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**LABS/R**

## **Synthesis and Recipe optimization – from research to application**

Industrial branches like combinative chemistry, galenical development or applications engineering often require a multitude of test runs in order to increase the yield of a synthesis or to optimize the properties of a product.

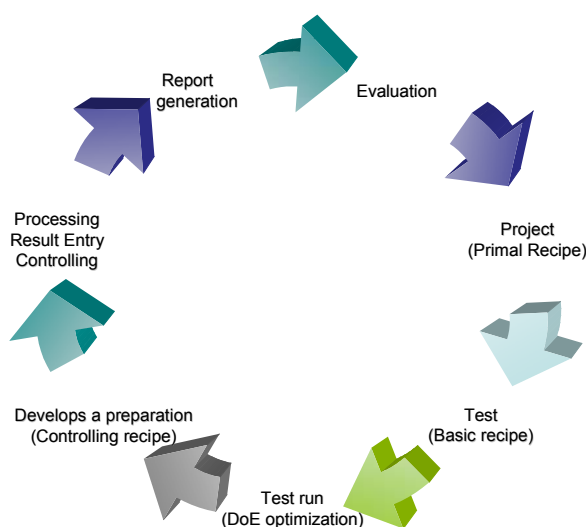
As a consequence a number of time-consuming tasks will become necessary, such as planning of multiple tests, control of production processes, complete documentation and last but not least a summary of all resulting evaluations. Often it will be difficult or even impossible to perform all these tasks in a proper manner.

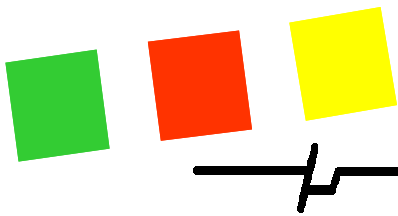
**LABS/R** as an integration platform supports the working processes starting from planning of tests up to the final evaluations.

In **LABS/R** you can map the complete workflow:

- Test planning
- Documentation of test runs
- Support of statistical test planning DoE based on already existing results
- Automatic processing of test preparations
- Collection of analytical and process accompanying results  
Support during evaluation and reporting.

The requirements of the NAMUR research group have been taken widely into account with respect to structuring of master data and the concept of data relation.





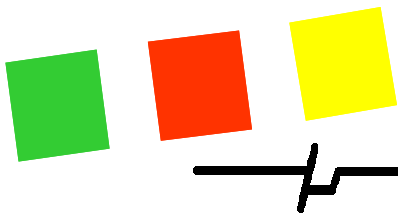
## Test Planning

### Project / Primal recipe

The test planning is organized in a multi-level arrangement. In a first step the project has to be described. To do so, information can be taken over even from external applications (research/development databases incl. chemical structure databases like e.g. MDL). In addition to the primal recipe a project contains the requirements as well as the objectives of the project.

The screenshot displays the '2925 - Modul 295' window in the ELAN software. The interface is divided into several sections:

- Project List:** A tree view on the left shows a hierarchy of projects, with 'F-05001-001' selected.
- Project Details:** The main area shows the 'Project ELAN' details for 'F-05001-001'. Fields include:
  - Project ID: F-05001-001
  - short name: Amadori compound
  - Description: Fructose-Alanin
  - type: CHEMISCH
  - Aim: Optimization of yield of Fructose-Alanin. Reducing Glucose as a byproduct.
  - Project File: F-05001-001
- Reaction scheme:** A section at the bottom shows a chemical reaction. On the left, a fructose molecule (a six-membered ring with multiple hydroxyl groups) reacts with an alanine molecule (a three-carbon chain with an amino group and a carboxyl group). An arrow points to the right, where the resulting Amadori compound is shown, which is a fructose ring with an amino group attached to the C2 position.



