add “outcome measurement” as a subclass of “process”
4. Stephan’s team: Please change users' roles in the Github repo, so Leon, Asiyah and Oliver can upload files to Github repo.

03/06/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Sumit Madan, Johannes Darms, Alpha Tom Kodamullil, Oliver He (yonggunhe@gmail.com)

- Use case COVID-19:
- Stephan: WHO - about 20 groups are developing vaccines
- Let’s plan for the conference paper submission for: ICBO-2020 (https://icbo2020.inf.unibz.it/): 8-10 pages
- Deadline of submission: April 20th.

Paper outline:

Title: CTO and its use for COVID-19

Google link to paper Draft:

https://drive.google.com/open?id=12BdgrKi5afBrdrRgRc_GVN0ChaMHRG_eO6lfJXG2qFw

CTO: clinical trial ontology that will be focused on clinical trials.

Introduction:

- What, Why, survey of history
- Main drive/datasources for CTO study: NIH clinicaltrials.gov
- Bottleneck of existing methods
- Our proposal.

Methods:

- Generate a full and functional version of CTO. → OPMI is now used for modeling and representation. Many terms will be moved to CTO.
- More terms from ontologies other than OPMI.
- Use case: COVID-19

Results:

- CTO top level hierarchy
- High level Design pattern (more like what is clinical trial and its key components and how they are linked together).
- Main drive/data source for CTO study: NIH clinicaltrials.gov
- Use case COVID-19:
    - Use CTO for NIH clinicaltrials.gov to classify COVID-19 clinical trials.
    - May link the data with other clinicaltrials resources like China, Europe, Japan, …

        - Literature mining for COVID-19 and vaccine (WHO is in development), maybe we can search in PubMed. (Search for “Draft landscape of COVID-19 candidate vaccines – 4 March 2020” at https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en/)
        - Do some demo using SPARQL/DL query.
        - Leon’s development of how NIH uses ontology for some prototype real clinical data representation and integration, and even better: how it can be linked to other RDF data in PubChem (like vaccine or drugs, etc.).
            - Leon: time tight, but prototype possible.
            - Maybe enough to show schema but not data?
            - This part may be itself a use case. → maybe in the future, not now.
- Figures/Tables:
    - Fig. 1: CTO high level hierarchy
    - Fig. 2. CTO design pattern (cross different hierarchical domains)
        - In OBO/BFO system: a term means an entity in reality. Different entities in reality have relations. The design pattern means here that we use relations to link different entities. It’s more like database schema, and how core terms are related together. It’s also UML in software design.
    - Fig. 3. NIH clinicaltrials.gov related figure.
    - Fig. 4. Literature mining figure.
    - Fig. 5. SPARQL/DL query figure?

Discussion

- >...

TO DO:

- Need to perform the CTO feedback and refinement if needed.
- Include transferring some terms from OPMI.
- Leon:
    - Check NIH clinical trials terms, and see which necessary/high level terms we do need to add for the CTO paper.
    - Then clinicaltrials.gov COVID-19 use case refinement.
        - See how many trials there.
- Stephan group
    - Stephan: CTO checking and
    - Perform literature mining
    - Alpha: Write some background.
- Asiyah
    - Design pattern.
    - Work with Leon on the NIH clinicaltrials tasks.
- Oliver
    - Prepare the figure 1 - high level CTO hierarchy draft
    - Write some background about coronavirus. May check China site info as well.
    - Disclosure: Oliver is writing a Coronavirus grant that may include this as a small part of the proposal.

02/28/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Sumit Madan, Johannes Darms, Alpha Tom Kodamullil, Oliver He

- Add Github-User-Ids of Asiyah, Leon and Oliver to CTO. (Asiyah Github id: linikujp, Oliver Github id: yongqunh, Leon Github id: leonqli)
- Use cases:
    - It would be good to have some coronavirus-related clinical trials as use cases.

