Particle Technology Series

Henk G. Merkus
Gabriel M.H. Meesters *Editors*

Particulate Products

Tailoring Properties for Optimal Performance

Springer

Particulate Products

Particle Technology Series

Volume 19

Many materials exist in the form of a disperse system, for example powders, pastes, slurries, emulsions and aerosols, with size ranging from granular all the way down to the nanoscale. The study of such systems necessarily underlies many technologies/products and it can be regarded as a separate subject concerned with the manufacture, characterization and manipulation of such systems. The series does not aspire to define and confine the subject without duplication, but rather to provide a good home for any book which has a contribution to make to the record of both the theory and applications of the subject. We hope that engineers and scientists who concern themselves with disperse systems will use these books and that those who become expert will contribute further to the series.

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ISSN 1567-827X
ISBN 978-3-319-00713-7 ISBN 978-3-319-00714-4 (eBook)
DOI 10.1007/978-3-319-00714-4
Springer Cham Heidelberg New York Dordrecht London

Library of Congress Control Number: 2013954059

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

For a long time, chemical engineering focused on the characterization, understanding, and designing of chemical processes for the manufacture of commodity chemicals. These processes typically contain several unit operations, which are continuously operated. The products generally consist of a single phase and their quality is usually defined in terms of, e.g., purity, hardness, calorific value, boiling point/range, and/or melting point/range. Typical examples are processes in the oil industry for production of gasoline, etc. As a result of the extensive chemical research in the twentieth century, knowledge and understanding of the general relationships between chemical structure of components and their properties significantly improved, and more complex products arose by formulation with different ingredients, each of which serving specific performance goals. A good example is the development of detergents from classical soaps via synthetic detergents and powders to detergent pearls, containing active material, enzymes, whiteners, etc.

Gradually, the focus changed to consumer products, often produced in batch processes, and product complexity increased through the presence of different phases. Also, particulate materials were more and more incorporated in these products. Nowadays, particulate products make up about 80 % of all chemical products. Here, performance properties no longer solely depend on chemical composition and structure but also on particle size, size distribution, and particle shape (and resulting microstructures). Although the field of particle technology has existed for several decades, in which several basic principles have been elucidated and many instrumental measurement techniques developed, it still offers many major challenges. Catalysts are a good example. Particulate properties, such as size, pore structure, and surface area, not only influence activity (reaction rate) and selectivity (ability to form the desired product) but also mechanical strength (attrition), pressure drop, deactivation, and regeneration possibilities. Concrete and paints are other examples, as can be seen in Chaps. 7, 12 and 13.

Consequently, good design of such products is not only science but also still an art. Besides knowledge and understanding of the basic relationships, a lot of creativity is required to combine component properties and technological capabilities into a commercial product that is desired or accepted by the market.

Design and development of these complex products is a complex process in itself. Thus, several books have been written on its basic principles as well as on how this process can be managed in an optimum manner. They typically contain some molecular structure – property relationships for chemical components and some historic cases of product innovation in addition to a general management scheme. However, very limited insight is given so far for particulate products.

Therefore, we invited experts in different product fields to write a chapter in this book that presents the state of the art for each specific type of complex particulate product. We are very pleased that many of them accepted this invitation and indebted for their contribution in which they share their experience. Their names and background has been listed separately. We hope and trust that the leads in one product field will promote advances in other fields.

Henk G. Merkus
Gabriel M.H. Meesters

Acknowledgment

The editors gratefully acknowledge Mr. Maurice Wedd for his contribution to clear English texts in this book.

Contents

Author Information

Dr. M. Cristina Bonferoni graduated in 1984 in chemistry and pharmaceutical Technology, in 1991 followed by a Ph.D. degree. She became assistant professor in 1993 and is associate professor since 2001. Her research interests concern preformulation and formulation of conventional and especially of controlled release formulations. Early work involved the characterization of hydrophilic polymers used in oral matrix tablets. Swelling/erosion and diffusion/dissolution processes involved in hydrophilic matrices have been studied. Rheological measurements (viscosity and viscoelasticity) under different conditions of pH and ionic strength were related to the performance of the polymer in hydrophilic matrices. Dr. Bonferoni's study of the rheological properties of mucoadhesive interface has contributed to the understanding of the mechanism of adhesion and the rationale choice of mucoadhesive polymers. Polymeric micelles for topical administration of poorly soluble drugs and the development of polymeric vehicles for the delivery of hemoderivatives are her most recent research interests . Dr. Bonferoni's research work resulted in 140 papers in scientific journals, 11 book chapters, 6 patents, and more than 200 contributions to scientific meetings.

Prof. Dr. Carla M. Caramella is professor of pharmaceutical technology and biopharmacy at the Faculty of Pharmacy, University of Pavia, with teaching responsibilities both in undergraduate and Ph.D. programs. She has been responsible for the Erasmus/Socrates programs for the Faculty since 1998. She has served as dean of the Faculty of Pharmacy in the years 2003–2006. From 2002 to 2005 she has acted as Director of the Interuniversity Consortium TEFARCOInnova. She serves in the EAB of *European Journal of Pharmaceutical Sciences*, *Journal of Pharmaceutical Sciences*, *Pharmaceutical Development and Technology*, *AAPS PharmSciTech*, *Journal of Drug Delivery Science and Technology* and *Journal of Drug Delivery*. She has been appointed as an expert by the Italian Agency for Medicines for the European Directorate of Quality of Medicines (Certification Division) and for EMA. In 2001, she was elected AAPS Fellow. She has been awarded by AFI (Association of Industrial Pharmacists) in 2002, in 2004, and in 2010 for her cooperation with the Association in the organization of scientific

events. In 2008, she became the first recipient of the prestigious "Ralph Shangraw Memorial Prize" created by the IPEC America Foundation. She has been the principal investigator of research project funded by the Italian Ministry of Education, by bank foundations, and by regional institutions. Her research interests are in the field of biopharmaceutics and drug formulation, including preformulation studies and controlled release dosage forms. Her present research interests are focused on the therapy of mucosal and skin disorders. She has published about 180 papers in journals, has co-authored 5 book chapters and 13 patents.

