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Selected illustrations of fractional factorial screening experiments

Illustrations choisies de plans d'expériences factoriels fractionnaires

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

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The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

In exceptional circumstances, when a technical committee has collected data of a different kind from that which is normally published as an International Standard ("state of the art", for example), it may decide by a simple majority vote of its participating members to publish a Technical Report. A Technical Report is entirely informative in nature and does not have to be reviewed until the data it provides are considered to be no longer valid or useful.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO/TR 12845 was prepared by Technical Committee ISO/TC 69, *Applications of statistical methods*, Subcommittee SC 7, *Applications of statistical and related techniques for the implementation of Six Sigma*.

Introduction

The Six Sigma[1] and international statistical standards communities share a philosophy of continuous improvement and many analytical tools. The Six Sigma community tends to adopt a pragmatic approach driven by time and resource constraints. The statistical standards community arrives at rigorous documents through long-term international consensus. The disparities in time pressures, mathematical rigor, and statistical software usage have inhibited exchanges, synergy and mutual appreciation between the two groups.

The present document takes one specific statistical tool (two-level fractional factorial design) and develops the topic somewhat generically (in the spirit of International Standards) but then illustrates it through the use of six detailed and distinct applications. The generic description focuses on the commonalities across the designs. The annexes containing the six illustrations follow the basic framework but also identify the nuances and peculiarities in the specific applications. Each example offers at least one “wrinkle” to the problem, which is generally the case for real Six Sigma applications. It is thus hoped that practitioners can identify with at least one of the six examples, if only to remind them of the basic material on fractional factorial designs that was encountered during their Six Sigma training. Each of the six examples is developed and analysed using statistical software of current vintage. The explanations throughout are devoid of mathematical detail – such material can be readily obtained from the many design and analysis of experiments textbooks (such as those given in the Bibliography).

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1) Six Sigma is a trade mark of Motorola, Inc.

Selected illustrations of fractional factorial screening experiments

1 Scope

This Technical Report describes the steps necessary to use and to analyse two-level fractional factorial designs through illustration with six distinct applications of this methodology.

NOTE 1 Each of these six illustrations is similar in that resource constraints precluded the possibility of naively running full factorial designs. Other commonalities among the six examples are noted [e.g. study objective, two levels for factors, response variable(s), factors affecting the response]. On the other hand, the individual illustrations have some salient features that are distinct.

NOTE 2 The examples suggest the spectrum of possibilities both in application area and in choice of fractional factorial designs. Fractional factorial designs can be used to identify important factors for subsequent investigation (screening design) and can in some cases provide a viable understanding of the process under study. Fractional factorial designs include screening designs and designs that have been popularized by Genichi Taguchi.

NOTE 3 Fractional factorial experiments are sometimes employed by individuals (so-called “black belts” or “green belts”) associated with Six Sigma methods. Six Sigma methods are concerned with problem solving and continuous improvement. A fractional factorial experiment can be a cost-effective tool for obtaining timely improvements of processes and products. Detailed discussions and treatment of other tools employed by Six Sigma practitioners can be identified in various ISO/TC 69/SC 7 documents.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 3534-1, *Statistics — Vocabulary and symbols — Part 1: General statistical terms and terms used in probability*

ISO 3534-2, *Statistics — Vocabulary and symbols — Part 2: Applied statistics*

ISO 3534-3, *Statistics — Vocabulary and symbols — Part 3: Design of experiments*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 3534-1, ISO 3534-2, ISO 3534-3 and the following apply.

3.1

analysis of variance
ANOVA
technique which subdivides the total variation of a response variable into components associated with defined sources of variation

NOTE Adapted from ISO 3534-3:—[2], definition 3.3.8. (The notes and example are not included here.)

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[2] To be published. (Revision of ISO 3534-3:1999)

3.2
binomial distribution

discrete distribution having the probability mass function

$$P(X = x) = \frac{n!}{x!(n-x)!} p^{x}(1-p)^{n-x}$$

where $x = 0, 1, \ldots, n$ and with indexing parameters $n = 1, 2, \ldots$, and $0 < p < 1$.

NOTE Adapted from ISO 3534-1:2006, definition 2.46. (The example and notes are not included here.)

3.3
block

collection of experimental units

NOTE Adapted from ISO 3534-3:—, 3.1.23. (The notes are not included here.)

3.4
centre point

vector of factor level settings of the form (a_1, a_2, ..., a_k), where all a_i equal 0, as notation for the coded levels of the factors

NOTE Adapted from ISO 3534-3:—, 3.1.38. (The note and example are not included here.)

3.5
design matrix

matrix with rows representing individual treatments (possibly transformed according to the assumed model) which can be extended by deduced levels of other functions of factor levels (interactions, quadratic terms, etc.) but are dependent upon the assumed model

NOTE Adapted from ISO 3534-3:—, definition 3.2.24. (The notes are not included here.)

3.6
full factorial experiment
factorial experiment

designed experiment consisting of all possible treatments formed from two or more factors, each being studied at two or more levels

NOTE Adapted from ISO 3534-3:—, 3.2.1. (The notes are not included here.)

3.7
interaction

combination of two or more factors

NOTE Adapted from ISO 3534-3:—, 3.1.15. (The notes are not included here.)

3.8
factor level

setting, value or assignment of a factor in accordance with the design region

NOTE Adapted from ISO 3534-3:—, definition 3.1.10. (The notes and examples are not included here.)

3.9
normal distribution
Gaussian distribution

continuous distribution having the probability density function

$$f(x)=\frac{1}{\sigma\sqrt{2\pi}}\mathrm{e}^{-\frac{(x-\mu)^2}{2\sigma^2}}$$

where $-\infty < x < \infty$ and with parameters $-\infty < \mu < \infty$ and $\sigma > 0$

NOTE Adapted from ISO 3534-1:2006, definition 2.50. (The notes are not included here.)

3.10
predictor variable
factor

variable that can contribute to the explanation of the outcome of an experiment

NOTE 1 The extent to which a given predictor variable can be controlled dictates its potential role in a designed experiment. Predictor variables can be controllable (fixed), modifiable (controllable only for short duration or at considerable expense) or uncontrollable (random).

NOTE 2 A predictor variable can include a random element in it or it can, for example, be from a set of qualitative classes which can be observed or assigned without random error.

NOTE 3 The term predictor variable is typically used in contexts involving the mathematical relationship among the response variable and predictor variable(s) or functions of predictor variables. The term “factor” tends to be used operationally as a means to assess the response variable as particular factors vary.

NOTE 4 A factor may be associated with the creation of blocks.

NOTE 5 “Independent variable” is not recommended as a synonym due to potential confusion with “independence” (see ISO 3534-1:2006, 2.4). Other terms sometimes substituted for predictor variable include “input variable”, “descriptor variable” and “explanatory variable”.

[ISO 3534-3:—, definition 3.1.4]

3.11
randomization

strategy in which each experimental unit has an equal chance of being assigned a particular treatment

NOTE Adapted from ISO 3534-3:—, definition 3.1.26. (The notes are not included here.)

3.12
replication

⟨experiment⟩ multiple occurrences of a given treatment combination or setting of predictor variables

NOTE Adapted from ISO 3534-3:—, definition 3.1.35. (The notes are not included here.)

3.13
repetition

performance of an experiment more than once for a given set of predictor variables not necessarily with a complete set-up of the predictor variables

3.14
split-plot design

experimental design in which the group of experimental units (“plot”) to which the same factor level assigned to the principal factor is subdivided (“split”) so as to study one or more additional principal factors within each level of that factor

NOTE Adapted from ISO 3534-3:—, definition 3.2.16. (The example and notes have not been included here.)

3.15
design resolution

⟨design of experiments; fractional factorials⟩ length of the shortest word in the defining relation

NOTE 1 Design resolution indicates the extent of aliasing among main effects and two-way and higher-order interactions.

NOTE 2 The design resolution describes the aliasing in a particular experimental design. The numerical length is generally given by upper case Roman numerals. The three most common practical situations are resolutions III, IV and V.

- For a **resolution III** design, main effects are not aliased with other main effects. This observation can be made by examining the expressions in the defining relation. For example, $I = ABD = BCE = ACDE$ includes the expressions I, ABD, BCE and $ACDE$ and counting the number of letters for each term (1, 3, 3 and 4, respectively for this example). The shortest length of these aside from 1 (corresponding to I) is 3, which is known as the length of the shortest "character string". At least one main effect is aliased with a two-way interaction. For example, for $I = ABD$ it would be the case that A is confounded with BD, B is confounded with AD and D is confounded with AB.
- For a **resolution IV** design, main effects are not aliased with other main effects or with any two-way interactions. At least one two-way interaction is aliased with another two-way interaction. For example, for the defining relation $I = ABCE = BCDF = ADEF$ includes the expressions I, $ABCE$, $BCDF$ and $ADEF$ and counting the number of letters for each term (1, 4, 4 and 4, respectively). The smallest value aside from 1 (corresponding to I) is 4, which is known as the length of the shortest "character string" for this design. For example, for $I = ABCE$, it would be the case that AB is confounded with CE, AC with BE, AE with BC, while A is confounded with BCE, B is confounded with ACE, C is confounded with ABE and E is confounded with ABC.
- For a **resolution V** design, main effects and two-way interactions are not aliased with any other main effects or with any other two-way interactions. For example, with $I = ABCDE$, it is clear that each main effect is confounded with a four-way interaction (A is confounded with $BCDE$) and each two-way interaction is confounded with a three-way interaction (AB is confounded with CDE).

NOTE 3 The higher the resolution, the more effects (main or interactions) can be estimated unambiguously, provided the higher-order interactions are negligible. Given a choice of two potential designs involving the same number of factors and experimental units, the design with the higher resolution should be selected. Fortunately, for most cases of k and p of practical interest, the most appropriate defining relations are recorded.

NOTE 4 Full factorial designs have no confounding. For most practical purposes, a resolution V is excellent and a resolution IV design may be adequate. Resolution III designs are useful as economical screening designs.

[ISO 3534-3:—, definition 3.2.6]

4 Symbols and abbreviated terms

The main symbols and abbreviated terms used in this Technical Report are given below.

Y	Response variable
A, B, C, D	Factors
AB, AC, AD, BC, BD, CD	Two-way interactions
ABC, ACD, BCD	Three-way interactions
$ABCD$	Four-way interactions
+1, −1	High and low settings
2^4	Four factors each at two levels
σ	Standard deviation

5 Generic description of fractional factorial designs

5.1 Overview of the structure of the examples in Annexes A to F

This Technical Report provides general guidelines on the design, conduct and analyses of two-level fractional factorial designs and illustrates the steps with six distinct applications given in the annexes. Each of the six examples in Annexes A to F follows the basic structure as given in Table 1.

The steps given in Table 1 apply to design and analysis of screening experiments in general. Each of the seven steps is explained below.

Table 1 — Basic steps in experimental design

Step 1	State the overall objective(s) of the experiment
Step 2	Describe the response variable(s)
Step 3	List the factors that might affect the response(s)
Step 4	Select a fractional factorial design
Step 5	Analyse the results – numerical summaries and graphical displays
Step 6	Present the findings
Step 7	Perform a confirmation run

5.2 Overall objective(s) of the experiment (Step 1)

Experiments are conducted for a variety of reasons. The primary motivation for the experiment should be clearly stated and agreed to by all parties involved in the design, conduct, analysis and implications of the experimental effort. There may be secondary objectives that could be addressed with this experiment but, in general, the focus is on identifying a subset of the factors that impact the response variable.

The ultimate outcome of the experiment might be to take immediate action on factor levels or to obtain a predictive model, both of which dictate some elements of the analyses. Further, the experiment could be recognized as the first step in an ongoing sequence of experiments to determine improvements to the product or process.

5.3 Response variable(s) (Step 2)

Associated with the objective of an experiment is a measurable outcome or performance measure. A response of interest could involve maximization (larger is better), minimization (smaller is better) or meet a target value (be close to a specified value). The response variable (denoted here by the variable Y) should be intimately (if not directly) related to the objective of the experiment. For some situations, there may be multiple characteristics of interest to be considered, although there is typically a primary response variable associated with the experiment. In other cases, multiple responses must be considered.

5.4 Factors affecting the response(s) (Step 3)

The response variable very likely depends in some unknown way on a variety of conditions. These could be set in the course of generating a response variable outcome such as a temperature or a time setting. These conditions are presumed to relate to controllable factors that may be continuous (temperature, concentration) or discrete (two assembly lines A or B, two vendors, two packaging styles, and so forth). For the fractional factorial experiments considered in this Technical Report, the experimental design process is simplified by selecting two levels for each factor to be varied in the experiment.

- For discrete factors, with only two possible settings, the levels are just these two settings.

- For continuous factors, discretion can be used in choosing the two specific values. In some cases, one setting could be the historical value and the other a proposed value. In other cases, the two settings could be nominal adjustments from the historical setting. In any event, the settings should be sufficiently far removed to have an opportunity to reveal an impact subject to the inherent uncertainty, while not being so disparate that the settings are unreasonable from a practical, safety or sensibility standpoint. The setting of levels of continuous factors benefits from an expert collaborating in the experiment.

There may be additional factors that could impact that response variable but may be deemed much less important than the chosen factors or are too difficult or expensive to control. Finally, it is the case that the factors are to be set independently from each other. It could, however, be discovered that the factors interact (the setting of one factor impacts how a second factor affects the response).

5.5 Select a fractional factorial design (Step 4)

It is usual that the number of factors thought to be important to experiment with is large, e.g. 10 or more. Designing an experiment to investigate all possible factors and their combinations would lead to excessively large experiments. For example, in studying only eight factors at two levels each, the number of experimental runs is 256. For three levels, this would be 6 561 runs! For most organizations, this would be a very extravagant use of resources. Thus, the need is there to design experiments using fewer runs but still giving the experimenter all of the important experimental results. Although this gives full information about the effects of the factors, it also delivers information about higher-order factor combinations that are of minimal practical utility. Consequently, a balance is sought to reduce the experimental effort without foregoing the information about main factors of interest by designing a fractional experiment.

The examples provided in the annexes use 6 to 15 factors with a maximum of only 40 runs to identify the critical factors.

A classical design consists of 16 runs obtained by considering all combinations of four factors with two possible levels. See ISO/TR 29901 for a description. Table 3 provides the basic layout in a standard order for ease of understanding. Each row of the table represents one set of experimental conditions that when run will produce a value of the response variable Y. The four factors are designated as A, B, C and D. For an individual factor, the level "–1" is the "low" setting, or one of the two levels if the factor is categorical. The level "+1" is the "high" setting, or the other level of the categorical factor. The column "Y" is a placeholder for the response value once a run has occurred.

This will provide unambiguous information about the following factors and their interactions, namely:

A, B, C, D, AB, AC, AD, BC, BD, CD, ABC, ABD, ACD, BCD and $ABCD$

For most practical applications, the higher-order interactions, e.g. ABC, are often taken as unimportant and can therefore, in a design, be discounted. This, therefore, becomes the way in which larger numbers of factors can be incorporated into designs that are intended for full factor combinations, albeit for a smaller number of factors.

It is imperative that the experimenter be aware of the exact pattern of main effects and the associated two-way interactions created by this discounting of higher-order interactions. A careless selection may inhibit the clear identification of the effects (be they main or two-way interactions). These aspects can be seen in the six different examples contained in the annexes.

Table 2 provides a useful summary of the shortcomings of certain designs. The table describes the three most common design resolutions. The examples in the annexes (see Table 4) refer to these resolutions.

Table 2 — Selected design resolutions

Resolution	Description
III	No main effects are aliased with any other main effect, but at least one main effect is aliased with two-factor interactions.
IV	No main effects are aliased with any other main effect or two-factor interactions, but at least one two-factor interaction is aliased with other two-factor interactions and at least one main effect is aliased with three-factor interactions.
V	No main effects or two-factor interactions are aliased with any other main effect or two-factor interactions, but at least one two-factor interaction is aliased with three-factor interactions and at least one main effect is aliased with four-factor interactions.

The design choice ultimately rests with the aforementioned considerations as well as resource constraints. Guidance of a general nature can be gleaned from the reference texts in the Bibliography. Increasingly, software packages contain useful guides to design selection and algorithms for optimal design where the problem is well defined.

Table 3 — Layout of a generic 2^4 full factorial design

Row number	A	B	C	D	Y	Run order
1	−1	−1	−1	−1	y_1	6
2	+1	−1	−1	−1	y_2	14
3	−1	+1	−1	−1	y_3	4
4	+1	+1	−1	−1	y_4	11
5	−1	−1	+1	−1	y_5	9
6	+1	−1	+1	−1	y_6	2
7	−1	+1	+1	−1	y_7	3
8	+1	+1	+1	−1	y_8	1
9	−1	−1	−1	+1	y_9	8
10	+1	−1	−1	+1	y_{10}	13
11	−1	+1	−1	+1	y_{11}	7
12	+1	+1	−1	+1	y_{12}	10
13	−1	−1	+1	+1	y_{13}	15
14	+1	−1	+1	+1	y_{14}	16
15	−1	+1	+1	+1	y_{15}	5
16	+1	+1	+1	+1	y_{16}	12

5.6 Analyse the results — Numerical summaries and graphical displays (Step 5)

At the completion of the conduct of the experiment, the y_i values would be replaced by the actual observed responses. Many statistical software packages exist to produce output to aid in the understanding of the results of the experiment. Of immediate concern is the determination of the impact of the factors individually on the response variable. By the nature of fractional factorial designs, it is hoped, if not presumed, that the main effects that are estimated are indeed attributable to the main factor although it is recognized that aliasing could be taking place.

Much of the analysis that is conducted for 2^4 full factorials (see ISO/TR 29901) is applicable here with the proviso that aliasing patterns must be recognized and properly evaluated. In particular, main effects plots, interaction plots, Pareto diagrams, normal and/or half-normal probability plots are relevant instruments of analysis. Although the emphasis of the analysis is likely to be graphical in its nature, additional supporting documentation, e.g. effects table, should be given.

5.7 Present the findings (Step 6)

Almost certainly, the conclusions from a screening experiment will constitute a description of the next phase of experimentation. Design of experiments is inherently sequential in nature and a screening experiment is frequently the first phase of investigation and is often followed by subsequent experiments with fewer factors and, sometimes, more levels. In some cases, the screening experiment supports a predictive model that can suggest alternative settings for the important factors. Although the process has not been fully optimized, superior settings may, in the meantime, have been identified.

Further, the experiment may reveal important interactions which may be, unfortunately, aliased with others. An example of this can be found in Annex C.

5.8 Perform confirmation runs (Step 7)

Confirming experiments are considered to be good “practice” in that they should provide the experimenter assurance that

a) the original experiment was correctly conducted,

b) the findings still hold true at a later point in time, and

c) there were no apparent “lurking” variables that were ignored in the original experimental design.

This being said, there are circumstances that preclude a confirmation run, e.g. time pressures due to commercial issues or matters of cost (resources) or management acceptance of the risk of a faulty screening experiment.

6 Description of Annexes A to F

6.1 Comparing and contrasting the examples

Six distinct examples of fractional factorial designs are illustrated in Annexes A to F. Each example follows the general template given in Table 1.

6.2 Experiment summaries

Table 4 summarizes the six examples detailed in the annexes and indicates aspects of the analyses that were unique to that experiment.

Table 4 — Experiment summaries found in annexes

Annex	Experiment	Business area	Resolution	Problem-specific aspects
A	Direct mail campaign	Marketing	IV	Proportion response variable, standard errors based on binomial distribution.
B	Polymer emulsion optimization	Chemical engineering	IV	Blocking, response transformation, two responses.
C	PVC foam formulation	Chemical engineering	III	Analysis of three responses with different levels of success, due to severe confounding of effects.
D	Insulin process validation	Pharmaceuticals	IV	Eight responses, blocking, factor levels expressed as a range, interest in no effect as a result.
E	Washing machine robustness	Mechanical engineering	Not applicable	Taguchi orthogonal arrays, inner/outer arrays.
F	Aggregated shipworm bacterium	Bioengineering	III, IV	Plackett-Burman design.

Annex A
(informative)

Direct mail marketing campaign

A.1 General

Mail material for a direct marketing campaign can be sent in a variety of packaging styles and with various textual and graphical cues to encourage a high response rate. Historically, the company had experimented with a small subset of their campaigns in which one aspect of the package would be varied. The company was receptive to a more sophisticated approach than their previous “one factor at a time” style. Management and the marketing firm that implemented the mailings in consultation with a statistician identified seven items that could be varied in the package sent to potential customers and decided on the specific fractional factorial design as described in the next subclauses.

A.2 Overall objective for the experiment

The objective of the experiment was to maximize magazine subscription response rate based on a direct mailing campaign[3].

A.3 Description of the process

A typical mailing involves solicitations to 400 000 potential subscribers. The actual package mailed can be varied regarding outer envelope design and other features that had previously enhanced response rate. For this study, the parent company opted to devote 40 000 packages to the experiment. The mailing itself is subcontracted to a third party that specializes in assembling these packages.

A.4 Response variable

A.4.1 Choice of variable

The response variable is the number of people who subscribed and paid (either by credit card or cheque).

A.4.2 Measurement of the response variable

Exactly 2 500 mailings went out for each combination of package contents. Subscribers were tracked to determine which package of materials they had been sent.

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[3] This example has been adapted from the article “Using a Fractional Factorial Design to Increase Direct Mail Response,” by J. Ledolter and A. J. Swersey (2006), *Quality Engineering*, **18**, pp. 469-475. Used with permission from the publisher, the American Society of Quality, Milwaukee, Wisconsin.

A.4.3 Relationship of the response variable to the objective of the experiment

A.4.3.1 General

The publisher expected a response rate of about 2 %. Further, the publisher wanted to be fairly certain to be able to recognize a 0,5 % increase and at least a decent chance of detecting a 0,25 % increase in response rate. The response rate is the critical factor in addressing the objective of the experiment as the package variations have roughly the same preparation cost. Of secondary interest is the proportion of positive responders who pay immediately as well, which avoids a later billing expense.

A.4.3.2 Description of each factor (continuous/discrete) to be varied

The factors chosen to be varied within the experiment were determined jointly by the publisher, the marketing firm involved in preparing the mailing and the statistical consultant. The factors are described as follows:

- presence/absence of an “Act now to respond/pay today” insert, a separate colour enclosure with the encouragement presented in a bold font, a copy of the cover of the next issue and a description of its contents; this insert also encourages prospective subscribers to pay at the same time as responding, to preclude a follow-up mailing requesting payment for those who indeed “acted now”;
- additional option of paying by credit card (rather than only by personal cheque);
- offer wording strength; an additional phrase encouraging the potential subscriber to send in the reply card and payment immediately in order to receive the next issue “hot off the press”;
- inclusion or non-inclusion of a bumper sticker;
- a guarantee that provides the opportunity to cancel the subscription and recuperate money for the issues not yet received (one option) or for the full subscription price (other option);
- testimonials that are inserts consisting of positive quotes from subscribers and possibly some celebrities;
- presence/absence of a phrase on the outer envelope with mild profanity (“ballsy” versus “gutsy”).

Each of these factors is categorical with two levels. Some incremental costs to the mailing are incurred with the variables that involve inserts.

A.4.3.3 Selection of levels (related to size of effect to be determined)

The factors used in the experiment and their associated levels are given in Table A.1.

Table A.1 — Factors

Factor	Level 1 (–1)	Level 2 (+1)
A: Act now	No “Act now” insert	“Act now” insert
B: Credit card	No credit card	Credit card
C: Offer hardness	Hard offer	Harder offer
D: Bumper sticker	No bumper sticker	Bumper sticker
E: Guarantee	Guarantee partial refund	Guarantee full refund
F: Testimonial	No “Testimonial” insert	“Testimonial” insert
G: Profanity	“Gutsy”	“Ballsy”

A.4.3.4 Other factors noted but not incorporated due to issues with controllability or relevance

No other factors were identified for the experiment.