Discussion on Primary purpose and primary outcome

- Purpose is the objective set up before the trial or any process. Outcome is the result after the trial. Primary outcome here may be primary outcome measurement.
    - Ref: https://prsinfo.clinicaltrials.gov/trainTrainer/WHO-ICMJE-ClinTrialsgov-Cross-Ref.pdf
- OPMI's primary purpose is a subclass of OBI:Objective specification:http://www.ontobee.org/ontology/OBI?iri=http://purl.obolibrary.org/obo/IAO_0000005
- One suggestion:
    - See OAE outcome discussion: https://jbiomedsem.biomedcentral.com/articles/10.1186/2041-1480-5-29
    - Generate a process term 'outcome measurement', which includes what, how, when, etc:
        - Has input:
        - Has measurement method:
        - Has object /purpose:
        - Has output: - outcome. So the output of 'outcome measurement' process is the outcome.
            1. Has event outcome: some event
            2. (Thought: Outcome is more like process role - maybe not right)
        - Has time-frame. (when to measure those endpoints across the whole course of the clinical trial)
    - Generate an information term 'outcome specification', which will be aligned with the 'objective specification'.
    - Maybe OBi can create something like 'study outcome specification' - can propose to OBI group.
    - For clinical trial, we will need 'clinical trial outcome specification'
        - Then under it, we can have primary, second, and other outcome …
        - Maybe add to the definition that the outcomes have to be **pre-specified** when designing the protocol. The pre-specification has to be emphasized either in the definition or in the label.
        - Difference between outcome and outcome specification: outcomes are pre-specified, while the outcome is the result. Probably, we can generate

a term called ‘outcome result description’ or ‘outcome measurement result’, or something like this, which will be used to describe the results.
    - We have clinical trial process. Before the process, we have the objective/goal, outcome specification, protocol, IRB approval. Then doing the trial process, where a last assay would be the outcome measurement. Then in the end of trial, we have the outcome measurement results. → We may generate a general clinical trial workflow figure based on this pipeline.
- We will create **“primary outcome**”.
    - Source: https://www.who.int/ictrp/network/trds/en/
    - Definition:
        Outcomes are events, variables, or experiences that are measured because it is believed that they may be influenced by the intervention.
        The Primary Outcome should be the outcome used in sample size calculations, or the main outcome(s) used to determine the effects of the intervention(s). Most trials should have only one primary outcome.
        For each primary outcome provide:
            1. The name of the outcome (do not use abbreviations)
            2. The metric or method of measurement used (be as specific as possible)
            3. The timepoint(s) of primary interest
    - Example:
        Outcome Name: Depression
        Metric/method of measurement: Beck Depression Score
        Timepoint: 18 weeks following end of treatment
- We will create “**secondary outcome**”
    - Key Secondary Outcomes
    - Source:
        - https://prsinfo.clinicaltrials.gov/definitions.html#PrimaryOMInfo
        - https://www.who.int/ictrp/network/trds/en/

- We will create “**other outcome**”
    - Other Pre-specified Outcome Measures
    - Source: https://prsinfo.clinicaltrials.gov/definitions.html#PrimaryOMInfo

Debug Leon’s Example:
Current Leon’s representation:
<http://rdf.ncbi.nlm.nih.gov/pubchem/clinicaltrial/NCT00061373>
<http://purl.obolibrary.org/obo/OPMI_0000294> "Steven Warach, MD, PhD|Principal Investigator|National Institute of Neurological Disorders and Strok
Should be represented as below. Depends on the visualization, the second triple maybe not needed. The relation ‘has clinical trial investigator’ has defined that the subjective has to be a clinical trial, and the objective has to be a clinical trial investigator’:

<http://rdf.ncbi.nlm.nih.gov/pubchem/clinicaltrial/NCT00061373> 'has clinical trial investigator' "Steven Warach, MD, PhD|Principal Investigator|National Institute of Neurological Disorders and Strok"
"Steven Warach, MD, PhD|Principal Investigator|National Institute of Neurological Disorders and Strok" 'is instance of' <http://purl.obolibrary.org/obo/OPMI_0000294>

02/14/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel

Leon's example:

- Primary purpose: http://purl.obolibrary.org/obo/OPMI_0000300
    - We do think it is different from "Primary outcome". And we may need to create a new term of "Primary outcome"... **Need to be discussed with all**.
- Drug administration (duplicated) needs to be addressed.
    - OAE_0000011 (subclass of Medical Intervention)
        - 3 votes for this term to be used:
    - DRON_00000031(subclass of Treatment)
- Drugs need to be linked to an ontology (which one? Depends on the final users? Use cases?)
- Need to create study types.

