Additional file 1

Superstructure-based process synthesis and economic assessment under uncertainty for solid drug product manufacturing

Kensaku Matsunami1, Fabian Sternal1, 2, Keita Yaginuma3, Shuichi Tanabe3, Hiroshi Nakagawa3, Hirokazu Sugiyama1,\*

1Department of Chemical System Engineering, The University of Tokyo,

7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-8656, Japan

2Department of Chemical and Bioengineering, Friedrich-Alexander-University Erlangen-Nürnberg,

Cauerstrasse 4, 91058 Erlangen, Germany

3Formulation Technology Research Laboratories, Pharmaceutical Technology Division, Daiichi Sankyo Co., Ltd., 1-12-1, Shinomiya, Hiratsuka, Kanagawa 254-0014, Japan

\*Corresponding author

sugiyama@chemsys.t.u-tokyo.ac.jp

Tel & Fax: +81-3-5841-7227

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# Supporting Information

## Calculation of the number of alternatives in a superstructure

The alternatives in a superstructure can be calculated by the following three steps.

### Step 1: excluding special processes

The processes including unit can be excluded from the superstructure because they are special compared with other processes. The two excluded processes are shown in Fig. S.1.



**Fig. S.1 Excluded processes in Step 1**

### Step 2: splitting into parts

The superstructure after excluding the special processes is shown in Fig. S.2. The ports that can be split are specified in Step 2 based on the streams, e.g., port 13 cannot be split because there is a stream from port 8 to 14. Consequently, six parts were obtained, as shown in Fig. S.3.



**Fig. S.2 A superstructure excluding special processes**



**Fig. S.3 Parts of the superstructure after Step 2**

### Step 3: calculating numbers

The total number of alternatives, [–], can be calculated as shown in Eq. (S.1):

|  |  |
| --- | --- |
| , | (S.1) |

where and represent the number of alternatives of the excluded processes and those of , respectively. The calculation of can also be done by repeating the steps described above. For part 1, for example, the stream from to port 8 can be excluded as a special process, and port 1 can be split as well. The number of alternatives from to port 1, and from port 1 to port 8 are 1 and 2, respectively. Then, becomes 3 (). Table S.1 summarizes the values of parameters. By applying Table S.1 to Eq. (S.1), was calculated as 9452.

**Table S.1 Values of parameters**

|  |  |
| --- | --- |
| Parameter | Value |
|  | 2 |
|  | 3 |
|  | 6 |
|  | 15 |
|  | 5 |
|  | 7 |
|  | 1 |

Table S.2 shows the breakdown of process alternatives in the superstructure.

**Table S.2 Breakdown of the investigated process alternatives**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Technology | Number | Dosage form | | Number |
| Batch | 8191 | Tablets | | 6750 |
| Continuous | 1261 |  | *Wet granulation* | *5400* |
| Total | 9452 |  | *Dry granulation* | *900* |
|  |  |  | *Direct compression* | *450* |
|  |  | Capsules | | 1352 |
|  |  | Granules | | 1260 |
|  |  | Powders | | 90 |
|  |  | Total | | 9452 |

## Details about the case study

The detailed results of sensitivity analysis for the top 20 highest sensitive parameters are summarized in Figs. S.4 and S.5.



**Fig. S.4 Results of sensitivity analysis in Scenario 1**



**Fig. S.5 Results of sensitivity analysis in Scenario 2**

## Contents of “SoliDecision”



**Fig. S.6 Data input tab for clinical development**



**Fig. S.7 Data input tab for commercial production**



**Fig. S.8 Data input tab for product demand**



**Fig. S.9 Result tab showing the best alternative for Scenario 1**