# Molecular Modelling Metered Dose Inhaler Suspension Formulations


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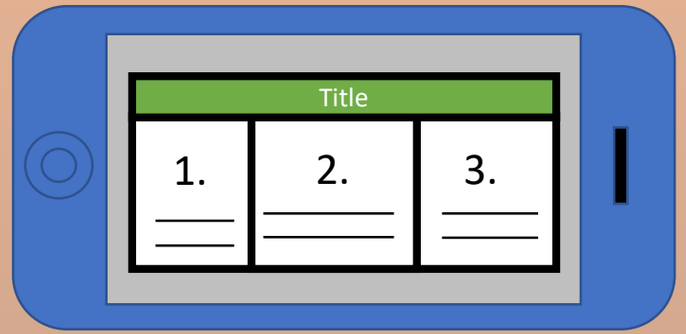
**Reading Guide:**

Each slide is a different section

Zoom into each panel

Read along from left to right

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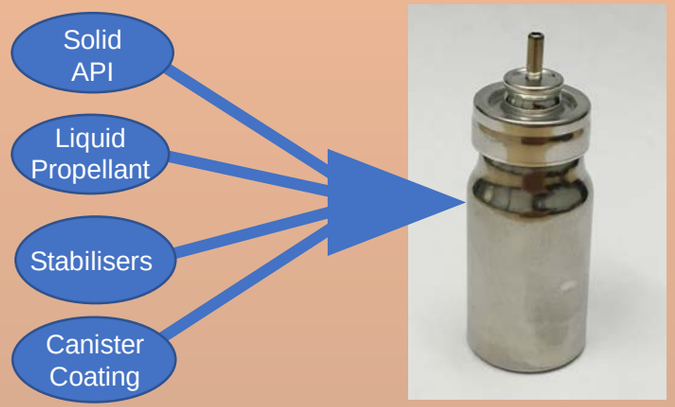
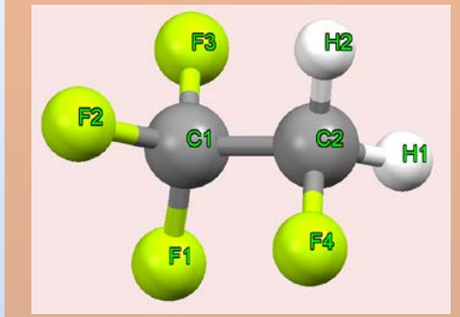
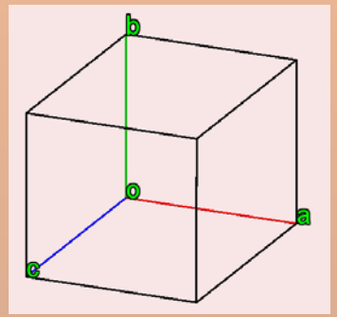
# 1. Introduction to Project




**CONTEXT**

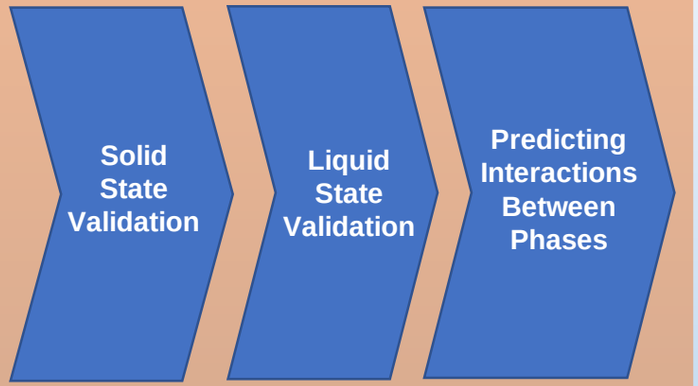
- Suspension formulations contain four key components
- Molecular modelling provides the ability to model specific surfaces of a crystalline particle
- Understanding interactions between different materials can potentially aid formulation development




**BACKGROUND**

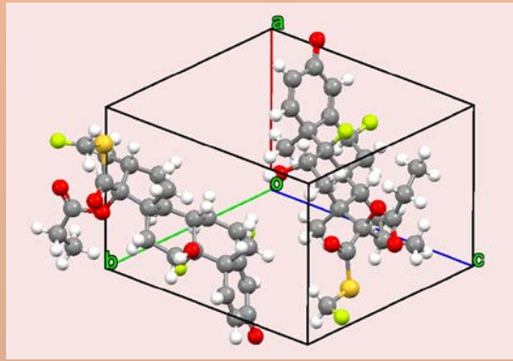
- Molecules are represented as spherical atoms connected by springs
- Atoms are assigned point charges and force fields calculate potential energy
- In crystallography molecular positions are specified relative to their unit cell
- This is used to define planes in the bulk structure




