S-L-1

Development of Drugs, Devices, and Drug-Device Combinations: Through the Eyes of the Regulator

presented to

The Korean Society of Applied Pharmacology
April 14, 1995

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DCRND Master Bibliography

Guidelines for Drug/Device Products

This document collects Center for Drug Evaluation and Research (CDER) and Center for Devices and Radiological Health (CDRH) guidance documents, citations to the primary literature, and other published and unpublished documents relevant to development and approval of drug/device combinations collected by the CDRH Division of Cardiovascular, Respiratory and Neurological Devices (DCRND). Since the Master Bibliography number represents an accession number, an alphabetical (by author) listing appears at the end of the document. Any citation marked with a *, is on file in the DCRND offices, 340B, in the Piccard Building (HFZ-450), 1390 Piccard Avenue, Rockville, MD 20850. All documents cited are in the public domain and most are available directly from the **Division of Small Manufacturers Assistance (DSMA)**, phone 800-638-2014 or 301-443-6597, fax 301-443-8818. Questions -- call Dan Spyker 301-594-2720, fax 301-594-3076, InterNet: DXS@FDADR.CDRH.FDA.GOV.

1.* US Congress (101st): Safe Medical Devices Act of 1990 (Public Law 101-629 - November 28, 1990) 104 STAT 4511-30 {DSMA order # 0025}

Abs: Amendment to the Federal Food, Drug and Cosmetic act to make improvements in the regulation of medical devices, and for other purposes. The 19 sections discuss device user facility reporting, distributor reporting, revision of 510(k) (substantial equivalence), reclassification, postmarketing surveillance, *et al.* (20 pages)

2.* USPHS DHHS FDA CDRH ODE: Reviewer guidance for computer controlled medical devices undergoing 510 (k) review. Office of Device Evaluation, Center for Device and Radiological Health, Food and Drug Administration, Rockville, MD. August 29, 1991.

Abs: Includes discussions of definition of level of concern, software development, review questions, and labeling. Discussions relate to both 510 (k) and PMA issues. Includes a glossary and a bibliography with 9 citations related to software engineering. (39 pages)

3.* USPHS DHHS FDA: Assignment of Agency Component for Review of Premarket Applications; Final Rule and Notice (21 CFR Part 3); Delegations of Authority and Organization; Office of the Commissioner and Center for Biologics Evaluation and Research, et al.; Final Rules (21 CFR Part 5). Federal Register, 56 (225) November 21, 1991: 58754-60.

Abs: Contains the regulations implementing some features of the Safe Medical Devices Act of 1990. This final rule puts in place the inter-center agreements between CDER and CDRH [10], CBER and CDRH [11], and CDER-CBER [12]. (20 pages)

4.* USPHS DHHS FDA CDRH: Closed loop blood pressure control device (P860035) Summary of Approval. Center for Drug Evaluation and Research, General Hospital, December 17, 1987.

Abs: Premarket approval application from IVAC Titrator Sodium Nitroprusside Closed Loop Module - Model 10K was approved for use in adult patients who require a nitroprusside infusion to control blood pressure following cardiovascular surgery. (15 pages)

5.* USPHS DHHS FDA CDRH: Summary of safety and effectiveness data for the Miles Laboratories Biostator Glucose Controller (P800032). Center for Drug Evaluation and Research, March 13, 1981.
Abs: This Glucose Controller was approved for short-term use (normally not more than 24 hours) to assist the physician in bringing the patient's blood glucose to the desired limits. (21 pages)

6.* Parnas DL, van Schouwen AJ, Kwan SP: Evaluation of safety critical software. Commun ACM 1990; 33(6): 636-48.
Abs: Researchers from Queens University in Kingston, Ontario, Canada outline methods and approaches for testing the reliability and trustworthiness of software including some of the crucial questions faced by software programmers and eventual users.(12 pages)

7.* Leveson NG: Software safety: Why, what, and how. Comp Surveys 1986; 18(2): 125-63.
Abs: This review from the computer scientists at University of California at Irvine gives an overview of software engineering, including definitions, analysis of modeling, design, human factors issues, hazard categorization, and hazard analyses. (39 pages)