A.4.4 Fractional factorial design

A.4.4.1 Choice of specific design

There are a multitude of possible designs that allow the investigation of the seven factors, each having two levels. The possibilities depend on the number of combinations to be considered which in turn impacts the number of runs considered. The publisher was willing to allocate a total of 40 000 mailings for the entire experiment. The designs considered are given in Table A.2.

Table A.2 — Design choices

Number of runs	Fraction size	Resolution	Confounding patterns	Comments
128	Full factorial	Full	None – All effects can be estimated	Benefits from estimating higher-order interactions are minimal
64	Half fraction	VII	Main effects confounded with six-way interactions Two-way interactions not confounded with other two-way interactions	Less costly than a full factorial but the additional benefits are minimal
32	Quarter fraction	IV	Main effects confounded with three-way interactions Some two-way interactions confounded with other two-way interactions	Slightly better confounding structure than the 16-run case but at twice the level of effort
16	One-eighth fraction	IV	Main effects confounded with three-way interactions Some two-way interactions confounded with other two-way interactions	Excellent trade off between level of effort and capability to estimate main effects free of two-way interactions
8	One-sixteenth fraction	III	Main effects confounded with two-way interactions Two-way interactions confounded with several other two-way interactions	Requires a follow-up experiment to separate main effects from confounding with two-way interactions

The two most viable designs were the 32-run one-quarter fraction and the 16-run one-eighth fraction, both of which are resolution IV (namely, main effects can be estimated to be free of two-way interactions, but there are some two-way interactions confounded with other two-way interactions). The larger experiments are simply too big for the benefits accrued (ability to estimate higher-order interactions which are unlikely to be significant). The small 8-run experiment would require a follow up experiment in order to resolve the two-way interactions. The 16-run experiment was chosen since it was felt that, with appropriate labelling of factors, the confounding structure could be accommodated. In particular, the factors A, B, C and D are set as if they would constitute a 2^4 full factorial design, in which all 16 combinations of the two levels of these factors are considered. The levels of the three additional factors are set according to $E = ABC$, $F = BCD$ and $G = ACD$.

Based on subject matter expertise in direct mailing, the experimenters believed that factors E and F were unrelated to each other and to the other factors (i.e. there should be no two-way interactions involving E and F). Factor G conceivably could entice the recipient to open the envelope, but once the contents were in hand, interaction between the slang expression on the envelope would not interact with the contents. In short, it was assumed, at the design stage, that all of the following two-way interactions would be negligible: AE, AF, AG, BE, BF, BG, CE, CF, CG, DE, DF, DG, EF, EG, FG.

The full confounding (alias) structure is given in Table A.3. Each of the main effects and plausible two-way interactions (in bold typeface in Table A.3) can be unambiguously estimated under the assumptions given in the previous paragraph.

Table A.3 — Confounding structure for the fractional factorial design

Generators: $E = ABC$, $F = BCD$, $G = ACD$

Defining relation: $I = ABCE = BCDF = ACDG = ADEF = BDEG = ABFG = CEFG$

Complete alias structure:

$\mathbf{A} = BCE = ABCDF = CDG = DEF = ABDEG = BFG = ACEFG$

$\mathbf{B} = ACE = CDF = ABCDG = ABDEF = DEG = AFG = BCEFG$

$\mathbf{C} = ABE = BDF = ADG = ACDEF = BCDEG = ABCFG = EFG$

$\mathbf{D} = ABCDE = BCF = ACG = AEF = BEG = ABDFG = CDEFG$

$\mathbf{E} = ABC = BCDEF = ACDEG = ADF = BDG = ABEFG = CFG$

$\mathbf{F} = ABCEF = BCD = ACDFG = ADE = BDEFG = ABG = CEG$

$\mathbf{G} = ABCEG = BCDFG = ACD = ADEFG = BDE = ABF = CEF$

$\mathbf{AB} = CE = ACDF = BCDG = BDEF = ADEG = FG = ABCEFG$

$\mathbf{AC} = BE = ABDF = DG = CDEF = ABCDEG = BCFG = AEFG$

$\mathbf{AD} = BCDE = ABCF = CG = EF = ABEG = BDFG = ACDEFG$

$AE = \mathbf{BC} = ABCDEF = CDEG = DF = ABDG = BEFG = ACFG$

$AF = BCEF = ABCD = CDFG = DE = ABDEFG = BG = ACEG$

$AG = BCEG = ABCDFG = \mathbf{CD} = DEFG = ABDE = BF = ACEF$

$\mathbf{BD} = ACDE = CF = ABCG = ABEF = EG = ADFG = BCDEFG$

$ABD = CDE = ACF = BCG = BEF = AEG = DFG = ABCDEFG$

Alias structure restricted to two-way interactions (main effects are clear of two-way interactions):

$\mathbf{AB} = CE = FG$

$\mathbf{AC} = BE = DG$

$\mathbf{AD} = CG = EF$

$AE = \mathbf{BC} = DF$

$AF = DE = BG$

$AG = \mathbf{CD} = BF$

$\mathbf{BD} = CF = EG$

As can be seen from Table A.3, each main effect and those two-way interactions likely to be of interest are confounded only with non-interesting two-way or higher interactions.

A.4.4.2 Design matrix (standard order and run order)

The design selected was the 16-run, one-eighth fractional factorial design, with seven factors (A, B, C, D, E, F and G). Table A.4 shows the design.

Table A.4 — Design matrix

Row number	A	B	C	D	E (= ABC)	F (= BCD)	G (= ACD)
1	–1	–1	–1	–1	–1	–1	–1
2	1	–1	–1	–1	1	–1	1
3	–1	1	–1	–1	1	1	–1
4	1	1	–1	–1	–1	1	1
5	–1	–1	1	–1	1	1	1
6	1	–1	1	–1	–1	1	–1
7	–1	1	1	–1	–1	–1	1
8	1	1	1	–1	1	–1	–1
9	–1	–1	–1	1	–1	1	1
10	1	–1	–1	1	1	1	–1
11	–1	1	–1	1	1	–1	1
12	1	1	–1	1	–1	–1	–1
13	–1	–1	1	1	1	–1	–1
14	1	–1	1	1	–1	–1	1
15	–1	1	1	1	–1	1	–1
16	1	1	1	1	1	1	1

Randomization was used in selecting 2 500 addresses out of the 40 000 addresses constituting the sampling frame. Considerable effort was expended to ensure that the third-party provider correctly assembled the mailed packages. There was no need to randomize the order with respect to the design matrix.

A.4.4.3 Centre points

Centre points were not selected for this experiment because the variables are categorical. Moreover, the response rate can be assessed as a binomial random variable with a nominal response rate of 2 % so that an independent estimate of the uncertainty can be calculated.

A.4.4.4 Replication and repetition

As mentioned in A.4.4.2, the mailings were sent to 2 500 potential subscribers. This experiment had neither replication nor repetition.

A.4.5 Analysis of results

A.4.5.1 Data acquired through the experiment and analysis considerations

The results from the experiment are given in Table A.5. They were keyed into a software programme called JMP4).

Table A.5 — Experiment results

Row number	*A*	*B*	*C*	*D*	*E*	*F*	*G*	Response rate %
1	–1	–1	–1	–1	–1	–1	–1	2,08
2	1	-1	–1	–1	1	–1	1	2,76
3	–1	1	–1	–1	1	1	–1	2,36
4	1	1	–1	–1	–1	1	1	3,04
5	–1	–1	1	–1	1	1	1	2,36
6	1	–1	1	–1	–1	1	–1	2,52
7	–1	1	1	–1	–1	–1	1	2,64
8	1	1	1	–1	1	–1	–1	2,64
9	–1	–1	–1	1	–1	1	1	2,40
10	1	–1	–1	1	1	1	–1	2,52
11	–1	1	–1	1	1	–1	1	3,24
12	1	1	–1	1	–1	–1	–1	2,12
13	–1	–1	1	1	1	–1	–1	2,12
14	1	–1	1	1	–1	–1	1	3,12
15	–1	1	1	1	–1	1	–1	1,96
16	1	1	1	1	1	1	1	3,20

The “Fit Model” in JMP generated the following results:

Singularity details

$$AE = BC = DF$$

$$AC = BE = DG$$

$$AG = BF = CD$$

$$AF = BG = DE$$

$$AB = CE = FG$$

$$BD = CF = EG$$

$$AD = CG = EF$$

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4) JMP is the trade name of a product supplied by SAS Inc. This information is given for the convenience of users of this Technical Report and does not constitute an endorsement by ISO of the product named. Equivalent products may be used if they can be shown to lead to the same results.

The confounding structure of the fractional factorial design is provided; it can be verified that it agrees with what was provided in Table A.4. This information is necessary to understand the parameter estimate results given in Table A.6.

Table A.6 — Parameter estimates

Term	Biased or zeroed	Estimate	Standard error	t ratio	Prob > $\|t\|$
Intercept	—	2,567 5	0,052 5	48,90	0,013 0
A	—	0,172 5	0,052 5	3,29	0,188 1
B	—	0,082 5	0,052 5	1,57	0,360 8
C	—	0,002 5	0,052 5	0,05	0,969 7
D	—	0,017 5	0,052 5	0,33	0,795 2
E	—	0,082 5	0,052 5	1,57	0,360 8
F	—	−0,022 5	0,052 5	−0,43	0,742 2
G	—	0,277 5	0,052 5	5,29	0,119 0
AB	Biased	−0,072 5	0,052 5	−1,38	0,399 0
AC	Biased	0,127 5	0,052 5	2,43	0,248 7
AD	Biased	−0,017 5	0,052 5	−0,33	0,795 2
AE	Biased	−0,042 5	0,052 5	−0,81	0,566 8
AF	Biased	0,102 5	0,052 5	1,95	0,301 3
AG	Biased	0,012 5	0,052 5	0,24	0,851 2
BC	Zeroed	0	0	—	—
BD	Biased	−0,037 5	0,052 5	−0,71	0,605 1
BE	Zeroed	0	0	—	—
BF	Zeroed	0	0	—	—
BG	Zeroed	0	0	—	—
CD	Zeroed	0	0	—	—
CE	Zeroed	0	0	—	—
CF	Zeroed	0	0	—	—
CG	Zeroed	0	0	—	—
DE	Zeroed	0	0	—	—
DF	Zeroed	0	0	—	—
DG	Zeroed	0	0	—	—
EF	Zeroed	0	0	—	—
EG	Zeroed	0	0	—	—
FG	Zeroed	0	0	—	—

With 16 combinations of the factors, 15 parameters are estimated — the intercept, seven main effects and seven sets of two-way interactions. At this point, the statistical package has not been “informed” of the nature of the response, so that the calculations proceed as if the response were a single value rather than the proportion of positive responses out of 2 500 attempts. Each effect can be estimated by the average response rate for the effect at the high level minus the response rate for the effect at its low level. Since the overall response rate is 2,57 %, the standard error of each of these estimated effects is $\sqrt{4(2{,}57)(100-2{,}57)/40\,000} = 0{,}158$ %. Two-way interactions can also be estimated but as has been noted, they are confounded with other two-way interactions.

Table A.7 — Estimation of effects

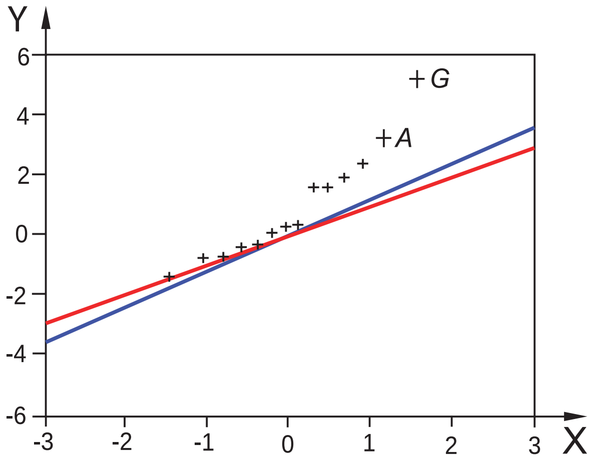
Term[a]	Coefficient	Effect	Standard error	z ratio	Prob $> \|z\|$
A	0,172 5	0,345	0,158	2,18	0,029
B	0,082 5	0,165	0,158	1,04	0,297
C	0,002 5	0,005	0,158	0,03	0,975
D	0,017 5	0,035	0,158	0,22	0,825
E	0,082 5	0,165	0,158	1,04	0,297
F	–0,022 5	–0,045	0,158	–0,28	0,776
G	0,277 5	0,555	0,158	3,51	0,000
AB + *CE* + *FG*	–0,072 5	–0,145	0,158	–0,92	0,359
AC + *BE* + ***DG***	0,127 5	0,255	0,158	1,61	0,107
AD + *CG* + *EF*	–0,017 5	–0,035	0,158	–0,22	0,825
AE + ***BC*** + *DF*	–0,042 5	–0,085	0,158	–0,54	0,591
AF + *DE* + *BG*	0,102 5	0,205	0,158	1,30	0,195
AG + ***CD*** + *BF*	0,012 5	0,025	0,158	0,16	0,874
BD + *CF* + *EG*	–0,037 5	–0,075	0,158	–0,47	0,636

[a] The most plausible of the interactions in each of the three term sums is in bold.

In Table A.7, the z ratio is the effect divided by the corrected standard error for each term as computed in Table A.6. The expression “Prob $> |z|$” refers to the probability that a standard normal variable is greater than z or less than $-z$.

The results in Table A.7 indicate the significance of factors A and G and a marginal AC interaction. The coefficients were generated in JMP and the results stored in a data sheet. The z ratio and Prob $> |z|$ were calculated using the formula feature.

In addition, the probability plot in Figure A.1 indicates potentially significant factors. However, the significance is based on a separate calculation that is not pertinent to the binomial response.



Key

X normal quantile

Y t ratio

The blue line is Lenth's PSE (pseudo standard error), from the estimates population.

The red line is the RMSE, i.e. root mean squared error, from the residual.

Figure A.1 — Probability plot

A.4.5.2 Pareto chart of effects

The relative size of the effects can be seen in the Pareto chart shown in Figure A.2.

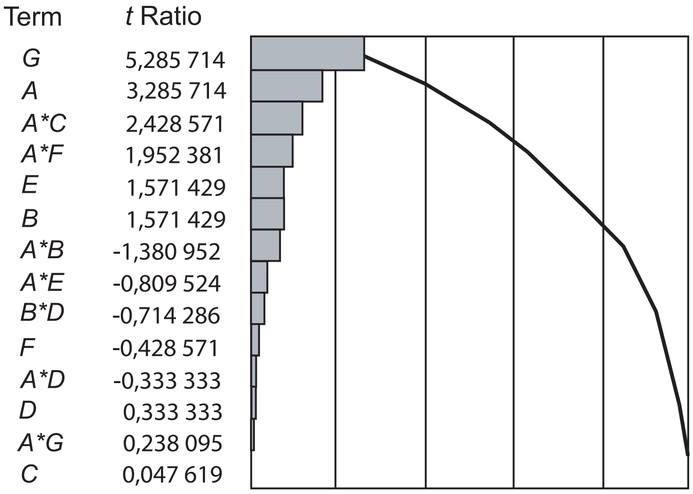


Figure A.2 — Pareto chart of estimates

A.4.5.3 Estimation of experimental error and standard error of effects

Each effect is estimated by the average response rate for the effect at the high level minus the response rate for the effect at its low level. Since the overall response rate is 2,57 %, the standard error of each estimated effect is $\sqrt{}[4(2,57)(100 - 2,57)/ 40\,000] = 0,158$ %.

A.4.5.4 Effects plots

Figure A.3 shows the main effects of the factors. The relative slopes of the lines are consistent with the significance of the factors *G* and *A*.

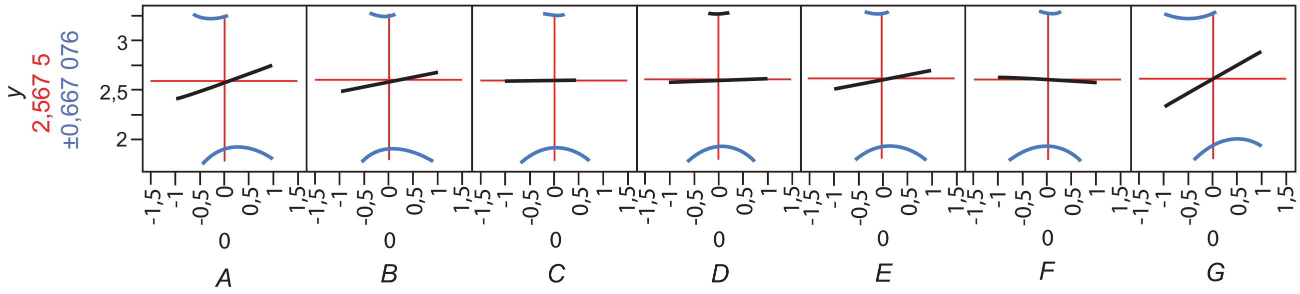


Figure A.3 — Effects plots

A.4.5.5 Interaction plots

Figure A.4 shows the interaction plots between the factors. The most noteworthy interaction is that between factors A (act now) and C (offer hardness).

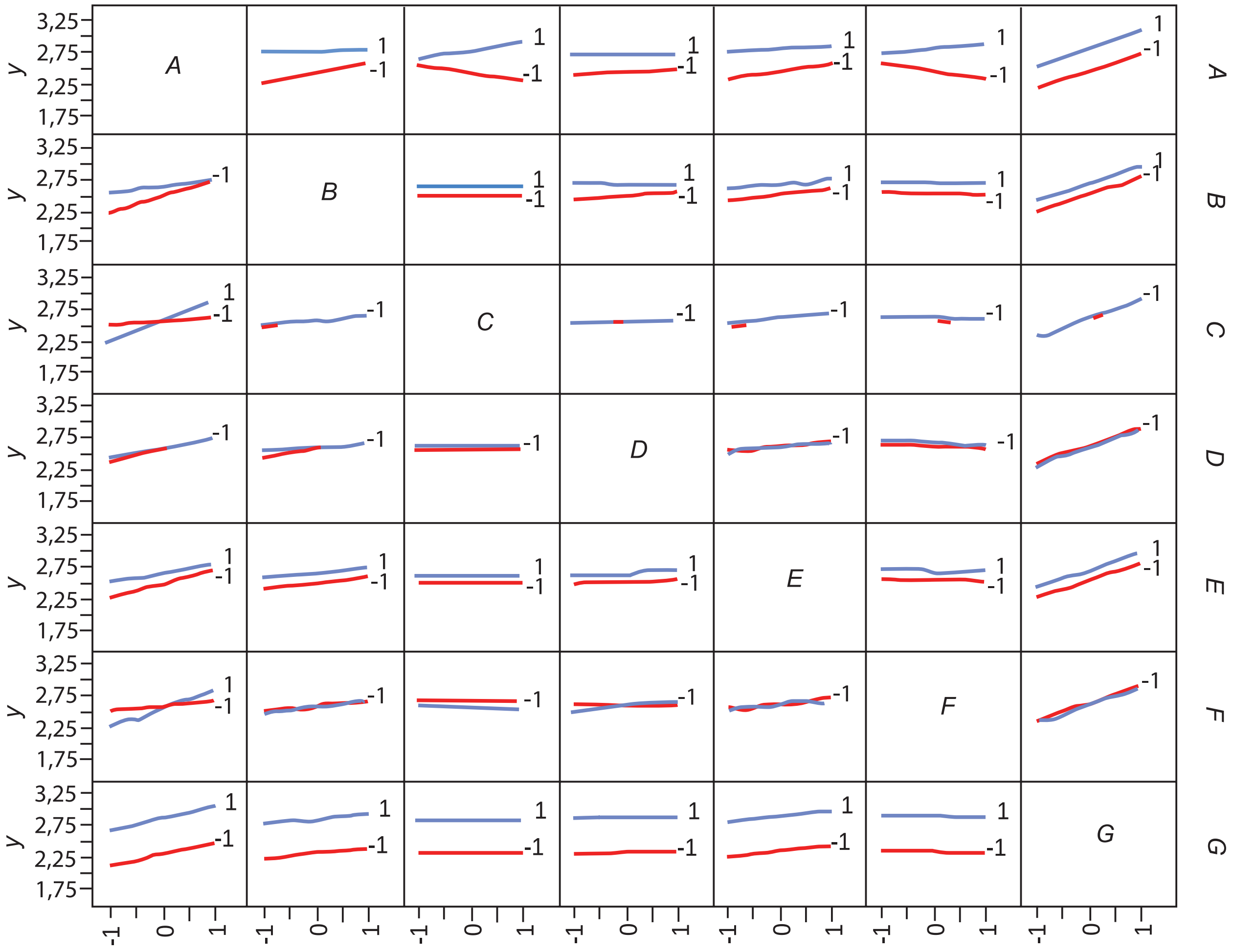


Figure A.4 — Interaction profiles

The interaction plots affirm the presence of an AC interaction. It appears that the “Act now” insert in conjunction with the harder offer wording was synergistically beneficial.

A.4.6 Presentation of findings

The experiment confirmed the benefits of using the word “ballsy” rather than the less vitriolic word “gutsy”. The “Act now” insert was supported, particularly when combined with the hard phrasing of the offer. The payment option, although not significant as a factor, led to a higher level of immediate payment. Finally, the bumper sticker and testimonial factors did not generate significant benefits, while incurring some costs. Likewise, the stronger guarantee did not generate appreciable improvement in response while having the possibility of costing the publisher additional money. Thus, it was decided not to include these options in the future.

A.4.7 Confirmation results

Subsequent mailings confirmed the benefits of offering the credit-card-payment option in addition to the personal-cheque option.

Annex B
(informative)

Optimizing a polymer emulsion

B.1 General

Overprint varnishes (OPV) and flexographic inks in the graphic arts business make use of a polymer emulsion that provides flexibility, water resistance and gloss. Production of this emulsion involves the importation of a resin from abroad before manufacturing. Production operators experience difficulties meeting lot-to-lot requirements for emulsion viscosity and particle size, as well as keeping production costs low, since a competitor is able to source this resin locally at lower prices. Documentation on the existing process was limited as the product was acquired during a merger of companies.

B.1.1 Overall objective for the experiment

The goal of this experimental work was to quickly identify a solution to the reaction problem by producing a polymer emulsion with specific viscosity and particle size characteristics while maintaining other product properties and characteristics5).

B.1.2 Description of the process

Seven reaction parameters were manipulated to understand how these changes influence viscosity and particle size of the polymer. The chemists wanted to identify the primary drivers (main effects) in this emulsion reaction and to control (block) for variability due to operator-to-operator and vessel-to-vessel differences. At this time, quantifying interactions is not important, but they must not interfere with the determination of main effects.

B.1.3 Response variable

B.1.3.1 Choice of response variables

Viscosity and particle size were the primary responses investigated in the experiment.

B.1.3.2 Measurement of the response variables

Viscosity was measured in centipoise (cps) using a Brookfield viscometer, using spindle #3 at 60 r/min. Particle size measurements were measured in nanometres (nm) using a Brookhaven BI 90 particle sizer.

B.1.3.3 Relationship of the response variables to the objective of the experiment

Viscosity and particle size are primary monitoring parameters used during production of the flexographic emulsion. Viscosity is monitored to assure end-use flow in printing conditions. Particle size impacts the clarity of the final coating on a printed surface.

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5) This example has been kindly donated by Rohm and Haas (Research Center, Pennsylvania), a wholly owned subsidiary of the Dow Chemical Company.

B.1.4 Factors affecting the response

B.1.4.1 Description of each factor (continuous/discrete) to be varied

The factors chosen to be varied within the experiment and their units of measurement are described, as follows:

- resin level (%),
- kettle initiator (%),
- co-feed initiator (%),
- process temperature (°C),
- sodium sulfate level (%),
- feed time (minutes),
- Disponil[6] level (%).

