

A Proposal of a Reference Model for the Pharmaceutical PDP Management

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Abstract

This paper presents a reference model for pharmaceutical Product Development Process. The model was created founded on renowned methods as Concurrent Engineering, Stage Gates and Product Based Business. It was developed using legislation and information from interviews with professionals of Brazilian pharmaceutical companies. The developed model contemplates three macro stages and seven phases, embracing from business opportunity recognition to product market launching. The purpose of this article is to introduce the reference model for the pharmaceutical body, since it represents an improvement compared to the general product development models presented in the literature. The reference model is also important in the pharmaceutical academic field, as a didactic tool.

Keywords: pharmaceutical product development process, reference model, product development management

Introduction

Since the 1990's product development has been considered under a broader standpoint, in which the idea of development centered in technical activities was substituted by the concept of business supported by product development. This new concept has been called, afterwards, Product Development Process (PDP) (Clark and Fujimoto, 1991; Cooper, 1994; Cooper et al., 1999; Patterson and Fenoglio, 1999; Corso and Pavesi, 2000; Crawford and Benedetto, 2000).

The main reason for this change was the important role played by products and services innovation in companies' outcome concerning competitiveness. To survive in the market,

companies had to increase the pace at which they developed their products, launching them before their competitors. Therefore, along the last twenty-five years several product development approaches were proposed, supported by methods and tools (Clark and Wheelwright, 1992; Clark and Wheelwright, 1993; Cooper, 1994; Pahl and Beitz, 1996). Each of them has particularly contributed to the evolution of this knowledge area. Among the development approaches, outstanding those that are considered under the expression *Integrated Product Development* (IPD) as *Concurrent Engineering* (CE) (Prasad, 1997; Hartley, 1998); *Stage Gates methodology* (SG) (Cooper, 1994; O'Connor, 1994; Cooper, Edgett, Kleinschmidt, 1999); *Product Based Business* (PBB) (Crawford and Benedetto, 2000; Koufteros et al., 2002); and more recently the *Lean* (L); *Design for Six Sigma* (DfSS) and *Maturity Models* (MM) considered as new approaches for IPD (Rozenfeld et al., 2006). Andreasen and Hein (1987), Kormos (1998) and Lovejoy and Srinivasan (2002) discuss IPD as a separate methodology, but Rozenfeld, Forcellini, Toledo, Amaral, Alliprandini, Scalice and Silva (2006) group CE, SG and PBB as being Integrated Product Development expressions.

In the same decade 1960, NASA (National Aeronautics and Space Administration) and the US Department of Defense (DoD) have developed tools to improve Project Management (PM) activities and to enhance project success. They were compiled, afterwards, by PMI (Project Management Institute) in the renowned PMBoK (Project Management Base of Knowledge) (Casarotto Filho et al., 1999; Dinsmore, 1999; Verzuh, 2000; Gasnier, 2001; Kerzner, 2002; Heldman, 2003; Vieira, 2003; Xavier, 2005). Accordingly to Kerzner (2002), the tools mentioned in PMBoK have influenced the Product Development area and, inversely, the Product Development methodologies have influenced and supported the PM subject growth.

Global pharmaceutical corporations, even dominating large markets and presenting a typical very long lasting product development process, have adhered, in the 1990's decade, to the product speed development concept and have reduced their development cycles significantly, as it is mentioned in related literature. The two approaches adopted by them include new PDP management practices (Boogs et al., 1999; Getz and Bruin, 2000; Hunt et al., 1998) and special technology development, directed to new drug discovery, identification and test (Gobburu and Chen, 1996; Wermuth, 1996; Gieschke et al., 1997; Cavalla, 1998; Hall, 1998; Gordon and Kerwin, 1998; Moos, 1998; Balant and Gex-Fabry, 2000; Weinstein, 2000; Wechsler, 2001). The changes in the pharmaceutical field may be attributed to the expiration of many drug patents in the 1980's what boosted the 'generic product' development by competitors, a medicine that presents the same properties of the reference product, and therefore may be interchanged with it, but which presents lower prices.

The generic medicine production in Brazil has been encouraged by the government in year 2000, mainly viewing the AIDS drug cocktail price reduction. Nevertheless, the Brazilian pharmaceutical industry scenario is dominated by few large multinational

pharmaceutical companies, that produce most of the medicine consumed in the country, and a large number of national companies, that attend a smaller market slice, mainly producing copies of medicines developed previously by the larger companies ('me too' or 'similar' products which may not be interchangeable with reference products). The government incentive to generic medicine has been decisive to some Brazilian pharmaceutical companies, which have considerably grown in the last seven years. More precisely, in 2005 the generic sales were stable, but increased considerably from 2006 to 2007, what made Brazil to become the most important market in South America, and the 8th medicine sales market in the world (Nascimento, 2007).

In this context, the development and launching of generic products in a fast pace is decisive for competition. Some companies observed that the existence of a formal product development process might reinforce product development success. To formalize companies' PDP practices is a global tendency and product development reference models, in addition to PDP methodologies and PM tools, play an important role in such formalization.

For this reason, the main objective of this paper is to introduce and discuss a reference model for the pharmaceutical product development process, focused in generic products.

Reference Models

The difficulty in describing how a product development process proceeds has significant reflects in the way this process is managed. How can a manager preview, plan and control the work of a team if the components do not have a common language; a minimum global vision of the project development or a perception of the expected contribution that project will bring to the company? In this sense it is very important to model the company business processes and register them as documents, including the product development process. Such product development documentation permits that a large number of people access the reality described in it and will be useful to structure new product development projects. Therefore it is called reference model (Rozenfeld et al., 2006).

Reference models have evolved from mere representations of the problem solution cycle (analysis, synthesis, simulation, evaluation and decision), also named as 'basic project cycle', to the four phases engineering project representation, from Pahl and Beitz, in 1960 decade (that includes design specification, conceptual design, embodiment project and detail design), up to the third type, the PDP phase model. The last type is a broader representation, since it includes: the product development relationship with the corporate strategic planning (CSP); the marketing practices (from pre-development phase), which are necessary for client demand assessment; the product strategic planning; apart of the descriptions of 'product and process projects', that are part of the 'basic project cycle', mentioned previously in Pahl and Beitz model (Roozenburg and Eekels, 1995).

A reference model may assume several formats. Some of them represent only the activities that must be performed in product development; other models detail what

procedures and methods are supposed to be adopted; they may include the evaluation criteria and mention what literature has to be consulted in order to accomplish a specific activity. The model may be a manuscript, manual or even a graphical representation available in intranet (Rozenfeld et al., 2006). They may be classified in generic models which may be adopted by different production companies or specific models, which describe a particular type of product development, as the model proposed in this paper.

Research Method

This proposal consists in the development of a specific reference model for pharmaceutical product development whose architecture was supported by three sources: (i) the Brazilian pharmaceutical companies’ professionals experience acquisition and legislation review; (ii) the selection of ‘best product development practices’ from literature, and (iii) information from project management gathering. The following items present the description of how these sources were investigated and how they contributed to the reference model development.

The Brazilian pharmaceutical companies’ professionals experience and legislation

The Case Study in a multi-case analysis was the research method adopted in this paper (Eisenhard, 1989) for the model development and the Delphi Method (Baxter, 2000) adaptation for the model validation. The qualitative approach was used for data collection and it was performed in two interview blocks. The objective in the first interview block was gathering information for construction of the reference model. The objective in the second interview block was the validation of the reference model. The latest was performed with the purpose of submitting the reference model to pharmaceutical professional analysis in relation to performance and applicability in the field. Table 1 resumes the information from companies and interviewed professionals’ characteristics.

Table 1 – Companies’ sizes and interviewed professionals areas.

| First block interview characteristics Reference model construction | | | Second block interview characteristics Reference model validation | | |
|---|-------------------------------------|------------------------|--|--|---------------------------------------|
| Company Size | Medium | Large | Company size | Medium | Large |
| Interviewed professional area | | | Interviewed professional area | | |
| Marketing and sales, R&D, Quality, Production, Medicine Registration | Company 1 Company 2 Company 3 | Company 4 Company 5 | Marketing and sales, R&D, Quality, Production, Administration, Costs, IT, Medicine Registration , Logistics, Production Planning and Control | Company A Company B Company C Company D | Company E* Company F Company G* |
| ANVISA professional | Generic product referee | | | | |

IT (Information Technology); R&D (Research and Development); and *Multinational companies.