Dr. Menno B. Claase received his master's degree in chemistry with honors at the University of Nijmegen. Subsequently he worked in the Polymer Chemistry and Biomaterials Group of Professor Jan Feijen at the University Twente, where he received his Ph.D. in 2004.

Immediately after, he started as head of R&D at BYK-Cera, Deventer, the Netherlands. There he was responsible for the development of wax additives for the coating and printing ink industry, especially the development and upscaling of micronized waxes.

In March 2007, he started working for DSM Powder Coating Resins as R&D manager of the powder coating application laboratory. Currently he holds the position of R&D manager application, Powder, Can and Coil at DSM Coating Resins.

Dr. David Fairhurst is president of Colloid Consultants Ltd., a company that offers consulting services (from exploratory research projects through formulation and characterization to product production) in the fields of cosmetics, personal care and pharmaceutics, and in all general areas of emulsion and dispersion technology and the methods to characterize them.

Dr. Franca Ferrari has received her Pharm. Sci. degree in pharmaceutical chemistry and technology at the University of Pavia in 1981 and Ph.D. in pharmaceutical analysis and technology, at the same university, in 1984. She became assistant professor in 1984 and associate professor in 1998 at the School of Pharmacy, University of Pavia, where she is presently active both in undergraduate and graduate education. From 2002 to 2010 she has been the coordinator of the II level Masters Course in Preformulation, Pharmaceutical Development and Control of Medicines. Her scientific expertise is in the field of dosage form technology and biopharmaceutical implications and includes: study of tablet disintegrants and of disintegration process, characterization of hydrophilic polymers (swelling and water uptake phenomena), characterization of semisolids by means of viscosity and viscoelastic measurements, evaluation and study of mucoadhesion mechanisms, and evaluation and study of absorption enhancement mechanisms. Dr. Ferrari's current research projects are in the field of the design and evaluation of drug delivery systems and include buccal and vaginal semisolid (gels, in situ gelling systems) and solid (films, matrices) formulations, micro- and nanoparticulate systems for ophthalmic delivery, and sponge-like dressings for cutaneous and mucosal application. Her research work resulted in

128 contributions published in scientific journals, 4 patents, 12 book chapters, and 250 contributions to scientific meetings.

Dr. Huan He was born in Zhejiang Province, China. He was awarded his bachelor's and master's degrees in civil engineering with honors from Beijing University of Technology in 2002 and 2005, respectively. He got his Ph.D. from Delft University of Technology in the Netherlands in 2010. Then, he started to work as a postdoctoral fellow in Laboratory of Building Materials of GeMMe group of University of Liège in Belgium. Recently, he obtained a position at the College of Civil Engineering and Architecture of the Beijing University of Technology in China. His main interests include road and bridge engineering, characterization, and numerical modeling of concrete materials, supplementary cementitious materials, etc. He is a RILEM TC-SCM committee member and serves as a reviewer for several international journals such as *Cement and Concrete Research*, and *Image Analysis and Stereology*.

Dr. Stéphen L.A. Hennart is a French citizen from Normandy. He graduated from the National Institute for Applied Sciences in Rouen, France, with a chemical engineering degree and from the University of Rouen with a Master of Science degree in organic chemistry. He performed his thesis at the Department of Research and Development, DSM Food Specialties, Delft, the Netherlands, with the support of the Delft University of Technology and was co-funded by the Marie Curie actions of the European Commission and DSM Food Specialties BV. The main research topic of his thesis entitled "Sub-micron grinding of a food product" is the optimization of preservatives in food coatings by means of particle size reduction..

After graduating, Stephen worked as Product Application Specialist with DSM Food Specialties, specializing on food safety and food quality with focus on antibiotic residues in milk and dairy products. Three years later, he decided to change company and country and started as Global Product Manager for Veterinary Diagnostics within the Qiagen Group in Hilden, Germany. Simultaneously, he takes responsibility for ELISA and PCR assays for the detection of animal diseases and for business development in France and Latin America.

Anthony J. Hickey is a distinguished fellow (appointed June 2012) and a senior research pharmacologist at Research Triangle Institute. Dr. Hickey has more than 30 years of academic and research experience in pulmonary biology, aerosol physics, powder dynamics, pharmacokinetics and drug disposition, formulation design, and device development. Since joining RTI in 2011, he has conducted research related to pulmonary drug and vaccine delivery for tuberculosis treatment and therapy. Additionally, Dr. Hickey is an adjunct professor of biomedical engineering at the University of North Carolina at Chapel Hill School of Medicine, emeritus professor of molecular pharmaceutics at the University of North Carolina at Chapel Hill Eshelman School of Pharmacy, and founder and president of Cirrus Pharmaceuticals, Inc. He has received many awards and honors and is an active member of several professional societies and committees, including the American Association for the Advancement of Science, American Association for Aerosol

Research and the Society of Toxicology. He is a fellow of the Society of Biology, the American Association of Pharmaceutical Scientists and the American Association for the Advancement of Science. Dr. Hickey holds 17 patents and has authored numerous books, book chapters, and more than 160 journal articles.