Each of these factors is continuous but for the purpose of this preliminary experiment, only two levels of each factor were used.

B.1.4.2 Selection of levels (related to size of effect to be determined)

The factors used in the experiment and their associated levels are given in Table B.1.

Table B.1 — Controlled factors

Factor	Level 1 (–1)	Level 2 (+1)
A: Resin level	26,50	32,50
B: Kettle initiator	0,48	0,72
C: Co-feed initiator	0,48	0,72
D: Process temperature	80,00	86,00
E: Sodium sulfate level	0,00	0,50
F: Feed time	144,00	216,00
G: Disponil level	0,48	0,96

B.1.4.3 Other factors, external to the experiment, that needed to be accounted for

Variability due to both operator-to-operator and vessel-to-vessel differences was believed to be non-negligible and needed to be isolated. Thus, the design was run in four blocks, where each block included experiments run under similar conditions, a given single operator and a given single vessel.

The associated levels for the blocking factors are given in Table B.2.

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[6] Disponil is the trade name of a product supplied by Cognis. This information is given for the convenience of users of this Technical Report and does not constitute an endorsement by ISO of this product.

Table B.2 — Blocked factors

Factor	Level 1 (–1)	Level 2 (+1)
Operator	Tara	Aaron
Vessel type	Small hood	Large hood

B.1.5 Fractional factorial design

B.1.5.1 Choice of specific design

The primary limitation in this experiment was time. A workable solution to the reaction problems was needed quickly to secure customers and turn them away from the competition. A maximum of 16 experiments could be accomplished in the available time. It was agreed that estimation of the interactions would be ignored at this stage and that, if needed, a follow-up experiment to refine the recommendation would be performed.

The experimental design chosen to fit all of these requirements is a blocked fractional factorial design of resolution IV in 16 runs, denoted 2_{IV}^{7-3}.

The full confounding (alias) structure is given in Table B.3.

Each of the main effects is confounded with a few three-term interactions, which the experimenter was willing to assume to be negligible. Aside from the block effects, only four “clusters” of two-term interactions can be uniquely estimated, a limitation acceptable to the experimenter, given the context explained above.

Table B.3 — Confounding structure for the blocked fractional factorial design

Factor generators: $E = ABC$, $F = ABD$, $G = ACD$

Block generators: 1 $= AB$, 2 $= AC$

Defining relation: $I = ABCE = ABDF = ACDG = AEFG = BCFG = BDEG = CDEF$

Complete alias structure:

[Estimated terms]	Aliased terms
$[A]$	$A + BCE + BDF + CDG + EFG$
$[B]$	$B + ACE + ADF + CFG + DEG$
$[C]$	$C + ABE + ADG + BFG + DEF$
$[D]$	$D + ABF + ACG + BEG + CEF$
$[E]$	$E + ABC + AFG + BDG + CDF$
$[F]$	$F + ABD + AEG + BCG + CDE$
$[G]$	$G + ACD + AEF + BCF + BDE$
$[AD]$	$AD + BF + CG$
$[AF]$	$AF + BD + EG$
$[AG]$	$AG + CD + EF$
$[BG]$	$BG + CF + DE$
$[ABG]$	$ABG + ACF + ADE + BCD + BEF + CEG + DFG$
[Intercept]	Intercept

Block generator – These effects are lost to blocks

[1] $= AB + CE + DF + ACFG + ADEG + BCDG + BEFG$

[2] $= AC + BE + DG + ABFG + ADEF + BCDF + CEFG$

[3] $= AE + BC + FG + ABDG + ACDF + BDEF + CDEG$

B.1.5.2 Design matrix

The design selected was the 16-run one-eighth fractional factorial design with seven factors (A, B, C, D, E, F and G). Table B.4 shows the design.

Table B.4 — Design matrix

Row number	Blocked factors	A	B	C	D	E (= ABC)	F (= ABD)	G (= ACD)
1	Tara/Large hood	26,5	0,72	0,72	80	0	216	0,96
2	Tara/Large hood	32,5	0,48	0,48	86	0,5	144	0,48
3	Tara/Large hood	26,5	0,72	0,72	86	0	144	0,48
4	Tara/Large hood	32,5	0,48	0,48	80	0,5	216	0,96
5	Aaron/Small hood	26,5	0,48	0,72	80	0,5	144	0,96
6	Aaron/Small hood	26,5	0,48	0,72	86	0,5	216	0,48
7	Aaron/Small hood	32,5	0,72	0,48	86	0	216	0,48
8	Aaron/Small hood	32,5	0,72	0,48	80	0	144	0,96
9	Tara/Small hood	32,5	0,48	0,72	80	0	216	0,48
10	Tara/Small hood	26,5	0,72	0,48	86	0,5	144	0,96
11	Tara/Small hood	32,5	0,48	0,72	86	0	144	0,96
12	Tara/Small hood	26,5	0,72	0,48	80	0,5	216	0,48
13	Aaron/Large hood	32,5	0,72	0,72	86	0,5	216	0,96
14	Aaron/Large hood	26,5	0,48	0,48	80	0	144	0,48
15	Aaron/Large hood	26,5	0,48	0,48	86	0	216	0,96
16	Aaron/Large hood	32,5	0,72	0,72	80	0,5	144	0,48

Randomization was used between each block and then within each block.

B.1.5.3 Centre points

Centre points were not selected for this experiment because of the time constraints.

B.1.5.4 Replication and repetition

Replication and repetition were not selected for this experiment because of the time constraints.

B.1.6 Analysis of results

B.1.6.1 Data acquired through the experiment and analysis considerations

The results from the experiment for both viscosity and particle size are given in Table B.5. They were keyed into a software programme called Design-Expert[7].

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[7] Design-Expert is the trade name of a product supplied by Stat-Ease, Inc. This information is given for the convenience of users of this Technical Report and does not constitute an endorsement by ISO of the product named. Equivalent products may be used if they can be shown to lead to the same results.

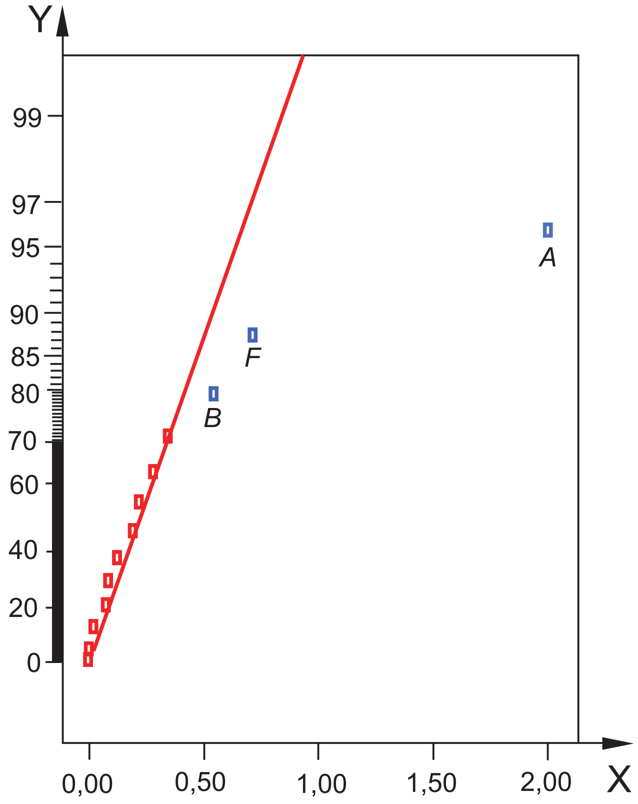
Table B.5 — Experiment results

Row number	Blocked factors	A	B	C	D	E (= ABC)	F (= ABD)	G (= ACD)	Viscosity cps	ln(viscosity) cps	Particle size nm
1	Tara/ Large hood	26,5	0,72	0,72	80	0	216	0,96	385	5,953 2	97
2	Tara/ Large hood	32,5	0,48	0,48	86	0,5	144	0,48	1 185	7,077 5	103
3	Tara/ Large hood	26,5	0,72	0,72	86	0	144	0,48	445	6,098 1	97
4	Tara/ Large hood	32,5	0,48	0,48	80	0,5	216	0,96	3 075	8,031 1	99
5	Aaron/ Small hood	26,5	0,48	0,72	80	0,5	144	0,96	252	5,529 4	116
6	Aaron/ Small hood	26,5	0,48	0,72	86	0,5	216	0,48	694	6,542 5	96
7	Aaron/ Small hood	32,5	0,72	0,48	86	0	216	0,48	11 700	9,367 3	102
8	Aaron/ Small hood	32,5	0,72	0,48	80	0	144	0,96	1 946	7,573 5	100
9	Tara/ Small hood	32,5	0,48	0,72	80	0	216	0,48	3 300	8,101 7	108
10	Tara/ Small hood	26,5	0,72	0,48	86	0,5	144	0,96	612	6,416 7	98
11	Tara/ Small hood	32,5	0,48	0,72	86	0	144	0,96	3 840	8,253 2	98
12	Tara/ Small hood	26,5	0,72	0,48	80	0,5	216	0,48	1 282	7,156 2	100
13	Aaron/ Large hood	32,5	0,72	0,72	86	0,5	216	0,96	4 740	8,463 8	100
14	Aaron/ Large hood	26,5	0,48	0,48	80	0	144	0,48	187	5,231 1	141
15	Aaron/ Large hood	26,5	0,48	0,48	86	0	216	0,96	388	5,961 0	96
16	Aaron/ Large hood	32,5	0,72	0,72	80	0,5	144	0,48	3 061	8,026 5	93

B.1.6.2 Emulsion viscosity analysis

Viscosity measurements often span several orders of magnitude. In this situation, a transformation of the data is useful for stabilizing the variance of the residuals. Here, the response “viscosity” has been transformed using natural logarithms and is subsequently denoted “ln(viscosity)”.

Normal probability plots of the estimate effects in the log-transformed viscosity data indicate that resin level, kettle initiator and feed time are important. These plots are shown in Figure B.1.



Key

X	effect
Y	half-normal % probability
A	resin level
B	kettle initiator
F	feed time

Figure B.1 — Probability plot for ln(viscosity)

A linear model containing the resin level, kettle-initiator level and feed-time effects explains 93 % of the observed variability in the ln(viscosity) data. This model is significant and all terms in this linear model are significant. The analysis of variance is shown in Table B.6.

Table B.6 — Analysis of variance for ln(viscosity)

Source	Sum of squares	Degrees of freedom	Mean square	F value	Prob $> F$	
Block	1,19	3	0,40			
Model	18,99	3	6,33	38,91	< 0,000 1	significant
A	16,01	1	16,01	98,46	< 0,000 1	
B	1,17	1	1,17	7,20	0,025 1	
F	1,80	1	1,80	11,08	0,008 8	
Residual	1,46	9	0,16			
Cor Total[a]	21,64	15				

[a] Cor Total = Totals of all the information corrected for the mean.

Model coefficient estimates, their standard errors and 95 % confidence intervals (CI) for the true coefficient are given in Table B.7. This information does not apply for blocks since block effects are random by definition. The purpose of blocking is solely to increase the power of detecting experimental factor effects.

Table B.7 — Estimation of effects

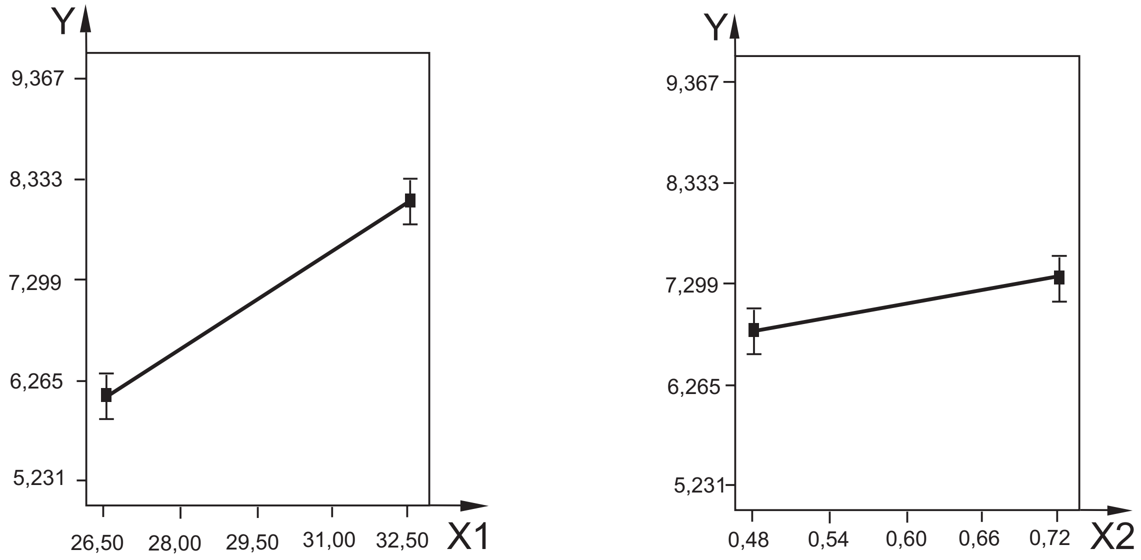
Factor	**Coefficient estimate**	**Degrees of freedom**	**Standard error**	**95 % CI Low**	**95 % CI High**
Intercept	7,11	1	0,10	6,88	7,34
Tara/Large hood	−0,32	3			
Aaron/Large hood	0,14				
Aaron/Small hood	0,37				
Tara/Small hood	−0,19				
A: Resin level	1,00	1	0,10	0,77	1,23
B: Kettle initiator	0,27	1	0,10	0,042	0,50
F: Feed time	0,34	1	0,10	0,11	0,56

The final equation in terms of coded factors is:

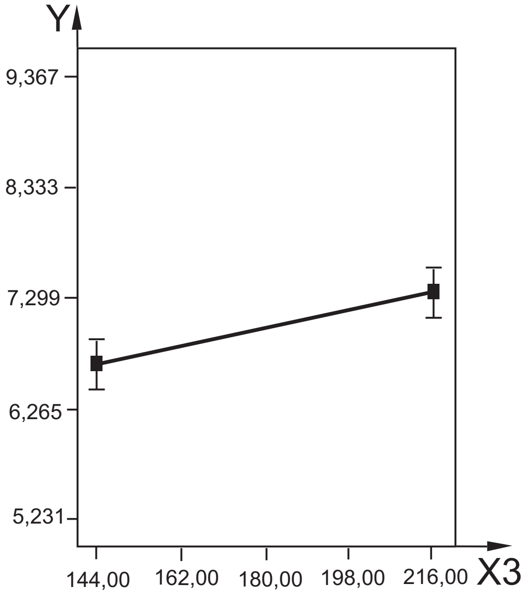
$$\ln(\text{viscosity}) = 7{,}11 + 1{,}00A + 0{,}27B + 0{,}34F$$

The predicted effects are shown in Figure B.2. To produce these plots, the factors not shown are set at their mid-level values.

The slopes of the lines are consistent with the significance of the factors.



a) *A*: **Resin level** **b)** *B*: **Kettle initiator**



c) *F*: **Feed time**

Key

X1 *A*: resin level

X2 *B*: kettle initiator

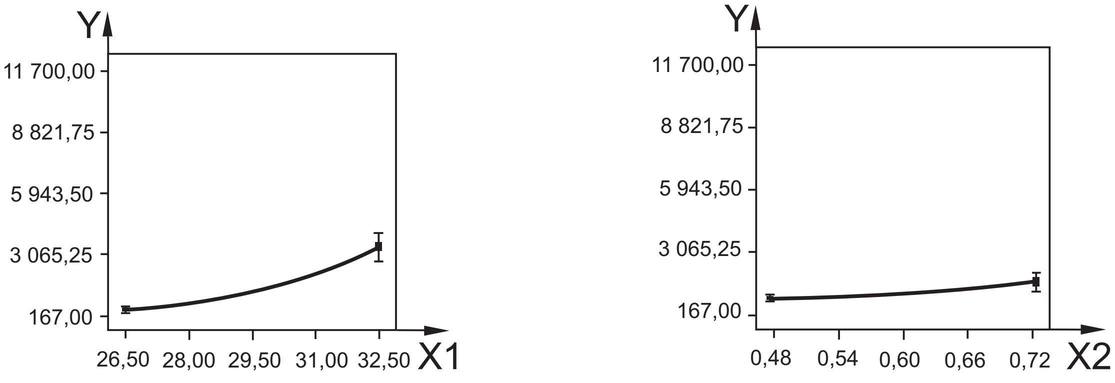
X3 *F*: feed time

Y ln(viscosity)

Factor		Actual factors		
		Figure B.2 a)	Figure B.2 b)	Figure B.2 c)
A:	resin level:	—	29,50 %	29,50 %
B:	kettle initiator:	0,60 %	—	0,56 %
C:	co-feed initiator:	0,60 %	0,60 %	0,60 %
D:	process temperature:	83,00 °C	83,00 °C	83,00 °C
E:	sodium sulfate level:	0,25 %	0,25 %	0,25 %
F:	feed time:	180,00 min	180,00 min	—
G:	Disponil level:	0,72 %	0,72 %	0,72 %

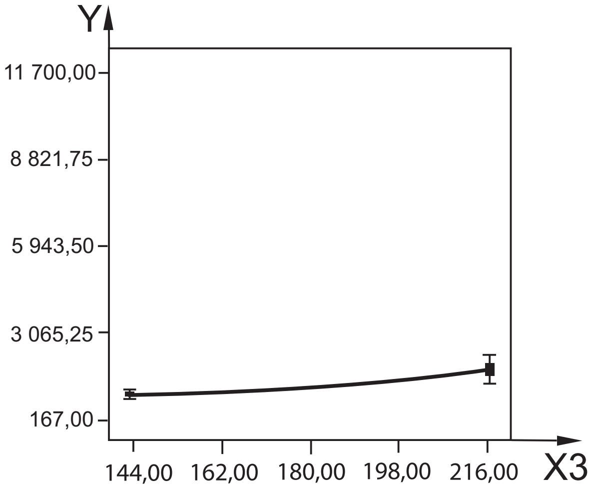
Figure B.2 — One-factor plots of *A*, *B* and *F* — Effects on viscosity plotted in transformed scale

The predicted effects can also be plotted in the original viscosity scale. They are represented in Figure B.3. It can be seen that the logarithmic transformation of viscosity allows for a simple way to fit nonlinear effects, as indicated in the plot of the effect of A.



a) A: **Resin level**

b) B: **Kettle initiator**



c) F: **Feed time**

Key

X1 A: resin

X2 B: kettle initiator

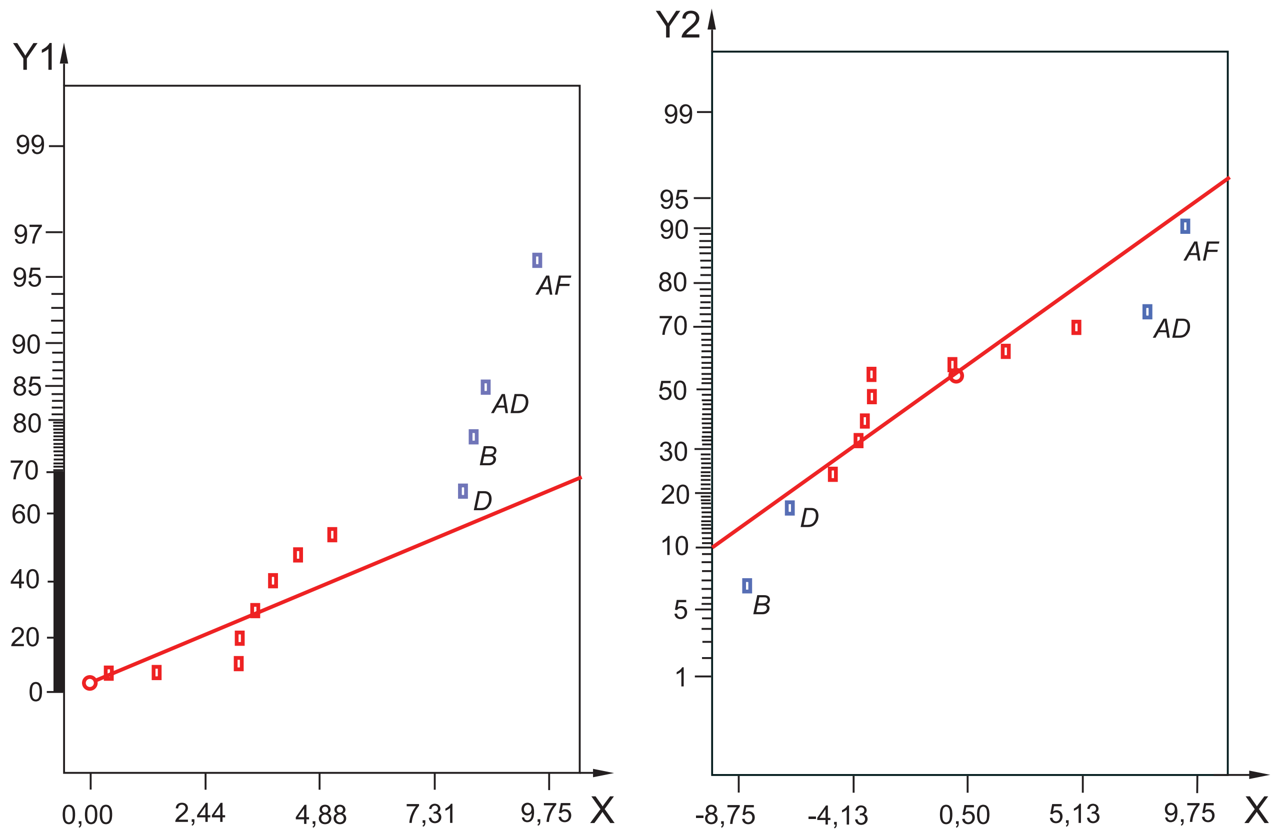
X3 F: feed time

Y viscosity

Figure B.3 — One-factor plots for A, B and F — Effects on viscosity plotted in original scale

B.1.6.3 Particle size analysis

The results from the analysis of the particle size data are not as apparent. The normal probability plots, shown in Figure B.4, suggest that kettle initiator (B) and process temperature (D) are important, as well as two apparent interactions, AF and AD. These interactions are not directly interpretable as they represent confounded clusters of two-factor interactions.



a) **Half-normal plot**

b) **Normal plot**

Key

X effect

Y1 half-normal % probability

Y2 normal % probability

A resin level

B kettle initiator

D process temperature

E sodium sulfate level

F feed time

Figure B.4 — Probability plots for particle size

A linear model containing kettle initiator (*B*), process temperature (*D*) and two sets of interactions explains 81 % of the observed variability in particle size. This model is marginally significant, as are the effects of *B* and *D*. The analysis of variance is shown in Table B.8. This model is not good enough to be used as a basis to get predicted particle sizes, but the information obtained about the effects of kettle initiator and process temperature are valuable and may be used to improve the production process.

Table B.8 — Analysis of variance for particle size

Source	Sum of squares	Degrees of freedom	Mean square	F value	Prob $> F$
Block	161,00	3	53,67		
Model	1 483,00	6	247,17	4,15	0,053 4
A	90,25	1	90,25	1,52	0,264 2
B	306,25	1	306,25	5,15	0,063 8
D	256,00	1	256,00	4,30	0,083 4
F	144,00	1	144,00	2,42	0,170 8
AD	306,25	1	306,25	5,15	0,063 8
AF	380,25	1	380,25	6,39	0,044 8
Residual	357,00	6	59,50		
Cor Total[a]	2 001,00	15			

[a] Cor Total = Totals of all the information corrected for the mean.

Model coefficient estimates, their standard errors and 95 % confidence intervals for the true coefficient are given in Table B.9. This information does not apply for blocks since block effects are random by definition. The purpose of blocking is solely to increase the power of detecting experimental factor effects.

