"Semi-finished kits" for synthetic cannabinoid receptor agonists: Analysis of a clandestine production site, seized samples from prisons and forensic casework, and their *in vitro* activity

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When China introduced a class-wide synthetic cannabinoid receptor agonists (SCRA) ban in July 2021, many new SCRAs emerged that circumvented the legislation; however, most of these were found to have little to no potency at the cannabinoid 1 (CB_1) receptor responsible for the psychoactive effects. An emerging new trend shows that potent SCRAs that were prevalent prior to the Chinese ban have remained on the market, likely as a result of a new production route, known as "semi-finished kits". "Semi-finished kits" involve the sale of a non-controlled precursor SCRA (e.g., MDMB-INACA) along with other reagents and instructions for converting the precursor into the desired controlled SCRA (e.g., MDMB-4en-PINACA) via a one-pot synthesis. This study reports the discovery of a clandestine production site for this type of synthesis using "semi-finished kits" found in Switzerland, profiling of seized samples from the Scottish prisons and forensic casework from the US likely prepared via "semi-finished kits", and the *in vitro* activity of such precursor and precursor/final product mixtures using CB_1 and CB_2 β-arrestin 2 recruitment assays and a CB_1 intracellular calcium release assay. The clandestine production site used an industrial kitchen pot with stirring mechanism, which when tested, was found positive for ADB-BUTINACA. A synthesis recipe was also recovered at the site. From January-November 2023, 125 samples seized from the Scottish prisons were found positive for one or more SCRAs, of which 47 samples (37.6%) contained a mixture of a precursor (MDMB-INACA) with a final SCRA (MDMB-4en-PINACA and/or MDMB-BUTINACA). Mixtures of a precursor and final product were also identified in seizures from the US in 2023/2024, including mixtures of MDMB-INACA and MDMB-4en-PINACA, as well as ADB-INACA and ADB-BUTINACA. Based on the *in vitro* CB_1 receptor activity, the precursors are much less potent than the final SCRAs (e.g., EC_{50} of MDMB-INACA = 3693 nM; EC_{50} of MDMB-4en-PINACA = 16.7 nM). We seek to raise awareness of the emergence of this new supply methodology observed in multiple countries. Indicators of the use of this methodology include the detection of significant amounts of precursors in the final products and a decrease in potency of the seized samples.