As described in Table 1, five national companies' professionals were interviewed in first block, from two large and two medium size companies, from the medicine and cosmetic fields. The selection criterion was the size of the companies, since small Brazilian pharmaceutical companies do not present, in general, a formal PDP nor develop generic medicines. The interviewed professional areas were those considered important for product development and it was respected the company development team or professional interview availability. A referee for generic product registration from ANVISA (*Agência Nacional de Vigilância Sanitária*), the Brazilian medicine registration body from the Government Health Ministry, was also interviewed for the reference model construction. Only one referee was interviewed in ANVISA, since the legislation information is of objective nature. The reference model was analyzed by professionals from seven companies, three large and four medium sizes (medicine, veterinary and cosmetic fields), concerning the model validation. The analysis was conducted in a collective approach inside each company, in which the interviewed group exchanged ideas and impressions about the model. The interviews lengths were two hours in average, in both blocks, and semi-structured questionnaires were used; their contents are presented in Table 2.

All interviews were recorded and, afterwards, submitted to transcription. The First block interviews were analyzed through internal comparison: between companies' information, and between the latest and the ANVISA referee information. The data gathered were important for construction of the reference model macro-phases and activities. The Second block interviews were analyzed through consensus ordination and importance ordination. Thus, the elements mentioned by the interviewed professionals about whom they agreed or disagreed were identified; as well as the model elements considered by them as interesting or object of concern. The elements mentioned by interviewed professionals from one company were compared with the opinion of interviewed professionals from

Table 2 – Questionnaires used in first block and second block interviews.

| Reference model construction questionnaire | Reference model validation questionnaire |
|---|--|
| Company questionnaire /interview steps | Company questionnaire /interview steps |
| (i) General information (company size, administrative structure, kind of product developed, market focus); (ii) Information from the development process (macro stages, phases, average development time, team, financial aspects); and (iii) Product registration difficulties and easiness, ANVISA x company relationship. | (i) General information (company size, administrative structure, kind of product developed, interviewed professionals skills and experience in product development); (ii) Reference model presentation (explanation about its characteristics, construction architecture and value); and (iii) Questions about resemblance between the reference model and the interviewed company's PDP (estimated similarity); opinion about observed failures or restrictions from the model. |
| ANVISA questionnaire | |
| (i) General information about the referee (experience time in ANVISA, experience as a referee for generic products dossiers); (ii) Information from generic products rules in pre-registration; registration and post registration stages; and (iii) Information from difficulties and easiness in ANVISA x companies relationship. | |

other companies, characterizing the internal comparison in Second block either. The data gathered in validation block interviews were important for changing, excluding or including activities in the reference model, or for reinforcing its value as a reference for generic product development in pharmaceutical companies.

The best product development practices from literature

The product development methods that support the reference model are Concurrent Engineering (CE), Stage Gates (SG) and Product Based Business (PBB). These theories, which are of the Integrated Product Development (IPD) methodologies type, have been adopted by companies and considered responsible for successful product development along the last years. The aspects of each approach that were integrated in the reference model will be presented.

Concurrent Engineering (CE) focuses in multidisciplinary teams, co-localized and simultaneous activities performance, mainly those that are independent. The physical co-localization of teams and multidisciplinary will depend on companies' culture, but the latest element is mandatory to development efficiency. Much rework may take place if the project of a new product is not simultaneously but, sequentially performed by organizational sector specialists. The application of tools and methods is important as IT (Information Technology); DfM (Design for Manufacturability); TQM (Total Quality Management); SPC (Statistical Process Control); DOE (Design of Experiments); QFD (Quality Function Deployment), among other methods and tool (Goldense, 1992; Hartley, 1998; Moffat, 1998; Kormos, 1998; Toni et al., 1999; Rozenfeld et al., 2006). Therefore, such tools were suggested in the reference model and may be observed in the detailed pictures of it (Paula, 2004).

Stage Gates (SG) is a methodology, which focuses in two aspects: business character of product development and product development process managerial control. The first aspect is guaranteed by the 'portfolio management methodology' that analyses what business-products the company is investing in. It is normally performed along Corporate Strategic Planning (CSP) implementation. Therefore the SWOT analysis tool (Strength, Weakness, Opportunity and Threats) may be present in this process phase. The process control aspect of SG is the phase transition evaluation/control which is systematically performed via process interruptions named 'gates'. The gates are generally located between important transition phases and they present a decision nature of process abortion; process modification or process maintenance. The gates may include control check lists that confirm the conclusion of the most important activities of that phase; although the document central managerial question is 'will the product development be continued in the next phase, changed or aborted?' The number of gates is a function of the risk level implicated in the product development process, but Cooper suggests six gates in his paper (Cooper, 1994; O'Connor, 1994; Cooper et al., 1999; Rozenfeld et al., 2006) that were incorporated in this reference model.

Product Based Business (PBB) is a methodology which reinforces the innovation mechanism, represented by two elements: the pair 'portfolio analysis-Corporate Strategic Planning' (from the strategic level) and by the activities of 'identification, selection and development of opportunities that were identified in the market' (from the tactical level). The business/company growth is a result of innovation in products or services since they must provide both, income and profit. The incomes from mature and new products maintain the innovation mechanism, since they may finance new market evaluation and technology acquisition. In this sense, a feedback mechanism is generated in terms of cash and information. The products must be followed after launch for all their lives (product life cycle management), and their performance in market must be measured. The information gathered from products feedbacks the development process for a new 'portfolio analysis-Corporate Strategic Planning' and the improvement cycle is maintained. In general, a Product Manager is the professional responsible for a specific class of product in the company (Paterson and Fenoglio, 1999; Crawford and Benedetto, 2000).

Summarizing, the IPD methodologies have in common the following best practices incorporated in the model: (i) a strong market orientation, based in the knowledge of clients demand; (ii) the practice of business opportunities screening, competitors benchmarking and portfolio management as support for decision in 'what projects to invest'; (iii) the practice of former technical, financial and economical analysis of projects, before product development; and (iv) the continuous analysis of products after launching, providing the feedback character of the PDP. The grouped practices (i) to (iii) form the Pre-Development Stage from product development process and the practice number (iv) outlines the Post Development Stage from this reference model. More details from the practices are presented in detailed version of the model (Paula, 2004).

Information from project management

The main contribution of Project Management (PM) methodology is its focus in project completeness. Some practices from PM have been proved to guarantee the completion and success of a project and they have been incorporated to the PDP, since product development is characterized as a project in an organization. In fact, a project is distinct from a routine activity, since it describes the performance of a group of activities which generate a unique product whose process presents start and conclusion proceedings, clearly executed in a period of time; i.e., a project is a temporary effort (PMBok, 2004).

The first effort in organizing a project is the thoroughly description of its scope. Most authors in PM indicate the use of WBS (Work Breakdown Structure) as an efficient tool for scope definition (Casarotto Filho et al., 1999; Dinsmore, 1999; Verzuh, 2000; Gasnier, 2001; Kerzner, 2002; Heldman, 2003; Vieira, 2003; PMBoK, 2004; Xavier, 2005). WBS is a hierarchical decomposition (top down flow chart) oriented to the project deliverables, including internal and external project products, aiming to reach project goals. This tool organizes the project global scope by its division in work packages that are decomposed

in activities. At the activity decomposition level it is finally possible to designate a person to execute it; to estimate performance duration for that activity; to calculate related costs and resources necessary for executing it and, as well, it is possible to define the activity control specification or the specification for its deliverable(s). Therefore, WBS is the first step of project planning, since it provides the base from which the project scope, time, human resources, cost, quality, risk and other plans derive. WBS may be presented as an indented list or in a graphic manner as it may be seen in Figure 1, which presents the first hierarchical level with nine resume tasks and task number 1 decomposed into work packages. These nine resume tasks and their decompositions are the information gathered from pharmaceutical professionals interviewed (their experience in Brazilian Pharmaceutical Companies) in addition to the best Product Development Practices, both mentioned in the items before. The nine resume tasks were decomposed in work packages that are represented in detailed pictures of the reference model in Paula (2004).

