

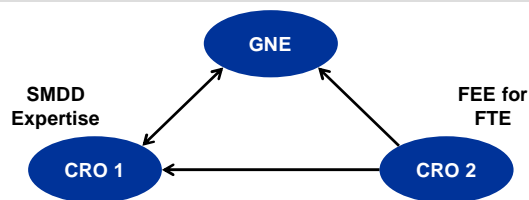
# DEGAS – Sharing and Tracking Target Compound Ideas With External Collaborators

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## Motivation

A significant number of the Small Molecule Drug Discovery (SMDD) projects at Genentech are collaborations with Contract Research Organizations (CROs).



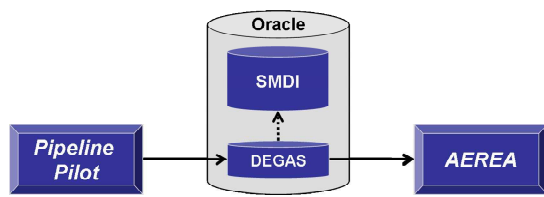
**Figure 1** Scientists at Genentech (GNE) and at CRO 1 make joint decisions. Synthesis requests are communicated to the chemists at CRO 2 who are assigned to the given project.

## DEGAS allows the sub teams to

- store target compound ideas and their profiles along with the team-based prioritization
  - Prerequisite for a transparent and well-documented decision process**
- track synthesis effort
  - Ensuring that the highest priority target compounds were being addressed**

## DEGAS Components

- The application is an integration of two very flexible software, Pipeline Pilot and AEREA.
- The DEGAS database is linked to the in-house database to enable novelty and availability check



**Figure 2** The database serves as link between Pipeline Pilot and AEREA. SMDI contains registered Genentech compounds.

## Register Target Compound Ideas

- Pipeline Pilot** is used by the computational chemists to make scientific software available to project teams
- An existing protocol for library enumeration, molecular property calculation, and the prediction of DMPK properties has been integrated

Library Enumeration completed  
Number of compounds loaded: 4  
Number of duplicate compounds: 0  
Number of failed compounds: 0  
Please check log files for details

Link to AEREA

**Figure 3** After the enumeration and registration of the compounds, the protocol reports the result to the user. A link to AEREA allows the seamless integration. Meanwhile the protocol for property computation is invoked and runs in the background.

## Prioritize Ideas and Track Synthesis

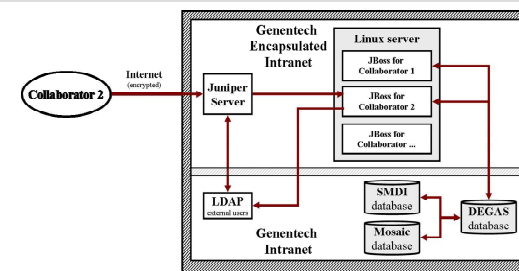
- AEREA** comes with interfaces for chemical searches, for report design, and for adding data entry columns
- Users can input data in the context of other information

#	Product Structure	Properties	Enter Product Estimate	Enter Priority	(Dis)Assign (Enter est. date)	Assigned To	Add Synthesis Report	Mark as completed
1		NW 345.03 TPSA 105.00 cLogP 6.5 2.20 cLogD 7.4 2.13 spKa (nb) 2.13 Rot. Bonds 5 cM (R/R/N) M/M/L cRP (R/R/N) S/M/L	Lower: 1000		04/27/2011 (Claim 20900)	Man-Ling Lee	<input type="checkbox"/>	<input type="checkbox"/>
2		NW 85.00 TPSA 85.00 cLogP 6.5 2.10 cLogD 7.4 2.13 spKa (nb) 2.13 Rot. Bonds 8 cM (R/R/N) M/M/S cRP (R/R/N) S/M/S	Library ground scoreFold 1			Man-Ling Lee	<input type="checkbox"/>	<input type="checkbox"/>

**Figure 4** Example of an editable report with the most frequently used columns. The cells of the "Add Synthesis Report" and "Mark as completed" columns are empty for the 2nd compound because its synthesis has not been assigned to any chemist. To create an assignment, a chemist enters the estimated completion date in the "(Dis)Assign (Enter est. date)" column. The refreshed page will display the text and check box for adding a synthesis report and for setting the completion flag.

## Access by Collaborators

- An external user only access the subset of data for which she is authorized
- Encapsulate each DEGAS instance from the internet, from the Genentech intranet, and from the DEGAS instances for other collaborators



**Figure 5** Infrastructure enabling collaborators to access Genentech internal applications. Genentech Informatics provides the Juniper and the LDAP servers for user authentication and authorization. The Linux server has restricted access to the Genentech Intranet.

## The Pilot Project Team

- Consists of three equal sized sub-teams across three continents
- Started eighteen months before the deadline for clinical candidate selection
- Needed to reduce lipophilicity to improve the attractiveness of synthesized compounds
- Team members evaluate the computed properties and state the rationale for each synthesis
- The project and chemistry leaders reviewed the status of the synthetic efforts and, if needed, re-assigned chemists to work on different target
  - The project team met the deadline for candidate selection**

### Acknowledgements

We like to thank the chemists in the pilot project team for their feedback and the GI team for their commitment to implement a secure infrastructure to expose DEGAS to the many collaborators.