Afrikanische Arzneipflanzen und Jagdgifte. Chemie, Pharmakologie, Toxicologie

Hans Dieter Neuwinger, Wissenschaftliche Verlagsgesellschaft mbH Stuttgart, Germany, 1998. 960 pp., DM 178.-; ISBN 3-8047-1550-8

With its detailed review of more than 270 common, but potentially toxic or medicinally interesting African plants, this book is outstanding in that it combines skilfully and concisely, in a single volume, a variety of information on the nature of these plants and on their use as hunting poisons.

The book is well organized and is divided into sections which deal with the respective plant families.

Each monograph covers a variety of subjects. The information includes both species and native name, habitat, a comprehensive botanical description of the plant and a study of its pharmacological and toxicological effects. The use of the plant as either a medication or as a hunting poison and the symptoms of the poisoning caused by the substance are described.

The monographs are illustrated by geographical and plant drawings and by structural formulae. Some beautiful plant pictures are also included.

A list of references is provided for each monograph and these should prove useful if more details on some specific subject were needed.

Furthermore, this book also includes several short but interesting chapters dealing with various topics such as larva poisons, poisons used for fishing and an impressive list of references on the traditional African medicines.

This book is a very good reference and should be recommended to medical practitioners, pharmacists, biologists, botanists and chemists. It deserves to be translated from German to English to ensure a wider distribution.

Fortunately, there are some people, who because of their passion, do not let knowledge such as this to be lost.

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Validation Fundamentals: How To, What To, When To Validate

William Gibson, Keith Powell-Evans (Editors), Interpharm Press, Buffalo Grove, IL, USA (1998)

The authors present a book which is intended to give an elementary introduction into the philosophy of validation as well as a guidance on how to do it.

In the first Chapter (pp. 1–36) 'What is validation?' validation is defined as 'the means by which the members of the pharmaceutical industry demonstrate to themselves, to governmental regulators and to the general public that they have taken, are taking and will take the best possible actions to secure the integrity of their products'. It is outlined that five validation categories are presently established: Process validation, Equipment and utilities validation, Computer validation, Analytical and Cleaning validation. A flow chart shows how each of these categories is broken down into the four qualification stages: Design Qualification (DQ), Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ). In further subchapters, the scope of the validation master plan as well as of the protocols of the various qualification stages is outlined.

Chapter two (pp. 37–50) gives a short overview on the history of validation. This summary is focused on the developments in the USA and the UK. With one exception, the contributions made by WHO or other European countries are not mentioned.

In Chapter 3, the following questions are raised: 'Why do we validate? How much does it cost?' The basic answer to the first question is given by the statement that 'the manufacturer is directed by GMPs and cGMP guidelines which he is bound to follow'. This is enforced by reference to the FDC Act, Section 401(a)(2)(B). The next statement however, 'Information on cost, efficiency and necessity are recorded in a familiar and understandable way' can not be deduced from the definition of validation given in the first chapter nor from the GMP or cGMP guidelines. It describes an often observed tendency of people involved in the validation business to penetrate all areas of pharmaceutical industry even if there is no direct link to the manufacture of drug products. The discussions on the cost of validation are not really helpful.

Chapter 4 deals with the question 'Who is responsible for Validation?'. A major role is assigned to the 'dedicated working party' which 'is convened to define, instigate, progress, collate, co-ordinate and, ultimately, approve the entire effort including all the documentation generated'. This working party includes preferably the following staff members: 'Head of quality assurance, Head of Engineering, Validation Manager, Production Manager' and Specialist validators from all areas. This team 'provides direction as well as controls the interdepartmental flow of information'.

In Chapter 5 the question is raised 'How does validation affect you?'. As already mentioned in Chapter 3 'only competent, qualified persons shall be active' in validation. 'This means trained personnel'. In Chapter 6 (pp. 79–97) 'Validation policy, Strategy Protocols and the Validation Report', the various issues mentioned in the headline are discussed at length. In addition, flow charts on protocol development, on the application of the validation process as well as on validation development conceptual activities are given. This information is completed by forms on the pages 1–4 of the validation report.