8.* Blum BI: Software Engineering: A Holistic View; Oxford University Press, New York , August, 1991.
Abs: This book from the Applied Physics Laboratory at Johns Hopkins University is due to be published late in 1992 should be a state of the art update on software engineering. (Table of Contents 4 pages)

9.* CDER: DRAFT Guidance to manufacturers on the development of required postmarket surveillance study protocols under section 522(a) (1) of the Federal Food, Drug, and Cosmetic Act . Center for Devices and Radiological Health, Draft 1992.
Abs: Document provides general guidance to manufacturers on implications of the post-marketing surveillance required for devices. Primary variables studied are morbidity and mortality in the population in whom the device has been used. Includes an outline of the surveillance protocol, study design, and reporting requirements. (13 pages)

10.* USPHS DHHS FDA: Intercenter agreement between the Center for Drug Evaluation and Research and The Center for Devices and Radiological Health. Version DDAGR25. October 29, 1991. {DSMA order # 0524}
Abs: The intercenter agreement between CDER and CDRH guides the selection of a lead center and details the interaction between the centers. (14 pages)

11.* USPHS DHHS FDA: Intercenter agreement between the Center for Biologics Evaluation and Research and the Center for Devices and Radiological Health. October 31, 1991. {DSMA order # 0521}
Abs: Intercenter agreement between CBER and CDRH guides the selection of a lead center and details the interaction between the centers. (12 pages)

12.* USPHS DHHS FDA: Intercenter agreement between the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research. October 25, 1991.
Abs: Intercenter agreement between CBER and CDER guides the selection of a lead center and details the interaction between the centers. (20 pages)

13.* Raemer DB, Bushman A, Varvel JR, Philip BK, Johnson MD, Stein DA, Shafer SL: The prospective use of Population Pharmacokinetics in a computer-driven infusion system for alfentanil. Anesthesiology, 1990; 73 (1): 66-72.
Abs: Evaluated the accuracy of a set of previously determined population pharmacokinetic parameters for alfentanil using data from an earlier study in which the drug had been administered using a computer-controlled infusion pump (CCIP). Conclusion was that a reasonably reliable and accurate target serum concentration of alfentanil can be achieved using the parameters in the CCIP study.

14.* Varvel JR, Donoho DL, Shafer SL: Measuring the predictive performance of computer-controlled infusion pumps. Jour Pharmacokin and Biopharm, 1992; 20 (1): 63-94.
Abs: Four measures proposed to quantitate the performance of CCIPs: median absolute performance error (MDAPE), median performance error (MDPE), divergence, and wobble. Advantages over previous measures identified. These measures allow the quantitation of overall performance or to compare the performance of CCIPs which differ in general approach, pump mechanics, software algorithms or pharmacokinetic parameter sets.

15.* USDHHS PHS FDA: Investigational Device Exemptions, regulatory requirements for medical devices, HHS Publication FDA 89-4159, August, 1989. Division of Small Manufacturers Assistance, Office of Training and Assistance FDA, Rockville, MD 20857.
Abs: This is a description of the Investigational Device Exemption which permits devices to be shipped in interstate commerce for clinical investigation to determine their safety and effectiveness. Requires safeguards for humans who are subjects of investigation, maintenance of sound ethical standards, and procedures to assure development of reliable scientific data. Deals with procedures, rules and safeguards. (98 pages).

16.* USDHHS PHS FDA: Premarket approval (PMA) manual, HHS publication FDA 87-4214, August, 1991. Office of Device Evaluation, FDA, Rockville, MD 20857.
Abs: Articulates the procedures considered essential in reviewing Premarket Approval Applications (PMAs). Submission requirements for safety and effectiveness data and information, criteria concerning acceptance of foreign studies, and rules applicable to alternative submissions are detailed.

