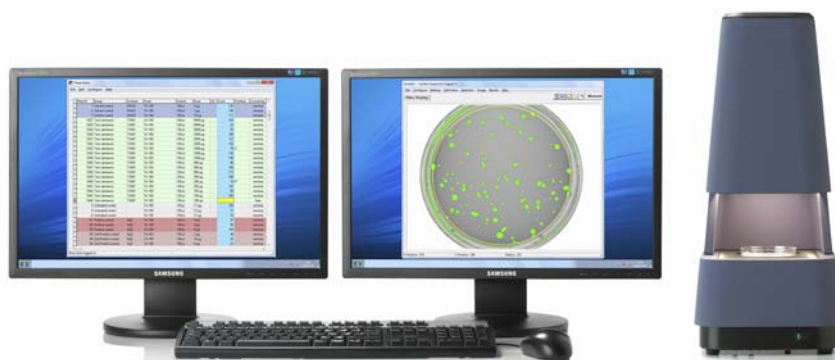


FOR THE BACTERIAL REVERSE MUTATION TEST



The **Ames Study Manager™** is an integrated suite of software for conducting the Ames Bacterial Reverse Mutation Test according to regulatory guidelines. It has been designed to fulfil the requirements of safety assessment laboratories in pharmaceutical, medical device and chemical companies as well as contract research organisations.

Ames Study Manager

- **Flexible study management**
accommodates any study design
- **Automatic plate counting**
in conjunction with the Sorcerer colony counter
- **Highly flexible configuration**
including the ability to share controls between experiments
- **Meet regulatory requirements**
with Ames Study Manager's comprehensive compliance options
- **Oracle database connectivity**
for optimal security of result and audit data
- **Configurable plate observations**
flag plates for observations such as precipitation
- **Links to the System Access Manager**
for GLP and FDA 21 CFR Part 11 compliance
- **Comprehensively tested and validated**
in accordance with our Quality Management System which is approved to ISO 9001:2008 incorporating ISO 90003

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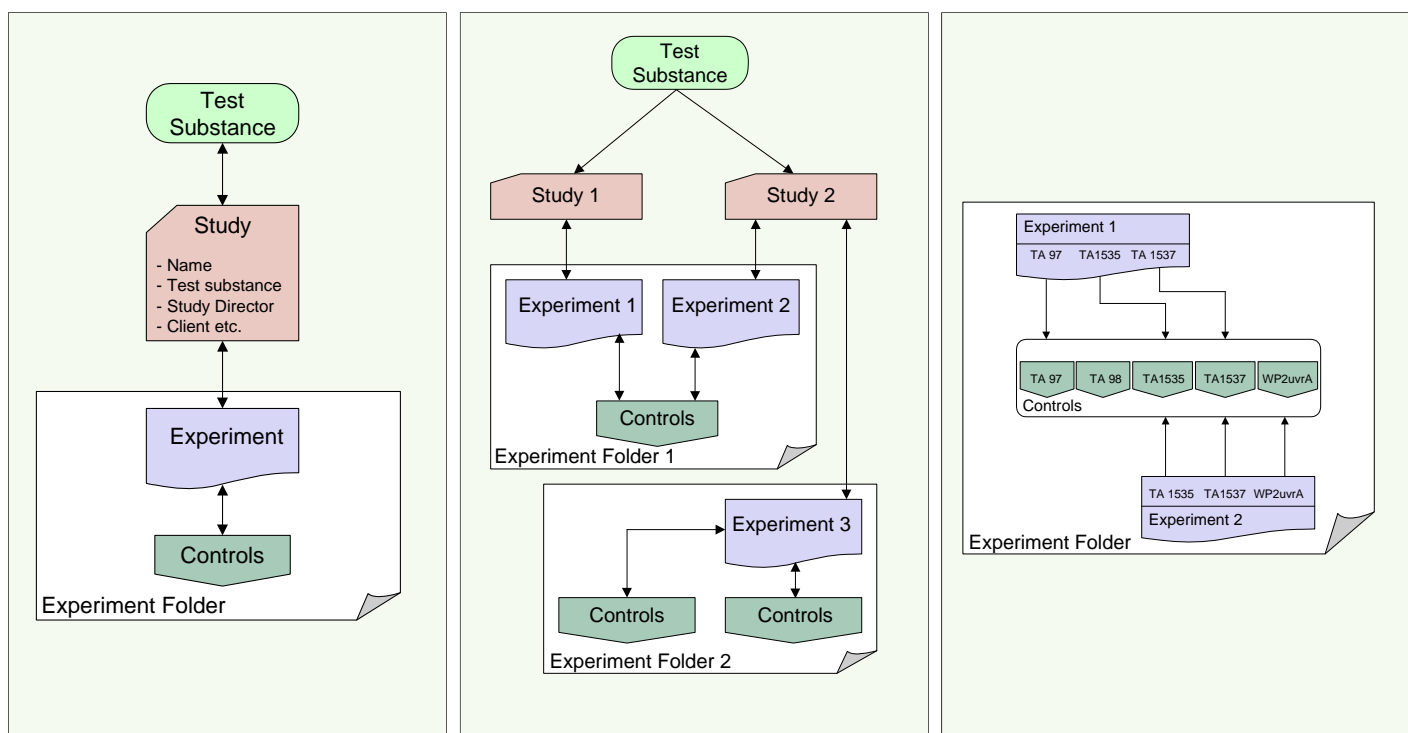
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Overview, Concept & Structure

