Laboratory Specific Standard Operating Procedures Mandated by the Settlement Agreement

General guidance regarding laboratory work with hazardous chemicals[1] is contained within the Chemical Hygiene Plan (CHP) and Chemical Use Guidelines. For certain chemicals, specific Standard Operating Procedures (SOPs) are required. An SOP is a document establishing a procedure for safely working with hazardous chemicals or processes in a laboratory. The July 25, 2012 Settlement Agreement between The Regents and the Los Angeles County District Attorney requires that chemicals on the Chemical Classification List[2] identified in Exhibit 1 of the Agreement (i.e. "*Exhibit 1 Chemicals*") require development of SOPs in accordance with the terms of the Agreement:

> "SOPs shall be written by laboratory personnel having the most experience and knowledge and who are routinely involved in the experimental process. The Principal Investigator and all personnel responsible for performing the procedures detailed by the SOP shall sign the SOP, acknowledging the contents, requirements and responsibilities outlined in the SOP. The SOP shall be reviewed. The review shall be conducted by qualified personnel. Authors of SOPs shall consider in developing, revising, and reviewing and approving SOPs, the usage and handling recommendations provided by the manufacturer."[3]

Developing SOPs[4]

UC maintains a website http://cls.ucla.edu/resources/sop-library with SOP templates and resources that may be referenced while developing SOPs. Your campus EH&S is also available to assist with the development of SOPs. SOPs must be developed prior to initiating any experiments with high-hazard chemicals and are to be maintained in the Laboratory Safety Manual[5] where they are available to all laboratory personnel.

The University is working on a quick authoring tool that will make the development and sharing of completed SOPs easier for all researchers. Intended for use directly by researchers who work with chemicals, "RADiCAL" is a Chemical Risk Management Tool that quickly determines banded safety operating parameters or if a detailed SOP is needed. Unlike static safety data sheet (SDS) our project is

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[1] Hazardous chemical means any chemical which is classified as a physical hazard or a health hazard, a simple asphyxiant, combustible dust, pyrophoric gas, or hazard not otherwise classified

[2] Exhibit 1 of the UC Agreement list both specific chemicals and chemical functional groups and properties that would classify a substance as an Exhibit 1 Chemical (e.g. a finely divided metal that may exhibit pyrophoric properties).

[3] *UC Settlement Agreement Appendix A Obligation 6*

[4] Adapted from *Living With The Laboratory Standard* The American Chemical Society committee on Chemical Safely

[5] SOPs shall be in a visible location within each laboratory and readily accessible to all laboratory personnel. Electronically available copies of the SOPs are acceptable to meet this provision, provided such SOPs are readily accessible to all laboratory personnel. *UC Settlement Agreement Appendix A Obligation 6*

research environment-centric and communicates pertinent information to the researcher so they can safely conduct an experiment (SOP). More information will be provided as the software tool becomes available.

Chemical Hazards

When drafting an SOP, the chemical hazards may either be evaluated by individual chemicals or by hazards of a chemical family. The chemical families used must be defined such that all the chemicals composing the family have similar physical and health hazards and common signs and symptoms of exposure. The conceptual basis for grouping of chemical exposures according to similar physical and chemical characteristics, intended processes/handling, and anticipated exposure scenarios (amount of chemical used and how workers would be exposed) is termed *control banding*. The final SOP for a control band of chemicals should provide appropriate guidance to enable personnel to safely work with the chemicals in the control band consistent with Cal/OSHA requirements.

To determine chemical hazards the Safety Data Sheet (SDS) for Exhibit 1 Chemicals should be referenced during SOP development. The SDS lists important information that will need to be considered, such as occupational exposure limits, type of toxicity, warning properties, and symptoms of exposure. If a new chemical will be produced during the experiment, an SDS will not necessarily be available. In these cases, the toxicity is unknown and it must be assumed that the substance is particularly hazardous, as a mixture of chemicals will generally be more toxic than its most toxic component.

It should be noted that the templates on the http://cls.ucla.edu/resources/sop-library website are developed based on a format following the National Academy of Science (NAS) Laboratory Chemical Safety Summary Sheets[6] (LCSS). As such the information provided is mainly limited to applicable Health and Safety information on a chemical. They are NOT an SOP by themselves but serve as an easy starting point for "laboratory personnel having the most experience and knowledge and who are routinely involved in the experimental process[7]" to write a completed SOP. A review of the SOP cannot be performed until the lab specific protocol/procedure portion is completed.

