Drug Development 2.0

Patient-centricity, crowdsourcing, data transparency and telemedicine – these novel trial design elements hail a transformation of the drug development model

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As investigators and participants in clinical trials, clinicians and patients stand on the front line of drug development. They experience first-hand the safety and efficacy of experimental treatments and intuitively understand the suitability of a clinical trial for generating useful data. These 'users' know the benefits and risks of treatments and trial designs on a personal level, rather than acting as passive observers – not just in terms of such factors as pharmacodynamic parameters, but also in terms of the effectiveness of the trial's data generation and collection mechanisms.

In a clinical trial, clinicians and patients work with the drug developer on a shared mission to determine the safety and effectiveness of an experimental treatment. Yet clinical trial design consistently prioritises the developer's perceived knowledge requirements over the user's ability to meet them. Additionally, the developer's needs may not be the most relevant for assessing the utility of a treatment. Partly as a result, the drug industry conducts a staggering number of complex and costly clinical trials that fail to produce useful findings. On an aggregate basis, according to the Tufts Center for the Study of Drug Development, pharmaceutical and biotech companies' spending on clinical research grew by nine per cent each year from 2004 to 2008, reaching $35 billion – nearly twice the $18 billion spent in 2000. Yet productivity has still been lagging (1).

The good news is that tools now exist for increasing the efficiency of clinical trials. Novel trial design elements being integrated into a new drug development model include patient-centricity, crowdsourcing, data transparency and telemedicine. Each is playing a role in transforming drug development and improving the efficiency of clinical trials. Collectively, they promise to significantly shorten the time and lessen the cost of drug development, while also potentially increasing its utility.

Patient-Centricity

The patient is becoming the driver of clinical innovation. This is true partly because electronic patient reported outcome (ePRO) tools provide investigators and developers with more timely data directly from the patient than they've had before. And personalised medicine, which is shifting the focus from large 'anonymous' clinical studies to much more customised clinical research approaches, is another reason to increase emphasis on patient-centricity (2).

But perhaps the most forceful driver is the patient community itself. Patients have become "more proactive about all aspects of their care", according to the social networking site, PatientsLikeMe (3). In addition, disease-specific portals like ThisIsMS have created flourishing online communities for tens of thousands of patients.

Janet Woodcock, Director at the US FDA's Center for Drug Evaluation and Research, explained the agency's perspective during a recent ECRI conference on patient-centeredness in policy and practice (4): "there's been a societal shift from medically defined assessment of treatment to patient-assessed impact." The FDA now references "patient centered drug development" as a key objective. According to Woodcock, "patient groups have often come to us, and they say they want to be on advisory committees for drug development. But we think the time to establish the standards for approval and [define what] should be taken into consideration for any given disease should be earlier."

Woodcock said that, through the FDA's Patient Centered Drug Development Initiative, the agency is attempting to develop better patient reported outcome measures – those targeted to the disease, of course, but also those that capture the "impacts of the treatment." She noted, "for many diseases, we may not have good existing measurement tools to quantify impact on the patient."

Woodcock also noted that capturing the impact of therapies needs to be done early in the drug development process: "developers should be thinking about this well before they have a candidate drug that they're studying."

Patient-Centricity at Work

Consistent with societal changes, the availability of new technologies and the FDA perspective voiced by Woodcock, the agency's patient-centric drug development initiative has moved past the goal-setting stage. In fact, the concept is now being put into practice with a new company's prototype crowdsourcing web platform launched in January 2012, which allows patients, physicians, researchers and other stakeholders to contribute to the design of clinical studies.

The platform's utility is initially being confirmed using generic compounds that have extensive safety records. The 'protocol builders' enabling 'the crowd' to participate in the design of proof-of-concept Phase 2 trials are currently accessible for the platform's first three candidates (the anti-hypertensive lisinopril, which is being repurposed as a treatment for multiple sclerosis; sulodexide as a potential treatment for peripheral vascular disease; and low-dose naltrexone as a candidate treatment for inflammatory bowel disease). These three projects are accepting ongoing collaborative input via the crowdsourcing web platform.