Besides WBS, project management methodologies recommend the use of matrices for human resources planning, in which the responsibilities for the project activities are established. Thus the team components have a clear vision of their and the others duties. Both WBS and an activity x responsibility matrix were used as elements for this pharmaceutical reference model construction and more details are available in Paula (2004). Aiming to control the PDP process, check lists were created for phase transition as recommended in Stage Gates and in PM. The gates in PM are called 'milestones', and differ from the first only by the fact that the milestones exist to call attention to an important fact inside project phase or between phases, not necessarily being a stop point for strategic decision, as to continue-or-abort the project, for instance. Therefore, the gates were adopted in this reference model, instead of milestones. Other tools from PM will not be discussed in this paper, although they may facilitate PDP implementation and management.

The Pharmaceutical Reference Model Presentation

The pharmaceutical reference model architecture developed from the sources mentioned before, presents three macro stages and seven phases, embracing from business opportunity recognition to product market launching. Figure 2 presents a general view of it.

Macro-stages, phases and organizational function structure

Figure 2 is an overview and its focus is the general aspects of the reference model, not the specific detailed work packages, presented in Paula (2004). The figure presents the three macro stages, seven phases, seven typical pharmaceutical organization functional sectors involved in PDP (grey flags on the left), six gates and phase work packages represented by internal boxes. The model is oriented from left to right, frontally fed by the Corporate Strategic Planning information, as recommended by IPD methodologies.

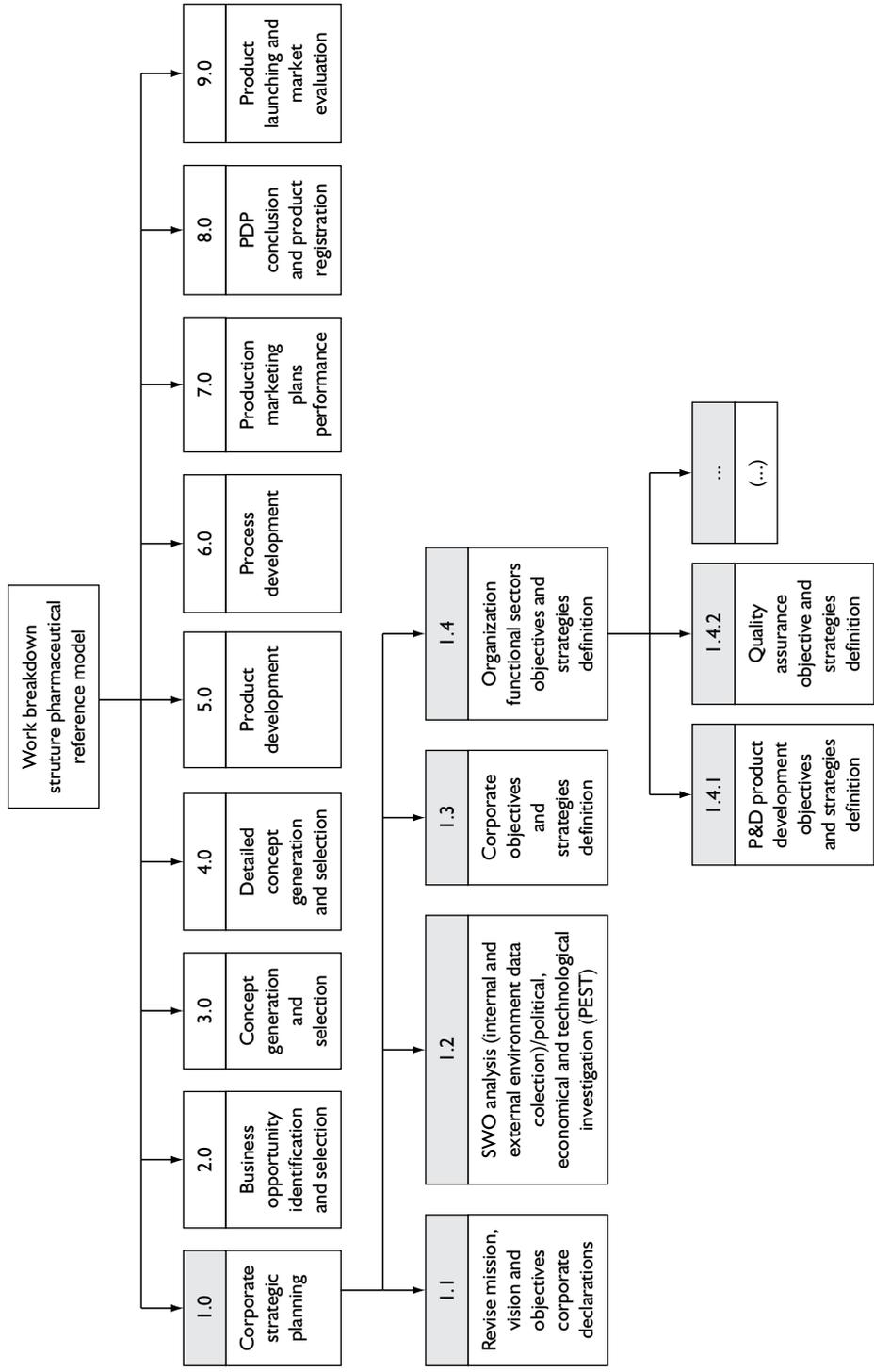
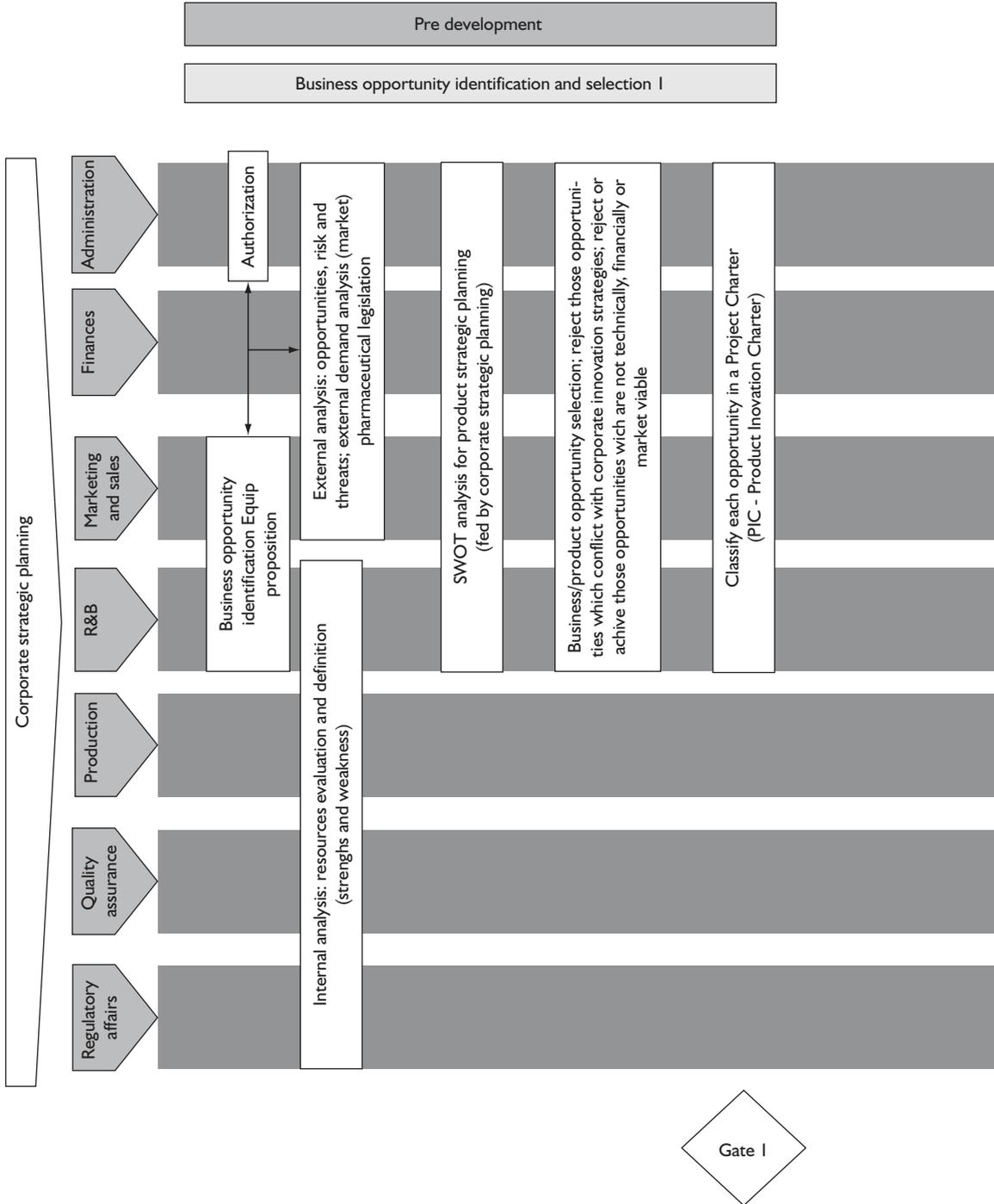


Figure 1 - Part of WBS from the pharmaceutical PDP reference model.