[6] LCSS provide basic information on the toxicity, flammability, reactivity, and explosivity of chemicals commonly used in research laboratories. Directions for handling, storage, and special instruction for first aid and emergency response are given.
[7] *UC Settlement Obligation A6*

Process Hazards

In addition to evaluating the hazards presented by the chemical in use, an evaluation of the experimental process (i.e. procedures) must be completed. It is important to consider the type and quantity of the chemical being used, along with the frequency of use. Key items to evaluate are the experimental design, equipment design, work space adequacy, and worker preparedness and qualifications. In addition the usage and handling recommendations provided by the chemical manufacture must be considered[8]. The SOP may include a step by step procedure or may alternatively list a number of parameters for which multiple procedures may be performed (e.g. reaction temperature not to exceed 100°C, quantities not to exceed100 micrograms.) SOPs for Particularly Hazardous Substances[9] (PHS) must include a description of a designated area[10], containment devices, decontamination and waste disposal procedures.

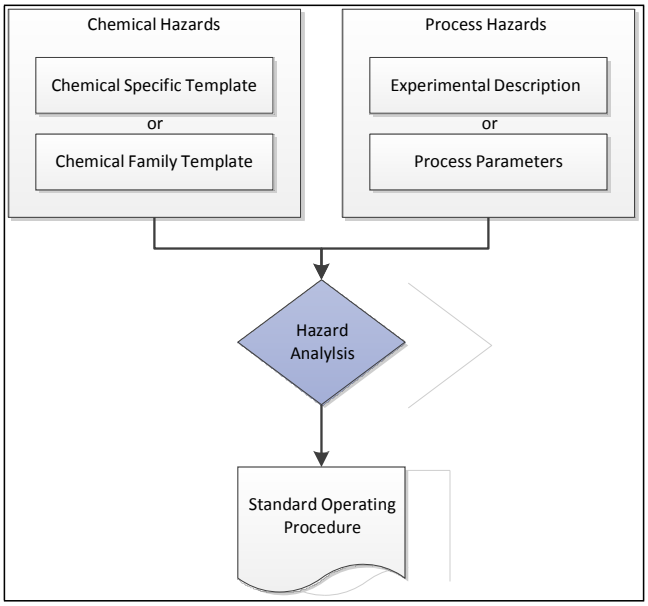

Figure 1
Conceptual Model for Developing SOPs Using a Risk Assessment.

[8] *UC Settlement Obligation A6*
[9] Particularly Hazardous Substances are defined by Cal/OSHA as: reproductive toxins, acutely toxic substances and select carcinogens, which include regulated carcinogens.
[10] A designated area may be defined as a hood, glove box, isolation cabinet, work area, or entire laboratory designed to isolate the worker from the substances

Table 2

Items to consider in performing a Risk Assessment

Excerpted from *Laboratory Chemical Hygiene – An AIHA[11] Protocol*

Through a literature review or discussion with colleagues, find out what is already known about the particular procedure or reaction system. Obtain safety information about the reactants.

In the absence of relevant information or when the proposed work is known to be original, cautiously conduct a very small scale preliminary experiment to assess the exothermic character and physical properties of the reaction system and its products.

When subsequently planning and setting up a larger-scale reaction, consider the following factors to ensure to the extent possible the safety of the experiment:

- Adequate temperature control: Is there sufficient capacity for both heating and cooling for both liquid and vapor phases?
- Proportions of reactants and concentrations of reaction components or mixtures: Minimize reagent concentrations to the extent possible.
- Purity of chemicals, absence of catalytic impurities, etc.
- Formation of peroxides in chemicals subject to peroxidation:
- Presence of solvents or diluents and viscosity of reaction media.
- Degree of agitation.
- Control of ignition sources in the presence of flammable liquids and gases.
- Control of reaction atmosphere.
- Control of reaction or distillation pressure and pressure relief threshold setting and capacity.
- Shielding from actinic (chemical change-producing) radiation.
- Avoidance of mechanical friction or shock to unstable or sensitive solids, and use of adequate personal protection if such materials will be isolated or dried (preferably without heating).
- Personnel shielding for potentially violent reactions.

Also, one should:

- Not allow hazardous systems involving poorly understood reactions to run unattended;
- Know the recommended first aid treatment in case of accidental chemical exposure; and
- Know what to do if:
  - the electric power fails
  - the cooling system fails
  - vessel pressure gets out of hand
  - water leaks into the reaction system
  - air leaks into the system
  - the reaction container fails and breaks or spills its contents

Remember that many explosions, fires, and asphyxiations are caused by the accidental combination of potentially dangerous substances.