Georgia K. Hinkley received a Bachelor of Science degree in biology and chemistry from Florida State University and is currently an Alumni Fellow with the Center for Environmental & Human Toxicology at the University of Florida. Her research focuses on factors influencing the agglomeration state of nanomaterials in the body and the effect of agglomeration on bioavailability. Her research also includes study of the maternal transfer and distribution of silver nanoparticles and its implications.

Dr. Saul M. Lemkowitz studied chemical engineering (B.Sc.) at Rutgers University in the United States. After working at Allied Chemical Europe in the Netherlands, he studied chemical engineering at Delft University of Technology (M.Sc., Ph.D.). He remained at Delft University, researching dust explosions and teaching explosion safety (later both with Prof. Hans Pasman). For almost 30 years, he has also taught explosion safety to industry. While formally retired, Dr. Lemkowitz still actively teaches at Delft University and to industry.

Dr. Gabriel M.H. Meesters has a B.Sc. and M.Sc. in chemical engineering with a major in BioProcessTechnology from the Delft University of Technology. He also has a Ph.D. in particle technology also from the same university. He worked at biotechnology companies like Gist-Brocades in the Netherlands, as well as for Genencor International and currently at DSM in research and development in the Netherlands. In all these functions he was working on formulation and product development. Since 1996, he has held a part-time position at the Delft University of Technology, as assistant professor at the faculty of Applied Sciences, first in the Particle Technology group, later the Nano-Structured Materials Group and currently in the Product and Process Engineering group. He has supervised over 15 Ph.D. students and more than 50 M.Sc. students. He has published around 60 refereed papers and holds around 15 patents and patent applications. He (co-)organized several international conferences in the field of particle technology and was president of the World Congress on Particle Technology in 2010.

Drs. Henk G. Merkus graduated in physical organic chemistry at the University of Amsterdam. He worked several years at the Royal Dutch Shell Laboratories in Amsterdam on research in the field of detergents and industrial chemicals, followed by development work on thermal wax cracking for production of $C_2 - C_{14}$ olefins and on acid-catalyzed synthesis of carboxylic acids from $C_3 - C_6$ olefins. Then, he made the change to analytical chemistry, involving both measurements and method development with a large variety of techniques and methods, first at Shell's process development department and later in the chemical engineering department of Delft University of Technology. Gradually, his analytical horizon widened: first surface area and porosity measurements were added to chemical analysis, later followed by particle size analysis. He is author of the book *Particle Size Measurements* (2009,

Springer) and many journal articles. Moreover, he participates in standardization activities regarding particle size measurement, both in the Dutch NEN and the ISO.

Dr. Tosko A. Misev has received his B.Sc. in chemical technology and Ph.D. in polymer technology from the University of Cyril and Methodius in Skopje, Macedonia, and M.Sc. in polymer technology from the University of Zagreb in Croatia. He started as Resin Plant Chemist at the chemical and pharmaceutical industry Alkaloid and then joined the Resin Business Group of DSM in the Netherlands, where he held the positions of R&D Manager Powder Coating Resins and R&D Director of the Coating Resin Group and R&D Vice President of DSM Desotech in the USA, a world leader in radiation curing coatings for optical fibers. In 2004, he returned to the Netherlands for the position of R&D Director of DSM Coating Resins until his retirement in 2011. His scientific activities primarily focused on resins for powder coatings and resulted in one book on powder coatings, co-authorship on two other books on the same subject, more than 20 publications and conference papers, and 21 patents.

Dr. Makio Naito received B.Sc., M.Sc., and Ph.D. degrees in chemical engineering from Nagoya University, Japan, in 1980, 1982, and 1987, respectively. He was with Hosokawa Micron Corp. from 1982 to 1993 and engaged in the R&D of powder processing technology. He joined Japan Fine Ceramics Center (JFCC), Nagoya, Japan, in 1993, where he focused on powder characterization and powder processing technology in ceramics manufacturing. He was Vice Director of JFCC from 2000 to 2002, and then became a professor at the Joining and Welding Research Institute (JWRI), Osaka University, Japan, in 2002. He continued focusing on important studies on innovative powder and nanoparticle processing to develop advanced materials about energy and environmental issues. He was promoted to be the Director of Smart Processing Research Center, JWRI in 2007, and is also the Vice Director of JWRI from 2009. In addition, he has served as a Director of Hosokawa Micron Corp. from 2005. His publications cover a wide range of studies in the fields related to the advanced materials. He has authored or coauthored more than 500 technical articles, including more than 200 refereed journal articles. He has contributed to 52 books including 13 books as an editor. He has received many awards, and is a Fellow of The American Ceramic Society.