At the outset it was clear that the Ames Study Manager should be able to accommodate the varied methodologies employed by different laboratories without compromising ease of use. Furthermore, it needs to be capable of handling large amounts of complex data. For these reasons, it was decided to interface the program to an Oracle relational database for security of data and audit trails.

Conceptually, the program links a particular *Test Substance* to one or more *Studies*. Each *Study* consists of one or an extended series of *Experiments*. An experiment consists of the treatment plates for all of the strains used, doses, number of replicates and metabolic activation.

The program is structured to allow concurrent strain-specific positive and negative (solvent and untreated) *Controls* with or without metabolic activation to be shared between different experiments whether they are part of the same or a different study. To achieve this, the program groups together plates generated as controls for a particular set of treatments into an *Experiment Folder*. Each folder will contain plates which share a common incubation time, method etc. In practice, an experiment folder is likely to contain details of all experiment and control plates to be created on a particular day.



This represents the most basic arrangement where a Study has a single Experiment with its one set of treatment plates linked to one set of control plates. The Experiment and Controls are held in a single Experiment Folder.

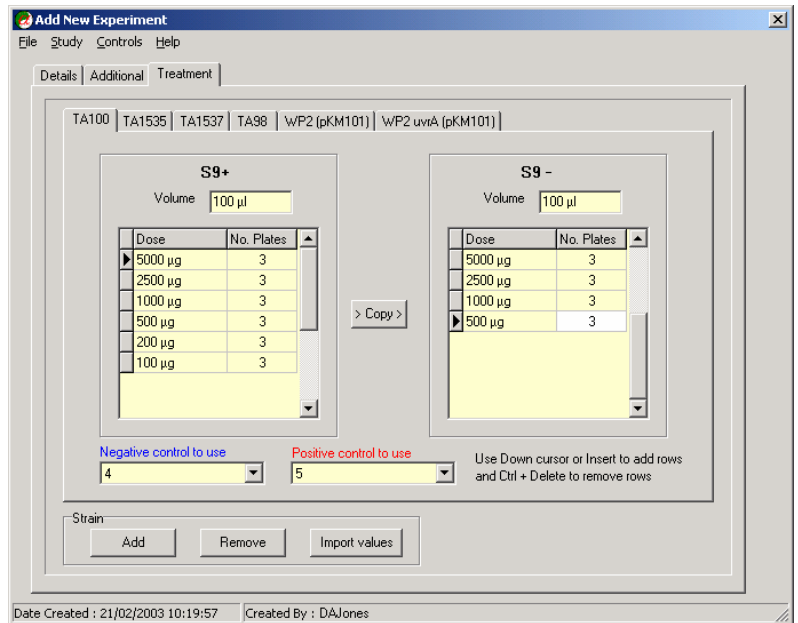
Here Folder 1 holds two Experiments sharing a common set of Controls and each Experiment is part of a different Study. Folder 2 has one Experiment linked to two sets of control plates. Study 2 consists of two Experiments from different folders.

Experiment treatment plates are linked to control plates for the same strain. Controls can be configured for each strain and may include Solvent, Untreated, 1 or 2 Positive controls and Viability plates. The scheme shown above has one set of Controls shared by two Experiments.

Creating Studies & Experiments

In routine use, most laboratories conduct their studies and experiments following a similar procedure and design. The Ames Study Manager makes extensive use of customisable *Templates* on which to base new studies, experiments etc. and thus avoid unnecessary repetition. Authorised users are able to independently configure Substance, Strains, Solvents, Positive control chemicals, Study types, Experiment templates, Negative control templates and Positive control templates.