## Test

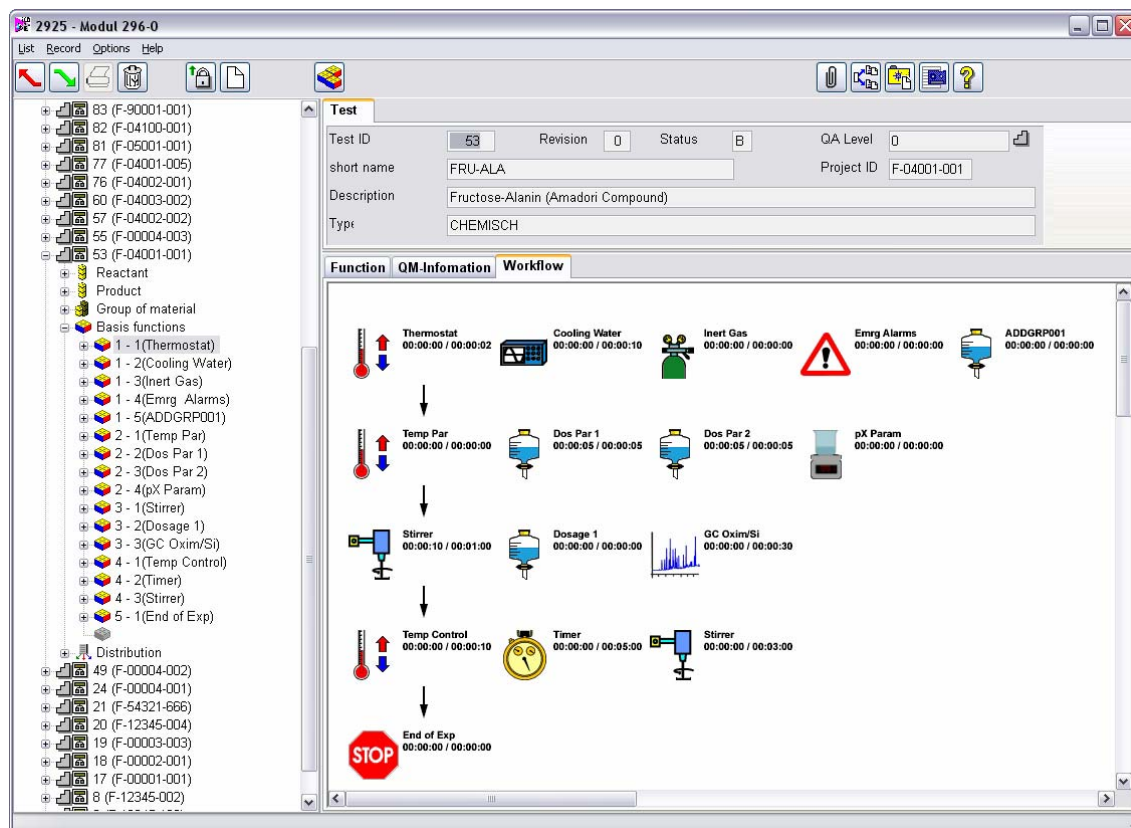
In each project you can define a set of various tests. Changes of the project arrangement underlie a version control system, including an automatic document distribution. A test describes in detail how the production process has to be performed.

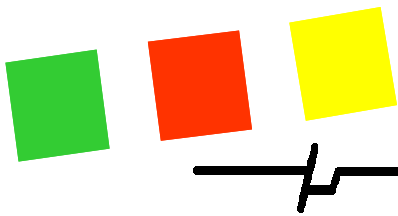
Test details include ...

- Involved materials
  - ◊ Materials/Chemicals
  - ◊ Solvent
  - ◊ Catalysts
  - ◊ Used substance groups
- Expected products/byproducts
- Basic operations of production (process steps)
- Methods for checking the manufactured products.

Depending on the type of test procedure (chemical synthesis / galenical development / application technique) the project arrangement offers all necessary calculations of the recipe (stoichiometric reactions, contents of help substances, active or equilibration agents).

Work flow in **LABS/R**:





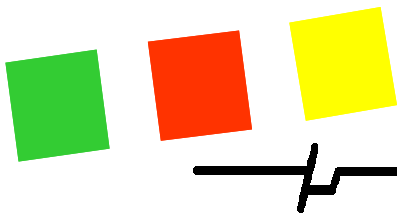
## Test runs

Based on the test and the already received results test runs can be set up. This procedure will be supported by the statistical test planning (DoE). A test run concretizes the test planning for the performed experiments in more detail.

- Applied laboratory equipment
  - ◊ Synthesis automates
  - ◊ Analytical instruments
- Educt materials
  - ◊ Batch information (purity, concentrations)
- Calculation of required educts/materials (with respect to the preparation quantities)
- Schedule planning of individual tests

A Gantt diagram helps you to find out if time conflicts would occur for the applied laboratory equipment because of parallel preparations.

