# Module 10: Safer Chemical Design Game – worksheet for students and instructors playing [www.gwiz.yale.edu](http://www.gwiz.yale.edu)

**KEY**



# Pre-Game Question

Speculate how molecular weight, lipid solubility, physical state (solid vs liquid) and vapor pressure of the detergent will impact absorption into the body.

Answers may vary: students may speculate that compounds with high molecular weight may have difficulty passing through membranes and that liquids are more likely to enter the body than solids. They may also speculate that chemicals which are lipid soluble are more likely to retain in the body and high vapor pressure can decide on the route of absorption (respiratory system).

# QUESTION 1

How do high and low values of the selected physicochemical parameters (molecular weight, lipid solubility, physical state) affect absorption? Was your pre-game prediction correct/incorrect?

Dermal absorption:

* Molecules with a molecular weight smaller than 400 Daltons are more likely to be absorbed through the skin.
* Chemicals with Log P between 0 and 5 are more readily absorbed through the skin.
* Chemicals in liquid state are likely to be absorbed more quicker than those in solid state.

Respiratory absorption:

* Molecules with a molecular weight smaller than 400 Daltons are more likely to be inhaled. Chemicals with Log P less than 0 tend to dissolve in mucus and do not pass through membranes easily.
* Chemicals with higher vapor pressure are more likely to be in the gas phase and thus are more easily inhaled.

# QUESTION 2

Using the game outcome, what is the HLB “sweet spot” which enables the detergent to be an effective cleaner and be nontoxic?

The HLB “sweet spot” value is 14.9916 and it corresponds to a Log P value of -0.1.

# QUESTION 3

Why do you think Log P and HLB are depended on each other? Tip: recall detergent’s structure

By definition, HLB hydrophilic-lipophilic balance of a surfactant is a measure of the degree to which it is hydrophilic or lipophilic. It calculates the value based on the chemical groups of the molecule. Detergents are made from hydrophilic heads and lipophilic tails, so whichever structure dominates decides on the character of the detergent.

Log P describes how well molecules are attracted to lipophilic layer (how well they dissolve in fat). Molecules with a higher log P tend to be more lipophilic and have a lower HLB value. In fact, their dependence is close to inversely proportional.

# QUESTION 4

Many detergents available on the market are designed for a specific function: be a good cleaning agent. As you can see from the game, it is relatively easy to control one parameter. When a company decides to design a product with a dual function like safety AND high performance, the task becomes more challenging. Why do you think that is?

Answers can vary, but the bottom line is that designing for two parameters should be difficult, especially given that the window of overlap for physicochemical properties is quite narrow.

In the game, were you able to design a detergent that will not absorb and have a high performance? Was it easy or difficult?

Answers may vary. Overall, designing for two parameters should be difficult.

Can you think of other examples of products from your daily lives, which perform a dual function?

Shampoos that biodegrade in the environment; or

cell phones that disassemble so that precious metals can be easily recovered or a

cheap water filter which is easy to use in developing countries

# QUESTION 5

Which molecules (high or low surface area) will enhance distribution through the membrane and why?

Molecules with a high polar surface area (more than 140) are less likely to penetrate through cell membranes; molecules with a low polar surface area (less than 60) will passively diffuse through membranes and distribute more readily in the body.

# QUESTION 6

Which functional groups impair excretion and contribute to accumulation in the organism?

Chloride, Fluoride or strongly lipophilic groups such as methyl.

# QUESTION 7

Why does branching play a critical role in biodegradation of the chemical?

Because it is more difficult for enzymes that might degrade a molecule to bind to that

molecule if more branches are present.

# QUESTION 8

Do the same functional groups that enhance biodegradation (Aquatic Toxicity Challenge) contribute to the increased performance?

Yes (carboxylic acid, alcohol and ester).

This allows the design of a molecule that’s both biodegradable and with increased performance by manipulating the same functional groups.

As future chemists, why do you think this is important to consider different functional groups and the role they play in the design process?

Because as a chemist you can entirely control the outcome of the design. And some groups may benefit one function, but impair the other, so as a chemist you need to make a conscious decisions which functional groups should be chosen. Ideally, a sweet spot is achieved.

What if instead of two parameters (safety and performance) you also need to consider cost as a third parameter?

The task becomes even more challenging if cost is a parameter. If the price becomes too high, then the product becomes not affordable and no one will benefit from it.

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