How to apply technology convergence in safety

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An analysis of the attrition of drug candidates from four major pharmaceutical companies

Michael J. Waring¹, John Arrowsmith², Andrew R. Leach³, Paul D. Leeson³,⁴, Sam Mandrell², Robert M. Owen⁵, Garry Pairaudeau¹, William D. Pennie⁶,⁷, Stephen D. Pickett³, Jibo Wang⁹, Owen Wallace⁶,⁷ and Alex Weir²

Abstract | The pharmaceutical industry remains under huge pressure to address the high attrition rates in drug development. Attempts to reduce the number of efficacy- and safety-related failures have focused on attrition rates and that additional work is required to address safety-related failures. Further cross-company collaborations will be crucial to future progress in this area.
An analysis of the attrition of drug candidates from four major pharmaceutical companies

Michael J. Waring1, John Arrowsmith2, Andrew R. Leach3, Paul D. Leeson3,4, Sam Mandrell2, Robert M. Owen5, Garry Pairaudeau1, William D. Pennie6,7, Stephen D. Pickett3, Jibo Wang9, Owen Wallace6,9 and Alex Weir2

Abstract | The pharmaceutical industry remains under huge pressure to address the high attrition rates in drug development. Attempts to reduce the number of efficacy- and safety-related failures have had limited success and it is clear that further cross-company collaborations will be crucial to future progress in this area.

<table>
<thead>
<tr>
<th>Termination reason</th>
<th>Period</th>
</tr>
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<tbody>
<tr>
<td>Clinical safety</td>
<td>48 (13%)</td>
</tr>
<tr>
<td>Commercial</td>
<td>23 (6%)</td>
</tr>
<tr>
<td>Efficacy</td>
<td>45 (11%)</td>
</tr>
<tr>
<td>Formulation</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Non-clinical toxicology</td>
<td>144 (40%)</td>
</tr>
</tbody>
</table>
Phase II and phase III failures: 2013–2015
Richard K. Harrison

Late failures = Expensive failures
‘omics technologies

Integrative strategies (technologies, data, models)

DRUG SAFETY PREDICTION
DRUG SAFETY PREDICTION

‘omics technologies

Genomics, transcriptomics, metabolomics, etc.

Integrative strategies (technologies, data, models)
‘omics technologies

Integrative strategies (technologies, data, models)

DRUG SAFETY PREDICTION

e.g. organs-on-a-chip

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DRUG SAFETY PREDICTION

‘omics technologies

Integrative strategies (technologies, data, models)

e.g. multi-component or multiscale modelling
Drug safety prediction

omics technologies

Integrative strategies (technologies, data, models)

Biomedical Big Data
Legacy data sharing to improve drug safety assessment: the eTOX project

Ferran Sanz¹, François Pogna², Thomas Steger-Hartmann³, Carlos Díaz⁴ and eTOX *

The sharing of legacy preclinical safety data among pharmaceutical companies and its integration with other information sources offers unprecedented opportunities to improve the early assessment of drug safety. Here, we discuss the experience of the eTOX project, which was established through the Innovative Medicines Initiative to explore this possibility.
Opportunity for better drug safety predictions

There is a wealth of the high quality toxicology data in the archives of the pharmaceutical companies.
Content of the eTOX database

- 8,881,217 Preclinical data points
- 8,196 Studies
- 1,947 Structures
Preclinical data
- eTOX data
- SEND data
- Other legacy data

Clinical data
- Clinical trials
- Labeling info
- Pharmacovigilance
- EHRs

Other data sources
- Tox21
- ChEMBL
- COSMOS
- DisGeNET
- VigiBase
- OpenFDA

Translational Safety Assessment
- Read-accross
- Visualization
- Modeling

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