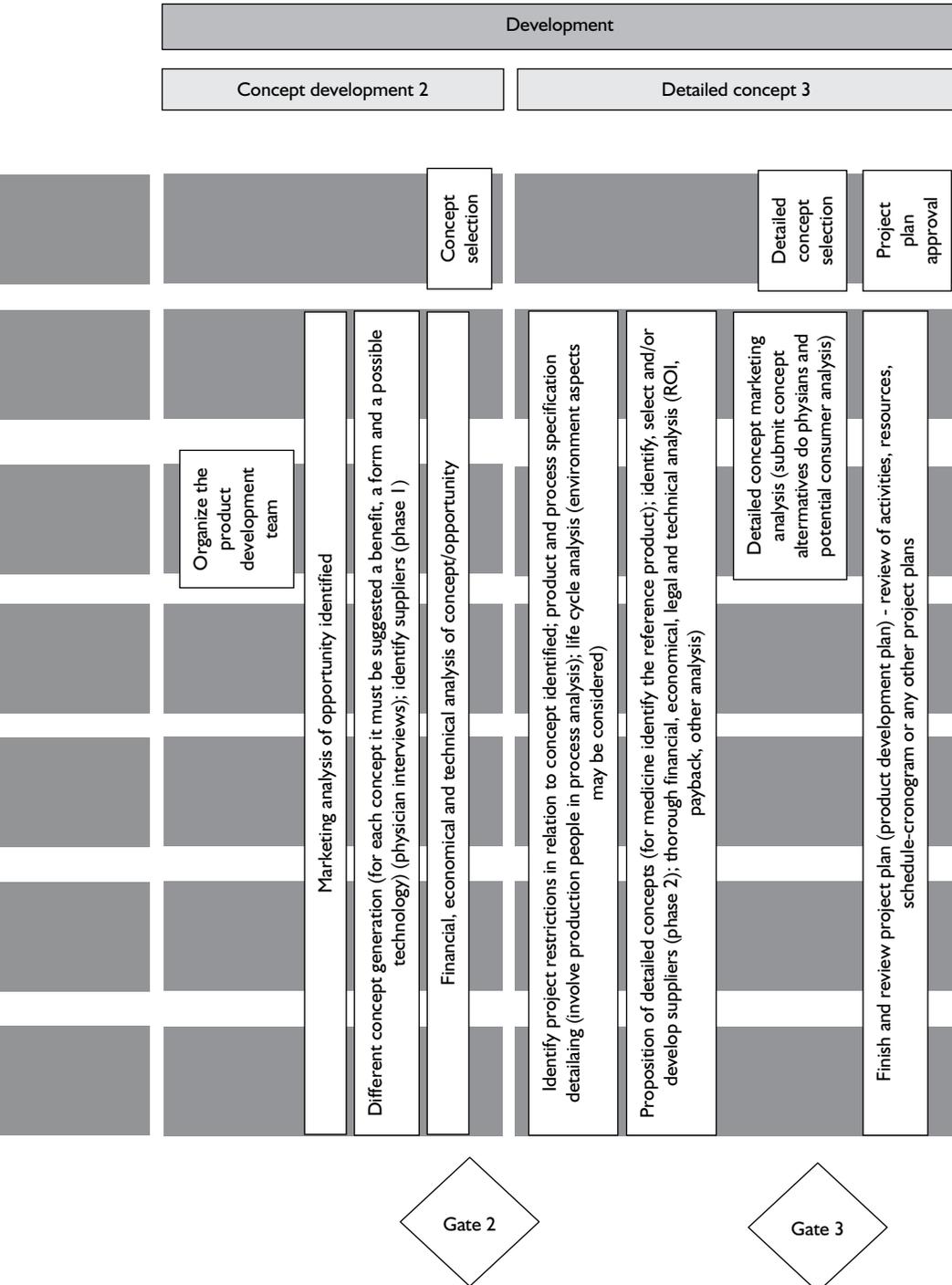
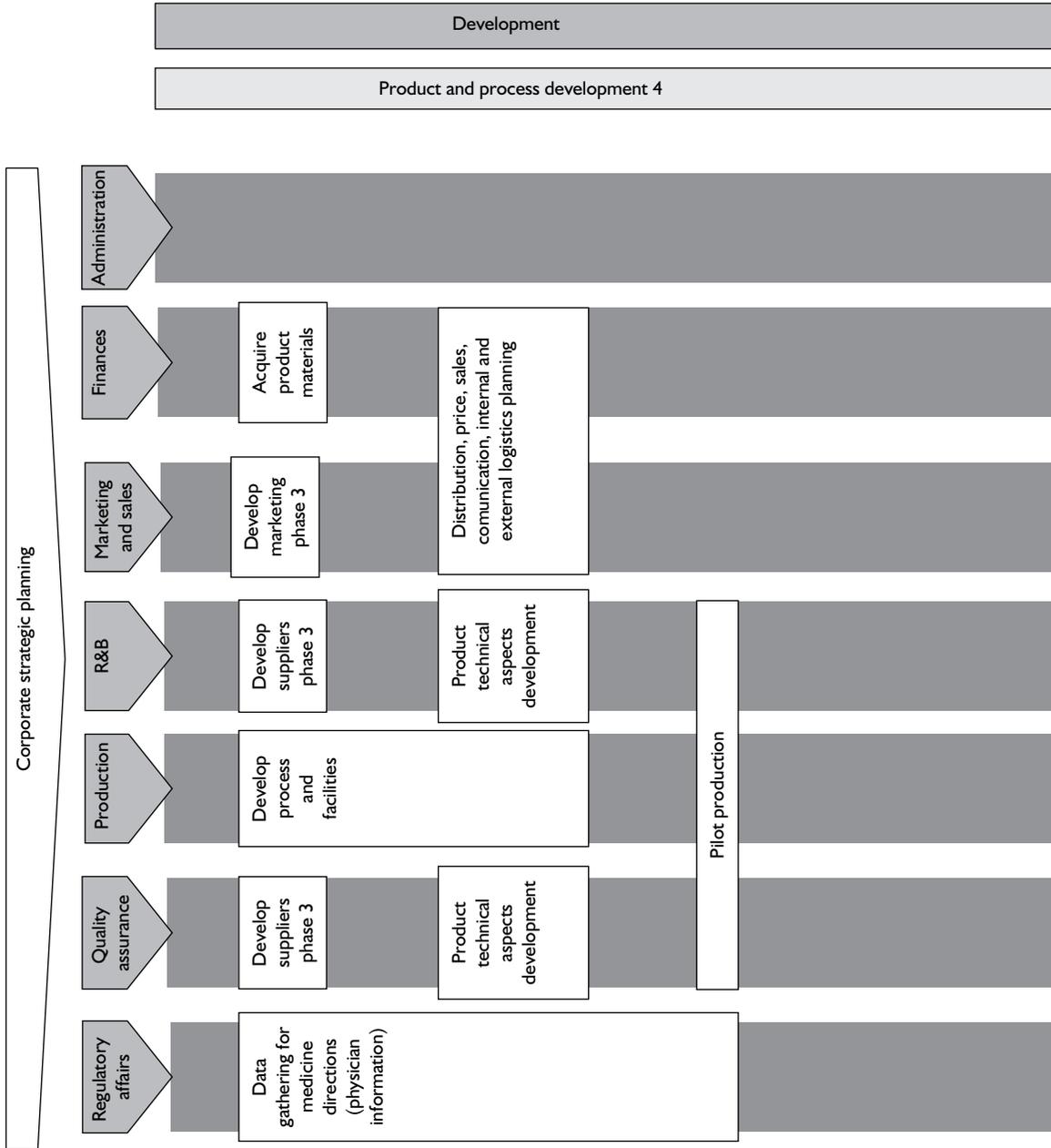


Figure 2 - Emphasis in general aspects: three macro stages (Pre-Development, Development and Post Development); seven phases (From Business opportunity identification and selection to Product Launching and market evaluation); team (horizontal dashed stripes under the white blocks) (white blocks represent work packages); and six gates between phases. Work packages are not emphasized in this figure (Source: adapted from Paula, 2004).