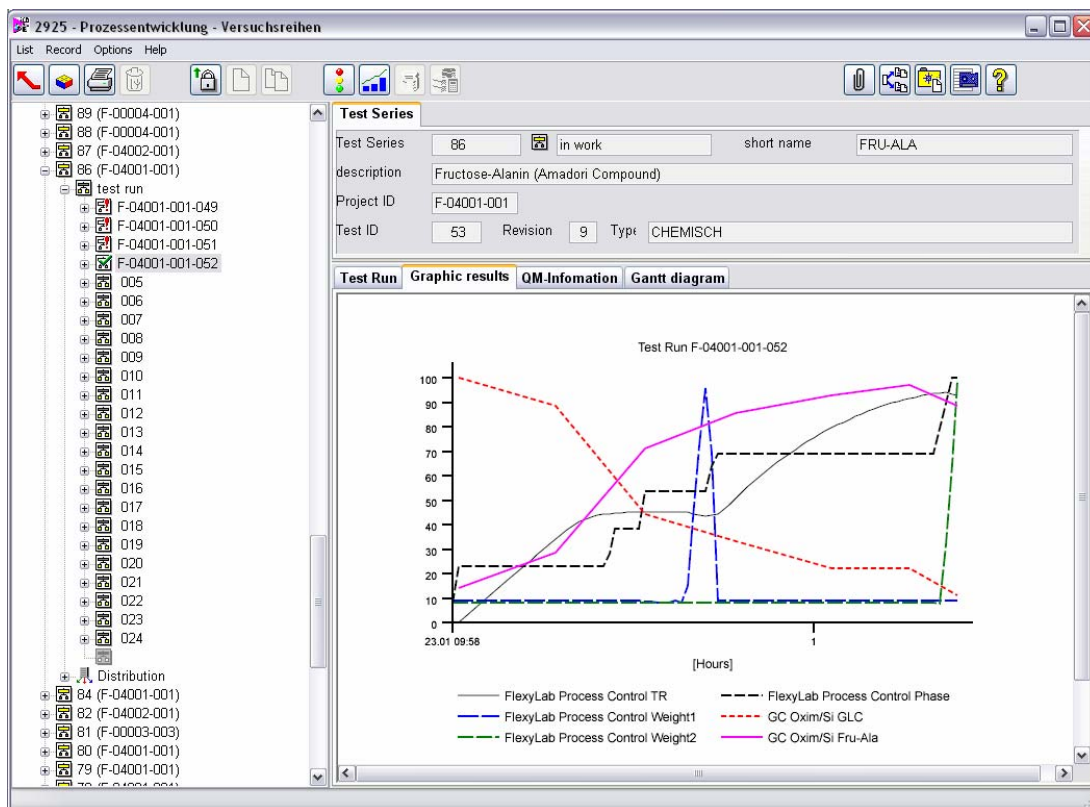
Test R	Temperature °C	Solvent	Ala Amount g	Fructose-Alanin %	Glucose %
1 F-04001-001-057	50.0000000	M001	1.0000000	80.0000000	4.0000000
2 F-04001-001-056	60.0000000	M001	2.0000000	[ 50.0]	[ 62.0]
3 F-04001-001-055	80.0000000	M001	1.0000000		
4 F-04001-001-058	90.0000000	M001	2.0000000	75.0000000	[ 6.00]



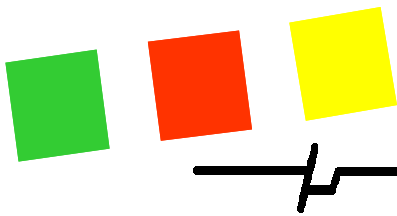
## Preparation Process

Based on the test runs, the laboratory preparations to be performed can be created automatically. Additionally, it is possible to set up a laboratory preparation manually by means of the existing master data (materials / agent groups), basic operations, basic functions as well as instruments. With the setup of the preparation controlling recipes will be arranged and transferred for the connected instruments (e.g. FlexyLab, HEL Chemscan, HP AutoMate, Surveyor, Anachem) or process control systems (e.g. Siemens PCS 7). As soon as the preparations are performed at automates/plants, process accompanying measured values will be collected. Of course, additionally you still have the possibility to enter measured values manually (e.g. from an offline analysis). Based on the measured values decisions may be taken promptly like for example the termination of preparation work.

The module of test series offers the possibility to display the collected result values graphically in a chart (result values may be e.g. process accompanying measured values, analytical result values of educts and products).



Starting from the graphic plot you can display the complete set of all measured values, that have been collected at a certain time point.