Prof. Dr. Ir. Hans J. Pasman graduated in chemical technology in 1961 at the Delft University of Technology and received the degree of Doctor in Technical Sciences working for Shell in 1964. He joined the Netherlands Organization for Applied Research TNO and worked in analytical chemistry, thermal stability of substances and explosiveness and investigated industrial accidents. Later he initiated gas and dust explosion research, risk analysis, and in particular consequence analysis methodology and a whole variety of defense-related subjects such as test methods, operations research, and systems analysis. He went through the ranks of TNO as research coordinator, institute director, and director of marketing and programs. At the same time, he was active as chairman of the Loss Prevention Working Party of the European Federation of Chemical Engineering organizing

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Dr. Elke Scholten received her M.Sc. in physical and colloid chemistry from the University of Utrecht. She received a Ph.D. from Wageningen University, the Netherlands, where she focused on protein-polysaccharide mixtures and related interfacial phenomena. She then joined the Chemical Engineering group at MIT, USA, from 2006 to 2008, where she worked with spinning and spraying techniques to create fibers and coatings. Then, she joined AKZO Nobel as a research scientist where she worked in the field of waterborne paints. In 2009, she returned to Wageningen University, where she currently holds a position as assistant professor in the Food Physics group. She mainly focuses on physical phenomena in food products, with a special interest in emulsions, gels, and fracture phenomena. One of her interests is molecular gastronomy.

Prof. Dr. Piet Stroeven was employed at Delft University of Technology from 1963 until his retirement in 2002, in a broad range of concrete technologies. Since then, he still is active as guest professor in the same university. His research experience includes a wide variety of subjects within the concrete field, such as shell structures, damage mechanics, optical methods for stress analysis, quantitative image analysis, alternative binders, fiber-reinforced concrete, and discrete element method. He has been awarded by ACI/CANMET (2001) and Wroclaw University of Technology (1999), and is appointed as honorary professor at Beijing Jiaotong University (1997). He has written about 1000 publications in journals, books, conference papers, reports, and reviews.

Dr. Paul Vercoulen received a master's in chemical engineering at the Delft University of Technology followed by a Ph.D. in powder technology at the same university. He started his industrial career at DSM in the area of Fine Chemicals. He held various positions within R&D and New Business Development of different DSM businesses and is currently (since 2011) responsible for the R&D and Innovation efforts of the Powder, Can & Coil Coatings Resins unit of DSM, located in Zwolle, the Netherlands.

Dr. Zhen Xu obtained his Ph.D. in 2010 in the Eshelman School of Pharmacy, University of North Carolina. His doctoral research in Dr. Anthony Hickey's lab focused on dry powder aerosol formulations for the treatment of asthma, with an effort on elucidating the heterogeneous microparticle interactions in the solid-state, and achieving cost-effective formulation screening and performance prediction. He is currently a postdoctoral fellow in the School of Pharmacy, University of

Maryland, contributing in the field of aerosol device technologies, using valvedii holding chamber and facemask systems for pediatric pulmonary delivery. He also earned a M.S. degree in chemistry previously at Michigan State University, where he worked on small molecule drug design and synthesis from the structural richness of carbohydrates.

Chapter 1
Introduction

Henk G. Merkus and Gabriel M.H. Meesters

When you can measure what you are talking about, and express it in numbers, you know something of your subject.
But if you cannot measure it, when you cannot express it in numbers, your knowledge is of a meager and unsatisfactory kind.

Lord Kelvin.

Abstract There is a great variety of industrial particulate products. Quality and performance of such products as well as their production processing depend upon the characteristics of the particulate ingredients and of product processing. These characteristics should be selected with due care in direct relation to product quality aspects. Measured data should be capable to discriminate between different product qualities, and the measurement quality should be sufficient. The last decades have shown a vast expansion and differentiation of measurement techniques as well as strong improvement of their quality. The design and selection of optimum particle characteristics for a variety of commercial products is the subject of this book. Its goal is to improve future product development. This chapter gives an introduction on product types, relevance of particle characteristics for product performance, schemes and statistical tools for optimum product development and design, and preferred particle characteristics in relation to product quality.

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H.G. Merkus and G.M.H. Meesters (eds.), *Particulate Products: Tailoring Properties for Optimal Performance*, Particle Technology Series 19,
DOI 10.1007/978-3-319-00714-4_1,

1.1 Objective of This Book

Particulate products make up around 80 % of all chemical products. Particle characteristics play an essential role in their quality and performance. The design of such products is the subject of this book. It can be used for improving existing products as well as for designing new products. Often, particulate products are composed of several ingredients. The particulate ingredients are not only solid particles, but they include all entities that have a difference in phase with their surroundings. Thus, products for consideration include dry powder mixtures, suspensions, emulsions and creams (liquid droplets in an immiscible liquid), sprays (droplets in gas) and foams (gas bubbles in a liquid or a solid material), etc. The other ingredients in the final products serve goals related to consistency, stability, taste, smell, etc.

The main objective of this book is to guide optimum design of particle characteristics of particulate ingredients in commercial products in relation to the required performance characteristics, both during processing and for the final product. Such designs start with good identification of the various performance aspects and understanding of their relationships with particle characteristics, viz. particle size distributions (PSD), particle shape, porosity and/or zeta-potential. The choice of optimum characteristic parameters requires such knowledge, in relation to desired performance tasks as well as for adequate specifications of both ingredients and products. Since very little seems to be published on the basic parameter choices to be made for particulate products, we asked various experts to write a chapter on this subject for a variety of important particulate products. We trust that their views will provide the available insight in the different, essential characteristics of composed particulate products. Their texts clearly show the different approaches taken in different product areas. This may lead to better understanding of the challenges in all product fields.

A further requirement for good product quality is that the particle parameters can be measured with sufficient precision, sensitivity and resolution. In addition to the information given for the products, a separate Chap. 3 deals with some major techniques for measurement of the parameters. It includes the quality of sampling, dispersion and measurement.