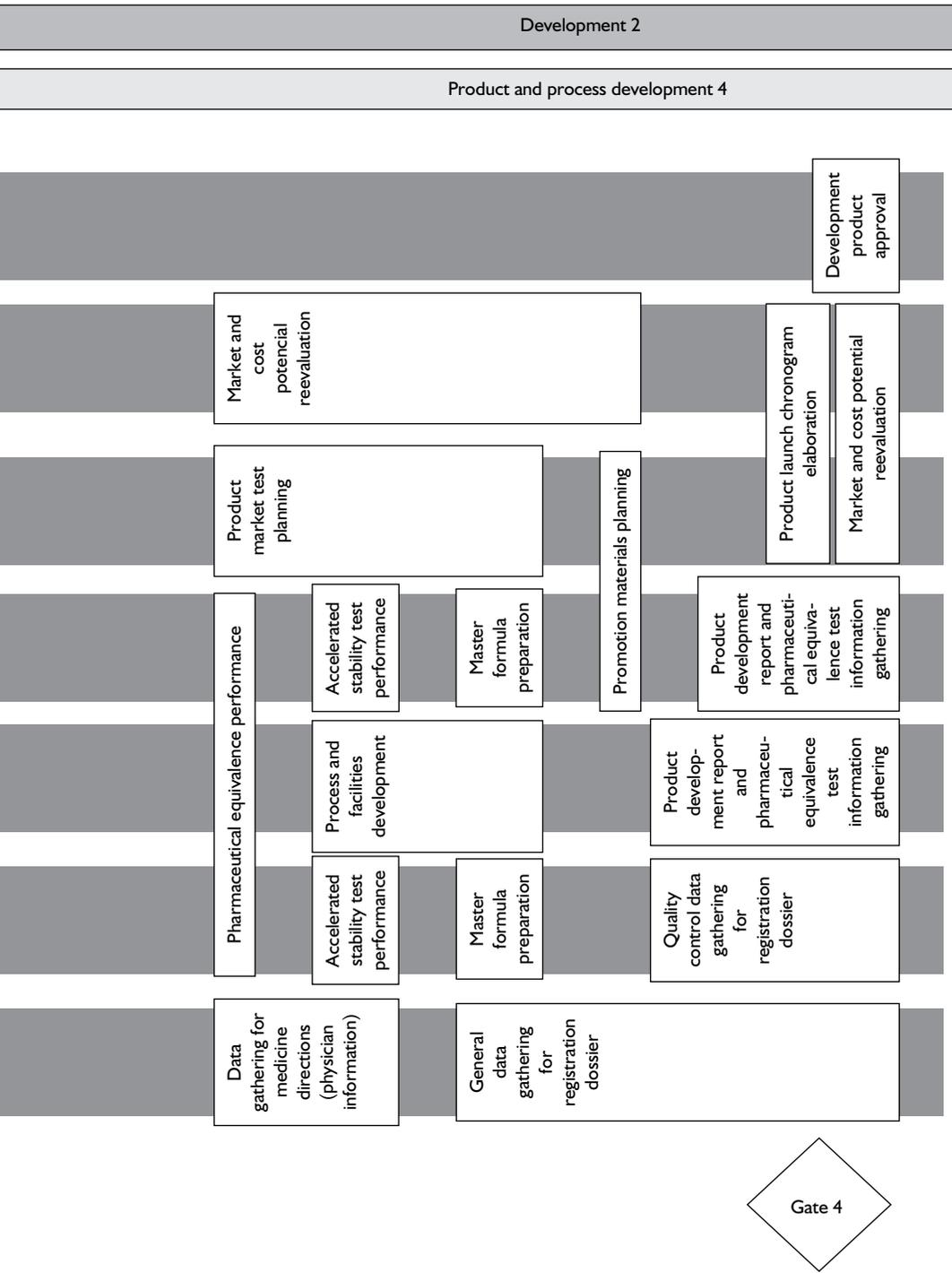
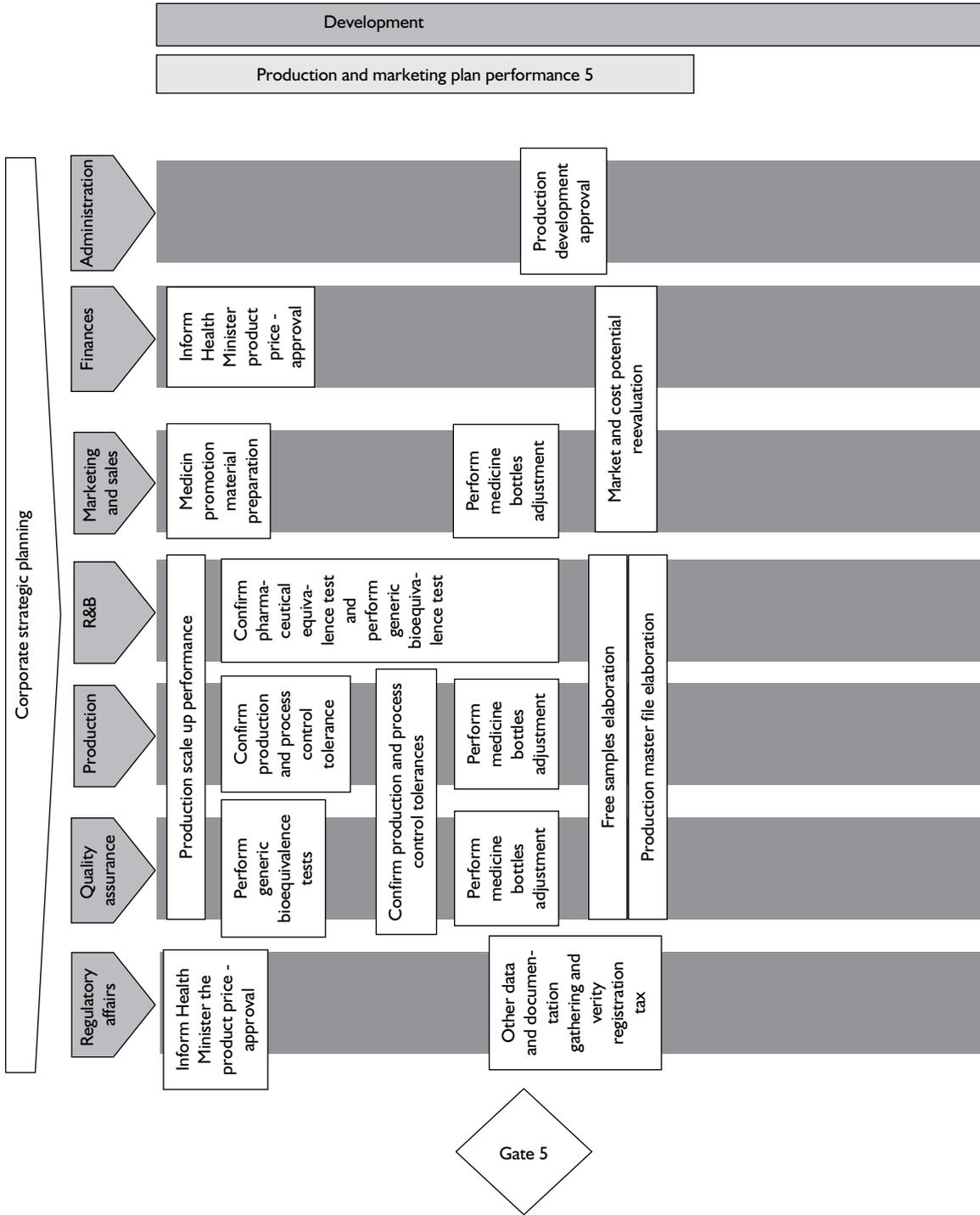


Figure 2 – Continued...