Table B.9 — Estimation of effects

Factor	Coefficient estimate	Degrees of freedom	Standard error	95 % CI[a] Low	95 % CI High	VIF[b]
Intercept	102,75	1	1,93	98,03	107,47	
Tara/Large hood	−3,75	3				
Aaron/Small hood	0,75					
Tara/Small hood	−1,75					
Aaron/Large hood	4,75					
A: Resin level	−2,38	1	1,93	−7,09	2,34	1,00
B: Kettle initiator	−4,38	1	1,93	−9,09	0,34	1,00
D: Process temp.	−4,00	1	1,93	−8,72	0,72	1,00
F: Feed time	−3,00	1	1,93	−7,72	1,72	1,00
AD	4,37	1	1,93	−0,34	9,09	1,00
AF	4,88	1	1,93	0,16	9,59	1,00

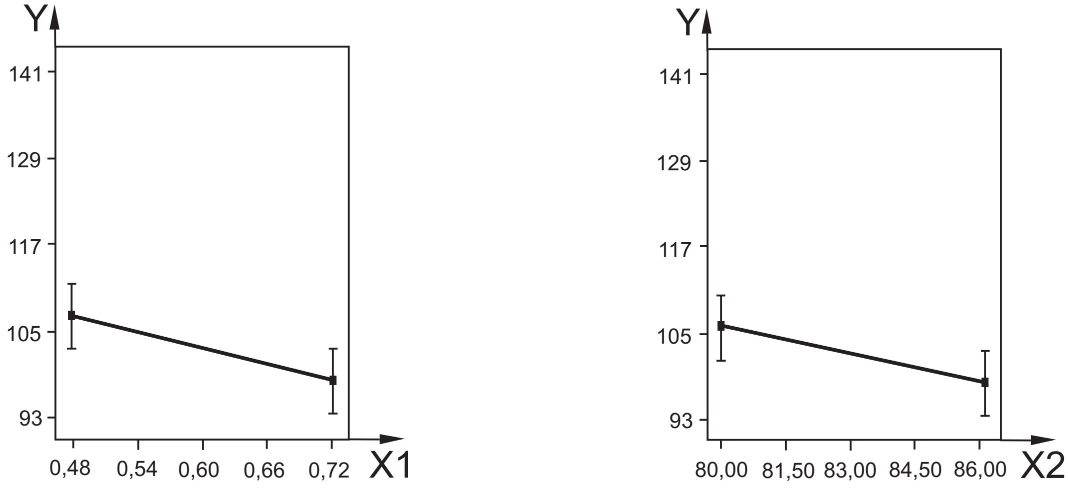
[a] CI = Confidence interval.

[b] VIF = Variation inflation factor.

The final equation in terms of coded factors is:

$$\text{particle size} = 102{,}75 - 2{,}38A - 4{,}38B - 4{,}00D - 3{,}00F + 4{,}37AD + 4{,}88AF$$

Note that the term 4,88AF could also be 4,88BD. The predicted effects are shown in Figure B.5. To produce these plots, all factors not shown are set at their mid-levels.



a) *B*: **Kettle initiator**

b) *D*: **Process temperature**

Key

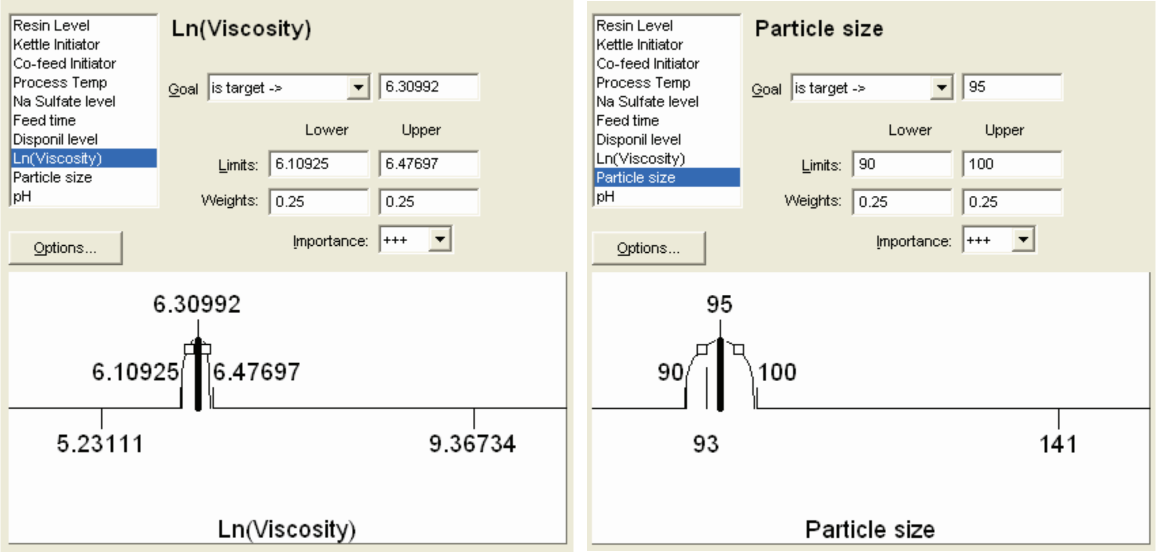
X1 *B*: kettle initiator
X2 *D*: process temperature
Y particle size

Factor	Actual factors	
	Figure B.5 a)	Figure B.5 b)
A: resin level:	29,50 %	29,50 %
B: kettle initiator:	—	0,65 %
C: co-feed initiator:	0,60 %	0,60 %
D: process temperature:	83,00 °C	—
E: sodium sulfate level:	0,25 %	0,25 %
F: feed time:	180,00 min	180,00 min
G: Disponil level:	0,72 %	0,72 %

Figure B.5 — One-factor plots for *B* and *D* — Effects on particle size

B.1.6.4 Optimization recommendations

To get good flexibility and gloss properties, this polymer requires viscosity to be in the range 450 cps to 650 cps with a desired target of 550 cps and particle size to be in the range 90 µm to 100 µm with a desired target of 95 µm. Using the software, desirability step functions were defined for each response, as represented in Figure B.5.



Ln(Viscosity)

Goal: is target -> 6.30992

	Lower	Upper
Limits:	6.10925	6.47697
Weights:	0.25	0.25

Importance: +++

Particle size

Goal: is target -> 95

	Lower	Upper
Limits:	90	100
Weights:	0.25	0.25

Importance: +++

Figure B.6 — Desirability curves (step functions) for in(viscosity) and particle size

The result of the optimization search process is a mapping of the overall joint desirability. Joint desirability ranges between 0 and 1 are obtained. A value of 0 is obtained if at least one of the response ranges is not achievable. A value of 1 is obtained if, and only if, all ranges are achieved and the exact target values are achieved. Table B.10 presents the results of eight optimization searches showing the levels of each process variable and the corresponding joint desirability values.

Table B.10 — Actual process conditions and joint desirability values obtained in eight optimization searches

Run	Resin level %	Kettle initiator %	Co-feed initiator[a] %	Process temperature °C	Sodium sulfate level[a] %	Feed time minutes	Disponil level[a] %	Viscosity cps	Particle size nm	Desirability
1	26,81	0,56	0,66	85,75	0,44	199,40	0,56	550	95,000 5	1
2	26,79	0,61	0,52	85,92	0,01	188,91	0,86	550	94,999 2	1
3	26,71	0,67	0,62	85,97	0,35	177,62	0,62	550	95,001	1
4	26,52	0,62	0,68	85,16	0,45	195,33	0,92	550	94,999 1	1
5	26,72	0,53	0,50	85,32	0,31	209,21	0,63	550	94,998 1	1
6	26,72	0,67	0,70	86,00	0,01	177,42	0,95	550	94,999 9	1
7	26,64	0,72	0,50	86,00	0,42	167,39	0,73	550	95,148	0,996
8	26,77	0,50	0,56	84,35	0,02	216,00	0,96	550	97,592 5	0,912

[a] Has no effect on optimization results.

B.1.7 Presentation of findings

This study indicates that emulsion viscosity is positively influenced by resin level, reaction feed time and kettle initiator level. Emulsion particle size is negatively influenced by kettle initiator level and process temperature. Preliminary use of the models developed here suggests that targeted values of emulsion viscosity and emulsion particle size can be achieved.

Variability due to operator differences and reactor hood difference was initially thought to be large and potential lurking variables. Blocking techniques were used to absorb this variation and improve the power of detecting small effects in the experiment. After completing the experiment, operator and reactor hood differences were found to be small and not considered in later experimentation. This was an unexpected but valuable piece of information. When differences in operator technique or reactor vessels exist, blocking serves as an active method of statistical control on the magnitude of the error term.

The results of the optimization exercise reported above will be validated. This involves running additional formulations at the recommended location and assessing the quality of the predictions relative to observed results. Alternatively, a smaller number of factors can be chosen for investigation in an experimental region defined by a reduced set of experimental ranges. The latter approach would yield better information about the aptness of the first order planar model fit to the data. If interactions are important in this system, an experimental design in a new region could help quantify the effects of the interaction and obtain better recommendations for validation runs.

B.1.8 Confirmation results

A set of confirmation experiments were completed to validate the results of the factorial experiment. The scale-up team confirmed the utility of the optimization results and quickly scaled an initial product to commercial quantities. Similar work was performed successfully by the scale-up team on other members of the flexographic emulsions. The family of flexographic emulsions described here were successfully transferred to the North American production facilities. The product line was successful in expanding its market leading position in spite of higher raw material prices.

Annex C

(informative)

Insight into PVC foam formulations[8]

C.1 General

This study discusses the formulation technology involved in the manufacturing of PVC foams. Typically, a PVC formulation will involve about a dozen ingredients (also referred to as additives) and will follow a complex manufacturing process. The number of characteristics measured on the product is large, on the order of about 35 responses. Some of these responses are highly correlated. Much is known about the way in which individual additives function, but a holistic approach is required to better understand the way a formulation functions as a whole. A fractional factorial experiment will support this holistic approach in a minimum number of runs which will allow economical use of laboratory time and equipment.

C.2 Description of the process

All formulations required to execute the experimental design were prepared using a high-speed mixer whose speed was varied to obtain a constant load on the motor. Process aid and blowing agents were added to the mixer at 120 °C, shortly before discharge to the cooler. This protocol is representative of most industrial practices. Samples were then tested using a variety of equipment as listed in C.3.2.

C.3 Response variable

C.3.1 Choice of response variables

Fifteen characteristics known to characterize foam formulations were measured in this experiment, thus maximizing the amount of information obtained from each formulation. In this example, the three most important responses for the analyst to study, namely fusion torque, hot expansion ratio and elongation at break, will be studied. Large values are desirable for all three properties.

C.3.2 Measurement of the response variables

A variety of laboratory equipment was used to generate the responses, including a torque rheometer, a capillary rheometer, a two-roll mill and a single screw extruder, all under fixed operating conditions.

C.4 Factors affecting the response

C.4.1 Description of each factor (continuous/discrete) to be varied

The study concentrates on nine factors related to the lubrication, filler, processing aid, nucleating and blowing agent components of a basis formulation. These factors are presented in Table C.1. Quantities are expressed in phr, or parts per hundred of PVC resin.

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[8] This example has been kindly donated by Rohm and Haas (European Laboratories), a wholly owned subsidiary of the Dow Chemical Company.

Table C.1 — Factors

Component type	Component	Parts per hundred of PVC resin
Nucleating agent	Calcium stearate	0,60
Lubricant	Partially saponified montanic acid ester	0,50
Lubricant	Oxidized polyethylene wax	0,40
Lubricant	Dicarboxylic acid ester	0,60
Lubricant	Hydroxy stearic acid	0,40
Filler	Ground Ca carbonate	3,00
Processing aid	Paraloid K-400[9]	5,50
Blowing agent	Sodium bicarbonate	1,50
Blowing agent	Azo dicarbonamide	0,20

C.4.2 Selection of levels (related to size of effect to be determined)

The factors used in the experiment and their associated levels are given in Table C.2.

Table C.2 — Controlled factors

Label in the analysis		Factor	Level 1 (−1)	Level 2 (+1)
A	CaSt	Calcium stearate	0,2	1,0
B	OPWax	Partially saponified montanic acid ester	0,3	0,7
C	AC680A[10]	Oxidized polyethylene wax	0,2	0,6
D	G60	Dicarboxylic acid ester wax	0,2	1,0
E	G21	Hydroxy stearic acid	0,1	0,7
F	95T	Calcium carbonate	1,0	5,0
G	K400	Paraloid K-400	4,0	7,0
H	BIN	Sodium bicarbonate	1,2	1,8
J	EPE	Azo dicarbonamide	0,15	0,25

C.4.3 Other factors, external to the experiment, that need to be accounted for

Other components in a typical PVC formulation such as resin, stabilizer, impact modifier and pigment were deemed less important regarding their impact on the responses and were fixed as constants in this experiment.

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[9] Paraloid K-400 is the trade name of a product supplied by Rohm and Haas. This information is given for the convenience of users of this Technical Report and does not constitute an endorsement by ISO of the product named.

[10] A-C 680A is the trade name of a product supplied by Rheochem™. This information is given for the convenience of users of this Technical Report and does not constitute an endorsement by ISO of the product named.

C.5 Fractional factorial design

C.5.1 Choice of specific design

The primary limitation in this experiment was the time required to obtain all 15 of the responses because of the need to use sophisticated, expensive equipment that were also needed to run other applications in the laboratory. With nine factors to be investigated, running a resolution III design appeared to be the only viable strategy to outweigh the all too common one-factor-at-a-time approach which would have otherwise been adopted. Sixteen experiments were proposed in a resolution III design denoted 2_{III}^{9-5}.

It was agreed that estimation of the interactions would be ignored at this stage. The experimenters were hunting for large effects, highly significant, that would guarantee an impact on the responses across widely different manufacturing environments, where processing conditions might differ from those in the laboratory.

Each of the main effects is confounded with two-term and three-term interactions.

C.5.2 Design matrix (standard order and run order)

The design selected was the 16-run one-eighth fractional factorial design with nine factors (A, B, C, D, E, F, G, H, J). Randomization was used to set the order of the experiments. Table C.3 shows the design. The layout is given in standard (std) order.

Table C.3 — Design matrix

Std	A: **CaSt**	B: **OPWax**	C: **AC680A**	D: **G60**	E: **G21**	F: **95T**	G: **K400**	H: **BIN**	J: **EPE**
1	0,2	0,3	0,2	0,2	0,1	1	4	1,2	0,25
2	1	0,3	0,2	0,2	0,7	1	7	1,8	0,15
3	0,2	0,7	0,2	0,2	0,7	5	4	1,8	0,15
4	1	0,7	0,2	0,2	0,1	5	7	1,2	0,25
5	0,2	0,3	0,6	0,2	0,7	5	7	1,2	0,15
6	1	0,3	0,6	0,2	0,1	5	4	1,8	0,25
7	0,2	0,7	0,6	0,2	0,1	1	7	1,8	0,25
8	1	0,7	0,6	0,2	0,7	1	4	1,2	0,15
9	0,2	0,3	0,2	1	0,1	5	7	1,8	0,15
10	1	0,3	0,2	1	0,7	5	4	1,2	0,25
11	0,2	0,7	0,2	1	0,7	1	7	1,2	0,25
12	1	0,7	0,2	1	0,1	1	4	1,8	0,15
13	0,2	0,3	0,6	1	0,7	1	4	1,8	0,25
14	1	0,3	0,6	1	0,1	1	7	1,2	0,15
15	0,2	0,7	0,6	1	0,1	5	4	1,2	0,15
16	1	0,7	0,6	1	0,7	5	7	1,8	0,25
17	0,6	0,5	0,4	0,6	0,4	3	5,5	1,5	0,2
18	0,6	0,5	0,4	0,6	0,4	3	5,5	1,5	0,2
19	0,6	0,5	0,4	0,6	0,4	3	5,5	1,5	0,2

C.5.3 Centre points

Three centre points were selected for this experiment (std 17 to std 19 in Table C.3), a maximum given the experimental circumstances described. Caution should be exerted when the number of centre points is small, (typically less than five) because of the small degrees of freedom used in the estimation of the pure error variance. The corresponding estimate (usually labelled MSE, or Mean Square Error) of the pure error variance should be carefully examined by the scientist to judge if it is larger or smaller than might reasonably be expected.

C.5.4 Replication and repetition

Replication (other than for the centre points) and repetition were not selected for this experiment because of the time constraints.

C.6 Analysis of results

C.6.1 Data acquired through the experiment and analysis considerations

The results of the experiment for the three responses of interest are shown in Table C.4.

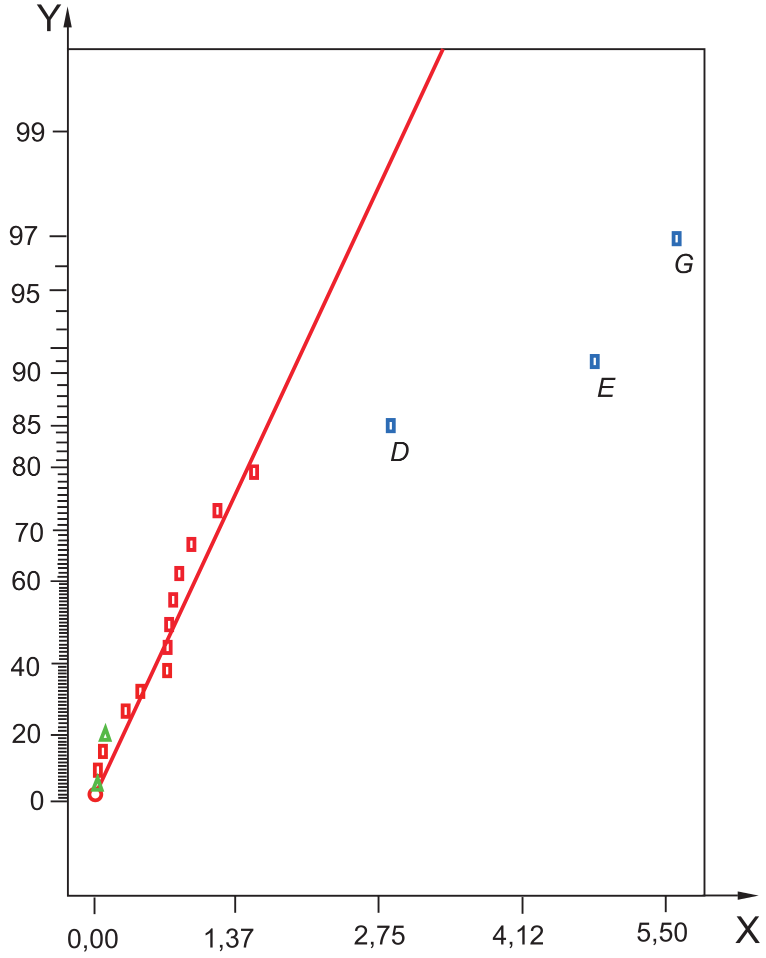
Table C.4 — Experiment results

Std	*A*	*B*	*C*	*D*	*E*	*F*	*G*	*H*	*J*	**Fusion torque** N·m	**Hot expansion ratio**	**Elongation at break** %
1	0,2	0,3	0,2	0,2	0,1	1	4	1,2	0,25	56	2,98	472
2	1	0,3	0,2	0,2	0,7	1	7	1,8	0,15	57,3	3,48	254
3	0,2	0,7	0,2	0,2	0,7	5	4	1,8	0,15	50,2	2,16	454
4	1	0,7	0,2	0,2	0,1	5	7	1,2	0,25	58	3,66	337
5	0,2	0,3	0,6	0,2	0,7	5	7	1,2	0,15	52,7	2,44	537
6	1	0,3	0,6	0,2	0,1	5	4	1,8	0,25	52	3,28	517
7	0,2	0,7	0,6	0,2	0,1	1	7	1,8	0,25	58,8	3,27	400
8	1	0,7	0,6	0,2	0,7	1	4	1,2	0,15	48,4	1,74	228
9	0,2	0,3	0,2	1	0,1	5	7	1,8	0,15	57,3	3,71	447
10	1	0,3	0,2	1	0,7	5	4	1,2	0,25	46,4	2,62	531
11	0,2	0,7	0,2	1	0,7	1	7	1,2	0,25	50,9	2,35	450
12	1	0,7	0,2	1	0,1	1	4	1,8	0,15	52,1	3,36	399
13	0,2	0,3	0,6	1	0,7	1	4	1,8	0,25	45,7	1,97	366
14	1	0,3	0,6	1	0,1	1	7	1,2	0,15	57,6	3,48	485
15	0,2	0,7	0,6	1	0,1	5	4	1,2	0,15	49,4	2,5	532
16	1	0,7	0,6	1	0,7	5	7	1,8	0,25	51,6	2,68	270
17	0,6	0,5	0,4	0,6	0,4	3	5,5	1,5	0,2	53,4	2,94	410
18	0,6	0,5	0,4	0,6	0,4	3	5,5	1,5	0,2	53,1	2,98	414
19	0,6	0,5	0,4	0,6	0,4	3	5,5	1,5	0,2	54,6	2.98	472

The results were keyed into a software programme called Design-Expert[11]. The analyses for each one of these three responses (fusion torque, hot expansion and elongation at break) are shown in C.6.2, C.6.3 and C.6.4, respectively.

C.6.2 Analysis of fusion torque

The normal probability plot in Figure C.1 indicates three factors (*E*, *D*, *G*) as highly significant. R-square for this model is 89 %. The analysis of variance, shown in Table C.5, shows no significant curvature nor lack of fit. The coefficient estimates for the model are shown in Table C.6. Plots of effects are displayed in Figure C.2.



Key

X effect

Y half-normal % probability

D G21

E 95T

G BIN

Figure C.1 — Half-normal probability plot for fusion torque

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[11] Design-Expert is the trade name of a product supplied by Stat-Ease, Inc. This information is given for the convenience of users of this Technical Report and does not constitute an endorsement by ISO of the product named. Equivalent products may be used if they can be shown to lead to the same results.

Table C.5 — ANOVA table for fusion torque

ANOVA for selected factorial model **Analysis of variance table (Partial sum of squares)**					
Source	**Sum of squares**	**Degrees of freedom**	**Mean square**	**F value**	**Prob $> F$**
Model	242,61	3	80,87	36,88	$< 0{,}000\ 1$
D	31,36	1	31,36	14,30	0,002 0
E	90,25	1	90,25	41,16	$< 0{,}000\ 1$
G	121,00	1	121,00	55,18	$< 0{,}000\ 1$
Curvature	2,16	1	2,16	0,99	0,337 6
Residual	30,70	14	2,19		
Lack of fit	29,44	12	2,45	3,89	0,222 3
Pure error	1,26	2	0,63		
Cor Total[a]	275,47	18			

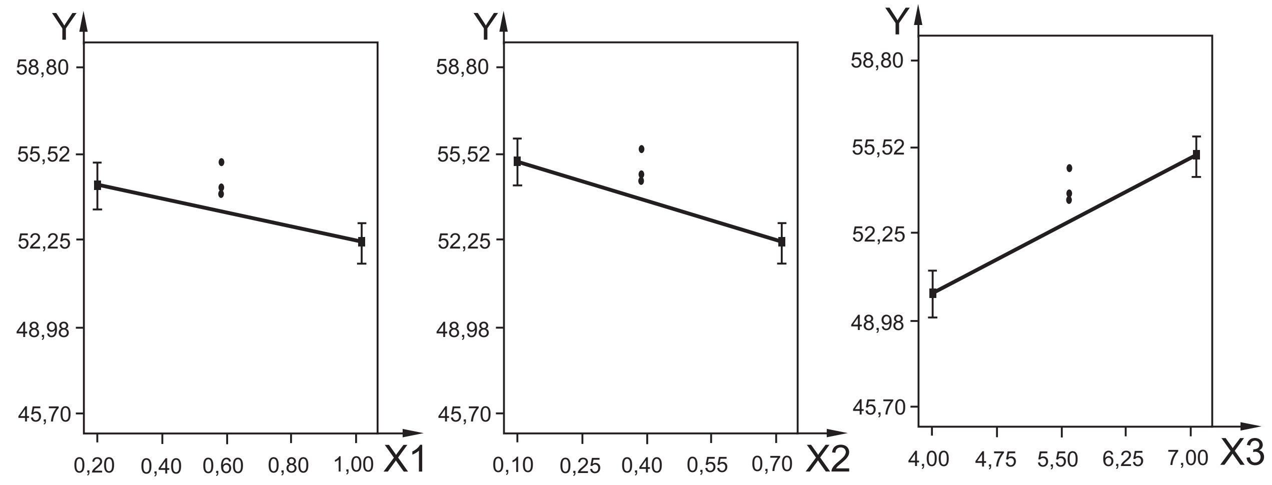
[a] Cor Total = Totals for all the information corrected for the mean.