From its launch date in late January through to mid-June, the open platform had attracted some 8,000 unique visitors. About 400 converted to registered users. Roughly two thirds of these are patients. All visitors – patients, healthcare professionals, and other interested individuals – can offer trial design ideas, some of which may be 'gold' for these formative development programmes. For example, patients participating in developing the MS protocol have proposed a novel efficacy measure – improvement in mobility – that has not been commonly used in MS trials.

To participate in the community effort, registered site users select the development programme of interest, before completing a questionnaire tailored to their expertise. Researchers, for example, are asked which patient populations to study, while patients are asked about their experiences with prior medications (5).

Crowdsourcing

As a side effect of the open-source approach to software development environments such as Linux, crowdsourcing is now being applied to numerous scientific disciplines and is becoming an effective tool for drug development. In clinical development, crowdsourcing permits anyone, in any location, to contribute to the design of clinical protocols by reviewing the posted protocol and all relevant data that has been collected to date, and adding their input to the evolving design. The idea is to tap into the wisdom of the crowd by having a large number of stakeholders address well-posed challenges. Expert curation separates the 'wheat' from the 'chaff.' A spirit of collaborative improvement, along with recognition by peers, catalyses further participation, as it has already in the software development community.

A proven example of the power of crowdsourcing in medical research was the recent elucidation of the crystal structure of retroviral protease by a group of online 'Foldit' gamers. In 10 days, two winning groups developed models that were close enough to the long-sought molecule to enable scientists to describe the entire structure. (6). Players are now applying the game technique to the more challenging work of protein design. Using this approach, researchers have created an enzyme with more than 18-fold higher activity than the original (7).

Rewarding participants for contributions is a necessary part of the crowdsourcing drug development concept. The forms of reward will evolve, but currently include professional development and industry networking benefits. Eventually it may also involve prizes and direct financial incentives.

Data Transparency

Data transparency feeds crowdsourcing – it's an enticement for those who can contribute unique perspectives because it builds trust and credibility.

Such transparency is currently perceived to be in direct conflict with the pharmaceutical industry's longstanding protection of intellectual property (IP). The transparency concept is a hard sell to companies that have made substantial investment in discovery and development, and for whom business success hinges on financial benefits generated from IP protection. Examples of successful value creation via open innovation and crowdsourcing in other industries (consumer products, for example) are helping to alleviate fears of incumbents. Recent initiatives by some pharmaceutical companies to pool drug discovery resources are encouraging in this regard. In a similar vein, in May 2012, NIH's National Center for Advancing Translational Sciences (NCATS) announced a major new initiative that matches drugs with interested researchers in an open setting.

The Value of Crowdsourcing: Case Study

Linux

Perhaps the most widely known example of crowdsourcing is the open-source computer operating system, Linux. Computer programmer frustration with the inaccessibility and limitations of proprietary operating systems in the 1980s and 1990s sparked the open software movement, much as the cumulative effect of clinical trial failures is now driving adoption of crowdsourcing in drug development.

Unlike drug developers, however, Linux's creators had no open-source development map to follow. First came the GNU project in the early 1980s. The GNU acronym stands for "GNU is not Unix," which perhaps reveals the mindset of those behind it. Their premise was that software should have no restrictions against copying or modification, to yield better and efficient computer programmes (10). This was the philosophy used initially to develop programming tools and, eventually, the crowdsourcing operating system of today that continues to be tweaked by professional programmers to meet their requirements.

OpenClinica

In the drug development world, an example of crowdsourcing is the OpenClinica Clinical Trial Management System for Electronic Data Capture (EDC) Clinical Data Management (CDM). Since its release four years ago, OpenClinica has spread to more than 100 countries and now boasts more than 12,000 community members.

OpenClinica grew out of frustration with proprietary electronic data capture (EDC) software (11). It is the product of internal and community-developed open source software.

Another hurdle has been the unwillingness of most drug companies to publish negative trial results. One reality of the pharmaceutical industry is that companies are competing to develop drugs that treat the same conditions. By publishing negative results, competitors might create opportunities to retool their own studies or pursue a different avenue of development. Nonetheless, calls for full disclosure of clinical trial data, both negative and positive, are on the rise and will provide further support for the transparency that is an integral part of this new model.