In the next sections of this introductory chapter, the relevance of particle characteristics for product behavior and methods for product design and development are illustrated.

1.2 Relevance of Particle Characteristics for Product Quality

Product quality can be identified in different ways. A simple definition is "*Conformance to product specifications*". Such specifications, however, are far from always sufficient to cover all performance aspects. Also, broader definitions have been formulated, which can be combined in:

"*The totality of features and characteristics of a product that bear on its ability to satisfy stated or implied expectations, needs and requirements of*

Table 1.1 Examples of quality aspects caused by particle characteristics

Product stability and 'structure' in dispersions
Dissolution rate, reactivity
Drying rate, efficiency
Rheological properties of powders, emulsions and suspensions: powder flowability, dosability, fluidization, viscosity, (non-) Newtonian behavior
Air dispersability, inhalation possibility
Filtration rate, removal possibilities
Pharmaceutical efficacy and side effects
Safety, toxicity, dusting, explosion sensitivity/severity
Catalytic activity and selectivity
Concrete/ceramic strength
Taste, mouthfeel, skin feel
Gloss, hiding power, transparency
Abrasive/polishing quality
Packing density and product porosity

customers in exchange for monetary considerations". Features and characteristics depend on product type. Typical examples are: performance, reliability, safety, toxicity, medical effects, appearance, taste, nutritional properties, texture, shelf life, etc.

The general concept is nicely covered in the following poem ([25] plus a little extension):

Quality is . . . giving a customer what he wants today,
at a price he is pleased to pay,
at a cost we can contain,
again, and again, and again;
and when more desires develop for the future
giving him something even better tomorrow.

There is a large variety of commercial products that have a particulate nature or contain particulate ingredients. Different industries produce such products. Examples for simple products or ingredients are abrasives, coal, filter aids, pigments, sand and sugar. Examples for composed products are polishers, agro-products, ceramics, chocolate, concrete, emulsions (in both dilute and concentrated form, e.g. milk, margarine and sunscreen), ice cream, medical inhalers, paint (both powder coatings and suspensions), powders for pharmaceutical tablets, sprays, toners, etc. Their chemical composition and possible specific (crystal) structure are primarily responsible for the basic material properties, such as hardness, color, taste, solubility, efficacy and safety. Particle characteristics take a second position for product quality. They are involved in many quality aspects, as illustrated in Table 1.1. A third important effect often comes from structural effects in dispersions resulting from attractive or repulsive forces between particles.

Particulate ingredients are either produced through a process of *size reduction* (crushing/milling/breakage/attrition, spraying, emulsification, de-agglomeration) or *size enlargement* (precipitation, crystallisation, polymerisation,

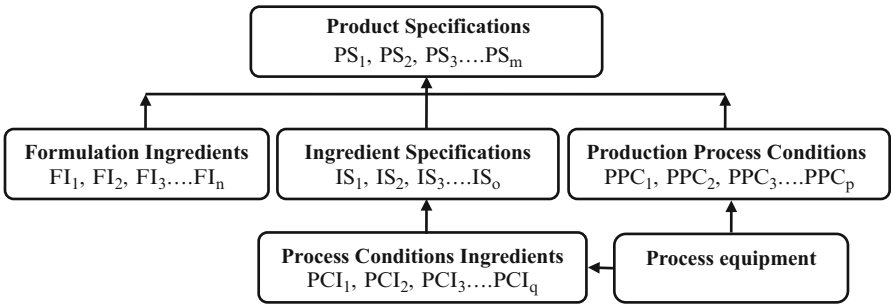

Fig. 1.1 Schematic of dependency of product specifications (*PS*) from formulation ingredients (*FI*), ingredient specifications (*IS*), process equipment, process conditions ingredients (*PCI*) and production process conditions (*PPC*)

compaction/granulation, extrusion, spray-drying). Often, a *classification* step in (hydro-) cyclones or by sieving/screening is integrated in the production process, for adequate control of the particle size distribution.

In order to obtain the desired quality at lowest possible costs, most products are formulated. This means that they contain several ingredients, each of which has a defined function or purpose, sometimes related to improved quality, sometimes to cost reduction. In addition to particles, there are e.g. wetting agents, flavoring agents and thickeners. Product quality and specifications are related to type, concentration and specifications of all ingredients as well as on (the control of) their production processes. Also, the choice of adequate process equipment is important. A general block scheme that relates the specifications of the end product to formulation ingredients, ingredient specifications, conditions of production processes and production equipment involved is given in Fig. 1.1.

Some of the general relationships between the quality of ingredients and product are known either from theory or from experimental results. Chapter 2 gives an overview of available relationships. For many products, however, adequate quantitative relationships are not (yet) available. There are several reasons for this lack of knowledge:

1. Particulate properties depend upon the chemical composition and (crystal) structure of the particles and, thus, upon their purity and route for preparation. Specific relationships are often required which may or may not be known.
2. Some ingredients cause synergistic or antagonistic effects within different product quality aspects, which complicates the relationships.
3. Some product properties are described in terms that do not yet allow an easy, direct translation to particle characteristics. Examples are sensory characteristics in ‘soft’ customer desires, e.g. ‘easy to swallow’, ‘mouthfeel’, ‘crispy’, ‘bite’, ‘creamy texture’ and ‘soft skin feeling’. Here, individual preferences and psychological factors play an important role in human perception.
4. The width of the PSD affects product properties. This is far from always incorporated in the PSD parameters chosen.
5. The results of size distributions of non-spherical particles may strongly depend on the technique used for determination. Also the product performance may

depend upon particle shape. Then again, application of a new ingredient or measurement technique causes that a new relationship has to be established.
6. Moreover, compromises must be found for particle characteristics in view of contradictory effects coming from different quality aspects or particle characteristics. Different products typically ask for different compromises.

