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editorial

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The seven types of drug discovery waste: toward a new lean for the drug industry

All things of value are defenseless – ***Lucebert, poet.***

Given the stakes that industry and society have in making drug discovery more successful, we need to find solutions to the productivity gap with any method imaginable. In this light, the application of methods adopted from manufacturing, such as lean thinking, kaizen and six sigma, is imperative, because they represent a rational approach to productivity increase [1–3]. For those who have not (yet) heard of these methods: kaizen focuses on continuous improvement, six sigma on minimizing defects and variability. The lean method attempts to improve processes by focusing on customer value and eliminating any activity that does not contribute [1].

Applying these methods to drug discovery however, is a challenge [2,3]. Lean thinking was originally developed in the Toyota factories and typically focuses on the optimization of repeated processes, such as car assembly [1]. The discovery of a drug, however, only happens once and is never repeated in that same way again. Even if one looks above the project level, at the general discovery process within a company, then applying lean is difficult because successful projects are so diverse that they all are statistical outliers (Table 1). To make things worse, manufacturing-lean relies heavily on quality control metrics, such as brake tests for cars, which it uses to differentiate poor products early [1]. In drug discovery, however, preclinical tests are often poorly predictive of final effect and many good drugs, such as carboplatin and aspirin, would not make it through standard control metrics. Implementing too much quality control leads to the loss of good projects in the nets that should catch bad projects. Because good projects are relatively rare, implementing lean, by standardizing drug discovery projects, may kill all good projects even before all bad projects are killed. This, in fact, worsens the productivity problem.

Nevertheless, lean has great potential for drug discovery. Typical lean values, such as customer focus and reduction of waste, are also important for drug discovery with its need for focus on the patient and high attrition rates. To make its biggest impact, however, lean needs to be implemented in a much more project-centred way than has been so far reported [2,3]. Lean-for-discovery should start with a project, define customers and steps that create value and then look for waste [1]. Doing this, a connection should be made to what past successful drug hunters perceived as good practice [4,5]. Only in this way, a sound analogy can be defined for the seven types of waste that the creator of lean, Taiichi Ohno, observed in the Toyota factories [1]:

1. *Transportation*. Unnecessary transport of parts under production.
2. *Inventory*. Stacks of parts waiting to be completed or finished products waiting to be shipped.
3. *Motion*. Unnecessary movement of people working on products.
4. *Waiting*. Unnecessary waiting by people to begin the next step.
5. *Over-processing*. Unnecessary steps in processing of the product.
6. *Over-production*. Inordinate volumes of products.
7. *Defects*. Inappropriate quality of products.

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TABLE 1

Important differences between manufacturing and innovation from a productivity optimization perspective

Manufacturing process	*Discovery project*
Technically characterized	Has never been done before
Repeated process	Only happens once
Standard procedure work	A role for experience and intuition
Quality tests are highly predictive	Quality tests can be deceiving
Each step can be studied and optimized	Study only possible in retrospect
Statistical outliers should be reduced	Diversity is the basis of success
False positive errors (allowing a faulty product on the market) are most costly	False negative errors (stopping a perfectly good product) are most costly
A focus on cost reduction is effective	A focus on productivity increase is effective
Experts should be interchangeable	Experts are a unique resource
Classic lean philosophy effective	A lean-for-discovery philosophy needed

Principles of lean thinking in discovery

Below is an outline of how taking the three basic steps of lean can lead to a definition of seven types of waste in drug discovery:

1. *Define customers*
   Paul Janssen, the most productive drug hunter ever, prompts us, in a true lean sense, to always keep the patients and doctors in mind: 'Any statement on the relative quality of a drug can only be meaningful in a statistical sense. In the final analysis, only the patient, his family and the treating physician can be the real judges, case by case' [4]. Without asking the customers, it is very hard to know if a new therapy needs primarily to be more efficacious, safe, accessible or affordable. Too many layers between drug discoverers and doctors are a competitive disadvantage, increasingly so as medicine gets more personalized.
2. *Identify process steps that create customer value*
   What is the value of an assay? For a contract research organization (CRO), which is subprocess-based, this is the data point that is sent to the customer, and which should be measured as reliably and cost-efficiently as possible [2]. For a discovery organization it should be the increased chance that a project is going to make it to the market. If the odds are increased by 0.001%, and if the final sale volume will be $1 bn, the value gained is $10^{-5} \times \$10^9 = \$10^4$. Another definition could be: the increased amount of money a project would make if it were sold or licensed. Well considered, all projects start as low value, but the more data are amassed and the more criteria it survives, the more value is created. Therefore it would be useful to keep track of the actual market value of projects and use this as an annual research productivity metric. In true lean spirit, customers need to assess this value.
3. *Reduce the process to its value creating steps*
   Getting rid of all nonessential activities could mean, for the process-based CRO, for instance, reducing the number of pipetting steps before reading the assay plates [2,3] and this is an example of the general popular conception of lean. For a discovery project, however, reducing waste means defining the optimal next experiment in the project, the one that most straightforwardly adds most value. Ideally this is a simple, quick test that convinces everybody, most importantly the customers, of how good the project is. This can be a standard test, but just as well a specifically tailored, highly creative experiment. Importantly, it is a test upon which experts agree that it scientifically tests a project-critical hypothesis. Reducing waste means getting rid of any other activities. This leads to a redefinition of the seven types of waste, drawing from nine years of pharmaceutical industry experience and discussion with numerous colleagues.

The seven types of waste in drug discovery projects

1. *Transportation*. Project loss because of movement across sites.
   Drug discovery transportation waste occurs when projects are transferred to other sites or teams. Transported projects have an increased chance of being dropped, neglected or having experiments redone. Therefore, hesitancy to adopt a project is a realistic drain on project value. This is sometimes called the NIH syndrome, the Not-Invented-Here syndrome.
2. *Inventory*. Projects waiting in archives instead of being out-licensed. When scientifically sound projects are halted for strategic reasons, or even through lack of resources, they degrade in value over time because of increasing competition, data loss, or expiring patent lifetime. It is important to realize this project value, for example, by timely out-licensing.
3. *Motion*. Unnecessary shifting of experts across projects.
   Any expert needs time to become familiar with a project's compounds and biological nuances. Moreover, part of the diversity that breeds success originates from every expert having his/her own philosophies and ways of working. Unnecessary shifts will set back the timelines of a project.
4. *Waiting*. Unnecessary waiting before doing crucial experiments.
   Time can be wasted in waiting for approvals or decisions, or in organizing non-standard approaches (organizational inflexibility). This all delays success and thereby reduces competitiveness. The remedy is sufficient empowerment of teams.
5. *Over-processing*. Too frequent reviewing and prioritization.
   Over-reviewing produces statistical averages, and reduces outliers. Over-processing accumulates false negative decisions and can, therefore, contribute to the extinction of good projects. Moreover, over-reviewing increases the chances of encountering dogmatic non-believers, leading to erroneous

project killing. As no project will get universal support, a successful project only needs sufficient support.

6. *Over-production*. Unfocused experimentation and too many projects. Within a project this refers to experimentation that does not aim to solve project issues. This can be because of lack of diversity and flexibility within the company, as well as poor project focus by, for example, technology oriented units. Prioritization can reduce the amount of projects, although it leads to inventory waste. A better approach is to remain committed to a limited amount of projects [5] (this is what biotech companies do better than pharma).
7. *Defects*. Faulty scientific data packages.
   This refers to delivering scientific data packages that fail to address the crucial issues of a project (poor science). If these are discovered at later stages, this results in delays and loss of project value. Experienced and self-critical project teams are essential in discovering (and repairing) weak spots early.

In conclusion, the application of lean to discovery projects needs a careful return to its basis. A first step is to appraise research in terms of customer value, which can lead to some surprising insights. As scientific data add most value when they answer a specific project problem, or inspire a new direction, a value-based view of research rewards creativity and tailored approaches, as well as project championship, factors known to be important for innovation. A value-based view also cautions against discontinuing projects without sound scientific reasons. Interestingly, all these lean-supported values have also been heralded as contributors to past drug discovery successes [4,5]. If we ever want to return to the productivity of the drug discovery golden age, minimizing the seven types of drug discovery waste will be a good start.

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