Chapter 7 (pp. 99–116) gives an answer to the question 'What Activities support the Validation Effort?' A series of

issues, all discussed in preceding chapters are already discussed in more detail. A flow chart shows how all these activities are tracked by the validation master plan. In Chapter 8 (pp. 105–110), all those who still might have reservations against the validation concepts outlined so far are informed about 'What are the Consequences of Not Validating?'. In Chapter 9 (pp. 111–116) 'For Whom Are We Validating?', we learn a little more on the C.V. of David Kessler and on the fact that a 'FDA inspector is a highly trained, overworked, little rewarded person who has the job of protecting the public from venal commercial interests of the major and minor drug companies'. Chapter 10 (pp. 117–150) teaches 'Preparing Standard Operating Procedures and the Validation Master Plan'. For this purpose forms of the first 8 pages of a SOP, two flow charts showing the Evolution of a Validation Master Plan (VMP) are given. In this context the different elements to be included into the VMP are discussed once more. Chapter 12 (pp. 151–156) is a Lexicon of Validation Terminology. In a series of Appendices (A–G) issues as 'Quality Control', 'Regulatory Approaches to GMP', the complex problem of 'Validation vs. Verification, Testing, Calibration and Qualification', 'The commitment to Validate', 'Validation vs. Verification', 'Revalidation and Requalification Studies' as well as 'ISO 9000 and Validation' are discussed.

It is not surprising that in a book of this kind the term 'quality' can be found on each page several times. However, it is surprising that nowhere in the book, a definition of the term 'quality' is given. Due to statements such as the following ones 'In-process materials shall be tested for identity, strength, **quality**, and purity as appropriate' (p. 25) or 'a drug product must be tested to ensure the safety, integrity, strength, performance and quality of the drug product' (p. 26). I am not sure whether the authors really know what 'quality' means. They define analytical validation as 'the evaluation of product quality attributes through testing' (p. 26). It is said nowhere who is defining quality, and at what stage of the product life cycle this has to happen. It is somehow remarkable that development is never mentioned in an entire book on validation. Product quality is not a product characteristic, per se, and therefore, it can not be tested for it. Product quality is defined by the extent to which predefined product quality attributes are realized. The list of performance related product quality attributes has to be defined for each drug product individually, in the course of its development. Reproduction related product quality attributes are defined partially by the different pharmacopoeias or again have to be defined during the upscale and transfer process of manufacturing into production.

In the development of a new testing procedure or of a new manufacturing process, validation has to be an integral part of the work and has to be performed by the same scientist. That is why we talk about good scientific practice or good manufacturing practice. In consequence, the validation life cycle begins at the moment when the decision to develop a new drug product is taken. User requirement specifications shall be defined as early as possible in the product development. However, in many cases, the final specifications can be defined only when the product development is almost completed. If process and analytical or equipment and utilities validation, is not performed on the basis of specifications and methods defined in the course of product and process development, there is a great danger that it turns into bureaucracy.

The book can be recommended to people who are experienced in drug product development. Without this experience the reader may get the impression that developing SOP's, protocols and reports is the most essential part in the development of a new drug product. Many of the flow charts are very helpful as a check list.

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Methods in Biotechnology (Natural Products Isolation, Vol. 4)
R.J.P. Cannell (Editor), Humana Press, Totowa, 1998. 479 pp., $89.50, ISBN 0-89603-362-7

Researchers from both industry and academia, present techniques for the extraction and isolation of natural products. The book is divided into 15 chapters. The first chapter, *How to Approach the Isolation of a Natural Product*, written by the editor himself, is an introduction to the natural products chemistry and to the principle of chromatography. Chapter 2, *Initial Extraction and Product Capture*, by F.P. Gailliot, is aimed at extraction of microbial fermentation broth and is divided into four sections that focus on laboratory-scale capture steps: solids removal, solvent extraction, solid phase extraction and expanded bed adsorption. Chapter 3, *Supercritical Fluid Methods*, by E. Venkat and S. Kothandaraman, is a broad overview of the use of supercritical fluid extraction (SFE) as a general extraction strategy. It also includes commercial applications of SFE of natural products. There are four chapters dealing with the isolation of natural products by chromatography. In Chapter 4, *Isolation by Low-Pressure Column Chromatography*, written by G.M. Salitburo and C. Dufresne, retention mechanisms are described, the type of stationary phases and the approaches to selecting column operation. A practical guide to packing and developing a column, as well as practical examples are provided. Chapter 5, *Isolation by Ion-Exchange Methods*, by C. Dufresne, gives up-to-date information on this popular technique, frequently used for the isolation of natural products. A