Product specifications are meant to guarantee that product quality/performance corresponds to expectation. At present, many specifications seem to come from subjective judgment based on experience. To our opinion, only a (semi)quantitative (mathematical) model that accounts for all effects, gives an optimum basis for setting the specification. This applies equally to the design and specification of both single and composed products. This is a major challenge for the future.

1.3 Product Development and Design

At this moment, there seem to be three main lines for development of new, complex products, viz. Technology Push, Market Pull and Quality Function Deployment/ House of Quality [22, 32]. Their main differences are the driving force for the development of the new product and the way of organizing and planning the development activities.

Technology Push is the conventional method for product design. Typically, all activities are done by a single responsible person or a small expert team within the same company. It is often based on the skills of that person or team. The individual or team may or may not consult the marketing people, R&D experts, production engineers and/or others, to define and develop the best products for that company. This should be done in relation to the company's strategic goals, while taking into account available and newly developed technologies. Thus, it reflects the optimum possibilities for new products in the view of the producer company to serve the market. The iPad is an example of pushed products. Test panels may be used to assess product quality. In this method, strict rules for planning and development are not prescribed and, often, decisions are made implicitly. For products having clear performance requirements, the method is adequate, provided that the above weak points are addressed.

Market Pull is the opposite approach for product design. Here, some group of 'customers' requests for a product with new properties. Examples are low-calorific foods and the bicycle with electric support. Often, its basis is improvement of an existing product, based on customer desires. However, for many products customer desires are too often, poorly defined.

Quality Function Deployment (QFD) or its basic element, *House of Quality* (HOQ), is a fairly new approach. It offers a good compromise between Technology Push and Market Pull. A production company usually takes the initiative. A new aspect is that all activities for the development of a new product are explicitly described and planned. This includes collection of all customer desires, including 'soft' ones, and their translation into measurable characteristics. Typically, customer input has a (much) stronger influence on product development than in the

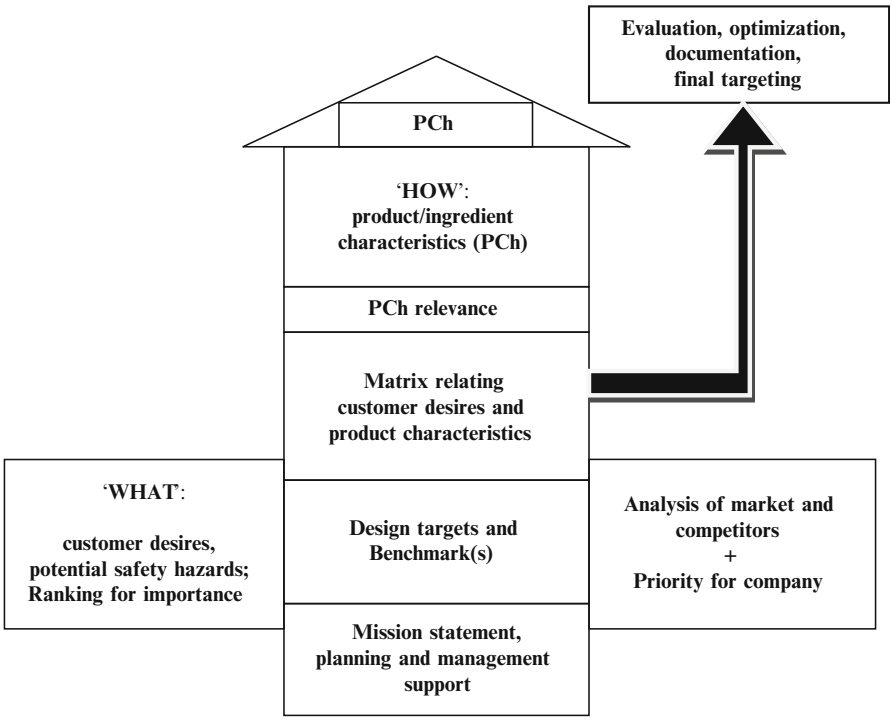

Fig. 1.2 Basic elements in House of Quality. (*PCh,* product characteristics)

Technology Push method [4, 5, 9, 11, 19, 21, 23, 27, 29, 31, 33]. In comparison to the Market Pull method, customer needs are more explicitly translated into measurable attributes. Consequently, it is useful in development of new products that the customer input as well as valuable chemical and engineering knowledge are combined. Note that different planning schemes are used, in relation to the type of product to be developed. A general scheme for the House of Quality method is presented in Fig. 1.2.

The basic steps are (for more details, see [9, 30]):

1. Prepare a clear, concise mission statement for the product and its development. This should include a short description of the product, its critical advantages over available products and its importance (priority) of the product for the producer company. The Mission statement should also include costs and the organization of the development, business goals for development time, profits and market share targets as well as assumptions and constraints related to the development.
2. Assure management support, plan all activities and set up a multi-functional expert team, in which as much expertise of colleagues as possible (marketing and R&D) is brought together for brainstorming, discussions, evaluation and decisions. Have a project leader appointed to lead the discussions effectively and to promote that planning schedules are met.