Table C.6 — Estimation of effects for fusion torque

Factor	**Coefficient estimate**	**Degrees of freedom**	**Standard error**	**95 % CI[a] Low**	**95 % CI High**	**VIF[b]**
Intercept	52,78	1	0,37	51,98	53,57	
D: G60	−1,40	1	0,37	−2,19	−0,61	1,00
E: G21	−2,38	1	0,37	−3,17	−1,58	1,00
G: K400	2,75	1	0,37	1,96	3,54	1,00
Centre point	0,92	1	0,93	−1,07	2,92	1,00

[a] CI = Confidence interval.

[b] VIF = Variation inflation factor.



Key

X1 *D*: G60

X2 *E*: G21

X3 *G*: K400

Y fusion torque

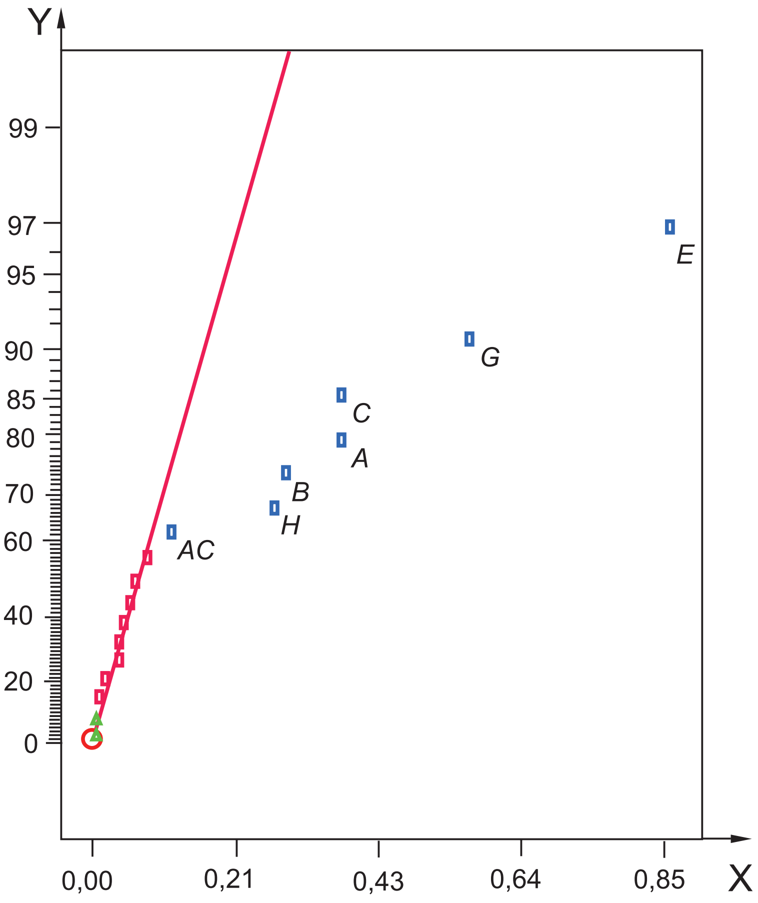
• design point

Factor	Actual factors		
	Figure C.2 a)	Figure C.2 b)	Figure C.2 c)
A: CaSt:	0,60 %	0,60 %	0,60 %
B: OPWax:	0,50 %	0,50 %	0,50 %
C: AC680A:	0,40 %	0,40 %	0,40 %
D: G60:	—	0,60 %	0,60 %
E: G21:	0,40 %	—	0,40 %
F: 95T:	3,00 %	3,00 %	3,00 %
G: K400:	5,50 %	5,50 %	—
H: BIN:	1,50 %	1,50 %	1,50 %
J: EPE:	0,20 %	0,20 %	0,20 %

Figure C.2 — One-factor plots — Effect of factors *D*, *E* and *G* on fusion torque

C.6.3 Analysis of the hot expansion ratio

The normal probability plot in Figure C.3 indicates six main effects (aliased), *A*, *B*, *C*, *E*, *G* and *H*, which are highly significant and one weak interaction term, *AC* (aliased), which is significant to a lesser extent. R-square for the model including all these seven terms is 99 %, perhaps suspiciously high. The analysis of variance, shown in Table C.7, shows no significant curvature, nor lack of fit. The coefficient estimates in the corresponding model are shown in Table C.8. The interaction between *A* and *C*, shown in Figure C.4, indicates a weak effect, thus was ignored, taking into account both practical significance and the risk of wrong interpretation due to aliasing. Removing *AC* from the model does not change the coefficients of the remaining terms, and has a minimum impact on R-square.



Key

X	effect
Y	half-normal % probability

A	CaSt
B	OPWax
C	AC680A
E	G21
F	95T
G	K400
H	BIN
J	EPE

Figure C.3 — Half-normal probability plot for the hot expansion ratio

Table C.7 — ANOVA table for the hot expansion ratio

ANOVA for selected factorial model

Analysis of variance table (Partial sum of squares)

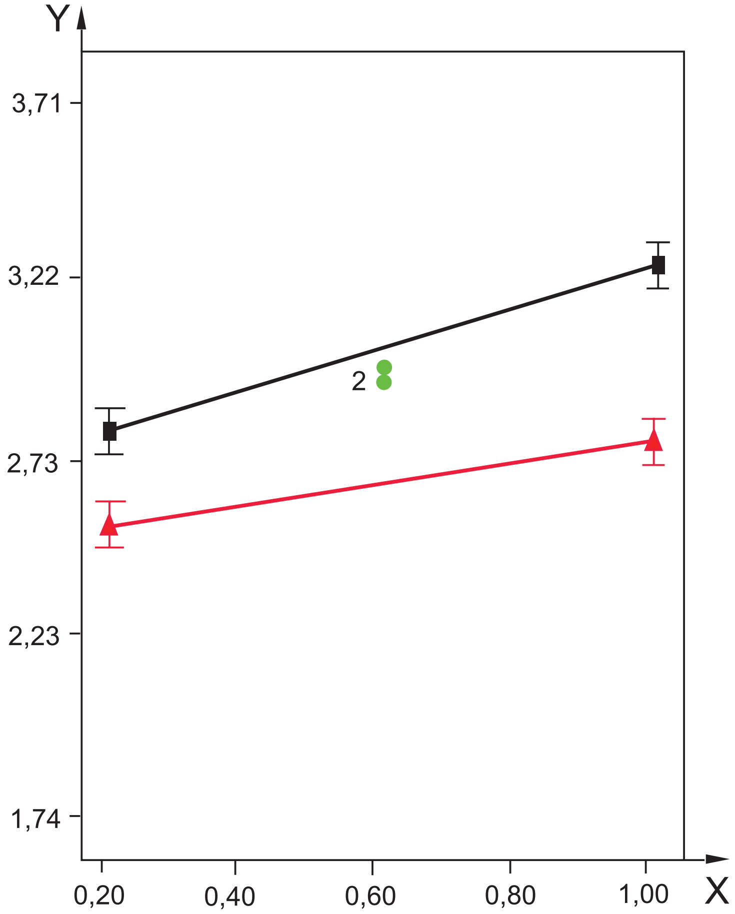
Source	Sum of squares	Degrees of freedom	Mean square	F value	Prob $> F$
Model	5,87	7	0,84	125,05	$< 0{,}000\,1$
A	0,53	1	0,53	79,52	$< 0{,}000\,1$
B	0,31	1	0,31	46,79	$< 0{,}000\,1$
C	0,55	1	0,55	81,71	$< 0{,}000\,1$
E	2,89	1	2,89	432,24	$< 0{,}000\,1$
G	1,24	1	1,24	185,51	$< 0{,}000\,1$
H	0,29	1	0,29	42,71	$< 0{,}000\,1$
AC	0,053	1	0,053	7,89	0,018 5
Curvature	0,032	1	0,032	4,70	0,055 3
Residual	0,067	10	$6{,}702 \times 10^{-3}$		
Lack of fit	0,066	8	$8{,}244 \times 10^{-3}$	15,46	0,062 2
Pure error	$1{,}067 \times 10^{-3}$	2	$5{,}333 \times 10^{-4}$		
Cor Total[a]	5,96	18			

[a] Cor Total = Totals for all the information corrected for the mean.

Table C.8 — Estimation of effects for hot expansion ratio

Factor	Coefficient estimate	Degrees of freedom	Standard error	95 % CI[a] Low	95 % CI High
Intercept	2,86	1	0,020	2,81	2,90
A: CaSt	0,18	1	0,020	0,14	0,23
B: OPWax	−0,14	1	0,020	−0,19	−0,094
C: AC680A	−0,19	1	0,020	−0,23	−0,14
E: G21	−0,43	1	0,020	−0,47	−0,38
G: K400	0,28	1	0,020	0,23	0,32
H: BIN	0,13	1	0,020	0,088	0,18
AC	−0,057	1	0,020	−0,10	−0,012
Centre point	0,11	1	0,052	$-3{,}093 \times 10^{-3}$	0,23

[a] Confidence interval.



Key

X *A*: CaSt

Y hot expansion ratio with the top line at *C* = 0,2 parts per hundred resin of AC680A and the bottom line at *C* = 0,6 parts per hundred resin of AC680A

● design point

■ *C* = 0,200

▲ *C* = 0,600

Actual factors

B OPWax = 0,50

D G60 = 0,60

E G21 = 0,40

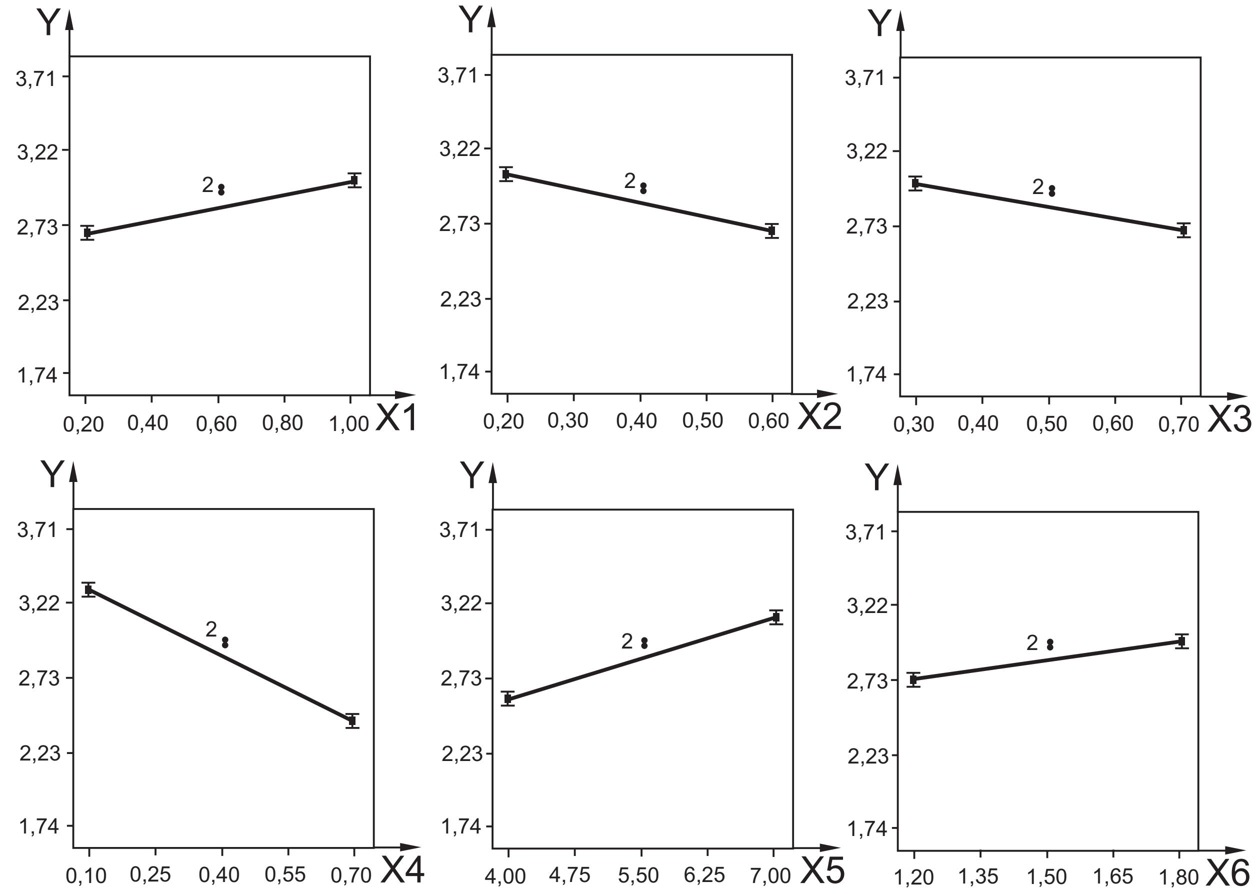
F 95T = 3,00

G K400 = 5,50

H BIN = 1,50

J EPE = 0,20

Figure C.4 — Effect of interaction between *A* (CaSt) and *C* (AC680A) on the hot expansion ratio



Key

X1 *A*: CaSt

X2 *C*: AC680A

X3 *B*: OnWax

X4 *E*: G21

X5 *G*: K400

X6 *H*: BIN

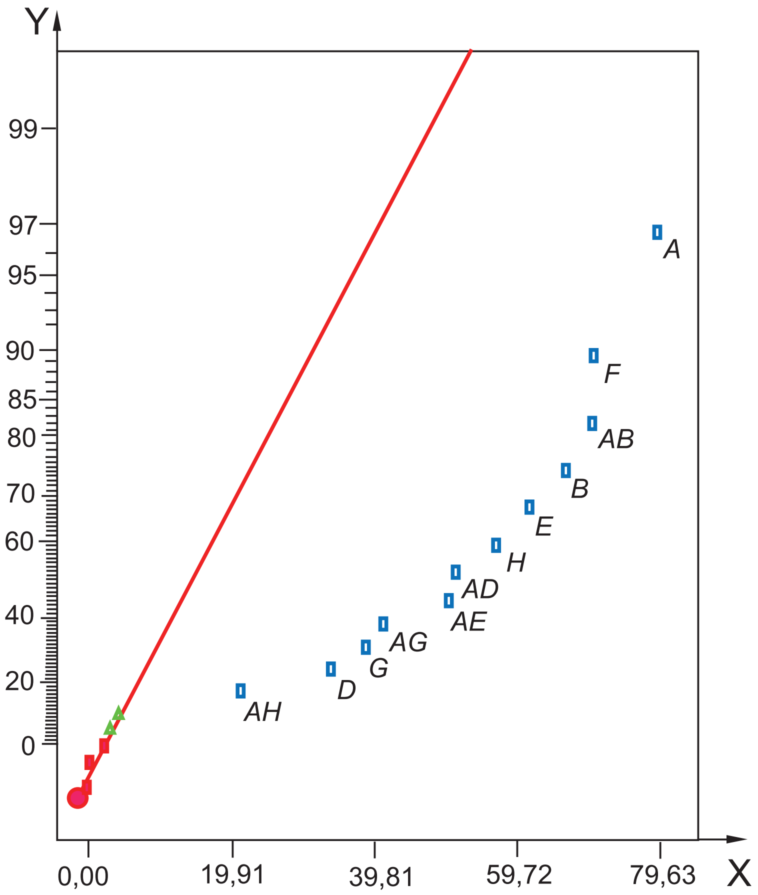
Y hot expansion ratio

Figure C.5 — Effect plots for the hot expansion ratio

C.6.4 Elongation at break

The normal probability plot in Figure C.6 indicates that there are possibly up to 12 significant effects (aliased) that, when included in the model, return an R-squared value of 98 %. The standard deviation, or RMSE, of 22,29 was believed by the experimenters to underestimate the noise in the system. In addition, some of the factors were affecting the response in an unexplainable direction. (The ANOVA table for elongation at break is presented in Table C.9.)

This might be the combined consequence of too few replicates and too many confounded effects in the estimation of the model coefficients, which obscures the practical interpretation of the results. It was decided to drop this response from further consideration.



Key

X	effect
Y	half-normal % probability
A	CaSt
B	OPWax
C	AC680A
D	G60
E	G21
F	95T
G	K400
H	BIN
J	EPE

Figure C.6 — Half-normal probability plot for elongation at break

Table C.9 — ANOVA table for elongation at break

Standard deviation	22,29	R-squared	0,984 2
Mean	419,74	Adjusted R-squared	0,946 4
Coefficient of variation	5,31	Predicted R-squared	0,952 0
PRESS[a]	7 585,11	Adequate precision	15,934

[a] PRESS = Predicted Residual Error Sum of Squares.

C.7 Presentation of findings

In both responses for which results were obtained, factor E and factor G turned out to be the most significant effects. Thus, Paraloid K400 and hydroxy stearic acid play a dominant role in determining the properties of the formulation. More K400 and less hydroxy stearic acid are needed to maximize the fusion torque and hot expansion ratio. The effects produced by other factors are of a lesser magnitude. No evidence was found to suggest that either K400 or hydroxy stearic acid had any significant interactions, either together or with other factors.

C.8 Confirmation results

Though it would have been desirable to confirm the results with a few additional runs, in this application the primary objective was not to check the accuracy of the model predictions but rather to identify major players affecting all or most responses studied, knowing that more experimenting was going to be needed at the customer sites. Thus, no confirmation runs were obtained. Given the general significance of factors E and G, it was safe to recommend their use as variables in experiments on an industrial scale and only consider the other factors where very specific modifications to the formulation behaviour were required.

Annex D
(informative)

Process validation for an insulin product

D.1 General

Both healthcare products and drugs must show stability under specified storing conditions. The exact rules are specified by regulatory bodies such as the Food and Drug Administration (FDA) in the USA. In this example, aspects of stability of an insulin product are the responses that are investigated, but the experiment is also a process validation study in the sense that stability of the drug for varying process parameters is being investigated.

D.2 Description of the process

In order to understand the experiment, it is sufficient to realize that it is a complicated chemical process where relevant process parameters are concentrations of chemicals, temperatures, filtration times, etc.

D.3 Response variables

D.3.1 Choice of variables

No single response variable reflects the stability or the degradation of the product. All response variables, except two, were differences between responses immediately after production and responses after storage at 4 °C for 18 months or after storage at 25 °C for 12 months. Only data from the storage at 4 °C for 18 months will be considered in this example.

Eight response variables were chosen for analysis. Table D.1 gives an overview of the response variables analysed. The first two, zinc and pH, are preparations of the product. The next one, labelled “HPLC assay U/ml”, expresses the potency of the drug, while the remaining five variables are related to degradation of the product.

Table D.1 — Response variables considered

Response	Description[a]	Name in analysis
Zinc (µg/ml)	Change 0-18 months 4 °C	Zinc018
pH	Change 0-18 months 4 °C	ph018
HPLC[b] assay U/ml	Change 0-18 months 4 °C	HPLC018
Higher molecular weight products	Change 0-18 months 4 °C	HMWP018
Dissolved insulin, total	Change 0-18 months 4 °C	disol018
Other insulin-related products (%)	Change 0-18 months 4 °C	Other018
Desamido insulin (A21, acid) HPCE[c] (%)	18 months at 4 °C	A21des18
Desamido insulin (B3, neutral) HPCE (%)	18 months at 4 °C	B3des18

[a] See D.3.1 for expanded descriptions.

[b] HPLC = High-performance liquid chromatography.

[c] HPCE = High-performance capillary electrophoresis.

D.3.2 Measurement of the response variable

The variables were measured right after production and again after storage for the stipulated amount of time. The response variables that were analysed were the differences of the values obtained after storage and the initial values measured right after production. Exceptions were the desamido values (the last two variables in Table D.1), where no initial values were measured because they were very small.

The measurements were obtained in two laboratories, and the fact that two laboratories were used makes it natural to run the experiment in two blocks corresponding to laboratories.

D.3.3 Relationship of the response variables to the objective of the experiment

The objective of the experiment is to study stability of an insulin product. In this light, one may say that the third variable of Table D.1, “HPLC assay U/ml”, is the most important aspect of stability, namely the potency of the drug after storage, whereas the last five variables of Table D.1 are used to study more subtle aspects of degradation.

D.4 Factors affecting the response

D.4.1 Description of each factor (continuous/discrete) to be varied

The factors of the experiment and their associated levels are given in Table D.2. The first six, denoted by the capital letters A to F, are process parameters that describe process conditions at different stages of production. Factors G and H describe the adjustments of the product after production, i.e. adjustment of the zinc level and the pH level. Note that zinc and pH are both factors of the experiment and response variables. The factors are continuous but for each factor, two levels are chosen.

D.4.2 Selection of levels (related to size of effect to be determined)

The eight factors used in the experiment and their associated levels are given in Table D.2.

Table D.2 — Factors

Factor	Low level	High level
A Time$_{2(\text{IV ins.sol.+ins/prot.sol.})+\text{filtering}}$	(−1) 70 ± 5 + 30 ± 5 min	(1) 55 ± 5 + 70 ± 5 min
B Temp$_{2(\text{ins/prot.sol.})}$	(−1) 20 °C ± 2 °C	(1) 27 °C ± 2 °C
C Time$_{4(\text{VII ins.sol.})}$	(−1) 30 ± 5 min	(1) 100 ± 5 min
D Temp$_{4(\text{VII ins.sol.})}$	(−1) 5 °C ± 3 °C	(1) 18 °C ± 3 °C
E Temp$_{2(\text{IV ins.sol.})}$	(−1) 5 °C ± 3 °C	(1) 18 °C ± 3 °C
F pH$_{2(\text{ins/prot.sol.})}$	(−1) 2,65 ± 0,03	(1) 3,25 ± 0,03
G Zinc$_{\text{prep.}}$	(−1) 25,0 ± 2,0 µg/ml	(1) 31,0 ± 2,0 µg/ml
H pH$_{\text{cryst, via mix}}$ = pH$_{\text{prep.}}$	(−1) 7,15 ± 0,03	(1) 7,40 ± 0,03

D.4.3 Other factors noted but not incorporated due to issues with controllability or relevance

No other factors were identified for the experiment.

D.5 Fractional factorial design

D.5.1 Choice of specific design

This design was constructed by embedding the factors E, F, G and H in the complete 2^4 factorial design defined by the factors A, B, C and D. The following definitions (aliasing) of the factors E, F, G and H in terms of factors A, B, C and D were used:

$$E = BCD$$

$$F = ACD$$

$$G = ABD$$

$$H = ABC$$

In addition, the experiment was run in two blocks, corresponding to the laboratories R_1 and R_2 where the measurements were made. The blocks were defined as

$$\text{Block} = ABCD$$

The resulting design with levels coded as –1 (low level) and 1 (high level) is shown in Table D.3.