Telemedicine and IT

The Drug Development 2.0 model – allowing patient/doctor-centricity through crowdsourcing and open data sharing – can be turbo-charged with telemedicine and information technologies. Consistent use of remote diagnostic techniques, and data transmission via computer, mobile devices and satellite links, make possible virtual clinical trials that are patient-centric in contrast to the traditional site-centric model with its costly, recruitment-limiting requirement of multiple clinic visits.

Telemedicine permits subject participation from home. In addition, in-home monitoring of trial participants may yield an improvement in data quality by minimising researcher bias and yielding more uniform data (8).

A wealth of newly developed mobile diagnostic devices promises data of at least equal quality to those obtained in-clinic. The fact that industry leader Pfizer initiated an all-electronic trial is testimony to the practical reality of this approach, even though the study finished early due to patient enrolment issues. Pfizer's Head of Clinical Innovation, Craig Lipset, has promoted an "app store of tools from telemedicine, which can help expand health IT connectivity." He said he views the use of telemedicine apps in clinical trials, which permit patient progress reports via smartphones and computers, as "a repurposing rather than inventing" (9).

Conclusion

Modern technology has provided several tools that support open innovation, crowdsourcing and decentralised data gathering – the infrastructure of Drug Development 2.0. When used in a patient-centric context, these tools will help transform clinical trials and make drug development a more successful and sustainable business model for the pharmaceutical industry.

References

1. Getz KA, Sizing up the clinical research market, *Applied Clinical Trials*, 1 March 2010, http://www.appliedclinicaltrialsonline.com/appliedclinicaltrials/article/articleDetail.jsp?id=660749
2. TranslationalMedicineOntology Internet Site, Translational Medicine Ontology: A Patient-Centric Ontology for Drug Development and Clinical Practice, http://code.google.com/p/translationalmedicineontology, accessed 20th March 2012
3. Williams DS, The value of openness, The PatientsLikeMe Blog, available at http://blog.patientslikeme.com/2007/12/13/the-value-of-openness, accessed 20th March 2012
4. Woodcock J, An FDA perspective on the critical role that patients play in the lifecycle of medical products, ECRI Institute 18th Annual Conference: Patient-Centeredness in Policy and Practice transcript, pp15, 29th November 2011, available at www.ecri.org/Documents/2011_TA_Conf/Transcripts/ECRI_Institute_2011_Conference_Session_8.pdf, accessed 20 March 2012
5. Weintraub A, Transparency launches as Linux of drug development, *Xconomy*, 23rd February 2012, available at www.xconomy.com/new-york/2012/02/23/transparency-launches-as-linux-of-drug-development/, accessed 20th March 2012.
6. The Promise of Open Protocol Development, Transparency Life Sciences available at, www.transparencyls.com/?q=node/12, accessed 20th March 2012, http://transparencyls.com/?q=node/12
7. Marshall J, Online gamers achieve first crowd-sourced redesign of protein, *Scientific American*, 22nd January 2012, http://www.scientificamerican.com/article.cfm?id=victory-for-crowdsourced-biomolecule2
8. Baum S, 4 ways to shake up the clinical trial process and cut costs, *MedCity News*, 1st February 2012, available at www.medcitynews.com/2012/02/4-ways-to-shake-up-the-clinical-trial-process-and-cut-costs, accessed 20th March 2012
9. Miller G, Pfizer's virtual trial: Open-source meets old pharma, *FierceBiotechIT*, 21st June 2011 available at www.fiercebiotechit.com/story/pfizers-virtual-trial-open-source-meets-old-pharma/2011-06-21, accessed 20th March 2012
10. Hasan R, History of Linux: New baby in [sic] the horizon, Department of Computer Science, University of Illinois at Urbana-Champaign, https://netfiles.uiuc.edu/rhasan/linux/, accessed 20th March 2012
11. Open Source Clinical Trial Software? Cool!, OpenClinica, available at www.openclinica.com/open-source-clinical-trial-software, accessed 20th March 2012
12. www.appliedclinicaltrialsonline.com/appliedclinicaltrials/CRO%2FSponsor/Sizing-Up-the-Clinical-Research-Market/ArticleStandard/Article/detail/660749, accessed 20 March 2012
13. www.scientificamerican.com/article.cfm?id=victory-for-crowdsourced-biomolecule2#comments%20and%20presents%20the%20challenge%20with%20colorful%20blocks.%20problems%20that%20would%20otherwise, accessed 20th March 2012

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