**MS28-2-5 Salt Formation between Two Frontline Antitubercular APIs: from Mechanochemistry to Spontaneous Formation**
**#MS28-2-5**

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**Abstract**
The discovery of novel active pharmaceutical ingredients (APIs) used to treat diseases like tuberculosis has slowed in recent years. First- and second-line therapies recommended by the World Health Organization (WHO) were introduced more than 50 years ago while the youngest member of the first line medicines consisting of rifampin, isoniazid, (S,S)-ethambutol and pyrazinamide were introduced in 1970. Issues relating to the rise of resistant strains, solubility, bioavailability, the 'pill burden' and the need to diversify the available treatments are paramount to producing new and effective treatments.[1,2]
Cocrystallization is an area of enormous interest owing to the facile manner in which it can be used to enhance the physicochemical properties of the parent APIs.[3] Herein we report on the salt formation between frontline antitubercular APIs (S,S)-ethambutol (free base) (ETMBTL) and pyrazinecarboxylic acid (PCBA), the active metabolite of pyrazinamide. Our attempts at preparing the salt included neat grinding, liquid-assisted grinding, solvent evaporation and co-sublimation. Moreover, the salt forms spontaneously when a 1:2 physical mixture of ETMBTL and PCBA is exposed to a relative humidity of 75% at 20 °C (see Figure 1).[4] The resulting salt was characterized by differential scanning calorimetry (DSC), powder X-ray diffraction (PXRD), Fourier transform-infrared spectroscopy (FTIR) and single-crystal X-ray diffraction (SCXRD).[1–5]

**References**
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Figure 1. Cocrystal formation