Table D.3 — Design matrix

	Experimental design									
Std	*A*	*B*	*C*	*D*	*E*	*F*	*G*	*H*	**Block/Number**	**Test number**
1	−1	−1	−1	−1	−1	−1	−1	−1	R_2 / 4	8
2	1	−1	−1	−1	−1	1	1	1	R_1 / 2	3
3	−1	1	−1	−1	1	−1	1	1	R_1 / 8	15
4	1	1	−1	−1	1	1	−1	−1	R_2 / 7	14
5	−1	−1	1	−1	1	1	−1	1	R_1 / 1	1
6	1	−1	1	−1	1	−1	1	−1	R_2 / 1	2
7	−1	1	1	−1	−1	1	1	−1	R_2 / 2	4
8	1	1	1	−1	−1	−1	−1	1	R_1 / 4	7
9	−1	−1	−1	1	1	1	1	−1	R_1 / 5	9
10	1	−1	−1	1	1	−1	−1	1	R_2 / 6	12
11	−1	1	−1	1	−1	1	−1	1	R_2 / 3	6
12	1	1	−1	1	−1	−1	1	−1	R_1 / 7	13
13	−1	−1	1	1	−1	−1	1	1	R_2 / 5	10
14	1	−1	1	1	−1	1	−1	−1	R_1 / 3	5
15	−1	1	1	1	1	−1	−1	−1	R_1 / 6	11
16	1	1	1	1	1	1	1	1	R_2 / 8	16

Although complete information about the settings of the factors in each run of the experiment is available from Table D.2 and Table D.3, it is advisable to write out detailed instructions about the settings of the factors in each run to the people who are running the experiment. An example of a description of a single experiment (run) from the design is given in Table D.4.

Table D.4 — Experiment (run) number 6 to be carried out in laboratory $R_2$12)

Process parameter		Level in experiment
A	$\text{Time}_{2(\text{IV ins.sol.+ins/prot.sol.)+filtering}}$	(1) 55 ± 5 + 70 ± 5 min
B	$\text{Temp}_{2(\text{ins/prot.sol.})}$	(−1) 20 °C ± 2 °C
C	$\text{Time}_{4(\text{VII ins.sol.})}$	(−1) 30 ± 5 min
D	$\text{Temp}_{4(\text{VII ins.sol.})}$	(1) 18 °C ± 3 °C
E	$\text{Temp}_{2(\text{IV ins.sol.})}$	(1) 18 °C ± 3 °C
F	$\text{pH}_{2(\text{ins/prot.sol.})}$	(−1) 2,65 ± 0,03
G	$\text{Zinc}_{\text{prep}}$	(−1) 25,0 ± 2,0 µg/ml
H	$\text{pH}_{\text{cryst, via mix}} = \text{pH}_{\text{prep}}$	(1) 7,40 ± 0,03

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12) Experiment (run) number 6 in laboratory R_2 corresponds to number 10 in the standard order.

Generators: $E = BCD$, $F = ACD$, $G = ABD$, $H = ABC$

Block generator: Blocks $= ABCD$

Defining relation: $I = BCDE = ACDF = ABDG = ABCH = ABEF = ACEG = ABEH$

$= BCFG = BDFH = CDGH = DEFG = CEFH = AFGH = BEGH$

$= ACDEFGH$

The length of the shortest word in the defining relation is four and this shows that the design is of resolution IV.

The complete alias structure for each factor contains 16 terms. The one for factor A, for example, is obtained from the defining relation by multiplying each term by A and using the rule that AA cancels:

$$A = ABCDE = CDF = BDG = BCH = BEF = CEG = BEH$$

$$= ABCFG = ABDFH = ACDGH = ADEFG = ACEFH = FGH = ABEGH$$

$$= CDEFGH$$

The complete alias structure for blocks is obtained by multiplying each term in the defining relation by $ABCD$ and recognizing that the terms AA, BB, CC and DD cancel:

Blocks $= AE = BF = CG = DH = CDEF = BDEG = CDEH$

$= ADFG = ACFH = ABGH = ABCEFG = ABDEFH = BCDFGH = ACDEGH$

$= BEFGH$

The alias structure restricted to two-way interactions is given in Table D.5.

Table D.5 — Alias structure of the two-factor interactions

Blocks $= J = AE = BF = CG = DH$
$AB = EF = DG = CH$
$AC = DF = EG = BH$
$BC = DE = FG = AH$
$AD = CF = BG = EH$
$BD = CE = AG = FH$
$CD = BE = AF = GH$

This means that main effects can be estimated to be free from two-factor interactions and that the $(8 \times 7)/2 = 28$ two-factor interactions are aliased in seven groups of four two-factor interactions. If specific two-actor interactions were expected to be active, it is important at this stage to inspect the alias structure to make sure that supposedly active interactions are not aliased. In this case, there were no such expectations.

D.5.2 Design matrix (standard order and run order)

The design selected was the 16-run one-sixteenth fractional factorial design with eight factors (A, B, C, D, E, F, G and H). The design is shown in Table D.3 in standard order, i.e. in the sense that the full 2^4 design in the defining factors A, B, C and D is given in standard order.

The runs were randomized within blocks. The number of each run within the specific block is shown in the "Block/Number" column of Table D.3.

D.5.3 Centre points

Centre points were not selected for this experiment.

D.5.4 Replication and repetition

Replication and repetition were not selected for this experiment.

D.6 Analysis of results

D.6.1 Data acquired through the experiment and analysis considerations

The results from the experiment are given in Table D.6. The first five columns are also the first five columns of the design matrix of Table D.3. The following eight columns are the response variables recorded. The names are the ones given in the last column of Table D.1. The final column gives the run number within block (laboratory), "r_w_b". In order to save space, the remaining factors are not listed, but they are defined in terms of the factors A, B, C and D as explained in D.5.1 as $E = BCD$, $F = ACD$, $G = ABD$, $H = ABC$, and block $= ABCD$.

The analysis was performed using the software R[13]. With 16 runs, it is possible to estimate 15 parameters in addition to the grand mean. The chosen parameters are the main effects of the eight factors A to H, the block factor J and an arbitrarily chosen two-factor interaction in each of the remaining six sets of aliased two-factor interactions in Table D.5. If a two-factor interaction should turn out to be significant, the alias pattern in Table D.5 as well as other significant factors will be considered before any conclusions are made.

We have a saturated model with no estimate for error so the analysis will be based on normal plots of effect supplemented with Lenth plots.

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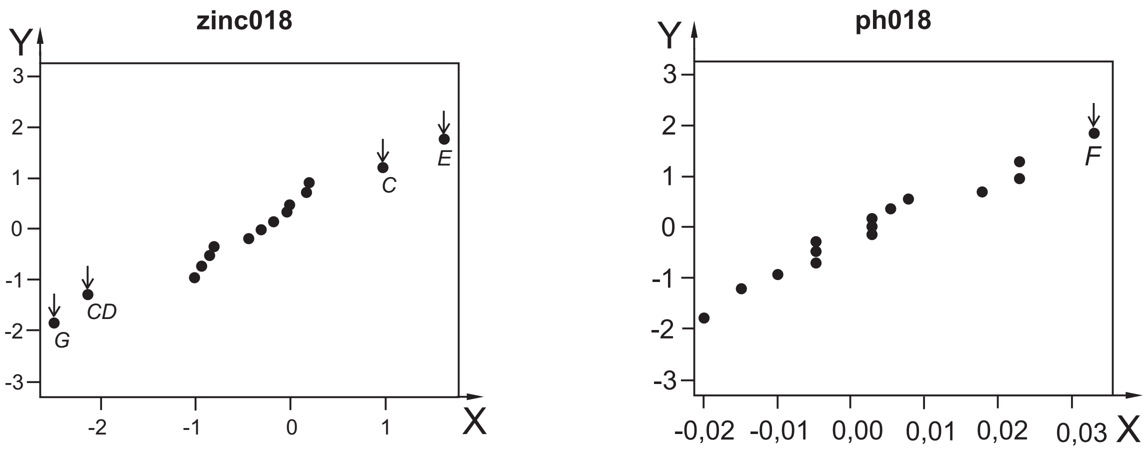
13) R is a free software environment for statistical computing and graphics. It compiles and runs on a wide variety of UNIX platforms, Windows and MacOS; see http://www.r-project.org/. This information is given for the convenience of users of this Technical Report and does not constitute an endorsement by ISO of this product.

Table D.6 — Experimental results

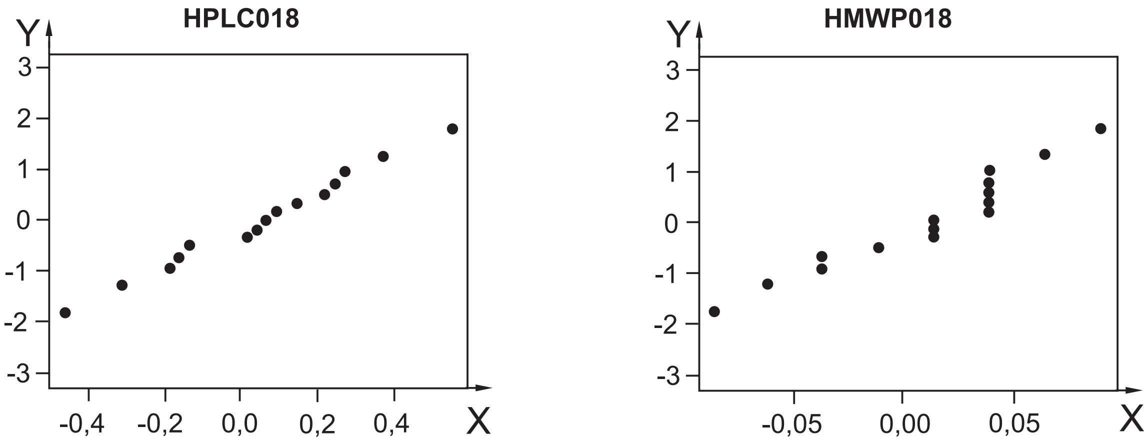
Std	*A*	*B*	*C*	*D*	Zinc018	Ph018	HPLC018	HMWP018	Disol018	Other018	A21des18	B3des18	r_w_b[a]
1	−1	−1	−1	−1	−5,5	−0,02	−0,9	0, 2	3,2	0,3	0,5	0,7	4
2	1	−1	−1	−1	−5,6	0,00	−0,8	0,3	2,8	0,5	0,6	0,7	2
3	−1	1	−1	−1	−3,1	−0,03	−0,5	0,2	4,4	0,6	0,6	0,8	8
4	1	1	−1	−1	−2,2	0,01	−0,4	0,2	3,4	0,4	0,6	0,5	7
5	−1	−1	1	−1	0,3	−0,01	−0,9	0,3	1,1	0,4	0,4	0,6	1
6	1	−1	1	−1	−1,7	0,01	−0,1	0,2	3,0	0,5	0,5	0,4	1
7	−1	1	1	−1	−2,8	0,05	−0,7	0,1	3,1	0,5	0,6	0,5	2
8	1	1	1	−1	0,1	−0,08	−0,2	0,2	0,7	0,6	0,7	0,6	4
9	−1	−1	−1	1	−2,0	0,02	−0,2	0,1	0,7	0,6	0,5	0,4	5
10	1	−1	−1	1	−0,4	0,00	0,6	0,3	−0,3	0,6	0,6	0,8	6
11	−1	1	−1	1	−1,3	0,02	−0,7	0,4	0,7	0,8	0,6	0,9	3
12	1	1	−1	1	−5,4	0,00	−0,1	0,1	4,4	0,8	0,7	0,6	7
13	−1	−1	1	1	−5,2	0,01	−0,7	0,2	0,7	0,6	0,5	0,6	5
14	1	−1	1	1	−2,4	0,03	−1,6	0,4	1,3	0,7	0,6	0,8	3
15	−1	1	1	1	−0,4	0,00	0,2	0,2	1,5	0,4	0,6	0,4	6
16	1	1	1	1	−6,4	0,03	−0,1	0,3	4,0	0,6	0,7	0,8	8

[a] r_w_b = run number within block (laboratory).



a) **Response variable zinc018**

b) **Response variable ph018**



c) **Response variable HPLC018**

d) **Response variable HMWP018**

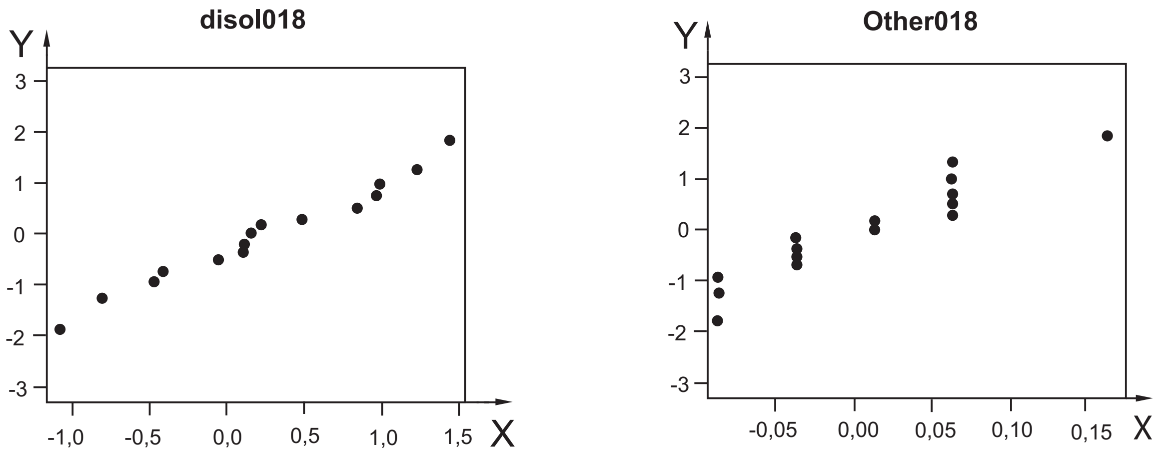
Key

X estimated effects

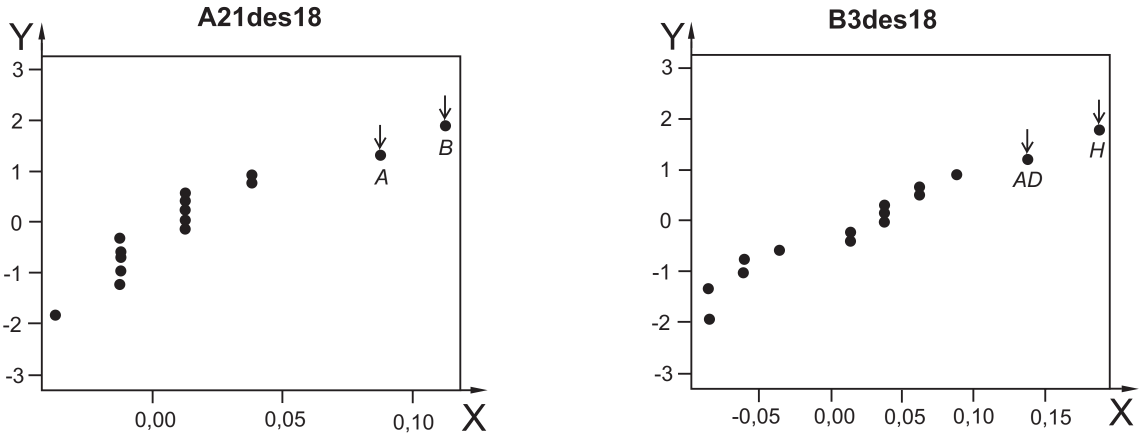
Y normal fractile

Figure D.1 — Normal plots of estimated effects for the response variables zinc018, ph018, HPLC018 and HMWP018

Estimated effects are along the horizontal axis. The points indicated by arrows and labelled are not indicative of significance. They are labelled for discussion in the text.



a) Response variable diso018 **b) Response variable other018**



c) Response variable A21des18 **d) Response variable B3des18**

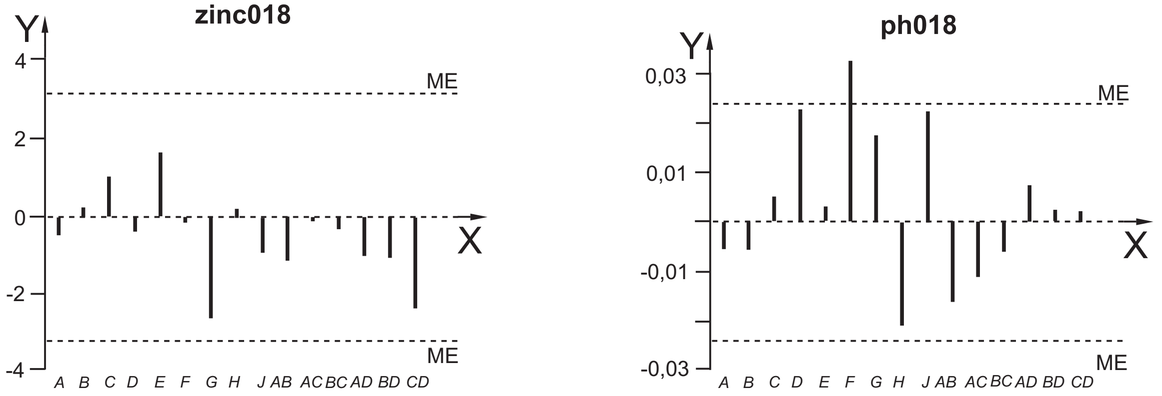
Key

X estimated effects

Y normal fractile

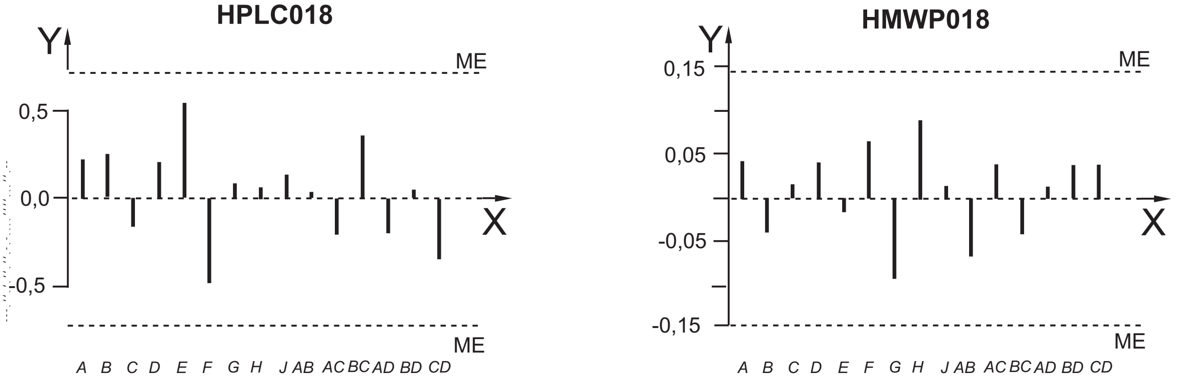
Figure D.2 — Normal plots of estimated effects for the response variables disol018, other018, A21des18 and B3des18

Estimated effects are along the horizontal axis. Estimated effects are along the horizontal axis. The points indicated by arrows and labelled are not indicative of significance. They are labelled for discussion in the text.



a) Response variable zinc018

b) Response variable ph018



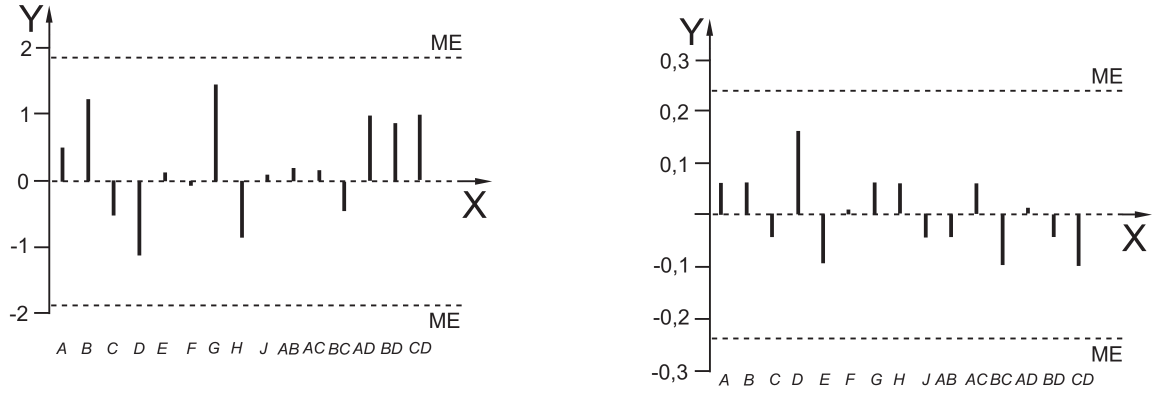
c) Response variable HPLC018

d) Response variable HMWP018

Key

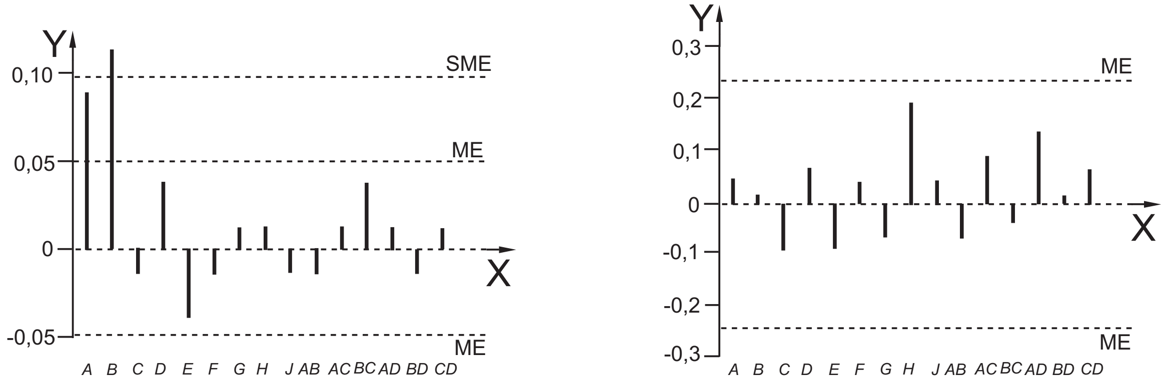
X	factors
Y	estimated effects
ME	margin of error
SME	simultaneous margin of error

Figure D.3 — Lenth plots of estimated effects for the response variables zinc018, ph018, HPLC018 and HMWP018



a) Response variable disol018

b) Response variable other018



c) Response variable A21des18

d) Response variable B3des18

Key

X	factors
Y	estimated effects
ME	margin of error
SME	simultaneous margin of error

Figure D.4 — Lenth plots of estimated effects for the response variables disol018, other018, A21des18 and B3des18

D.6.2 Analysis of results — Normal plots

The normal plots of the estimated effects for the eight response variables in Table D.1 are collected in Figures D.3 and D.4.

The estimated effects are average responses at the high level minus the average responses at the low level. Here, the normal plots are used in the following way. Straight lines are fitted to the points by eye with emphasis on the central points. Negative estimated effects that lie to the left of the line and positive estimated effects that lie to the right of the straight line are considered to be active. Only the normal plots for responses zinc018, A21des18 and B3des18 show estimated effects that may seem active.

In the normal plot for the response zinc018, it is tempting to plot a straight line based on the 11 central estimates which leads to the conclusion that G, CD, C and E are active factors. But numerically the estimate of E is not larger than some of the 11 central estimates, so either E is active and even more factors must be considered as active, or E is not active. The choice was made to not consider E as active. Then, if E does not deviate too much from the straight line neither does C, thus leaving G and CD as the only potentially active effects.

For the response A21des18, the evaluation of the normal plot is straightforward. Clearly, the positive estimated effect A and B are to the right of a straight line defined by the remaining estimates.

For the response B3des18, the situation is similar but not as clear. Active effects, if any, are AD and H, but it is not obvious that the points deviate significantly from a straight line defined by the remaining estimates.

The Lenth plots in the following subclause will be used to support the tentative conclusions already made.