Stephan showed CTO:

- CTO defined (imported from NCIT) the "primary outcome measure" and "secondary outcome measure", however, the mother class of these terms is " study protocol".
    - Suggest to change the relation of "is_a" to "part_of"
- CTO has imported "study design" from OBI. However, the subclasses of OBI_"study design" do not reflect the clinical study design well.
- "Study design" is related to "study type". This relation was not developed in OBI. We may need to work out this piece. There is no need for a term labeled as "study type", because all subclasses of "clinical study"/"human study"
- Add "preclinical study"
- ClinicalTrials.gov changes "phase 0" to "early phase 1"
- Investigated the subclasses of "medical intervention". The "Gene therapy" should be a subclass of " biologic intervention" (ERO_0001553). Other classes such as "medical procedure" and "therapeutic intervention" need to be defined more specifically, because the current definition is too broad. Ideally the interventions should cover: **drugs, biologics (vaccines and genetic therapies may be subclasses of biologics), devices, behaviour or therapeutic, dietary supplements, combination product, diagnostic areas**.

02/07/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Oliver He, Sumit Madan

Team reviewed the current CTO on github (https://github.com/ClinicalTrialOntology/CTO).

Action item:

1. Oliver to upload the OPMI to Ontobee so Stephan's team will extract most latest terms to CTO.
2. Stephan to review CTO and delete non-domain specific terms, such as children terms under vaccination, or medical intervention.
3. Leon will provide a use case so we will have a clear vision.
4. Stephan and Asiyah may also think about their use cases.
5. Exchange emails about schedule change.

Planning to have a paper submitted to ICBO in May.

https://icbo2020.inf.unibz.it/

https://www.iaoa.org/jowo/2020/

Submission deadline not known yet, likely May or June. Asiyah and Leon need one month approval time. So we need to finish our manuscript by April.

For this submission, we need:

1. Finish all Leon's terms needed for clinicaltrials.gov.
2. Generate a full and functional version of CTO. → OPMI is now used for modeling and representation. Many terms will be moved to CTO.
3. Use case studies:
    a. A major one is Leon's.
    b. Asiyah plans to have another use case.
    c. Stephan may have some literature mining use case..

1/31/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel, Oliver He

TO DO:

- Import OBI inclusion criterion and exclusion criterion - replace OPMI ones.
- Continue our discussion on Study Design, study type, …

1/17/2020

Attendees: Leon Li, Asiyah Yu Lin, Stephan Gebel and his colleagues

- Inclusion criterion (the reason why it is added?)
- coordinate the development of OPMI and new CTO.
- Currently in OPMI, there is no inclusion criterion, and the exclusion criterion is not under eligibility criterion -- is a mistake? -- Note on 1/31/2020: Oliver will import from OBI
- Provide use cases for defining term to move forward. For example, we looked at the term age and subclasses in CTO, and this arrangement needs to discuss. -- Note on 1/31/2020: Stephan team will upload CTO in a couple of days.

1/3/2020

Attendees: Leon Li, Asiyah Yu Lin, Oliver He

Added new terms in OPMI:

- Inclusion criterion, under eligibility criterion
- Primary registry identifier
- Secondary registry identifier
- Primary registry identifier role
- Secondary registry identifier role
- Identifier role

TODO:

- Secondary identifier:
    - Clinicaltrials.gov definition: https://prsinfo.clinicaltrials.gov/definitions.html#SecondaryIds
    - WHO definition: https://www.who.int/ictrp/network/trds/en/
- Study type:
    - Refs:
        - https://www.who.int/ictrp/network/trds/en/ #15
        - https://prsinfo.clinicaltrials.gov/definitions.html#StudyType
    - allocation
    - interventional study model
    - Masking
    - Assignment
    - Purpose

12/20/2019

Attendees: Leon Li, Asiyah Yu Lin, Oliver He, Stephan Gebel, Alpha Tom Kodamullil

TODO:

- Secondary identifier:
- Study type:
    - Refs:
        - https://www.who.int/ictrp/network/trds/en/ #15
        - https://prsinfo.clinicaltrials.gov/definitions.html#StudyType
    - allocation
    - interventional study model
    - Masking
    - Assignment
    - Purpose

12/13/2019

Attendees: Leon Li, Asiyah Yu Lin, Oliver He

Added new terms in OPMI:

- Investigation agent
- Sponsor
- Primary sponsor
- Secondary sponsor
- Collaborator
- Principal investigator
- Sponsor investigator.