A logical procedure is followed to create a study starting with entering details of the test substance (Name, CAS no., Physical nature etc). An appropriate study type is selected and details for the new study are entered.



The study is then linked to the substance. An experimental folder is created into which experiments and associated controls are placed. Experiments are generated using the experimental templates which include details of strains, treatment doses, activation, no. of replicate plates etc. Each experiment within the folder is then linked to a study and to one or more sets of control plates. Finally, a table is generated showing the plate identifiers ready for count data to be captured.

Plate counting and data capture

Group	Plate ID	Replicate	Contents	Volume	Dose	Strain	S9	Count	Postfixes
Test substance	370	2 of 3	Compound X	100 ul	250 ug	WP2 uvrA	+	125	
Test substance	371	3 of 3	Compound X	100 ul	250 ug	WP2 uvrA	+	119	P
Test substance	372	1 of 3	Compound X	100 ul	100 ug	WP2 uvrA	+	111	
Test substance	373	2 of 3	Compound X	100 ul	100 ug	WP2 uvrA	+	143	
Test substance	374	3 of 3	Compound X	100 ul	100 ug	WP2 uvrA	+	130	C
Solvent control	115	1 of 5	Water	100 ul	100 ul	TA 100	-	81	
Solvent control	116	2 of 5	Water	100 ul	100 ul	TA 100	-	76	
Solvent control	117	3 of 5	Water	100 ul	100 ul	TA 100	-	82	
Solvent control	118	4 of 5	Water	100 ul	100 ul	TA 100	-	83	
Solvent control	119	5 of 5	Water	100 ul	100 ul	TA 100	-	83	
Solvent control	123	1 of 5	Water	100 ul	100 ul	TA 100	+	92	
Solvent control	124	2 of 5	Water	100 ul	100 ul	TA 100	+	103	
Solvent control	125	3 of 5	Water	100 ul	100 ul	TA 100	+	93	
Solvent control	126	4 of 5	Water	100 ul	100 ul	TA 100	+	92	
Solvent control	127	5 of 5	Water	100 ul	100 ul	TA 100	+	87	
Untreated control	120	1 of 3				TA 100	-	90	
Untreated control	121	2 of 3				TA 100	-	83	
Untreated control	122	3 of 3				TA 100	-	82	
Untreated control	128	1 of 3				TA 100	+	91	
Untreated control	129	2 of 3				TA 100	+	95	
Untreated control	130	3 of 3				TA 100	+	84	
Positive control	95	1 of 3	NaA	100 ul	2 ug	TA 100	-	463	
Positive control	86	2 of 3	NaA	100 ul	2 ug	TA 100	-	419	
Positive control	87	3 of 3	NaA	100 ul	2 ug	TA 100	-	410	
Positive control	88	1 of 3	2AA	100 ul	2 ug	TA 100	+	194	
Positive control	89	2 of 3	2AA	100 ul	2 ug	TA 100	+	202	
Positive control	90	3 of 3	2AA	100 ul	2 ug	TA 100	+	253	

The program allows individual plate counts to be either entered manually or captured directly from automatic colony counting systems such as **Sorcerer** from Perceptive Instruments.

During data entry/capture, prompts will require entry of reasons for any changes made and the user is able to apply postfixes e.g. P to indicate precipitation. These can be entered for a specific plate or applied across replicate plates, strains or treatment dose. Additional comments can also be entered as appropriate. Counting can be suspended at any time to be continued later.

When used with the Sorcerer colony counter, the two programs combine to create a totally integrated package for the Ames test. Counts are requested from within the Ames Study Manager with a single key press and are instantly returned and displayed in the plate editor. It is possible to re-read or manually override the automatic plate counts if necessary. In this situation, the user will be prompted to enter a reason for the change.

Database tables & report generation

All information generated during the course of creating and conducting a study is sent directly to secure, independent database tables within Oracle. The physical location of the database is fully configurable and audit trail tables can be stored independently of the core data tables if desired.

All information stored in the database is accessible using SQL Scripted query commands. SQL functionality can be fully utilised to generate custom reports and to provide historical control data.

The Ames Report Generator allows the user to browse through a hierarchical view of each element of a study or experiment in order to request automatically generated customisable Microsoft Word reports. These reports are password protected for extra data security.

The program provides a choice of experiment report formats that include number, mean & standard deviation of revertant colonies for all strains, treatments & controls for +/- S9. The standard OECD format report also includes ratio of treated and positive control plate counts to solvent control counts.