[11] American Industrial Hygiene Association

Risk Assessment

After determining both the chemical hazards and the process hazards a risk assessment must be performed. This is illustrated in Figure 1. **The risk assessment process is the most critical step in developing the SOP.** The Principal Investigator (PI) I will need to use judgment to determine the appropriate level of controls needed to allow for the reasonable safety of those performing the described experimental process. There are many different methodologies[12] to conduct a risk assessment. Table 2 provides a listing of key factors to evaluate during the risk assessment. It is important to understand that changes to either the chemical involved or the experimental process affect the risk assessment and may alter the controls documented in the SOP. The PI must re-review the SOP whenever changes occur that increase the risks beyond what was originally included in the original SOP.

Prior Approval

For Exhibit 1 Chemicals, circumstances requiring prior approval from the PI must also be addressed in laboratory-specific SOPs. These circumstances are based on the inherent hazards of the material being used, the hazards associated with the experimental process, the experience level of the worker, and the scale of the experiment. Some examples of circumstances that may require prior approval include development of a new experimental process, working alone in a laboratory, unattended or overnight operations, the use of highly toxic gas of any amount, the use of large quantities of toxic or corrosive gases, the use of extremely reactive chemicals (e.g., pyrophorics, water reactive chemicals), or the use of carcinogens.

Whenever there is a significant change in chemical amounts, new equipment, new chemicals, new procedure, or new work space, or a situation where one must work alone, approval must be given prior to startup to determine that conditions now exist to protect the worker, the community, and the environment[13]. Depending on conditions, the following signatures should be obtained indicating approval of new work space or equipment, or changes of an existing procedure.

[12] The American Chemical Society is developing a guidance document that will describe a number of risk assessment methodologies appropriate for laboratory environments. This publication is expected in early 2013. In the interim seek advice from your campus EH&S department.

[13] The SOP shall be amended and subject to additional review and approval by the Principal Investigator where changes or variations in conditions, methodologies, equipment, or use of the chemical occurs, or when it is reasonably apparent that

You may wish to add others to this list.

- Chemical hygiene officer
- Safety engineer
- Industrial hygienist
- Principal Investigator
- Laboratory personnel

exposure to injury or illness may be increased or adversely effected by any anticipated or an unanticipated condition arises when an approved SOP is utilized, or where the scale of any reaction Or application has increased beyond the capacity of the equipment or apparatus outlined or described in the original SOP, or the increased scale of any reaction or application had not been evaluated and approved within the scope of the original SOP. *UC Settlement Agreement Appendix A Obligation 6*

Carcinogens

Those substances regulated by OSHA as "carcinogens"; listed as "known to be carcinogens" by the National Toxicology Program (NTP); and listed as Group l "carcinogenic to humans" by the International Agency for Research on Cancer (IARC). A substance is also considered to be carcinogenic if it is listed by IARC Group 2A, "probably carcinogenic to humans", or 2B, "possibly carcinogenic to humans"; or under the category, "reasonably anticipated to be a carcinogen", by NTP.

Reproductive Toxins

Chemicals that affect the reproductive capabilities including adverse effects on sexual function and fertility in adult males and females, as well as adverse effects on the development of the off-spring.

Highly Toxic Materials

Those substances that have met any of the criteria listed below.

Exposure route	
Oral (mg/kg bodyweight)	≤ 50
Dermal (mg/kg bodyweight)	≤ 200
Inhalation - Gases (ppmV)	≤ 500
Inhalation - Vapors (mg/l)	≤ 2.0
Inhalation – Dusts and Mists (mg/l)	≤ 0.5

All substances of unknown toxicity used in the laboratory must be considered highly toxic.

APPENDIX A
SUGGESTED APPROACH FOR DEVELOPING LAB SPECIFIC SOPS
(Dr. John Palmer, UCSD Chemistry Department)

Prioritize:

1. Identify any Exhibit 1 Chemicals in your laboratory's "Inventory"
    a. See: http://www.ehs.uci.edu/programs/labres/UCSettlement_UCIPlan/ChemicalClassificationList.xlsx
2. Realistically ask yourself which are needed.
    a. Are they involved in processes and experiments conducted routinely?
    b. Is their use really anticipated in the immediate future (4-6 weeks)?
        i. NOTE: Can you dispose of them? (EHS will help)
    c. If not needed "immediately" – can the materials be designated in a way that insures they are NOT used until the required lab specific SOP is developed ("tagged-out Not in Use")?
        i. Various methods tagging-out use are acceptable:
            1. Lab-inventory electronic listing clearly designating "locked-out" materials.
            2. A clear identifying tag, bag, or label.
            3. The physical segregation 'out of inventory' of materials awaiting SOPs
3. Organize your lab's remaining list by "degree of hazard" (use the concept of "Control-Banding"). Take into account:
    a. Inherent hazards (physical, chemical, toxicological, etc.)
    b. Manipulative or equipment hazards (special skills or familiarity required)
    c. Amounts used (if large scale use or scale up equates to higher risk?)
    d. Special mitigation factors (small quantities only – in a glove box = lower risk).
4. Appropriately sub-group remaining materials by dominant hazards. This can be done by process or by chemical family attributes. You might group several similar chemicals together in one SOP (all alkyl-aluminum compounds). Be sure you are considering all the involved chemical and physical hazards of the process)

Assign the remaining high-priority list appropriately across the lab's researchers and then, as a group, vet the resulting SOPs for accuracy and consistency so that common safety factors are properly emphasized. Insure everyone is familiar with the contents of your lab SOPs. It will help if you also summarize a basic set of conditions which will be found in all (or most of) the lab's SOPs, such as: "work is to be conducted in a laboratory hood using approved safety glasses and lab coat." Any process or chemical which requires personal approval for each use by the PI should also be uniformly designated.

So, you have large synthetic lab - but you've already managed to cut down you're list of 75 high-hazard "listed" chemicals to a more manageable 15 needing immediate SOP development. How do you accomplish this?

A. Write each lab specific SOP's from "scratch". Choose a representative blank template and fill out required elements manually from various resources (a lot of effort).
    a. See your campuses' recommended template, or download a blank template at: http://www.ehs.uci.edu/programs/sop_library/UCSOPtemplate.docm

B. Use a chemical specific template from the UC repository and modify it to include laboratory specific use and guidance information (not too bad but you still have to tie the chemical(s) together with a lab process or experiment and consider the risks).
C. Borrow and modify an appropriate and completed SOP from a colleague using the same chemical(s) in the same processes/experimental procedures as you do on the same scale. (This method should be a lot easier – but someone has to go first and you have to vet their information as appropriate to your lab).
D. Any combination of the above. Take a chemical SOP template together with a combination of appropriate SOP resources and combine them (cut-and-paste). The final SOP needs to describe PPE and other lab requirements to be met in safely conducting the named experiment, process, or chemical use.

APPENDIX B
CENTER OF LABORATORY SAFETY SOP TEMPLATES

The SOP templates provided on this website are developed based on a format following the National Academy of Science (NAS) Laboratory Chemical Safety Summary Sheets (LCSS). As such the information provided is mainly limited to applicable Health and Safety information on a chemical. They are NOT an SOP by themselves but serve as an easy starting point for "laboratory personnel having the most experience and knowledge and who are routinely involved in the experimental process" to write a completed SOP. A review of the SOP cannot be performed until the lab specific Protocol/Procedure portion is completed.

Users of these templates need to complete the following:

1) Add lab specific contact information.
2) Add pertinent lab specific protocol/procedure instructions to the protocol/procedure section.
3) The PI must review the SOP and acknowledge the "contents, requirements and responsibilities outlined in the SOP."
4) Researchers who perform that laboratory protocol/process must understand the SOP, sign and date on the last page.

Researchers are expected to understand the correct steps to be performed as detailed in the SOP, including the hazards present in the experiment and the proper safety controls required. By signing the form individual researches are acknowledging that they understand the contents, requirements and their responsibilities outlined in the SOP.

If you have any questions, please contact your local EH&S for assistance. If you identify any errors or have comments regarding these templates please contact: labsafety@ucop.edu

APPENDIX C
INSTRUCTIONS FOR COMPLETING STANDARD OPERATING PROCEDURES

To be in compliance with the Cal/OSHA Laboratory Standard, laboratory-specific Standard Operating Procedures (SOPs) are required. Your Chemical Hygiene Plan document does not provide specific SOPs for the hazardous chemical or hazardous substance use operations or procedures in your particular laboratory. If your laboratory research involves the use of Exhibit 1 chemicals or PHS, you must develop laboratory-specific SOPs to supplement the information found in the EH&S Laboratory Safety Manual and Chemical Hygiene Plan. You may work with your departmental safety committee and EH&S, as required.