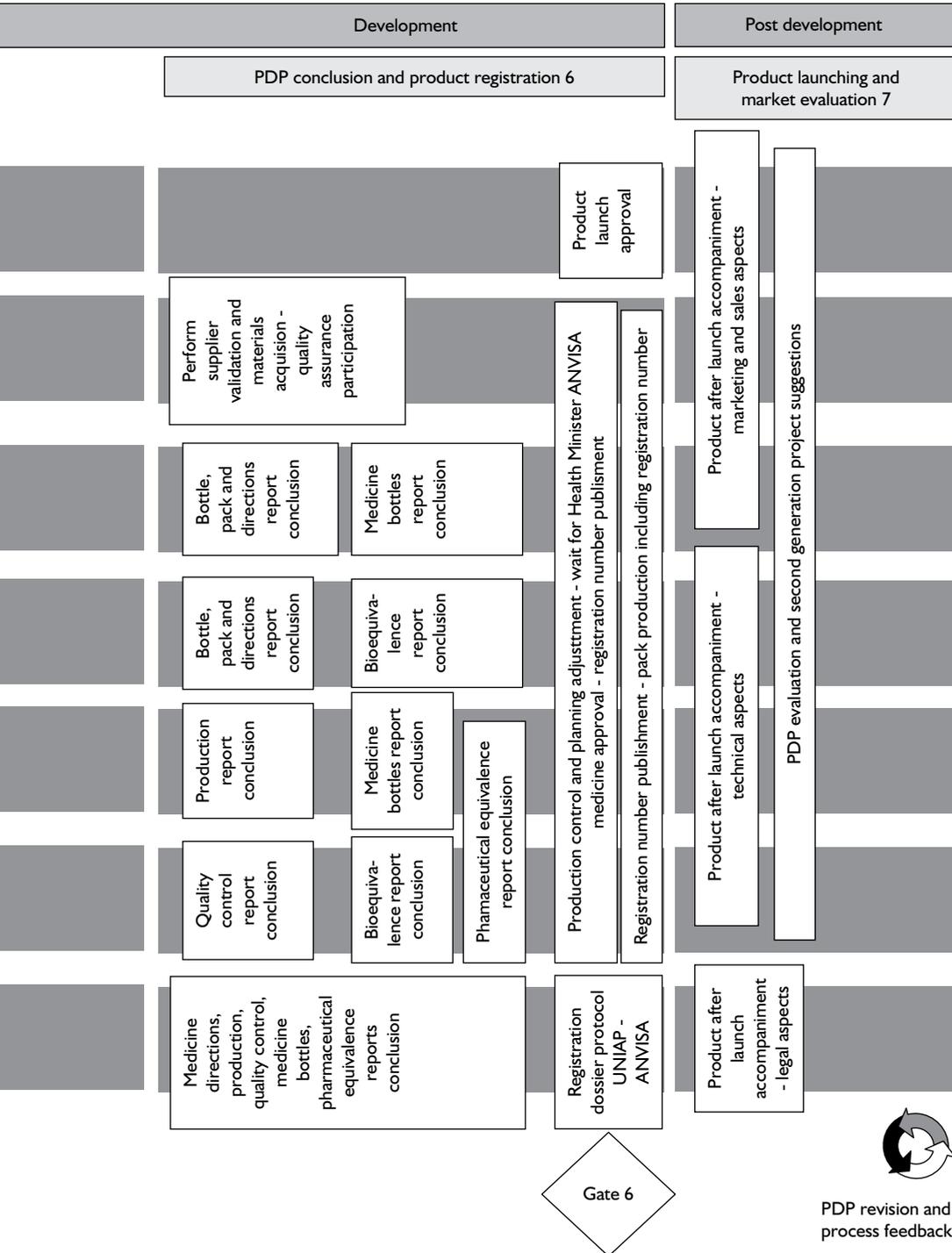


Figure 2 – Continued...

The three macro-phases are named pre-development, development and post development. Pre-Development complies the business opportunity identification and selection, as well the definition of a project manager and a team to perform the other subsequent PDP phases. The Development macro-phase embraces five phases: (i) concept development; (ii) detailed concept; (iii) product and process development; (iv) production and marketing plan performance; and (v) PDP conclusion and product registration. The Post-Development macro stage consists of only one phase (product launching and marketing evaluation). Underneath the internal boxes (the boxes represent the work packages from WBS) there are seven grey shaded horizontal stripes, which reflect the functional sector involvement along the entire PDP. Sometimes a single box covers six shaded lines, indicating that this specific work package is under the responsibility of all the six organization functional sectors beneath it. As it shows, the IPD recommended multifunctional team is included in the reference model, augmenting the chances of 'doing right for the first time'.

The organization functional sectors typical in Brazilian pharmaceutical companies are: administration, finances, marketing and sales, R&D, production, quality assurance and regulatory affairs. The interviews showed that the functional organization structure still predominates in medium and large Brazilian pharmaceutical companies, although there are multifunctional product development teams. In smaller companies, the number of team components is most of the time restricted, since the same professional may assume more than one function in the company. In general the product development management is responsibility of R&D or marketing and sales professionals, depending on the typical level orientation to market in the company's PDP and depending on its culture.

The pharmaceutical PDP reference model control

The reference model presents six gates, similar to those of the Stage Gates methodology. They are located between phase transitions, in which a decision of abortion, phase modification or process maintenance may occur. A check list and specific control documents were created for each gate, as it is observed in Table 3. Along the first three gates of the model (between the three respective phases), it is possible to notice the increase of financial risk. At the first gate the financial investments are relatively low, since no physical product development has occurred yet (product opportunity identification phase). Further, in the second gate, product prototypes may be constructed (concept phase), augmenting phase two expenses; but the third gate of this macro-stage, the transition between 'detailed concept identification and selection' and 'product and process development', is the most risky and delicate. The product and process development phase involves the physical development of the product and the process (Figure 2), generally performed at high expenses. Such gate is an important transition and strategic point in the reference model. Therefore, the control documents used in this gate are three: (i) the check list (used to control the phase activities completion); (ii) detailed product protocol (including financial and technical information for administrators strategic analysis); and (iii) project

plan (that presents project specifications for the product development team). The other four gates are controlled by the documents listed in Table 3 (more document details are published in Paula, 2004).

Table 3 - Pharmaceutical reference model macro-stage, phases, gates, and main documents.

| Macro stage | Phase | Gate | Control documents | Document description |
|-------------------------------------|---|--|----------------------------------|---|
| Pre development | Business opportunity identification and selection | 1 | Check list | List of phase activities completion control and authorization for process maintenance |
| | | | Product Innovation Charter (PIC) | Description of business/product opportunity |
| | | | PIC archive | Archive for PIC files classification |
| Development | Concept development | 2 | Check list | List of phase activities completion control and authorization for process maintenance |
| | | | Product Protocol | Description of product benefit, form and technology, i.e, product concept |
| | Detailed concept | 3 | Check list | List of phase activities completion control and authorization for process maintenance |
| | | | Detailed Product Protocol | Detailed description of product, including market information, product-process specifications and tolerances, financial, technological data |
| | | | Project Plan | File with project specifications for the product development team from different organizational functions |
| | | | Project chronogram | Chronogram with PDP activities distributed in a line time |
| | | | Activity x responsibility matrix | Matrix with activities and Human resources responsibilities |
| | Product and process development | 4 | Check list | List of phase activities completion control and authorization for process maintenance |
| | | | Phase Register Dossier reports | Reports from product and process development demanded for registration by ANVISA |
| | Production and marketing plan performance | 5 | Check list | List of phase activities completion control and authorization for process maintenance |
| | | | Phase Register Dossier reports | Reports from product and process development, demanded for registration by ANVISA |
| | | | Product/process master file | Document with all product and process control specification for quality control and assurance |
| | PDP conclusion and product registration | 6 | Check list | List of phase activities completion control |
| | | | Register Dossier | Document with product/process information submitted for registration by ANVISA |
| | Post development | Product launching and marketing evaluation | PDP feedback | Check list |
| PDP history and project lessons | | | | Summary of documents used for project control, as check lists, approvals, reports and learned lessons |
| Marketing and technical information | | | | Data from post approval tests; data from stability tests and from marketing analysis of the product |

The last gate, named 'PDP feedback', guarantees the process character of the model, since the information generated along the process will provide feedback for the initial phases of future developments. In this sense the information may be classified in strategic data and data from the product/process properly speaking, including the lessons learned (good and bad results from PDP). Information management requires special routines and will not be part of the scope of this paper. Authors from Project Management area recommend the formal conclusion of a project, in the form of a meeting where these lessons may be commented and the knowledge reinforced in the team. This practice is, therefore, suggested in this reference model.

