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Purge ratio vs Spike & Purge, who wins?

A real case during an API production

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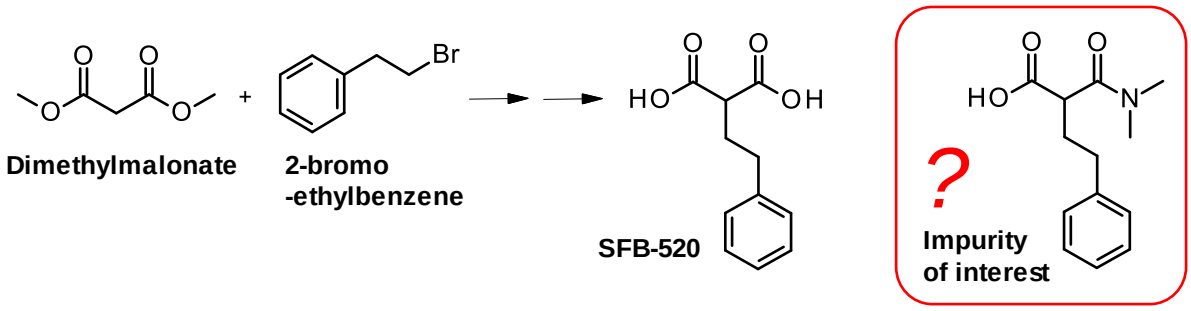
In order to satisfy the requirements of Regulatory Agencies regarding the production and release of an Active Pharmaceutical Ingredient (API), many factors need to be taken into account.

Many resources, both in terms of time and money, may need to be invested to ensure that the specifications set for both the starting materials and intermediates are enough to guarantee the production of an API with an analytical profile complying with ICH regulations.

While a purely theoretical approach can minimize both costs and timelines, can it take the place of experimental studies while yielding comparable assurances of success?

We present here the case of an impurity considered critical and detected in the initial steps (Scheme 1) of the synthetic process of Sodium Phenylbutyrate. In the work carried out the theoretical "Purge Ratio" approach of determining the fate of each impurity was compared with the experimental approach of "Spike & Purge" of the impurity previously identified and synthesized.



Scheme 1

References:

[1] C. Barber et al. Regulatory Toxicology and Pharmacology, 2017, 90, 22-28

[2] A. Teasdale et.al. Org Process Res Dev, 2013, 17, 221-230