17.* USDHHS PHS FDA CDRH: Premarket Approval (PMA) Manual Supplement.Office of Training and Assistance, HHS Pub FDA 91-4245, August 1991. Division of Small Manufacturers Assistance, Center for Devices and Radiological Health, FDA, Rockville, MD 20857.
Abs: Supplements the 1986 PMA manual with guidance re: changes in compliance policy, procedural issues, and development of an adequate investigational plan. Does not deal with changes due to SMDA 90 changes. This document is pretty much packed full of goodies including: current GLP guidelines (Good Lab Practices), sections of protocol development and submissions by Richard Chiacchireini (HFZ-160, Biometrics), and a dozen of the ODE Guidance memos including Device Labeling. (87 pages)

18.* USDHHS PHS FDA : Premarket Notification: 510(k), Regulatory requirements for medical devices, HHS Publication FDA 90-4158, August, 1990. Division of Small Manufacturers Assistance, Office of Training and Assistance, FDA, Rockville, MD 20857.
Abs: Deals with responsibilities of manufacturers to adequately determine whether a proposed device change or modification requires 510(k) review by FDA. Defines the extent to which manufacturers must demonstrate adequate safety and effectiveness of new device as compared to marketed device. Also defines the premarketing notification process as it was intended to facilitate the placing of devices in the marketplace with a minimum of difficulty. (69 pages)

19.* CDRH ODE: ODE Guidance Memoranda (Blue Book), Publication # T92-2, March, 1992. Center for Device and Radiological Health, FDA, Rockville, MD 20857.
Abs: This volume collects the current ODE policies and procedures dealing with:PMA, 510(k), IDE, and Administrative issues. Current issue includes 51 memoranda. You should have a copy of the table of contents, 3 pages. Entire document = many pages.

20.* Shafer Steven L, MD: STANPUMP Manual, PAVAMC, Palo Atto, CA. May 10, 1991.
Abs: This 12 page manual outlines the capabilities and limitations of the PC-based program for driving an infusion pump (Harvard Pump 22 or IMED C2) to either a target plasma level or target effect site concentration. Steve's address is Anesthesiology Service (112A), PAVAMC, 3801 Miranda Avenue, Palo Alto, CA 94304; Office 415-852-3414, fax 415-852-3414, home 415-965-7450, cellular 415-722-7840.

21.* Bailey PL, Stanley TH: Package inserts and other dosage guidelines are especially useful with new analgesics and new analgesic delivery systems. Anesth Analg 1992; 75:873-5
Abs: Anesthesiologists from U of Utah say a few kind words about the package insert (label) for transdermal fentanyl (Duragesic).

22.* Miller L, Abou-Donia M, Rudd D, Samara B, Schmith V, Huffman C, Wargin W, RaymondR, Lai A, McRainey M, Hutson B, higgs M, Woolf J:: NDA Day: The approval of a neuromuscular blocking agent. J Clin Res Pharmacoepidemiol 1992; 6: 271-284.
Abs: The folks from Burroughs Wellcome comment on the changing FDA philosphy (PK/PD, Individualization of Dosage, Interactive NDAs) and their experience with the doxicurium NDA Day. They conclude thet "although the demands on the sponsor and the FDA are considerable, the NDA Day process represents an advance in the review process that results in the faster introduction of new drugs into the marketplace."

23.* Harter JG: New drug approval -- it's a whole new ball game. First Princeton Conference on Drug Development: Highlights of a Symposium. October 3-4, 1991: 29-32. Excerpta Medica, Amsterdam.
Abs: A brief description of the philosophy, structure and function of the Pilot Drug Evaluation Staff.

24.* Basaral M, Petre J: Recommendations for specifications and operator interface design for medical infusion pumps. Biomedical Instrumentation Technology 1992; Sept/Oct: 364-70.
Abs: Anesthesiologist & engineer from Case suggests the hardware and user interface design (including chapter 1 if the user manual) for general-purpose infusion pumps.

25. Shabot MM: Standardized acquisition of bedside data: the IEEE P1073 medical information bus, Int Clin Monit Comput 1986; 6: 197-204.

26. McKinley S, Cade JF, Siganporia R, Evans OM, Mason DG, Packer JS: Clinical evaluation of closed-loop control of blood pressure in seriously ill patients. Crit Care Med 1991; 19: 166-70.