Finally, it is important to mention that inside each phase it may be defined several milestones or project marks, for example: materials entering the process, important team meetings, chronogram disbursement and other events considered relevant by the team.

Reference model detailed representations: work packages and activities

Details in the reference model are represented by: (i) work packages from the overview model (distributed in all the seven phases) from Figure 2 and by (ii) the work packages decomposed in activities that are shown in graphic representations of each phase, as exemplified in Figure 3.

Figure 3 shows larger boxes (the work packages) covering the organizational function sector involved, the parallel activities, represented by smaller boxes inside the larger ones, and gate 1. Figure 3 is the exploded graphic representation of the first phase shown in Figure 2. As observed, concurrent development from CE is provided by the parallelism of independent activities described in the smaller boxes of this figure. It means that the organizational function sectors work in parallel, performing independent activities not sequentially, thus reducing development cycle. The detailed pattern of this reference model is a differential in the product development literature and it is an advantage for those pharmaceutical companies, which do not have a formal PDP yet. The model helps the generic product development team to remember all tasks necessary to successfully develop this kind of medicine. On the other hand, it is an inspiring model for companies that intend to structure PDP, even for new product development, since the model comprises the best development practices.

The interviews with Brazilian professionals showed that the pre-development stage and the first two phases from Development stage are the least structured in their companies. In contrast, PBB literature and other IPD methodologies devote most of the product success to the innovation pattern from pre-development, concept generation and detailing activities performance. Therefore, the pre-development is considered a foremost contribution of this reference model to the pharmaceutical area. Table 4 resumes the important work packages suggested in this macro-stage, as well the other macro-stages work packages from the model, since it is not possible to present all graphic representations in this paper. The

detailed graphic representation of work packages and activities for all phases is available in Paula (2004).

Special attention may be given to the italicized words in Table 4, since they describe the important work packages for generic medicine development and, therefore, are specially performed in pharmaceutical processes. These work packages were decomposed in activities in the graphic phase representations available in Paula (2004). The other work packages not italicized in Table 4 reflect the best practices from IPD methodologies and they are also performed in development processes of other product types. The graphic representation also indicates the organization function sector, which is responsible for the work package and its respective activities.

Further Discussion

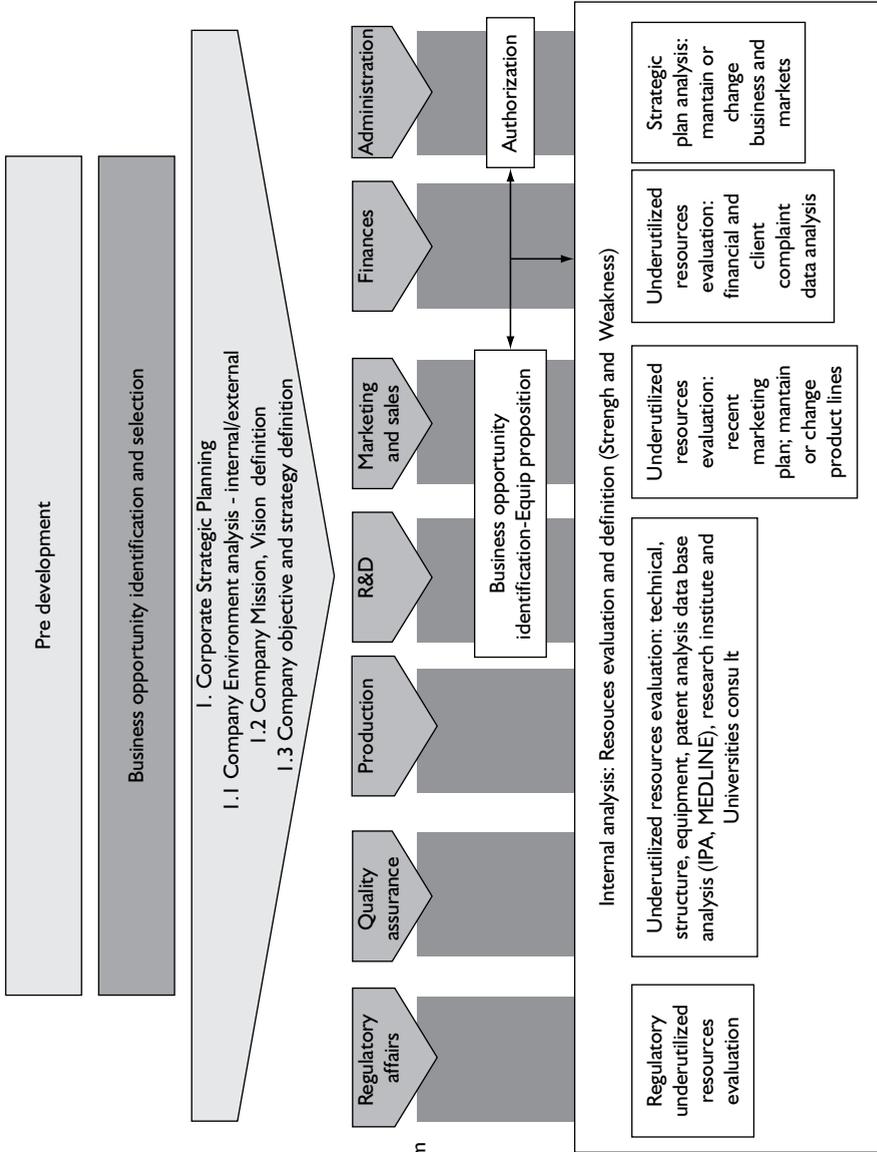
Conclusions

The qualitative approach adopted in the construction of the reference model proved to be efficient, since it permitted to gather information from professionals in a deeper manner, generating the model work packages. The choice of companies from medium and large sizes was adequate, since their development processes and relationship with ANVISA presented particularities, and the different types of business these companies develop brought more robustness to the final reference model. The same differences would not be so clear if the interviews included small companies; moreover the smaller companies hardly ever produce generic medicines.

The interview with the ANVISA referee was important for the delineation of legislation related workpackages in all macro-stages and phases. Furthermore, it was possible to notice the distance that still existed, at the time of the interviews, between the Registration Agency and the professionals, mainly those from medium pharmaceutical companies. Fortunately from 2004 on, some changes have occurred in direction to faster dossiers analysis and generic medicine registration in ANVISA. In spite of this fact, more efforts have to be made in order to improve the communication between the Agency and the regulatory functional sectors of companies. Actually the future goal is to create a partnership between companies and the Agency.

The interviews in the construction phase were important for the reference model configuration, since each company PDP was modeled in block 1 interviews and the final graphic reference model format was consequence of them. The second block interviews were important for validation and adjustments made in the final model. The adapted Delphi method proved to be efficient for the validation phase.

As mentioned before, professionals from seven pharmaceutical companies, totalizing 40 people with large experience in pharmaceutical product development expressed their