Submitted to OBI an issue tracker:
https://github.com/obi-ontology/obi/issues/1099
(***note***: the responsible party role definition needs update.)

Asiyah is going to ask the German group to have a representative to join our weekly meeting.

12/06/2019
Attendees: Leon Li, Asiyah Yu Lin, Oliver He

Sponsor and collaborator:

- There are primary (lead) and secondary sponsors in clinical trials. (https://prsinfo.clinicaltrials.gov/trainTrainer/WHO-ICMJE-ClinTrialsgov-Cross-Ref.pdf)
- Collaborator usually serves as secondary sponsor?
    - In clinicaltrials.gov, they

Added new terms in OPMI:

- Primary sponsor role
- Secondary sponsor role.
- Principal investigator role
- Sponsor investigator role.
- Investigation collaborator role

11/22/2019
Attendees: Leon Li, Asiyah Yu Lin, Oliver He

We added several new “contact” related terms, and made their definitions.

Use case discussion:

- We will find three clinical trial use cases from the clinicaltrials.gov website, one from cancer vaccine clinical trial, one from medical device clinical trial, and one to be selected from Leon.
-

11/15/2019:

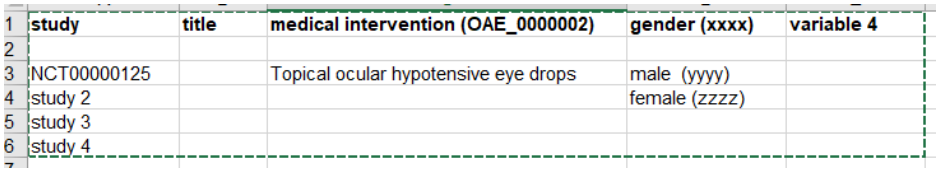
Attendees: Leon, Asiyah Yu Lin, Oliver He

We added several “contact” related terms.

Use case discussion:

- Identify a clinical trial use case, which came from the clinicaltrials.gov website.
- Such a use case is defined as a study stored in the clinicaltrials.gov website, which contains all the standard information and can be used as a representative model for our ontological study. A nice choice would be something related to cancer vaccine clinical trial.
- Once we find and finalize such a use case, then we can extract the information from the clinicaltrials.gov and then try to map each itemized information to ontology.
- Then use

Excel format of the data:



	study	title	medical intervention (OAE_0000002)	gender (xxxx)	variable 4
2					
3	NCT00000125		Topical ocular hypotensive eye drops	male (yyyy)	
4	study 2			female (zzzz)	
5	study 3				
6	study 4				

Question: To what levels we need to add ontology to the above data format? In addition to the header items, do we also need to add ontology mapping for the inside data such as “Topical ocular hypotensive eye drops”.