27. Jannett TC, Kay GN, Sheppard LC: Automated administration of lidocaine for treatment of ventricular arrhythmias. Med Prog Technol 1990; 16: 53-9.

28.* Temple R, Witt A, et al: Final Report of the Committee for Clinical Review - Based on a review of Selected Medical Device Applications. Food and Drug Administration, Center for Drug Evaluation and Research, Rockville, MD. March 1993 {DSMA order # 0802}
Abs: An *ad hoc* group of clinical & statistical reviewers (n=13) formed at Commissioner's request reviewed selected pending and approved device applications (n-16). Findings include failure to utilize the most appropriate control, under powered, poor specification of patients entering studies, failure to define endpoints, and failure to use (consider) blinded evaluation. Recommendations included: earlier and greater interaction between reviewers & sponsors and better use of advisory committees in improving data quality.

29.* USPHS DHHS FDA: (21 CFR Part 820) Medical Devices; Current Good Manufacturing Practice (CGMP) Regulations; Proposed Revisions; Request for Comments; Proposed Rule. Federal Register 58 (224) November 23, 1993: 61952-86.
Abs: Modifies CGMP to replace "quality assurance program" with more comprehensive quality system requirements c/w ISO 9001 "Quality Systems Part I - Specification for Design/Development, Production, Installation, and Servicing" thereby integrating international quality system terminology into CGMP.

30.* World Medical Association: World Medical Association Declaration of Helsinki -- Recommendations guiding physicians in biomedical research involving human subjects. The World Medical Association, Inc., September 1989, 17.C, Original: English, Cedex, FRANCE, 4 pages.

Abs: The original version, adopted in Helsinki, Finland, June 1964, has been revised in 1975 in Tokyo. in 1983 in Venice, and this version in September 1989 in Hong Kong. Includes an introduction, Basic principles (12 points), Clinical Research (6 points), and Non-clinical Biomedical Research (4 points).

31.* Kessler DA, Feiden KL: Faster evaluation of vital drugs. Scientific American 1995; March: 48-54.

Abs: David compares the 6.6 year "Standard Approval Process" to 6.2 year EXPANDED ACCESS ("parallel Track" and "Treatment" IND", and the 4 year ACCELERATED PROCEDURES (:Approval Based on Surrogate Markers" and Telescoped Trials") with help from a medical writer Karyn Feiden and Bob Temple, David Feigal; Janet Woodcock, and Randy Wykoff.

32.* Gore A: From Red Tape to Results -- Creating a Government that Works Better & Costs Less -- Report of the National Performance Review. US Government Printing Office, Pittsburgh, PA, September 7, 1993 (revised September 10, 1993), 168 pages. see also Executive Summary, same date & title, 21 pages.

Abs: This is the report of the 6 month National Performance Review (NPR) begun 3/3/93 and using federal employees instead of outside consultants. Recommendations fall into 4 categories: (cutting red tape, putting customers first, empowering employees to get results, and cutting back to basics). See especially recommendations for DHHS (page 141), **Creating Quality Leadership & Management** (page 160), and **Transforming Organizational Structures** (page 160).. Available *via* InterNet: ACE.ESUSDA.GOV, then choose 4. Americans Communicating, then 8. National Performance Review. Also available from Superintendent of Documents, phone 202-783-3238, fax 202-512-2250

Guidelines for Drug/Device Products

Single Line Listing - Alphabetical by Author

21. Bailey PL, Stanley TH: Package inserts and other dosage guidelines.. Anesth Analg 1992; 75:873-5
24. Basaral M, Petre J: Recommendations for ..pumps. Biomedical Instrumentation Technology 1992
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29. USPHS DHHS FDA: (21 CFR Part 820) CGMP..Proposed Rule. Federal Register 58 1993
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14. Varvel JR,: Measuring performance, Journ Pharmacokin and Biopharm, 1992; 20 (1): 63-94.
30. World Medical Association: Declaration of Helsinki.. biomedical research involving human subjects. 1989