Below are instructions for completing the laboratory-specific SOPs with the corresponding template. Templates for all of the specifically listed Exhibit 1 chemicals and chemical families are found at http://cls.ucla.edu/resources/sop-library. Please contact your designated Laboratory Safety Officer with any questions or comments you may have while completing your SOPs. Completed SOPs are reviewed by the Laboratory Safety Officer during annual inspections.

The University is working on quick authoring tool that will make the development and sharing of completed SOPs easier for all researchers.

1. Type of SOP

- **Process**: the SOP will be for a process such as distillation, synthesis, etc.
- **Hazardous chemical**: the SOP will be for an individual chemical such as arsenic, formaldehyde, nitric acid, etc.
- **Chemical Family:** the SOP will be for a chemical family such as aluminum alkyls, Cadmium compounds, heavy metal salts, etc.

2. Describe the Process, Hazardous Chemical or Chemical Family

- **Process**: Briefly describe the process and name all the hazardous chemicals or substances used in the process
- **Hazardous chemical**: Provide the name of the chemical. Include the full name, common name, and any abbreviations used for the chemical
- **Chemical Family:** Name the chemical family and list the name of the chemicals in this family used or stored in your laboratory

3. Potential Hazards

Describe all the potential hazards for each process, hazardous chemical or chemical family. Describe the potential for both physical and health hazards. Health hazards include carcinogens, toxic or highly toxic agents, reproductive toxins, irritants, corrosives, sensitizers, hepatotoxins, nephrotoxins, neurotoxins, agents which act on the hematopoietic systems, and agents which damage the lungs, skin, eyes, or mucous membranes. State the potential for chronic and/or acute health hazard effects of the chemical(s).

Physical hazards include radioactivity, cryogen, high temperature, electrical, compressed gas or other pressure systems, UV light, laser, flammable or combustible, corrosive, water-reactive, unstable, oxidizer, pyrophoric, explosive, or peroxide formers.

4. Circumstances Requiring Prior Approval

Discuss the circumstances under which this particular process, hazardous chemical or chemical family will require prior approval (if any) from the PI/Laboratory Supervisor or Chemical Hygiene Officer. The circumstances may be based on such criteria as: the inherent hazards of the material(s) used the hazards of the experimental process, the experience level of the worker, the scale of the reaction, etc. Some examples of circumstances that may require prior approval include unattended or overnight operations, use of explosives or pyrophorics, use of highly toxic gas

in any amount, use of large quantities of toxic or corrosive gases or use of carcinogens.

5. Personal Protective Equipment (PPE)

Identify the required PPE for the process, hazardous chemical or chemical family. PPE includes, but is not limited to: gloves, aprons, laboratory coats, safety glasses, goggles, masks, respirators, or face shields.

6. Engineering Controls

Describe or list engineering controls that will be used to prevent or reduce employee exposure to hazards. Examples of engineering controls are fume hoods, glove boxes, interlocks on equipment, and shielding of various kinds.

7. Special Handling and Storage Requirements

Describe the storage requirements for hazardous substances, including special containment devices, special temperature requirements, special storage areas or cabinets, chemical compatibility storage requirements, etc. State the policy regarding access to the substance(s). Provide the exact storage location in the laboratory. Describe any special procedures, such as dating peroxide forming chemicals on receipt, opening and disposal, or testing after an appropriate amount of time has passed. Describe safe methods of transport, such as in a secondary container using a low, stable cart, or using two hands to carry the chemical container.

8. Spill and Accident Procedures

Describe special procedures for spills, releases or exposures (e.g., neutralizing agents, use of fluorescence to detect materials, etc.). Indicate how spills, accidental releases and exposures will be handled. List location of the following emergency equipment: chemical spill clean-up kit, first-aid kit, emergency shower, eyewash, and fire extinguisher.

9. Decontamination Procedures

Describe specific decontamination procedures for equipment, glassware or work areas.

10. Waste Disposal Procedures

Describe the anticipated waste products as well as how waste will be collected and disposed.

11. Designated Area

Indicate the designated area established for experiments using particularly hazardous substances (PHS). A portion of a laboratory bench, a piece of equipment, the fume hood, or the entire laboratory may be considered as a designated area for experiments using PHS.

12. Safety Data Sheet (SDS) Location

State where the SDSs are kept for the chemicals, or hazardous substances, used in the laboratory. Indicate the location of other pertinent safety information (e.g., references, equipment manuals, etc.).

13. Protocols

Insert a copy of your specific laboratory procedures for the process, hazardous chemical or chemical family.