**THIS POSTER**

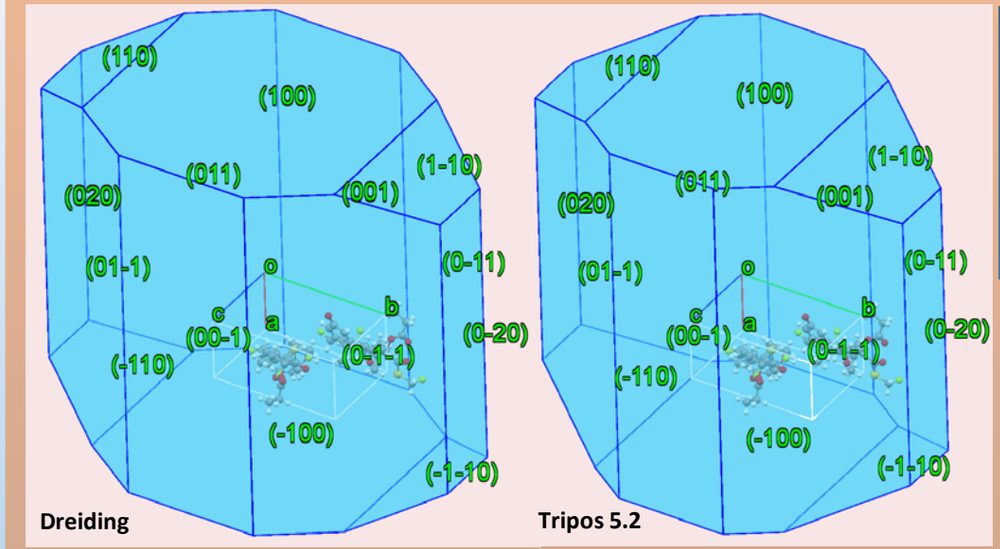
- Phases must be simulated and validated individually before being combined
- This poster shows validation of fluticasone propionate's (FP) solid crystal structure
- Also, validation of liquid propellant HFA-134a

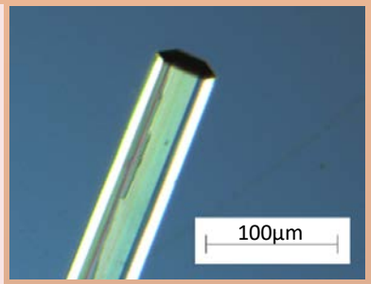
# 2. Solid State of Fluticasone Propionate

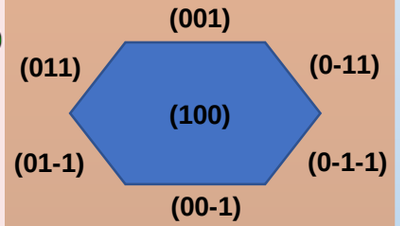



## METHOD

- FP's crystal structure data came from the DAXYUX entry[1]
- Hydrogen positions were optimised and point charges assigned using AM1 method within MOPAC[2]
- Program habit98[3] calculated interaction energies using generic force fields Dreiding[4] and Tripos 5.2[5]

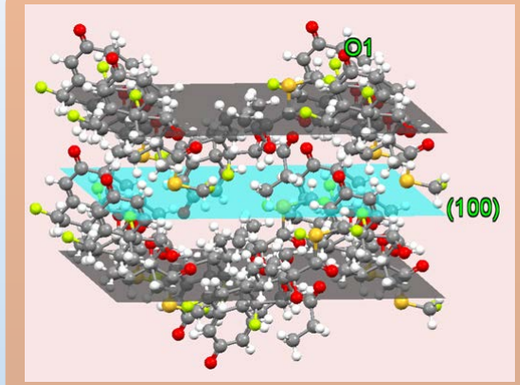



## MORPHOLOGY VALIDATION

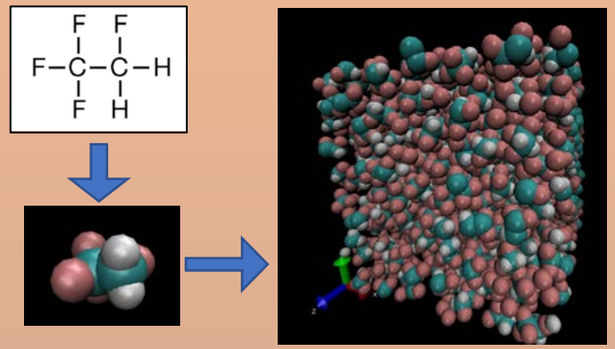
- In this model, each face's growth rate was proportional to attachment energy
- Both force fields predicted a morphology that resembled the hexagonal profile of FP crystals from slow evaporation in methanol




