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# Bring out your dead

**Despite recent progress, only a fraction of the drug industry's shelved compounds are shared with the research community. Could online collaborative research offer a solution?**

Failure—punctuated by the odd success—is an integral part of drug discovery and development. And industry is very vocal about the burden of its failed compounds in inflating the cost of bringing a drug to market—now purportedly $2.56 billion according to the latest Tufts study. Industry is less forthcoming, however, when disclosing the thousands of 'failed' drug assets to the wider research community. In recent years, both the US National Center for Advancing Translational Sciences (NCATS) and the UK Medical Research Council (MRC) have made progress in coaxing de-prioritized compounds out of company vaults, with the latter announcing last month it had brought together "the world's largest collection of de-prioritized compounds"—68 in all. But for drug repurposing of failed compounds to truly realize its potential, additional mechanisms need to be found that incentivize both large and small companies to release data so that they can be accessed and searched by the crowd.

Drug repurposing, or repositioning, is nothing new. Historically, it has often been a serendipitous process in which chance clinical observations suggest new indications for an approved drug or drug candidate. In recent years, compounds stalled in drug company pipelines due to lack of efficacy have received particular attention for repurposing. Such compounds are useful because they already have extensive information on safety and efficacy. Indeed, according to the Institute of Medicine, repurposed drugs can be approved faster (within 3–6 years of program initiation), at as little as ~60% the cost and with three times lower attrition rates than a drug from a traditional discovery program.

Two flagship initiatives that crowdsource researcher ideas for new uses are the NCATS' Discovering New Therapeutic Uses for Existing Molecules program and the MRC's Industry Asset Sharing Initiative. Key facets of either program are the provision of boilerplate collaborative research agreements, which streamline the legal and administrative burden between participating researchers and companies, and an open crowdsourcing application process followed by a closed second stage governed by cooperative agreements. Participants can apply for new use intellectual property (IP), with the companies donating the compounds getting first right of refusal.

Thus far, NCATS and MRC have succeeded in engaging eight companies from the entire industry. Although it is a promising start, it represents a tiny fraction of all discontinued programs.

Uptake has been slow for several reasons. First, the drug industry is conservative, particularly when repurposing initiatives might throw up safety signals about lucrative drugs in portfolios. Second, company insiders may dismiss crowdsourcing expertise—after all, they 'know' their compounds best (the NIH 'not-invented-here' problem). And third, sharing compounds and data for crowdsourcing has significant resource implications.

To work with NCATS or MRC, a company must rally all the relevant data on a discontinued compound; must locate internal champions with relevant expertise (who may be working on another asset or have left the company); must appoint an individual to oversee the program (who would otherwise be working on another project in the organization); and, most importantly, must manufacture sufficient quantities of the compound at clinical grade to supply a trial. Industry insiders estimate these direct and 'opportunity' costs may total up to $1 million per compound.

Clearly, this is prohibitive for many companies, especially the majority of small-to-medium-sized enterprises. Even if their overheads are less, most biotech companies have insufficient time, staffing and resources to participate in an NCATS/MRC collaboration. For companies that run out of funding, assets and IP are often left in limbo.

One alternative to the NCATS/MRC programs would be to create an online platform where users could upload data about shelved compounds in return for royalty options, milestone payments, and exclusive and non-exclusive licenses if compounds are taken forward. These online solutions could provide collaborative environments in which drug-related data would be uploaded, linking out to repositories like PubChem or ChEMBL. Researchers could either work in open environments to discuss ideas, organize research, and network or collaborate in private environments where proprietary information would be shared with a defined group.

The question is, who would build such a resource?

One thought is the European Union–funded Innovative Medicines Initiative (IMI). IMI has the authority, industry/academic contacts, and financial muscle to put the technology together in short order. Failing this, several internet-based collaborative platforms might also moonlight for this purpose. For example, Collaborative Drug Discovery's (CDD) 'Vault' cloud-based offering to mine biological and chemical data has securely hosted over 250,000 user logins for 10 years now; Cures Within Reach is launching the CureAccelerator platform later this year, which has similar capabilities and the ability to network with funders.

The movement of drug discovery from silos in companies and other organizations to online platforms that enable collaborations with researchers across the globe is not going to happen overnight. But it is coming.

It will be enabled by the increasing ability to integrate molecular and structural data about compounds, data from electronic medical records and high-throughput large-scale phenotyping and genotyping technologies. It will be facilitated by greater transparency in disclosing clinical data on drugs, exemplified by the European Medicines Agency's decision to publish from this month onwards complete clinical study reports for all marketing authorization applications. And it will be driven by the recognition that crowdsourcing the global research community can invigorate drug development with new ideas.

The upshot will be that collaborative drug discovery will become accessible to all companies, large or small, across the industry. If that means failures can be shared more widely, resources diverted from making the same mistakes and a greater number of failed compounds turned into successes, the sooner the better.

Corrected after print 8 January 2015.

# Erratum: Bring out your dead

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In the version of this article initially published, the cost of bringing a drug to market was incorrectly stated as $2.3 billion. The correct amount, as per the Tufts study referenced in the article, is $2.56 billion. The error has been corrected in the HTML and PDF versions of the article.