3. Collect information from potential customers on their qualitative desires (needs, wants and benefits) for the stated product through interviews of individual or groups of users/customers. Translate these into short 'quality tools' (the WHATs or NEEDS or Voice of the Customer). Make sure that the expert team defines these tools as clearly as possible. For interpretation and translation of 'soft' customer desires, product engineers and trained user panels may be helpful.
4. Identify potential hazards of both product and ingredients with respect to human and environmental safety and integrate these aspects in the group of customer needs.
5. Give a ranking to all customer needs in view of their importance and list them in order of importance (CN_1, CN_2, ..., CN_n). Three levels of ranking will generally suffice, e.g. 1 (low) – 3 (medium) – 9 (high) [9, 23, 26]; often these levels are indicated by specific symbols or colors to allow a rapid overview. Here too, trained user panels may be helpful.
6. Investigate and judge the market situation and competition. Select one or two (competitive or own) products to act as 'benchmarks' for quality.
7. Translate all customer desires, including 'soft' ones, and any hazards into measurable characteristic product parameters (the HOWs or Voice of the Company).
8. Investigate and describe the positive (synergistic) and negative (antagonistic) interrelationships between these characteristic product parameters and design trade-offs (in a matrix in the roof of the House).
9. Investigate and set up quantitative relationships between customer desires, potential hazards, importance for producer and characteristic parameters of product and/or ingredients and give them a weighting (in the central matrix, the Relationship Room).
10. Investigate the feasibility of (additional) ingredients and production processes to meet the desired characteristic product parameters and estimate the production costs.
11. Choose the best product and manufacturing process, and define the operational goals for the characteristic product parameters, both values and margins.
12. Evaluate the results in terms of potential, risks and regulatory issues for the producer company in the development team, and set targets. Address intellectual property in terms of patents and/or secrecy.
13. Define targets, benchmarks and specifications for product and/or ingredients and equipment and conditions for the production process.
14. Document all considerations and results well for eventual future use.

A major advantage of this approach is that it provides good planning opportunities as well as an objective overview of customer desires and market potential in relation to production possibilities and requirements. For example, the relation between 'soft' customer needs and product/ingredient characteristics, such as PSD parameters, is addressed explicitly. Another advantage is that it contains a weighting for priorities and costs. Hence, it provides a repository for product

planning information. However, full application of all aspects of Quality Function Deployment/House of Quality requires a lot of time and money, although mathematical procedures for effective judgment are available. Therefore, often only its basic concept is used to improve planning and analysis of product development as well as for reference in subjective judgments. Based on adequate knowledge and planning, QFD has proven in several fields of application (e.g. ships, electronics, cars and food) to decrease both cycle time and costs for product development, despite the substantial expert time needed initially for collection, discussion and translation of customer information [4, 5, 11, 23, 29].

The application of QFD can be extended through the sequential use of similar schemes for planning, process design, production and process control, in a Planning Matrix, a Design Matrix, a Manufacturing/Operating Matrix and a Control Matrix [9, 26, 29].

It should be noted that the present QFD schemes seem to be used primarily for improvement of existing products and not for development of highly innovative products. A reason may be that customer needs are not yet clear for such products and that production processes and/or product composition still have to be invented. Here, the Technology Push approach with an open mind for applications seems to be more appropriate.

QFD/HOQ design schemes are often rather abstract and seem to be mainly directed towards management. For the design and manufacture of our complex type of products, the core activities for chemists and engineers are expressed in the following ten-step template [12, 34]:

I. Prepare a clear, concise **mission statement** for the product and its development.
II. Identify **needs** for the envisaged product and translate them into measurable attributes and (preliminary) specifications.
III. Generate **product ideas** (ingredient characteristics, ingredients and products) that may satisfy these needs.
IV. Determine (or estimate) **quantitative relationships** between product performance parameters and product composition and ingredient characteristics.
V. **Select** the most promising product ideas, in relation to performance and quality as well as to potential safety hazards.
VI. Generate **ideas** for **manufacturing** processes of both ingredients and product.
VII. Investigate and set up **quantitative relationships** between product performance and the manufacturing process(es) and process conditions.
VIII. **Select** the best manufacturing process possibilities (batch/continuous, flow sheet, equipment and operating conditions), in relation to both least complexity and costs.
IX. **Evaluate** most promising ideas and **select** the best combination of product and process, plus final specifications and process control parameters.
X. **Set up** equipment and **prepare** a test portion of the product.

A review for the management can be envisaged to get support and to enable a go/no-go decision for the next steps, e.g. at the end of steps I, V, VIII and IX of this template. Then, also costs and human and environmental safety can be considered. The steps in this template fit well within the QFD scheme, but they are more explicitly defined. In step II, product users are interviewed and their needs are translated into measurable attributes and specifications. The emphasis in steps III to V rests on specialized chemists. On the basis of knowledge, experience, literature and experiments, they should select the most promising ingredients and products. The same holds for specialized engineers in steps VI to VIII for the manufacturing equipment and process conditions. Note that an existing plant may be the starting point to ideas for a new product line. Optimum decisions in step IX depend on the total group of chemists and engineers. Reference [34] provides examples and background for some creams and pastes. References [12, 22, 32] give numerous examples for a wide variety of chemical products, illustrating the choices to be made in the design steps. Scientific and empiric backgrounds are discussed as well as differences in the various steps for different types of products.

