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DOES QUALITY ASSURANCE APPLY TO DEVELOPMENT PLANNING?

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Quality Assurance is a well established discipline, not least in the healthcare industry where ethical and regulatory considerations require the application of strict quality criteria to the final product delivered to patients.

Less often are Quality Assurance criteria applied to more intangible aspects of human endeavour, such as planning and forecasting. We need look no further than government deficit projections to realize that this is a lamentable omission. And deficit financing is not an option for industry.

In our dynamic society, patients as well as professionals have come to expect continually improving healthcare options. Therapeutic innovation is essential if we want a better cure tomorrow. However, the research and development costs for a new drug are already astronomical and will continue to escalate.

Efficient planning is therefore a critical component in the management of scarce R&D resources and in selecting new agents for clinical investigation with the ultimate prospect of licencing. Several parameters, ranging from safety and efficacy to environmental concerns and marketability, define the innovative character of a new treatment modality. All must be considered in the evaluation process.

Evidence supporting the risk/benefit ratio requires us to think first of all in terms of safety and efficacy. However, the importance of pharmacoeconomic considerations is growing. Factors such as better cost-effectiveness compared to existing treatments, more convenient dosage or administration and a positive effect on hospital bed utilization are likely to determine the marketability of a new treatment. And since an adequate return on investment is critical to ensure the financial health of our industry - and funding for future R&D - these parameters must be thoroughly considered in the planning process.

New product development planning is a complex process. Through its different phases, some parameters directly involve R&D; others are the responsibility of the new business development and marketing departments. Yet most planning parameters are interrelated and likely to have some degree of relevance to everyone involved in the development of a new product . A thorough understanding of the clinical characteristics of a therapeutic innovation is critical to the new business planner, just as understanding the pharmacoeconomic considerations and intended market niche will enable the clinical research director to develop an optimal clinical trials programme.

Ultimately, the quality of the planning will have a profound effect on time to market(s) and the commercial success of a therapeutic innovation. However, R&D and business development departments are no less likely than politicians to make unrealistic assumptions. For this reason, Quality Assurance has an important role in the planning process. The more rigorously it is applied, the better the chances of avoiding costly and time-consuming mistakes.

For this reason we have drawn up a list of Quality Assurance criteria applicable to the planning process in R&D, clinical investigation and new business development. The criteria are divided into categories. The list is by no means exhaustive and we would welcome your thoughts and comments on other criteria and other areas. Meanwhile we trust that the present review will stimulate interest and raise our readers' awareness of the formidable array of different considerations that must be taken into account if we are to create better therapies for tomorrow's patients.

EFFICACY CRITERIA

1. Is the innovation effective in an indication for which there is no effective approved product?

2. Is the innovation more effective than approved products in those patients who respond to treatment?

3. Is the innovation effective in patient subpopulations for which approved products are ineffective?

4. Does the innovation significantly increase the proportion of treatment responders?

5. Does the innovation have a more specific action than approved products?

6. Does the innovation offer additional therapeutic benefits?

7. Does the innovation allow single-drug treatment where multi-drug treatment is required with approved products?

8. Does the innovation resolve signs and symptoms more rapidly than approved products?

SAFETY CRITERIA

Compared to approved products:

1. Does the innovation have a better safety profile in terms of less serious adverse effects?

2. Does the innovation have a better safety profile in terms of the overall incidence of adverse effects?

3. Is the innovation less likely to induce tolerance, dependence, withdrawal or rebound phenomena?

4. Does the innovation have a better safety profile in terms of the incidence of serious adverse drug effects?

5. Is the innovation less likely to produce unacceptable interaction with food or commonly used medications?

6. Does the innovation have a broader therapeutic margin?

7. Is the innovation less likely to produce changes in laboratory tests, vital signs or ECGs?

PRECLINICAL PHARMACOLOGY CRITERIA

1. Does the innovation act on a single target organ or functional system while approved products act at more than one site?

2. Does the innovation have a selective molecular action site, while approved products do not?

3. Does the innovation have a specific receptor binding site, while approved products do not?

4. Does the innovation have defined molecular characteristics, while approved products do not?

5. Does the innovation have a defined mechanism of action, while approved products do not?

TOXICOLOGY CRITERIA

Compared to approved products:

1. Does the innovation have a cleaner profile in mutagenicity tests?

2. Does the innovation have a cleaner profile in reproduction tests?

3. Does the innovation have a cleaner profile in acute toxicology tests?

4. Does the innovation have a cleaner profile in subchronic toxicology tests?

5. Does the innovation have a cleaner profile in chronic toxicology tests?

6. Does the innovation have a cleaner profile in carcinogenicity tests?

PHARMACODYNAMIC CRITERIA

1. Is the innovation a new release form that represents a significant technical advance, with adequately documented pharmacodynamic action and therapeutic relevance?

2. Does the innovation have a better defined dose-response relationship than approved products?

3. Does the innovation have a more appropriate onset and duration of action than approved products?

4. Does the innovation have a better defined therapeutic dose than approved products?

5. Does the innovation have an established dosing regimen compared to approved products?

PHARMACOKINETIC CRITERIA

Compared to approved products:

1. Does the innovation have a more adequate pharmacokinetic profile related to the active substance or to a new drug delivery process?

2. Is the innovation delivered to its site of action in an effective concentration during the desired period?

3. Does the innovation have a better bioavailability?

4. Does the innovation release active metabolites that are less toxic?

5. Does the innovation have more favourable ADME characteristics?

6. Does the innovation release fewer pharmacologically active metabolites?

7. Does the innovation have more favourable protein binding characteristics?

PRODUCTION CRITERIA

1. If the new agent is a physiological biological substance, does a manufacturing innovation lead

to the production of a medicinal product?

2. Is the innovation generated by a new drug generation process that represents a significant technical advance?

3. Is the innovation produced industrially by a new drug production process that represents a significant technical advance?

PHARMACOECONOMIC CRITERIA

1. Does the innovation permit outpatient treatment whereas hospitalization is needed with approved products?

2. Does the innovation permit shorter hospital stays than approved products?

3. Can surgical intervention be avoided by use of the innovation?

4. Can the innovation be administered by a more convenient route than approved products?

5. Does the innovation allow less frequent dosing or a shorter duration of treatment than approved products?

6. Does the innovation result in improved survival?

7. Does the innovation provide patients with a better quality of life than approved products?

ENVIRONMENTAL CRITERIA

1. Is industrial production of the innovation associated with significantly reduced environmental concerns compared to approved products?

2. Is industrial production of the innovation more compatible with environmental protection objectives?

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