D.6.3 Analysis of results — Lenth plots

The Lenth plot is a graphical illustration of Lenth's procedure to decide which factors are active. Based on the estimated effects an estimated standard error is calculated. Two multiples of the estimated standard error are calculated: the margin of error (ME) and the simultaneous margin of error (SME). If we entertain the hypothesis before the experiment that a certain effect is active, an appropriate test is to consider it active if the absolute value of its estimate exceeds the ME. For screening purposes, the SME is used. A factor is considered active if the absolute value of its effect estimate exceeds the SME. The Lenth plot illustrates this procedure by placing the factors along the horizontal axis and representing the estimated effects by vertical lines. Horizontal lines represent the ME and the SME, so it is easy to see which effects exceed one or the other. Note that the SME is always larger than the ME, so the SME may not show in all Lenth plots.

The Lenth plots of the estimated effects for the eight response variables in Table D.1 are plotted in Figure D.3 and Figure D.4.

For the response zinc018, the conclusion is that no factors are active. This conclusion is consistent with the discussion of the normal plot. It is indeed possible to fit a straight line that is close to all points.

For the response ph018, the factor F exceeds the ME line, so if that had been a specific hypothesis before the experiment, F would have been considered to be an active factor. But it was not the case, so it has to exceed the SME line to be considered active.

The response A21des18 is the only variable with an estimated effect, B, exceeding the SME.

D.6.4 Presentation of results

The results are summarized in Table D.7. As already explained in D.6.2 and D.6.3, A21des18 is the only variable showing an active effect. The experiment has indicated that the process is stable within the process window considered.

Table D.7 — Summary of results

Response	Analysis	Comments
Zinc (µg/ml)	Change 0-18 months 4 °C	no effects detected
pH	Change 0-18 months 4 °C	no effects detected
Higher molecular weight products	Change 0-18 months 4 °C	no effects detected
Dissolved insulin, total	Change 0-18 months 4 °C	no effects detected
HPLC assay U/ml	Change 0-18 months 4 °C	no effects detected
Other insulin-related prod. (%)	Change 0-18 months 4 °C	no effects detected
Desamido insulin (A21, acid) HPCE (%)	18 months at 4 °C	Temp_2 effects (factor B)
Desamido insulin (B3, neutral) HPCE (%)	18 months at 4 °C	no effects detected

D.6.5 Confirmation results

In this case, no confirmation experiment or single confirmation run was performed.

Annex E
(informative)

Washing machine experiment

E.1 General

Washing machines are usually repairable items and consumers want the interval between repairs to be as long as possible. The service organizations, whose job it would be to provide assistance in any repair, are also interested parties. The fewer times a washing machine breaks down, the lower the associated costs to the service organization.

During the development programme for a new washing machine, the design engineers test different subsystems of the new machine and record, amongst other things, the number of cycles to failure for the subsystem. Design engineers attempt to design subsystems and components that will perform well in spite of many different usage conditions, such as the water type, that the machines will encounter during their lives.

E.2 Overall objective for the experiment

A washing machine manufacturer, developing a new range of machines, was interested to know if certain design changes would lead to greater reliability. The following paragraphs describe an experiment performed by the design engineers to better understand which design of tub and which certain operating conditions are most robust against some of the usage factors the washing machines are expected to face. A Taguchi design with inner (for the design variables) and outer (for the usage factors) arrays was chosen.

E.3 Response variable

E.3.1 Choice of variable

The response (Y) chosen for the experiment was the “mean cycles between failure” (MCBF).

A signal-to-noise ratio (“biggest is best”), $\varDelta_{\mathrm{b}}$, was chosen to analyse the data.

$$\varDelta_{\mathrm{b}} = -10\log_{10}\left[\frac{1}{N}\sum\left(\frac{1}{Y_i^2}\right)\right]$$

where

Y_i are the observations;

N is the number of observations.

The greatest MCBF is indicated when this expression is maximized. An analysis of the results of the experiment shows that the levels of the design factors which maximize the signal-to-noise ratio indicate a design that gives the greatest reliability in spite of the behaviour of the noise factors.

E.3.2 Measurement of the response variable

Six washing machines were built for each arrangement of the design factor levels (runs). They were all run in a laboratory and continuously cycled to failure. Each machine had a counter fitted to it to record the number of cycles. For each run, the MCBF was calculated and used in the analysis of the experiment. Depending on the nature of the failure, a washing machine would be repaired and then cycled to failure again. In this way, several machines were repaired several times during the experiment.

E.3.3 Relationship of the response variable to the objective of the experiment

The MCBF is directly linked to the objective of the experiment, i.e. to determine the design considerations that provide a greater number of cycles between failure with least variability once subjected to usage factors.

E.4 Factors affecting the response

E.4.1 Description of each factor (discrete) to be varied

The factors chosen to be varied within the experiment were determined using the knowledge of the design engineers and technical staff. These were:

B: Tub type

C: Detergent type

E: Wash temperature

Additionally, the usage factors chosen were:

A: Wash load

D: Water type

F: Wash frequency

All of the chosen factors were treated as discrete variables as indicated in E.4.2.

E.4.2 Selection of levels (related to size of effect to be determined)

The factors used in the experiment and their associated levels are listed in Table E.1.

Table E.1 — Factors

Factor	Level 1	Level 2
B Tub type	Design A	Design B
C Detergent type	Liquid	Powder
E Wash temperature	Low	High
A Wash load	Half	Full
D Water type	Soft	Hard
F Wash frequency	Low	High

E.4.3 Other factors noted but not incorporated due to issues with controllability or relevance

Other factors that might have been considered but were not included in the experiment are given in Table E.2.

Table E.2 — Excluded factors

Factor	Reason for exclusion
External air temperature	Air temperature external to the machines was not regarded as important to the response by engineers as the internal temperatures were likely to be much higher.
External humidity	Considered irrelevant as the humidity levels within the machines were likely to be much more important.
Operator	As long as the operator placed the detergent in the correct location and shut the door properly, engineers regarded the operation of the machines as automatic.

E.4.4 Independence of factors

The factors selected for the experiment were regarded as independent of each other.

E.5 Experimental design

E.5.1 Inner array

The design selected for the “inner” array was a Taguchi L_8 design giving full resolution. With only three design factors, this was thought to be appropriate.

Table E.3 shows the design. The numbers “1” and “2” in the first three columns of this table refer to the level of the factor.

Table E.3 — Inner array

B	C	E	**Run**
1	1	1	1
1	1	2	2
1	2	1	3
1	2	2	4
2	1	1	5
2	1	2	6
2	2	1	7
2	2	2	8

NOTE The design is printed in “standard order” and not randomized since all runs were conducted concurrently.

Because the design was a full factorial, there were no aliased factors.

E.5.2 Outer array

The usage factors comprised the “outer” array. As there were three usage factors, each at two levels, it was decided to use a Taguchi L_4 design and perform a half fraction since interactions were regarded as unimportant.

Table E.4 shows the design.

Table E.4 — Outer array

A	*D*	*F*	**Run**
1	1	1	1
1	2	2	2
2	1	2	3
2	2	1	4

E.5.3 Full design

The full design is shown in Table E.5.

Table E.5 — Full design

				F	1	2	2	1
				D	1	2	1	2
Run	*B*	*C*	*E*	*A*	1	1	2	2
1	1	1	1					
2	1	1	2					
3	1	2	1					
4	1	2	2					
5	2	1	1					
6	2	1	2					
7	2	2	1					
8	2	2	2					

E.5.4 Centre points

Centre points were not selected for this experiment because two of the factors in the inner array were regarded as categorical (binary) factors making the creation of centre points very difficult.

E.5.5 Replication and repetition

The washing-machine-development laboratory could not accommodate any more experimental time or space than that allocated to carry out the 8 × 4 experiment shown above. Therefore, there was no replication of any of the experimental runs.

For each experimental run, there were eight machines providing repetition.

E.6 Analysis of results

E.6.1 Data acquired through the experiment and analysis considerations

The results from the experiment are given in Table E.6. They were keyed into a software programme called MINITAB™14). Plots from this programme are shown in Figures E.1 to E.4.

Table E.6 — Experimental results

				F	1	2	2	1
				D	1	2	1	2
Run	*B*	*C*	*E*	*A*	1	1	2	2
1	1	1	1		278,1	367,2	463,8	310,9
2	1	1	2		342,0	355,1	451,7	253,9
3	1	2	1		393,0	406,2	356,0	349,8
4	1	2	2		421,0	411,9	530,7	377,8
5	2	1	1		431,7	444,8	541,4	433,3
6	2	1	2		581,9	519,1	615,7	462,8
7	2	2	1		465,3	500,6	575,0	422,1
8	2	2	2		686,4	699,6	942,8	643,2

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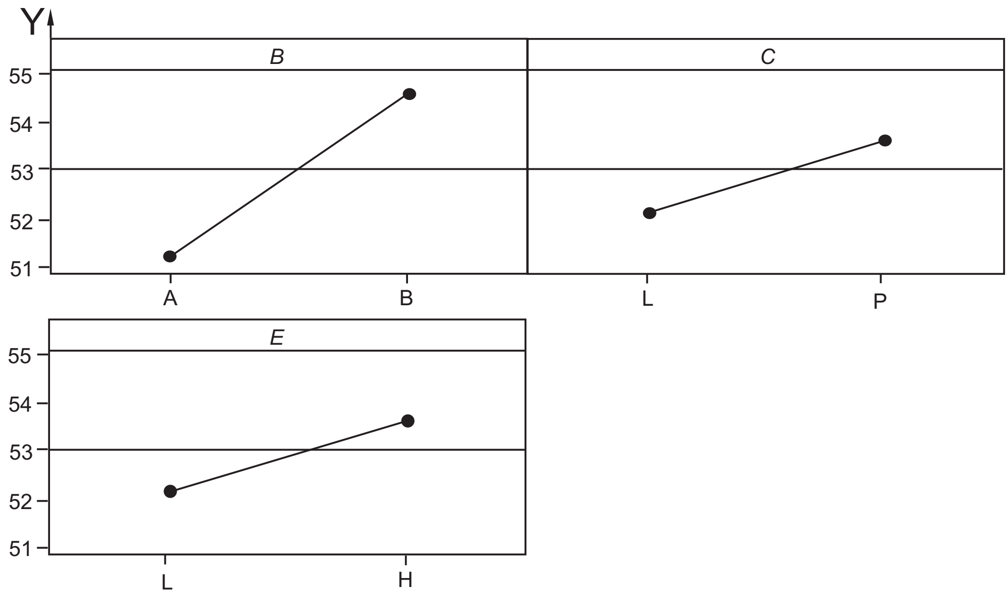
14) MINITAB is the trade name of a product supplied by Minitab Inc. This information is given for the convenience of users of this Technical Report and does not constitute an endorsement by ISO of the product named.

E.6.2 Analysis of the signal-to-noise ratio



Key

Y mean of signal-to-noise ratios (signal-to-noise: larger is better)

B tub type, i.e. design A or design B

C detergent type, i.e. liquid (L) or powder (P)

E wash temperature, i.e. low (L) or high (H)

Figure E.1 — Main effects plot for signal-to-noise ratios — Data means

Table E.7 — ANOVA — Signal-to-noise ratios

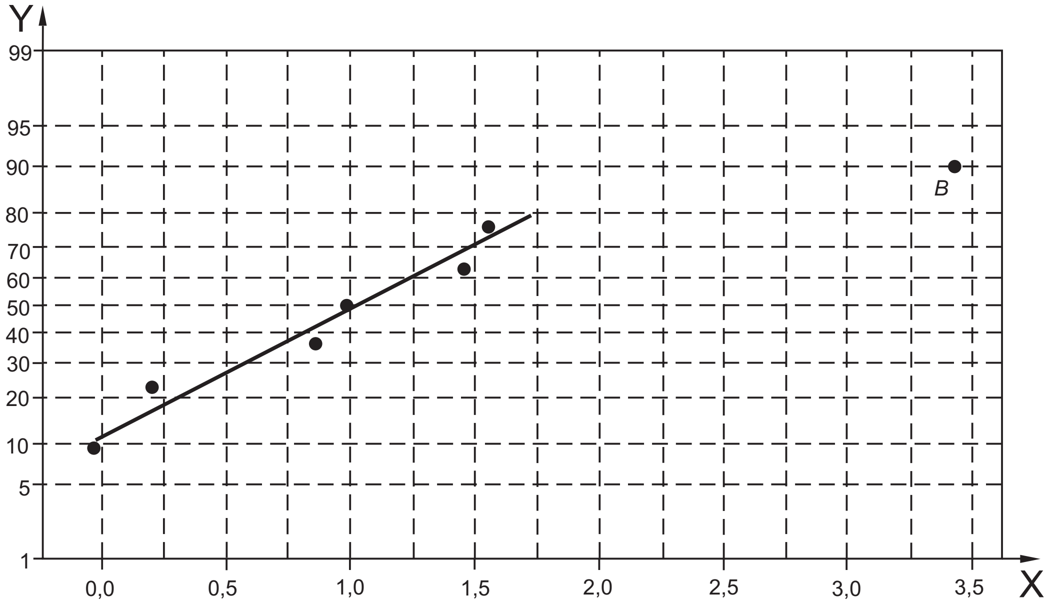
Source	Degrees of freedom	Seq SS[a]	Adj SS[b]	Adj MS[c]	*F* value	*p* value
B Tub type	1	23,276 7	23,276 7	23,276 7	277,72	0,038
C Detergent type	1	4,783 1	4,783 1	4,783 1	57,07	0,084
E Wash temperature	1	4,209 4	4,209 4	4,209 4	50,22	0,089
BC	1	0,001 4	0,001 4	0,001 4	0,02	0,917
BE	1	1,935 3	1,935 3	1,935 3	23,09	0,131
CE	1	1,474 1	1,474 1	1,474 1	17,59	0,149
Residual error	1	0,083 8	0,083 8	0,083 8		
Total	7	35,763 9				

[a] Seq SS = Sequential sums of squares.

[b] Adj SS = Adjusted sums of squares.

[c] Adj MS = Adjusted mean square.

The analysis indicates that factor B is significant at the 0,05 level with C and E marginally significant at the 0,10 level. As the p values for the interaction terms are all above 0,10, they were regarded as not significant. Because only one degree of freedom was available to assess the residual error, a probability plot was drawn of the effects of the factors to better assist the determination of significance. This was done for all of the responses.



Key

X signal-to-noise effect

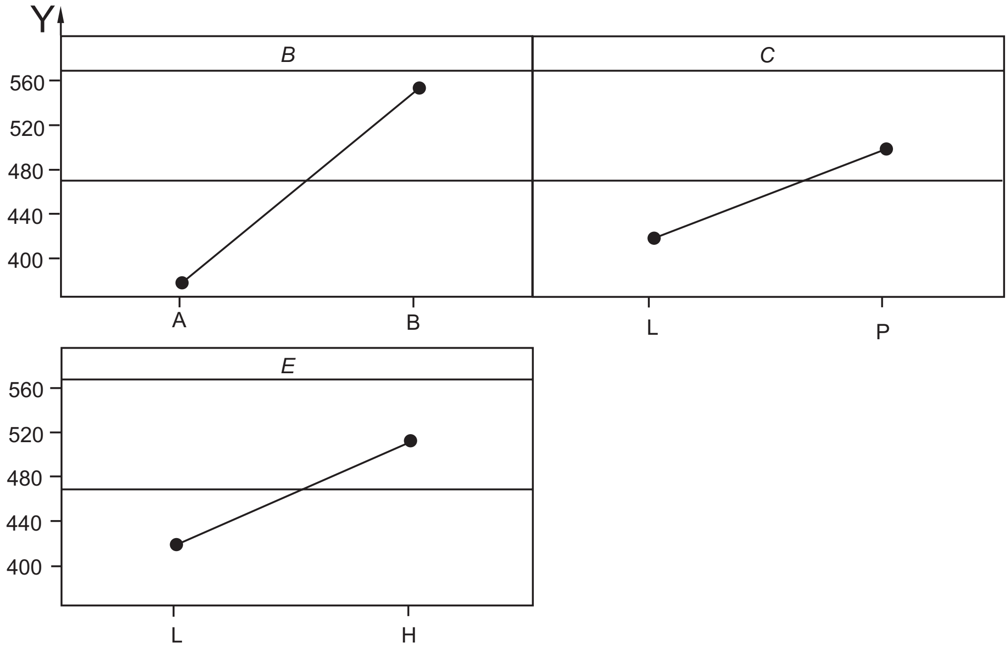
Y percent

B tub type

Figure E.2 — Normal probability plot of signal-to-noise effect

To improve the model, the analysis was then re-done (see E.6.3), removing the interaction terms from the model fitted.

E.6.3 Analysis of MCBF means



Key

Y mean of means

B tub type, i.e. design A or design B

C detergent type, i.e. liquid (L) or powder (P)

E wash temperature, i.e. low (L) or high (H)

Figure E.3 — Main effects plot for means — Data means

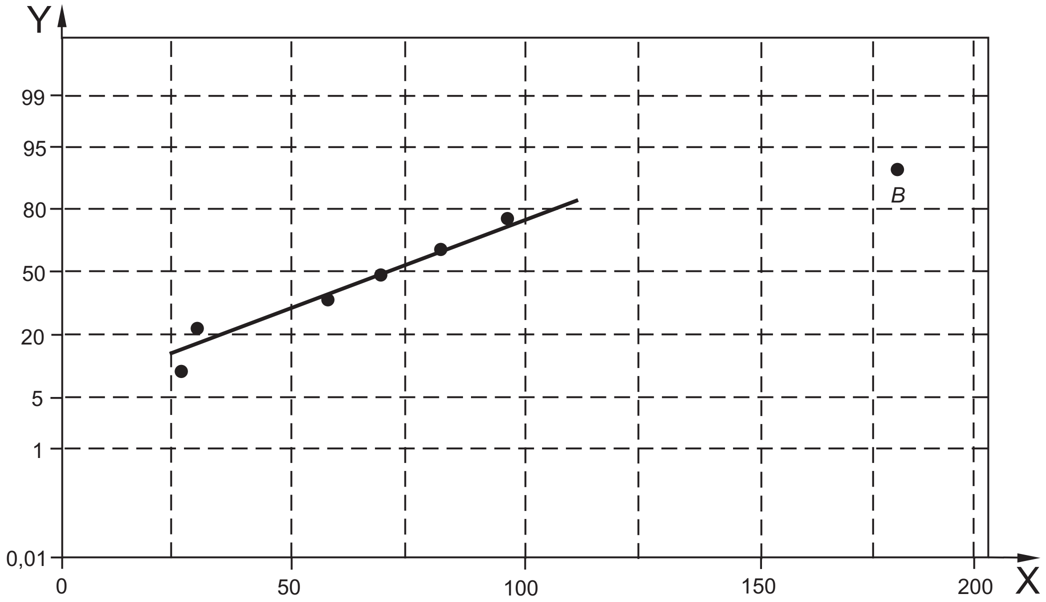
Table E.8 — ANOVA — MCBF

Source	Degrees of freedom	Seq SS[a]	Adj SS[b]	Adj MS[c]	*F* value	*p* value
B Tub type	1	65 549	65 549	65 549	46,02	0,093
C Detergent type	1	13 778	13 778	13 778	9,67	0,198
E Wash temperature	1	18 925	18 925	18 925	13,29	0,170
BC	1	1 805	1 805	1 805	1,27	0,462
BE	1	9 769	9 769	9 769	6,86	0,232
CE	1	6 821	6 821	6 821	4,79	0,273
Residual error	1	1 424	1 424	1 424		
Total	7	118 071				

[a] Seq SS = Sequential sums of squares.

[b] Adj SS = Adjusted sums of squares.

[c] Adj MS = Adjusted mean square.



Key

X mean effect

Y percent

B tub type

Figure E.4 — Probability plot — MCBF

The analysis indicates that factor B is marginally significant at the 0,10 level. As the p values for the interaction terms are all above 0,20, they were regarded as not significant. The analysis was then re-done, removing those interaction terms from the model fitted.

E.6.4 Revised analysis of signal-to-noise ratio

Table E.9 — Revised ANOVA — Signal-to-noise ratios

Source	Degrees of freedom	Seq SS[a]	Adj SS[b]	Adj MS[c]	F value	p value
B Tub type	1	23,277	23,277	23,276 7	26,64	0,007
C Detergent type	1	4,783	4,783	4,783 1	5,47	0,079
E Wash temperature	1	4,209	4,209	4,209 4	4,82	0,093
Residual error	4	3,495	3,495	0,873 7		
Total	7	35,764				

[a] Seq SS = Sequential sums of squares.

[b] Adj SS = Adjusted sums of squares.

[c] Adj MS = Adjusted mean square.

The analysis shown in Table E.9 confirms that factor B (tub type) is significant at the 0,05 level with C (detergent type) and E (wash temperature) marginally significant at the 0,10 level.

E.6.5 Revised analysis of MCBF means

Table E.10 — Revised ANOVA — MCBF

Source	Degrees of freedom	Seq SS[a]	Adj SS[b]	Adj MS[c]	F value	p value
B Tub type	1	65 549	65 549	65 549	13,29	0,022
C Detergent type	1	13 778	13 778	13 778	2,78	0,171
E Wash temperature	1	18 925	18 925	18 925	3,82	0,122
Residual error	4	19 819	19 819	19 819		
Total	7	118 071				

[a] Seq SS = Sequential sums of squares.

[b] Adj SS = Adjusted sums of squares.

[c] Adj MS = Adjusted mean square.

The revised analysis in Table E.10 indicates that factor B (tub type) significantly affects the MCBF at the 0,05 level but that factors C (detergent type) and E (wash temperature) are not significant. Thus, the new design is unaffected by the detergent type used and the wash temperature.

NOTE Although in the usual application of the Taguchi method, the above analysis would be all that is performed, it would be considered good practice if a standard deviation were calculated per run to assess the variation induced by the usage factors. This might be regarded as important here, since the signal-to-noise ratio (the larger the better) selected for this study does not really describe variation. Clause E.7 contains the analysis of ln(S). It shows no factor significantly affected by the variability.

E.6.6 Presentation of results — Optimization recommendations

One of the objectives for the new washing machine design was to produce a machine that maximized the MCBF with the least variability when subjected to the usage factors water type, wash load and wash frequency.

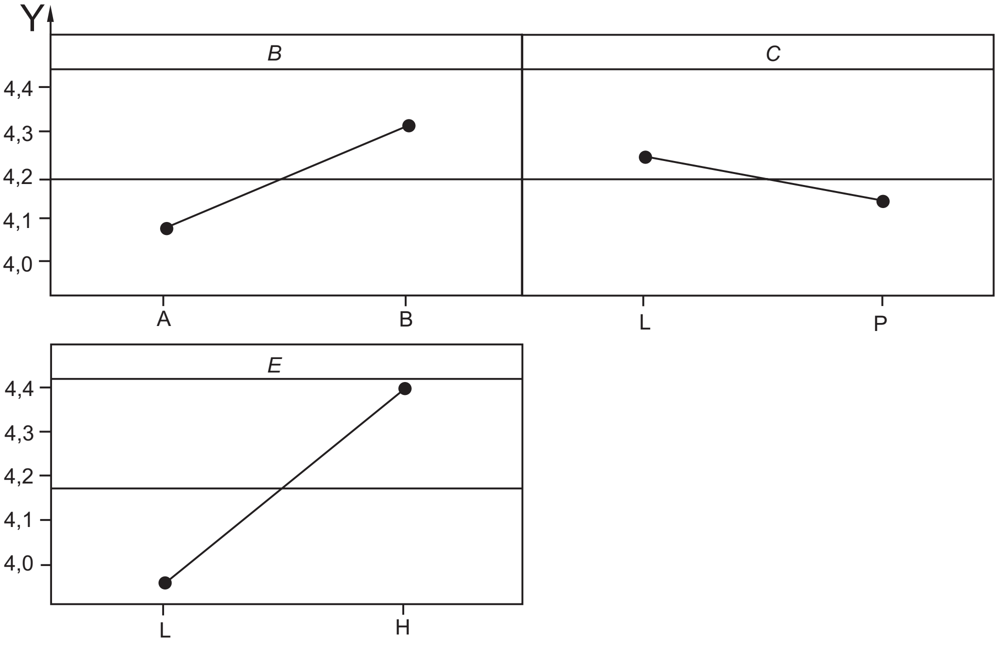
The signal-to-noise ratio used here cannot indicate which factors influence variability. This is only achieved from the analysis of the standard deviation. Regarding the output in E.7, none of the factors had any effect on the variability. Therefore, the recommendation was to select the factors to maximize the MCBF.