## Reporting

When the preparation handling has been completed a report can be generated automatically and distributed by taking into account a distribution list. Such a report will contain information on the developing of synthesis and inspection of the synthesized materials. LABS/R contains an open report tool interface which enables the authorized user to apply his preferred report tool for generating report templates. The standard system already contains a multitude of general report templates based on the MS Office products, Oracle Reports as well as on the iCD report format FreeForms.

Reports can be generated at any step of the recipe optimization:

- for a single preparation
- for a test run
- for a test
- for the complete project

Furthermore, it is possible to send the report to an external application (e.g. a research database). The module of scheduled reports allows arranging user-defined automatic report generation and distribution in regular intervals.

## Evaluations

All information, starting from the project structure up to the single measured value is stored in a central SQL database. This advantage guarantees a selective and easy to use evaluation of data.

**Evaluation Test Series 79 – F-04001-001**  
 Document: P:\projekte\p376\Testinstallation\labs\release\vbms\ular\F-04001-001-79.doc  
 released: 16.08.2004  
 Status: 2  
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**Description of Experiment**

Project-No.: V12345      Fructose-Alanin (Amadori Compound)      Step: 1  
 Versuch: 536  
 Apparatus: FlexLab001  
 Laboratory: PD

**List of Materials**

	Material	Formula	[g/cm]
Reactant	A001 L-Alanin	C3H7NO2	1,0000
Reactant	G001 Glucose	C6H12O6	1,0000
Solvent	M001 Methanol	CH4O	0,7867
Solvent	W001 Water, HPLC	H2O	1,0000
Product	F002 Fructose-Alanin	C9H17NO7	1,0000
Byproduct	F001 Fructose	C6H12O6	1,0000

**Used Batches and Amount**

List of Materials

Material	Batch	MAmount	Test Run
A001 - L-Alanin	L-2004-101220	1,00 g	001 002 003 013 014 015
A001 - L-Alanin	L-2004-101220	1,57 g	004 006 008 016 017 018
A001 - L-Alanin	L-2004-101220	2,33 g	007 009 009 019 020 021
A001 - L-Alanin	L-2004-101220	3,00 g	010 011 012 022 023 024
G001 - Glucose	Merck-1234567	10,00 g	001 002 003 004 005 006 007 008 009 010 011 012 013 014
M001 - Methanol	L-323-234567	10,00 g	015 016 017 018 019 020 021 022 023 024
W001 - Water, HPLC	PuraChem-1234	10,00 g	001 002 003 004 005 006 007 008 009 010 011 012

**Comments**

Aim:  
 Optimization of yield.  
 Reduced quantity of byproducts  
 Realization:  
 Reaction vessel under nitrogen.  
 Cleansing using cation exchanger.  
 Lyophilisation.

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Author: \_\_\_\_\_      Witness: \_\_\_\_\_      Witness: \_\_\_\_\_  
 Date: \_\_\_\_\_      Date: \_\_\_\_\_      Date: \_\_\_\_\_

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**Results for Test Series**

Run	Status	Experiment	Ala GAmount [g]	Solvent	Temperature [°C]	Fructose-Alanin [%]	Glucose [%]
001	F	F-04001-001-022	1	M001	50	25,0	10,0
002	F	F-04001-001-023	1	M001	75	26,0	12,0
003	F	F-04001-001-024	1	M001	100	27,0	12,0
004	F	F-04001-001-025	1,67	M001	50	28,0	10,0
005	F	F-04001-001-026	1,67	M001	75		
006	F	F-04001-001-027	1,67	M001	100		
007	A	F-04001-001-028	2,33	M001	50		
008	A	F-04001-001-029	2,33	M001	75		
009	A	F-04001-001-030	2,33	M001	100		
010	A	F-04001-001-031	3	M001	50		
011	A	F-04001-001-033	3	M001	75		

**Comments**

003 Temperature to high. Glucose deutlich zu hoch. Glucose caramellises in reaction vessel.

**Result**

	Stoff	MW [g/mol]	Formel	[g/cm <sup>3</sup> ]	Versuch#/aufe
Product	F002 Fructose-Alanin		C9H17NO7	1,0000	001
Byproduct	F001 Fructose		C6H12O6	1,0000	002

Analysis:      IMS: Identity conforme [X]

Evaluation:  
 Quantity of L-Ala has no effect on yield.  
 Tests continue in further series.

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Author: \_\_\_\_\_      Witness: \_\_\_\_\_      Witness: \_\_\_\_\_  
 Date: \_\_\_\_\_      Date: \_\_\_\_\_      Date: \_\_\_\_\_