All approaches for design of composed chemical products show three similarities:

- They require basic data that are necessary for optimum design of the new product
- They require basic data that are necessary for optimum design of the manufacturing process
- They use similar ways for optimal application of these data in the design.

The basic product data are measurable, characteristic (particulate and other) features that relate best to assumed or expressed customer desires. For ingredients, they include the influence of wetting and stabilizing agents, fillers, viscosity improvers, taste enhancers, etc. Their basic relationships may come either from theory or from experiments. Chapter 2 gives examples of existing relationships.

The basic process data usually relate to equipment, such as crystallizers, emulsifiers, homogenizers, (colloid) mills, mixers and sterilizers, where the influence of mechanical forces, shear forces and cooling/heating dominate in the quality of the product.

1.4 Particle Characteristics for Product Quality and Process Control

Relevant particle characteristics for particulate product performance include aspects of the particle size distribution (PSD), particle shape, particulate concentration, porosity and/or zeta-potential. Sometimes, the relationship between performance and particle characteristics are known from theory or literature. Often, however, this is not the case and research is necessary to find both best characteristics and functional relationships [15]. Characteristic parameters are preferred when

their relationships with product quality and performance are based on both good correlation and understanding of their physical background. The parameters that are regarded essential must be laid down in specifications for ingredients and product, which are meant to distinguish good and poor products. Thus, they should correlate well with product quality and have adequate measurement possibilities. Note that redundancy of specifications may lead to unnecessary costs for measurement and contradictory results for quality. For control of the production process, sometimes, alternative parameters are used in relation to process parameters. The relevant size parameters depend on the product as well as on the precision with which they can be measured.

Following PSD parameters for particulate ingredients seem logical choices from the product point of view [20]:

- Mean size of the distribution, weighted according to number, area, volume, etc., depending on application and theoretical background. The mean value has the advantage that the contributions of *all* particles to the performance are taken into account.
- Size of the largest particle if this value is essential to product quality. Sometimes, the D_{90} or the fraction of particles larger than a stated size is used instead, in view of easier determination.[1]
- Fraction of particles smaller than a stated size (e.g. 45 μm) or the D_{10} if these smaller particles are essential to product quality[1].
- The width of the size distribution, in addition to one or some PSD parameters chosen, expressed as ratio D_{90}/D_{10}, D_{84}/D_{16} or the width parameter of a modeled distribution[1].
- Stated volume fractions in given size classes to minimize voids, e.g. in sand for concrete (see Chap. 7).

It is again remarked that particle size measurement of non-spherical particles, which are normal in industrial products, may yield distributions of equivalent sphere diameters that depend on the physical principle applied in the technique. Thus, different techniques generally yield different PSD results, the more so when the particles' aspect ratios significantly differ from 1 (for more information see Chap. 3). This weakens, of course, the physical basis for relationships between PSD characteristics and product performance aspects.

Note that PSD's are sometimes characterized by model equations, which contain a size location parameter as well as a distribution width parameter. Typical examples are: normal, log-normal, Rosin-Rammler (or Weibull) and Gaudin-Schumann distributions. Such model parameters, however, seem to be more useful for identification and explanation of particulate production processes and for process control purposes in existing equipment than for relating PSD parameters

[1] In all cases an indication has to be given for the type of weighting of the value, viz. by number, area or volume, etc. and for the measurement technique.

to product performance. For, often, real size distributions do not follow these equations over their full range.

Note further that the median (D_{50}) of a PSD is *not* suitable to qualify products, since it is a statistical parameter that has no basic relationship to product quality. For, it does neither reflect information about the width of the PSD nor about the presence of outlying particles, which may damage product quality. In combination with some other characteristic PSD parameters, however, the D_{50}[1] can be suitable for both process control and for testing measurement precision and bias of instruments with standard samples.

Particle shape characteristics may involve [20]:

- Macro-shape features, related to the 3-dimensional form of the particles, as expressed e.g. in aspect ratio
- Meso-shape features, related to the general aspects of roundness and angularity
- Micro-shape features, related to rugosity and smoothness as well as porosity and other structural heterogeneities.

At this moment, typical shape characterization concentrates on only one or two of the main shape features. Typical examples are aspect ratio, angularity, porosity and surface area. Also, modeling is sometimes used. Examples are (1) evaluation of the contours of two-dimensional particle projections in a so-called Fourier series, specific coefficients of which being used in correlation with specific performance features, and (2) expression in terms of fractal dimension [20]. So far, shape characteristics are mostly used for qualitative characterization of product performance. Only porosity features are used quantitatively.

For product specifications as well as process control, techniques and procedures for sampling, dispersion and measurement should be applied that have a known, fit-for-purpose quality. This means, for example, that both precision and sensitivity for the selected parameters must be adequate to distinguish between different product qualities. All procedures should be laid down in written form, for important products preferably in international standards (ISO, EN, ASTM, etc.). This simplifies international trade.

The following aspects should be addressed during development of particulate products:

1. Product composition, basic data and application(s)
2. Consumer desires for product quality and translation into measurable attributes
3. Potential hazards and regulations with respect to human and environmental safety
4. Critical behavior/performance aspects in quantitative terms for differentiation between good and poor products
5. Production process(es) and equipment used for ingredients and product, e.g. crystallization, (colloid) milling, mixing, polymerization, precipitation
6. Role of ingredients and/or production process conditions for product behavior/performance, in qualitative relationships as well as quantitative property functions for product and process(es)