From the analysis of means, having factor B set to level 2 will bring a higher value of MCBF.

Given that, in practice, the user of the washing machines will choose what temperatures to wash at and what detergent will be used, the expected MCBF will be 560,4. Given "average" washing demand, this equates to an approximate mean time between failure of 3,6 years.

The findings of the experiment assisted the engineers in designing a very successful washing machine that performed much better than its predecessors. The new machine was perceived by customers as very reliable.

E.7 Analysis of ln(S)



Key

Y mean of ln(S)

B tub type, i.e. design A or design B

C detergent type, i.e. liquid (L) or powder (P)

E wash temperature, i.e. low (L) or high (H)

Figure E.5 — Main effects plot — ln(S)

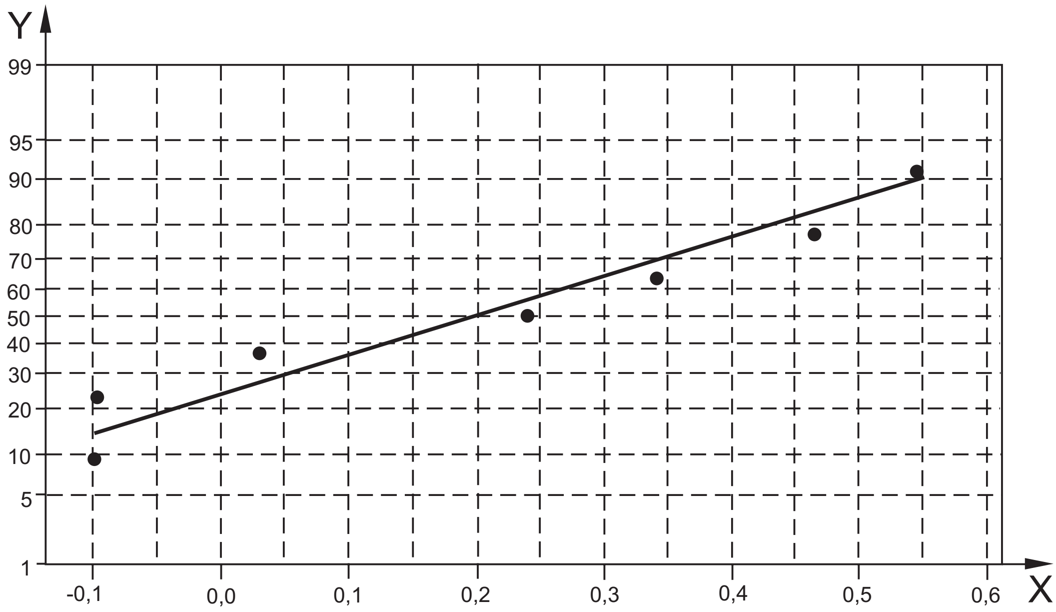
Table E.11 — ANOVA — ln(*S*)

Source	Degrees of freedom	Seq SS[a]	Adj SS[b]	Adj MS[c]	*F* value	*p* value
B Tub type	1	0,114 04	0,114 045	0,114 045	5,92	0,248
C Detergent type	1	0,018 54	0,018 539	0,018 539	0,96	0,506
E Wash temperature	1	0,432 48	0,432 478	0,432 478	22,46	0,132
*B*C*	1	0,592 55	0,592 551	0,592 551	30,77	0,114
*B*E*	1	0,001 78	0,001 779	0,001 770	0,09	0,812
*C*E*	1	0,233 35	0,233 350	0,233 350	12,12	0,178
Residual error	1	0,019 26	0,019 259	0,019 259		
Total	7	1,412 00				

[a] Seq SS = Sequential sums of squares.

[b] Adj SS = Adjusted sums of squares.

[c] Adj MS = Adjusted mean square.



Key

X ln(*S*) effect

Y percent

Figure E.6 — Normal probability plot – ln(*S*)

Annex F
(informative)

Aggregated shipworm bacterium

F.1 General

The marine shipworm hosts a symbiotic parasite commonly known as the shipworm bacterium (*teredinobacter turnirae*) which has been found to have commercial applications in impacting nitrogen levels in media by producing cellulolytic and proteolytic activities. The bacterium grows in rod-like or clump-like fashions and can produce extracellular proteolytic activity. A more desirable growth morphology is in the form of aggregates which, if grown at an exponential rate, can be commercially viable.

F.2 Overall objective for the experiment

The inability of the shipworm bacterium to grow exponentially in aggregates suggests the impedance owing to a medium component. As there are many such candidates, a screening experiment was sought to identify key inhibitors, recognizing the possibility of some interactions.

A Plackett-Burman 20-run design was chosen along with its 20-run fold-over as a likely second phase of experimentation. Eventually, a response surface design was employed using the three most critical components that impacted growth.

This annex adapts the experiment and results from a study by Ahuja, Ferreira and Moreira [2].

F.3 Response variable

F.3.1 Choice of variable

Cell growth was determined via an optical scanning procedure which converts observed optical density values to dry cell weight of biomass. Proteolytic activity was determined by a protease assay, resulting in response variable Y outcomes measured in micrograms (µg) of azocasein digested per hour.

F.3.2 Measurement of the response variable

A rigid protocol was followed for each run of the experiment and measurements were performed as described in F.3.1 in duplicate.

F.3.3 Relationship of the response variable to the objective of the experiment

Microbial growth proceeds at a rate proportional to the biomass concentration. To capture the limitations to the growth, the response was determined by measuring growth at 8 h and 36 h.

F.4 Factors affecting the response

F.4.1 Description of each factor to be varied

Various medium factors were chosen as candidates that impact growth. The components are given in the form of their chemical composition or other description, as follows:

1 NaCl

2 KCl

3 $MgSO_4 \cdot 7H_20$

4 $MgCl_2 \cdot 6H_20$

5 $CaCl_2 \cdot 2H_20$

6 HEPES

7 K_2HPO_4

8 Na_2CO_3

9 Sodium citrate$\cdot 2H_2O$

10 $Fe_2(SO_4)_3 \cdot H_2O$

11 H_3BO_3

12 $MnCl_2 \cdot 4H_2O$

13 $ZnSO_4 \cdot 7H_2O$

14 $Na_2MoO_4 \cdot 2H_2O$

15 $CoSO_4 \cdot 6{,}5H_2O$

16 $CuSO_4 \cdot 5H_2O$

17 Sucrose

18 NH_4Cl

NOTE Components 1, 6 and 17 were ultimately held constant throughout the experiment and were used for consistency checks by the original experimenters. Henceforth, these variables are treated as unvaried and not suitable for further analysis.

F.4.2 Selection of levels (related to size of effect to be determined)

The factors used in the experiment and their associated levels are given in Table F.1.

Table F.1 — Factors and levels

Factor		Lower level g/l	Higher level g/l
2	KCl	0,4	1,6
3	$MgSO_4{\cdot}7H_2O$	1,9	7,6
4	$MgCL_2{\cdot}6H_2O$	1,5	6,0
5	$CaCl_2{\cdot}2H_2O$	0,4	1,6
7	K_2HPO_4	$1{,}53 \times 10^{-2}$	$6{,}12 \times 10^{-2}$
8	Na_2CO_3	$1{,}00 \times 10^{-2}$	$4{,}00 \times 10^{-2}$
9	Sodium citrate$\cdot 2H_2O$	$4{,}56 \times 10^{-3}$	$1{,}82 \times 10^{-2}$
10	$Fe_2(SO_4)_3{\cdot}H_2O$	$3{,}14 \times 10^{-3}$	$1{,}25 \times 10^{-2}$
11	H_3BO_3	$2{,}90 \times 10^{-3}$	$1{,}16 \times 10^{-2}$
12	$MnCl_2{\cdot}4H_2O$	$1{,}80 \times 10^{-3}$	$7{,}2 \times 10^{-2}$
13	$ZnSO_4.7H_2O$	$2{,}00 \times 10^{-4}$	$8{,}00 \times 10^{-4}$
14	$Na_2MoO_4.2H_2O$	$4{,}00 \times 10^{-5}$	$1{,}60 \times 10^{-4}$
15	$CoSO_4{\cdot}6{,}5H_2O$	$4{,}84 \times 10^{-5}$	$1{,}94 \times 10^{-4}$
16	$CuSO_4{\cdot}5H_2O$	$8{,}00 \times 10^{-5}$	$3{,}20 \times 10^{-4}$
18	NH_4Cl	1	4

As is apparent from Table F.1, the higher level of each component was set at four times the lower level.

F.4.3 Other factors noted but not incorporated due to issues with controllability or relevance

No other factors were identified for inclusion in the experiment.

F.4.4 Independence of factors

The factors selected for the experiment were considered as independent of each other.

F.5 Experimental design

F.5.1 Design chosen

A 20-run Plackett-Burman design was chosen for the experiment.

NOTE 1 The numbers “–1” and “1” in Tables F.2 and F.3 refer to the lower and higher levels of the factors, respectively, as defined in Table F.1.

NOTE 2 The design is presented in “standard order” but was run in a randomized order.

Table F.2 — Initial 20-run Plackett-Burman design factor

Run number	2	3	4	5	7	8	9	10	11	12	13	14	15	16	18	*Y*
1	1	–1	–1	1	1	1	–1	1	–1	1	–1	–1	–1	–1	1	0,048
2	1	1	–1	–1	1	1	1	–1	1	–1	1	–1	–1	–1	1	0,039
3	–1	1	1	–1	1	1	1	1	–1	1	–1	1	–1	–1	–1	0,039
4	1	–1	1	1	–1	1	1	1	1	–1	1	–1	1	–1	–1	0,029
5	1	1	–1	1	–1	–1	1	1	1	1	–1	1	–1	1	–1	0,044
6	–1	1	1	–1	1	–1	–1	1	1	1	1	–1	1	–1	–1	0,041
7	–1	–1	1	1	1	1	–1	–1	1	1	1	1	–1	1	1	0,046
8	–1	–1	–1	1	–1	1	1	–1	–1	1	1	1	1	–1	–1	0,041
9	–1	–1	–1	–1	1	–1	1	1	–1	–1	1	1	1	1	1	0,026
10	1	–1	–1	–1	1	1	–1	1	1	–1	–1	1	1	1	–1	0,038
11	–1	1	–1	–1	–1	1	1	–1	1	1	–1	–1	1	1	1	0,035
12	1	–1	1	–1	–1	–1	1	1	–1	1	1	–1	–1	1	1	0,031
13	–1	1	–1	1	–1	–1	–1	1	1	–1	1	1	–1	–1	1	0,034
14	1	–1	1	–1	–1	–1	–1	–1	1	1	–1	1	1	–1	1	0,037
15	1	1	–1	1	1	–1	–1	–1	–1	1	1	–1	1	1	–1	0,033
16	1	1	1	–1	–1	1	–1	–1	–1	–1	1	1	–1	1	–1	0,036
17	1	1	1	1	1	–1	1	–1	–1	–1	–1	1	1	–1	1	0,03
18	–1	1	1	1	–1	1	–1	1	–1	–1	–1	–1	1	1	1	0,034
19	–1	–1	1	1	1	–1	1	–1	1	–1	–1	–1	–1	1	–1	0,031
20	–1	–1	–1	–1	–1	–1	–1	–1	–1	–1	–1	–1	–1	–1	–1	0,039

Subsequently, the fold-over to the 20-run Plackett-Burman design of Table F.2 was run and the results were combined. Table F.3 provides the runs and the corresponding responses (again reporting the average of the duplicates for the responses).

Table F.3 — Foldover of the Plackett-Burman design factor of Table F.2

Run number	2	3	4	5	7	8	9	10	11	12	13	14	15	16	18	Y
1	–1	1	1	–1	–1	–1	1	–1	1	–1	1	1	1	1	–1	0,044
2	–1	–1	1	1	–1	–1	–1	1	–1	1	–1	1	1	1	–1	0,038
3	1	–1	–1	1	–1	–1	–1	–1	1	–1	1	–1	1	1	1	0,039
4	–1	1	–1	–1	1	–1	–1	–1	–1	1	–1	1	–1	1	1	0,04
5	–1	–1	1	–1	1	1	–1	–1	–1	–1	1	–1	1	–1	1	0,039
6	1	–1	–1	1	–1	1	1	–1	–1	–1	–1	1	–1	1	1	0,039
7	1	1	–1	–1	–1	–1	1	1	–1	–1	–1	–1	1	–1	–1	0,043
8	1	1	1	–1	1	–1	–1	1	1	–1	–1	–1	–1	1	1	0,041
9	1	1	1	1	–1	1	–1	–1	1	1	–1	–1	–1	–1	–1	0,039
10	–1	1	1	1	–1	–1	1	–1	–1	1	1	–1	–1	–1	1	0,043
11	1	–1	1	1	1	–1	–1	1	–1	–1	1	1	–1	–1	–1	0,05
12	–1	1	–1	1	1	1	–1	–1	1	–1	–1	1	1	–1	–1	0,051
13	1	–1	1	–1	1	1	1	–1	–1	1	–1	–1	1	1	–1	0,051
14	–1	1	–1	1	1	1	1	1	–1	–1	1	–1	–1	1	–1	0,052
15	–1	–1	1	–1	–1	1	1	1	1	–1	–1	1	–1	–1	1	0,049
16	–1	–1	–1	1	1	–1	1	1	1	1	–1	–1	1	–1	1	0,052
17	–1	–1	–1	–1	–1	1	–1	1	1	1	1	–1	–1	1	–1	0,048
18	1	–1	–1	–1	1	–1	1	–1	1	1	1	1	–1	–1	–1	0,052
19	1	1	–1	–1	–1	1	–1	1	–1	1	1	1	1	–1	1	0,048
20	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0,049

F.5.2 Centre points

Centre points were not selected for this experiment as the experiment is a screening experiment and the relative magnitudes of the various components is of greater interest than their pure statistical significance.

F.5.3 Replication and repetition

Measurements were performed as repeats. The two values obtained are not pure replicates, hence, only the average of the two values for each run are reported in Tables F.2 and F.3.

F.6 Analysis of results

F.6.1 Data acquired through the experiment and analysis considerations

The results from the experiment are given in Table F.4. These results correspond to combining the original 20 runs with the fold-over runs and estimating parameters. The responses were entered into a software programme called JMP7™[15].

Table F.4 — Experimental results — Parameter estimates

Term	Estimate	Standard error	*t* ratio	Prob > |*t*|
Intercept	0,040 95	0,001 194	34,29	< 0,000 1
×2	−0,000 15	0,001 194	−0,13	0,901 1
×3	−0,000 2	0,001 194	−0,17	0,868 4
×4	−0,001 1	0,001 194	−0,92	0,366 2
×5	0,000 15	0,001 194	0,13	0,901 1
×7	0,001 45	0,001 194	1,21	0,236 6
×8	0,001 55	0,001 194	1,30	0,206 7
×9	0	0,001 194	0,00	1,000 0
×10	0,000 75	0,001 194	0,63	0,536 0
×11	0,000 95	0,001 194	0,80	0,434 2
×12	0,001 8	0,001 194	1,51	0,144 8
×13	0,000 05	0,001 194	0,04	0,967 0
×14	0,000 6	0,001 194	0,50	0,620 0
×15	−0,001 05	0,001 194	−0,88	0,388 1
×16	−0,001 2	0,001 194	−1,00	0,325 1
×18	−0,001	0,001 194	−0,84	0,410 7

The three leading effects are: 7 (K_2HPO_4), 8 (Na_2CO_3) and 12 ($MnCl_2 \cdot 4H_2O$).

These effects can also be identified from the half-normal probability plot given in Figure F.1.

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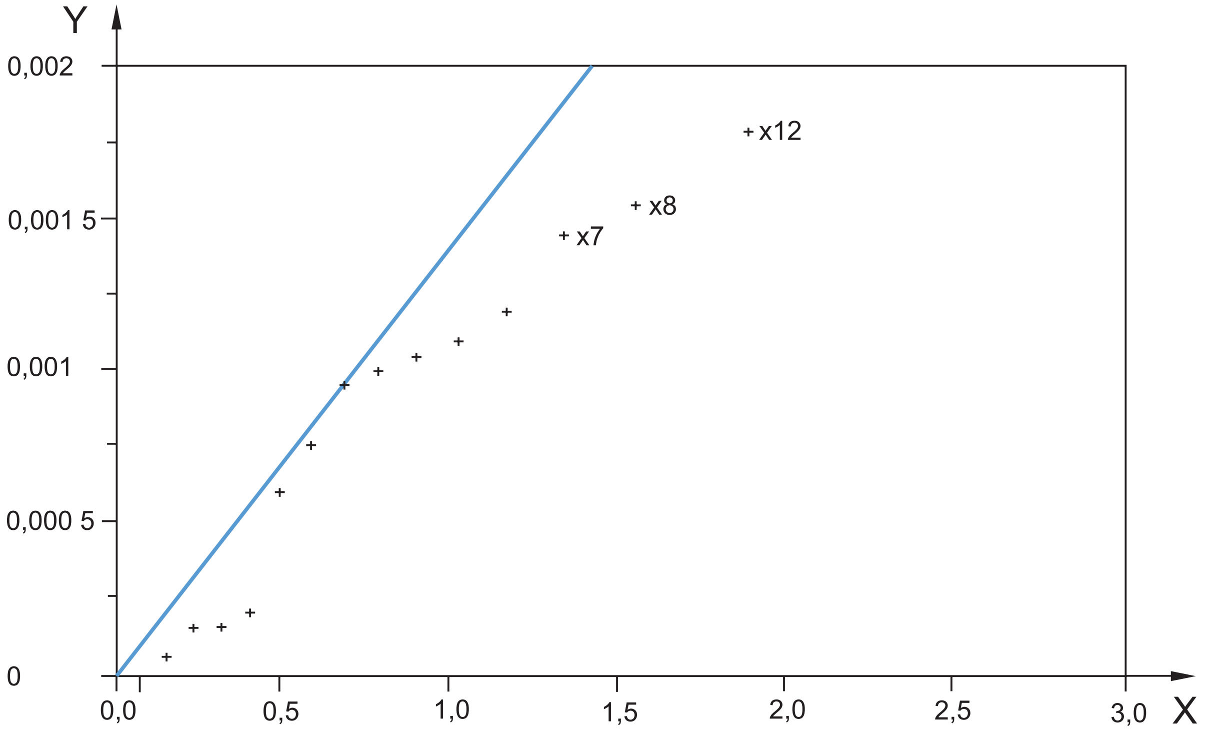
[15] JMP7 is the trade name of a product supplied by SAS Institute Inc. This information is given for the convenience of users of this Technical Report and does not constitute an endorsement by ISO of the product named.



Key

X normal quantile

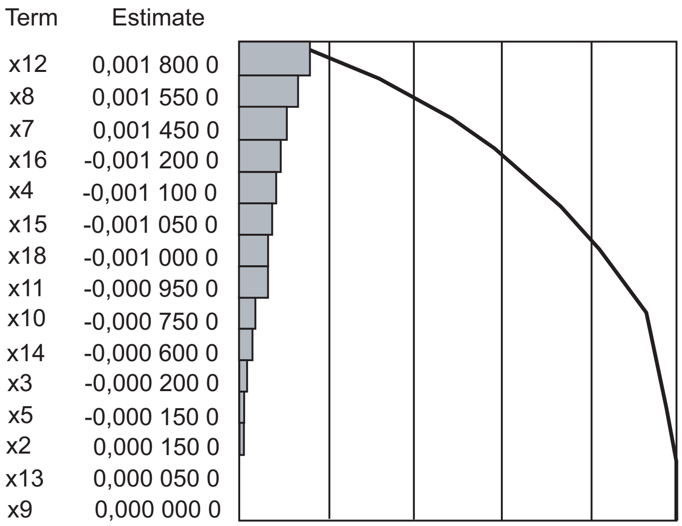
Y estimate

NOTE The blue line is Lenth's PSE, from the estimates population.

Figure F.1 — Half-normal plot

F.6.2 Pareto chart of effects

The same ranking of effects is observed in the Pareto plot given in Figure F.2.



Term	Estimate
x12	0,001 800 0
x8	0,001 550 0
x7	0,001 450 0
x16	-0,001 200 0
x4	-0,001 100 0
x15	-0,001 050 0
x18	-0,001 000 0
x11	-0,000 950 0
x10	-0,000 750 0
x14	-0,000 600 0
x3	-0,000 200 0
x5	-0,000 150 0
x2	0,000 150 0
x13	0,000 050 0
x9	0,000 000 0

Figure F.2 — Pareto plot of effects

The effects plot given in Figure F.3 provides an indication of the impacts of the three leading effects.

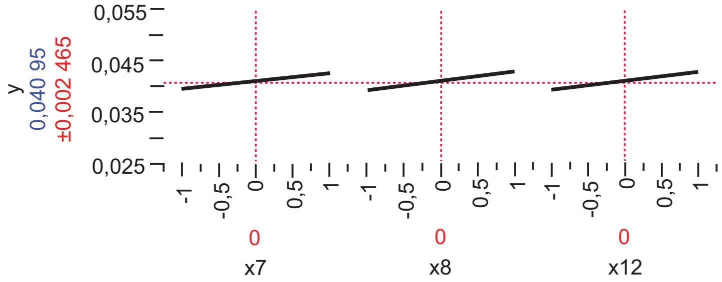


Figure F.3 — Estimation of the response as a function of the effects ×7, ×8, ×12

Each effect can be estimated by the average response for the effect at the high level minus the average response for the effect at the low level. The standard error of effects is obtained in the software using the usual regression framework (there are 24 degrees of freedom for estimating error in the combined analysis). The objective of the experiment was to identify the leading inhibitors of the aggregate growth which diminishes the interest in the statistical significance aspects.

F.7 Presentation of findings

Three factors were identified for subsequent use in optimizing the conditions present in the medium for culturing the bacterium. Estimates of the effects can be carried out individually on each of the 20 original runs and the 20 fold-over runs. These produced different combinations of leading factors which is attributable to the presence of interactions. By folding over the original design and combining the results, a resolution IV design was achieved which gave main effects clear of two-way interactions. A follow-up response surface experiment built upon the lessons learned in the screening experiment.

F.8 Comments on design choice

As originally described, the experimenters focused on screening 18 factors which were potential inhibitors of aggregate growth of shipworm bacterium. The 20-run Plackett-Burman design is excellent for this circumstance. Recognizing the potential impact of aliasing of main effects with two-way interactions, they chose to augment the original 20 runs with the 20-run fold-over set of runs, yielding a resolution IV design.

In executing the design, the experimenters chose to fix three of the original 18 factors, so that only 15 variables were actually varied. Under this situation, an alternative design would have been the 32-run 2^{15-10} fractional factorial design which is resolution IV. Perhaps a greater level of sophistication is necessary to implement this alternative design.

In any event, to the credit of the experimenters, they were able to shepherd the resources to conduct a 40-run experiment that ultimately identified three factors contributing to the inhibition of aggregate growth of shipworm bacterium that subsequently were optimized to obtain improved biomass production. The Plackett-Burman experiments used are vastly superior to one-factor-at-a-time strategies or other haphazard approaches.

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