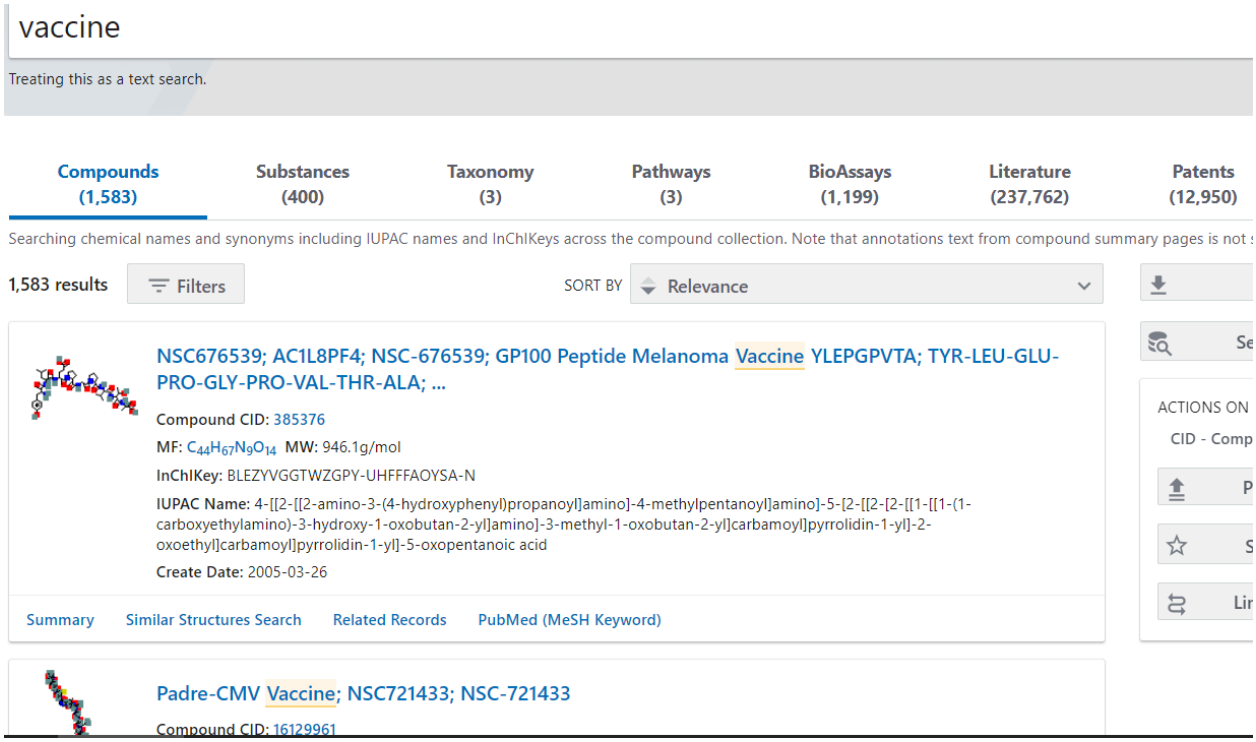
Plan:

Get as much detail as possible. For example, if we don’t have an ontology term for “Topical ocular hypotensive eye drops”, we may use the term “drug administration”. It might be good to include ontology terms for “Topical ocular hypotensive eye drops” and other drug administration. Such information would be good to support advanced computer-assisted reasoning and analysis.

One idea: We can identify a list of clinical trials under the same theme (e.g., cancer vaccine studies). Then use ontology to standardize all these studies. Then we can use ontology power (e.g., hierarchical classification, reasoning) to automatically query and analyze … → such a thing may be good material to show in publication.

Another idea: By doing so, you can link your clinical trial data to other datasets in your system. The other databases include: PubChem, proteins , diseases, patents, literature, …. See PubChem website: https://pubchem.ncbi.nlm.nih.gov/#query=aspirin

https://pubchem.ncbi.nlm.nih.gov/#query=vaccine



11/8/2019 meeting:
Attendees: Leon, Asiyah Yu Lin, Oliver He

Country:
WHO maintains the country list and associated trials:
http://apps.who.int/trialsearch/ListBy.aspx?TypeListing=1

We will use GAZ as our default country representation, Which uses the geographic location as the parent term:
http://www.ontobee.org/ontology/GAZ?iri=http://purl.obolibrary.org/obo/GAZ_00000448

Primary outcomes and secondary outcomes:
NIH describe them as descriptional text:
https://prsinfo.clinicaltrials.gov/definitions.html#PrimaryOMInfo
Quote:

> “Primary Outcome Measure Information *
> Definition: A description of each primary outcome measure (or for observational studies, specific key measurement[s] or observation[s] used to describe patterns of diseases or traits or associations with exposures, risk factors or treatment).

Note: "Primary outcome measure" means the outcome measure(s) of greatest importance specified in the protocol, usually the one(s) used in the power calculation. Most clinical studies have one primary outcome measure, but a clinical study may have more than one."

https://prsinfo.clinicaltrials.gov/definitions.html#SecondaryOMInfo
Japan clinical trial example: https://rctportal.niph.go.jp/en/detail?trial_id=jRCTs021190009