## SURFACE CHEMISTRY

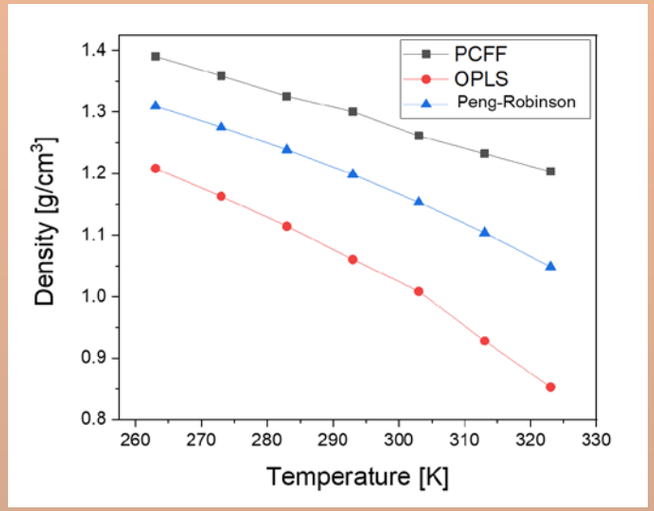
- Morphology model shows the chemistry of each face
- (100) face exposes the hydrogen bond accepting O1 atom
- Large cavities between molecules

# 3. Liquid Propellant HFA 134a



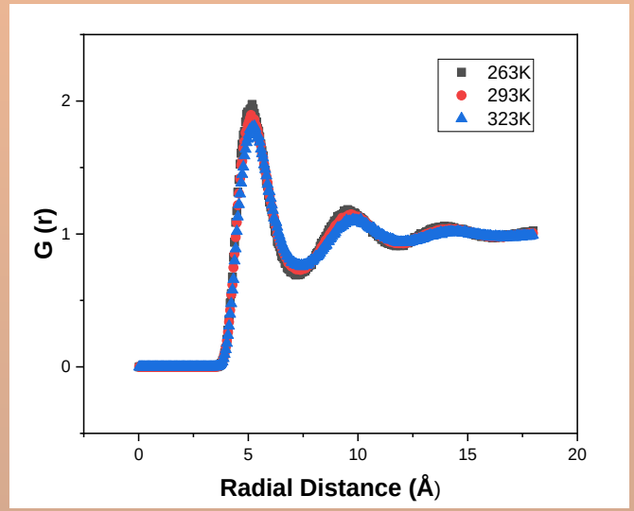

## METHOD

- 463 HFA-134a molecules were simulated in a cubic box using molecular dynamics code DL_Poly 4.09[6]
- Atomic point charges came from the force fields being tested; OPLS[7] and PCFF[8]
- Volume could change with conditions of constant target temperature and pressure; ranging from 263 to 323 K and 5.6 atm, respectively
- Equilibration lasted 500 ps and sampling 1.2 ns




## VALIDATION

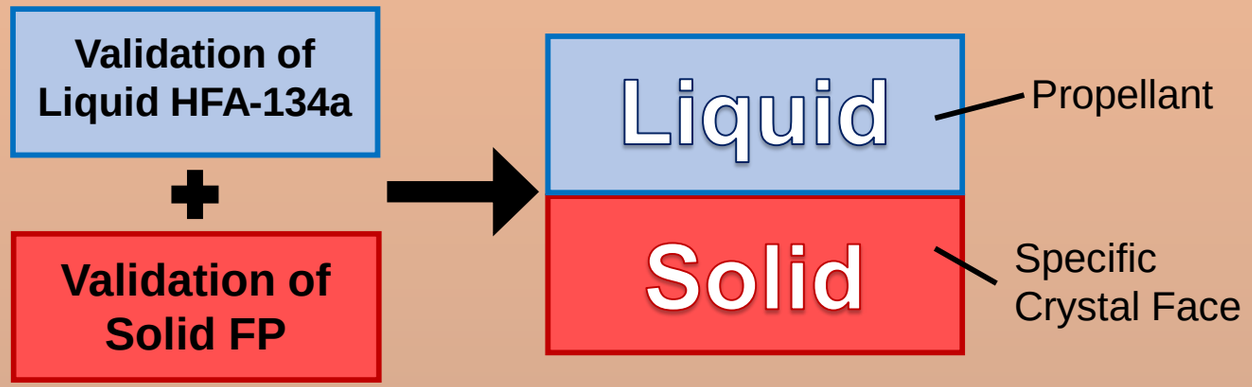
- Thermal expansion was compared to physical values from the Peng-Robinson equation of state
- It showed a difference in density of +/-10 % for the PCFF and OPLS force fields respectively




## STRUCTURE OF LIQUID

- Radial distribution function (RDF) of PCFF simulations show higher peaks at lower temperatures
- It also resembled a previous Monte Carlo simulation[9] which further validates the results

# 4. Conclusion and Future Work




- Molecular models of the solid and liquid phase were validated against physical values
- The different chemistry of FP's crystal surfaces was highlighted and structure of liquid HFA-134a was observed with an RDF plot
- The two phases will be combined to measure the free energy of wetting of different faces
- Then, further work will use this method to look at other materials in formulations

# 5. References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