Multifunctional team

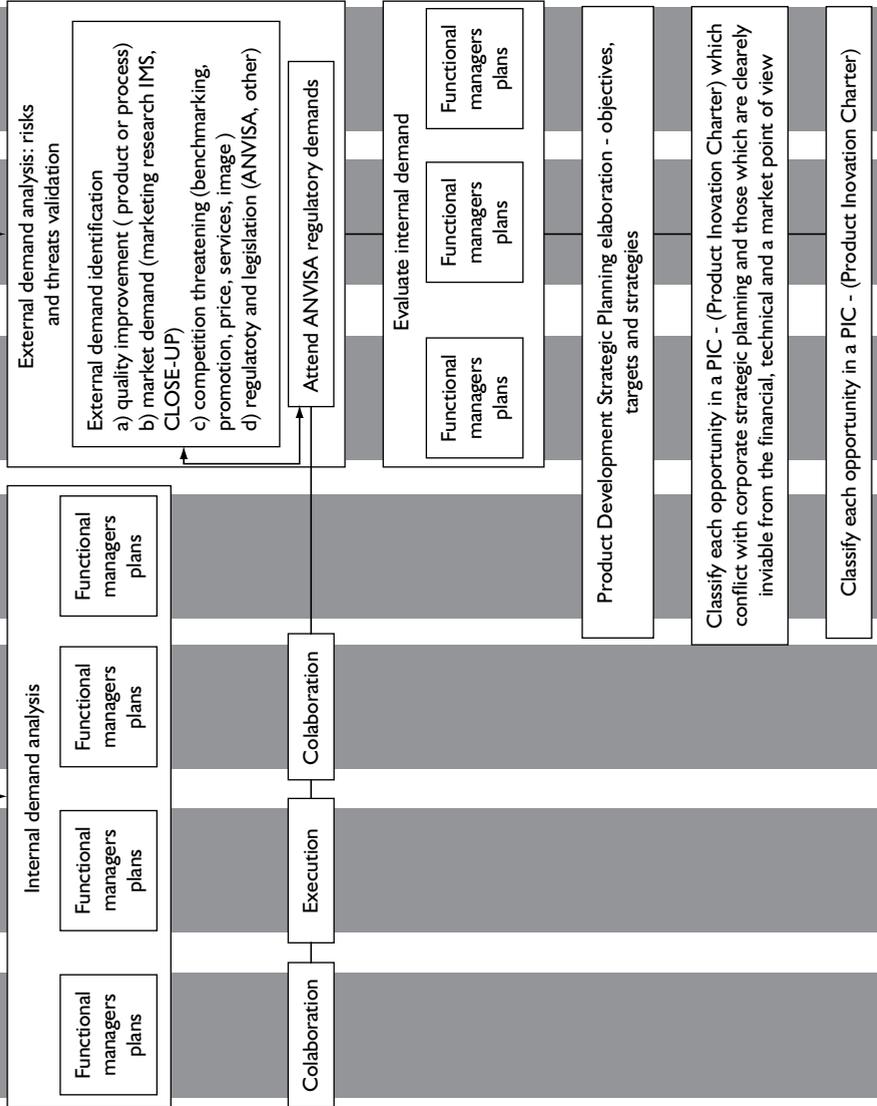


Figure 3 - Detailed graphic view from the Business opportunities identification and selection phase from the PDP reference model (Pre Development macro-stage) (IMS, CLOSE UP marketing research companies contracted).

Table 4 – Pharmaceutical reference model macro-stage, phases and work packages.

| Macro stage | Phase | Work packages from WBS - short description | |
|------------------|---|---|---|
| Pre development | Business opportunity identification and selection | Internal and external data gathering (includes pharmaceutical legislation information) | |
| | | SWOT analysis for Product Strategic Planning (fed by Corporate Strategic Planning) | |
| | | Business/product opportunity identification, selection and PIC classification | |
| Development | Concept development | Marketing analysis of opportunities identified | |
| | | Different concept generation (for each concept it must be suggested a benefit, a form and a possible technology (it is important to do conduct interviews with physicians at this phase) (its time to identify suppliers – Phase 1) | |
| | | Financial, economical and technical analysis of concept/opportunity | |
| | Detailed concept | Proposition of detailed concepts (For generic medicine it's time to identify and analyze the reference product; its time to select and/or develop suppliers – Phase 2) | |
| | | Detailed concept marketing analysis (submit concept alternative to physicians and potential consumers analysis) | |
| | | Thorough financial, economical, legal and technical analysis (Return on Investment, payback, other analysis) | |
| | | Product and process specification detailing (involve the production people in processes analysis); Life Cycle Analysis (environment aspects may be considered) | |
| | | Detailed product protocol analyzes and development approval (create project plan) | |
| | | Product and process development | Generic medicine bench development; generic equivalence and accelerated stability studies; process control, validation and specifications development |
| | | | Marketing plan development |
| | Production and marketing plan performance | Generic medicine scale up | |
| | | Production execution; marketing plan execution | |
| | | Perform generic medicine bioavailability studies and stability studies | |
| | PDP conclusion and product registration | Submit registration dossier to ANVISA; organize Process Control Planning; finalize Product Master File ; Publish Product registration number; produce generic free samples; submit price to ANVISA | |
| | | Prepare promotional material and sales training; conclude project and save development historical | |
| Post development | Product launching and marketing evaluation | Product launching and sales; finalize stability studies; | |
| | | Make marketing, technical, sales, and suppliers analysis; follow product performance; continuous gathering of product information | |

impressions about the reference model in block 2 interviews. All the interviewed experts recognized the importance of PDP management, although some of the companies still present a product development not fully formalized. Companies A, B and C, of medium sizes for example, possess PDP phase similarities with some development phases and with the post development macro-stage of the reference model. In relation to the pre-development stage and to the first two phases from Development macro-stage (concept identification

and detailing) it is less structured. The larger companies D, E, F and G present a more structured pre-development macro-stage, and company G practically execute all the phase activities mentioned in the model. It is important to mention that E and G are multinational companies that develop innovative products, being therefore, more structured.

The professionals in general appreciated the Pre-Development, concept identification and detailing descriptions in the model, since there is no parallel in pharmaceutical literature. They also valued the control documents suggested in the model. Some activities dependencies were discussed mainly by professionals from company G, what imposed changes in the model. Changes or criticism in work packages were not frequent and the interviewed professionals appreciated the graphical characteristic of the model. They commented that such format is easily understood by the team components and the overview provided by Figure 2 facilitates the identification of a particular task in the global process. This fact permits a team component to establish a relation between his work and the work of other components and to valorize his participation in the overall product development.

The generality of the model was considered large, since it was analyzed and approved by experts from companies that produce human/veterinary medicines and cosmetics. The macro-stages and phases are independent on the product under development, but the work packages and activities, specially the latest, have to be defined product to product, when adopting the model.

Some other aspects must be considered. Although the model is supported by development methodologies, CE tools for example, were not widely commented in it. The tools mentioned before in literature review have been proved to bring efficiency and efficacy to product development. The Design for Six Sigma development approach, for instance, is a current successful evidence of this. It is a limitation of this reference model to present these tools, since the tools applicability has to be analyzed at each development case.

On the other hand, tools as corporate Strategic Planning and Product Strategic Planning are recommended. The marketing methodologies are mentioned in all macro-stages, reinforcing the market orientation of the model. The practice of business opportunities screening, competitors benchmarking and portfolio management as support for decision in 'what projects to invest'; the practice of former technical, financial and economical analysis of projects, before product development; the continuous analysis of products after launching, providing the feedback character of the PDP, are essential parts of the model.

The managerial aspects of the reference model are attributed to: the broad scope description guaranteed by the WBS or the hierarchical indented activity list, which were transformed in a graphic representation of the process; the process segmentation, that facilitates risk management, process execution and control, since its complexity is crescent from the begin to the end; the clear indication of organizational function sector activities and work packages in the graphic representation; the decision making and quality control

gates, with their check lists and process documentation; the model feedback activity which stimulates the process cyclic quality improvement.

This reference model adoption may be easily performed by the following steps: (i) to perform the company PDP analysis/description followed by comparison with the reference model; (ii) team definition and further adjustment of the activities that will be necessary for generic product development, using WBS representation (the activities chosen from the reference model will depend on the company culture and the available structure); (iii) WBS activities decomposition in other management plans (time or chronogram; infrastructure, materials and equipment; acquisitions; human resources; risk; communication and quality plans, as prescribed in Project Management subject); (iv) process implementation and control of reference model documents and plans; (v) product development conclusion and feedback; and (vi) market product accompaniment.

Finally, some advantages of the reference model, mentioned by the interviewed professionals, include: the possibility of speeding product development; the possibility of using it to support training activities of recently contracted people and trainees; to be used for convincing administrators of investments in new resources, since the model provides a wide vision of development process; to facilitate process simulations, information management and rationalization; focus in waste minimization (time, resources, rework); the standardization of development practices, among others. The reference model is also important in the pharmaceutical academic field as a didactic tool. Some of its limitations comprise: the necessity of further activity detailing and tools definition; to perform a deeper analysis of activity dependency when the model is adopted. Possibly the company culture and infrastructure may difficult model implementation, mainly in small or medium companies that still work under an organizational function approach, instead of the process approach, and at last, the necessity of model revision if the registration legislation is changed. More significant changes must be done in the reference model activities for its application in innovative products development.

This reference model contributed to the product development state of the art evolution in the pharmacy field and it is introduced by this paper. It represents an improvement compared to general product development models presented in the literature and may be useful to guide or adjust the PDP of pharmaceutical companies.

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