Study Name: Ind01 Experiment: Exp4176 Assay Conditions: Standard plate incorporation assay		Study Code: 1065 Date Filed: 21/07/02 Contact: 240792				
Strain	Compound	Dose level per plate	Without metabolic activation Mean revertants per plate	S9 Ratio treated / solvent	Individual revertant colony counts	
TA 98	Ind01	5000 ul	2.3	0.0	0.0	1, 2, 1
		2500 ul	3.7	1.5	0.1	5, 2, 4
		1000 ul	22.0	7.0	0.7	19, 17, 20
		500 ul	30.0	7.5	0.9	33, 20, 28
		250 ul	33.7	11.7	1.1	47, 25, 29
		100 ul	28.0	4.4	0.9	33, 26, 23
Water			32.0	11.2	37, 39, 43, 16, 25	
Unreated Control			37.7	10.0	36, 28, 49	
TA 100	Ind01	5000 ul	8.0	7.5	0.7	9, 15, 0
		2500 ul	34.0	27.2	2.7	179, 137, 116
		1000 ul	118.0	3.3	1.4	120, 115, 116
		500 ul	126.0	23.1	1.5	110, 134, 100
		250 ul	102.0	8.1	1.0	94, 104, 105
		100 ul	88.0	16.8	1.1	94, 74, 105
Water			82.0	2.0	81, 76, 83, 83	
Unreated Control			80.0	3.0	76, 83, 81	
TA 153	Ind01	5000 ul	3.0	4.4	0.2	8, 1, 0
		2500 ul	4.0	2.0	0.3	3, 7, 2
		1000 ul	16.7	6.0	0.8	5, 10, 17
		500 ul	8.3	4.3	0.6	8, 13, 4
		250 ul	13.7	4.2	1.0	9, 17, 15
		100 ul	11.0	1.0	0.8	10, 11, 13
Water			14.2	4.3	21, 14, 10, 15, 11	
Unreated Control			16.0	3.0	16, 19, 13	
TA 157	Ind01	5000 ul	10.3	7.5	0.7	3, 18, 10
		2500 ul	7.3	4.4	0.3	17, 3, 2
		1000 ul	6.0	0.4	0.4	6, 6, 6
		500 ul	10.7	3.1	0.7	5, 15, 12
		250 ul	14.3	4.2	0.9	19, 15, 11
		100 ul	18.7	2.1	1.2	17, 21, 18
Water			23.6	3.6	14, 16, 21, 16, 11	
Unreated Control			20.3	3.2	19, 16, 24	
WP2 verA	Ind01	5000 ul	33.7	27.5	0.7	7, 62, 33
		2500 ul	32.0	7.0	1.0	45, 23, 29
		1000 ul	113.0	6.0	2.3	121, 116, 109
		500 ul	96.7	23.0	1.9	71, 101, 118
		250 ul	109.3	5.0	2.1	114, 104, 110
		100 ul	122.7	16.9	2.4	137, 127, 104
Water			31.0	6.4	33, 38, 49, 34, 41	
Unreated Control			31.0	6.6	37, 44, 32	
TA 98	2 NF	1 ul	763.7	93.7	23.9	861, 674, 756
TA 100	N/A	2 ul	426.7	28.0	3.0	463, 418, 410
TA 153	N/A	2 ul	397.7	40.2	42.1	577, 372, 644
TA 157	9 AC	2 ul	39.7	16.2	2.5	35, 37, 37
WP2 verA	BN20	1 ul	110.0	33.0	8.0	791, 790, 849

Study Name: Ind01 Experiment: Exp4176 Assay Conditions: Standard plate incorporation assay		Study Code: 1065 Date Filed: 21/07/02 Contact: 240792											
Dose Level Per Plate	Strain	Number of Revertants, (Mean) +/- SD											
		TA 100	TA 153	WP2 verA	TA 98	TA 157							
S9-Mix (-)	Unreated Control	76 (80)	16 (16)	29 (23)	96 (95)	3 (3)	0 (0)						
		83	19	3.0	44	6.6	101	6.6	2	1.7	0	0.6	
		81	15	2	52	2	2	1					
	Solvent Control (Water)	81 (81)	21 (18)	52 (51)	88 (88)	37 (32)	14 (16)						
		76	2.9	14	4.3	28	6.6	115	10.6	39	11.2	16	3.6
		82	10	49	107	43	21						
	5000 ul	9 (8)	8 (3)	7 (3)	29 (46)	1 (1)	3 (10)						
		15	7.5	1	4.4	62	27.5	64	17.6	2	0.6	10	7.5
		0			44								
	2500 ul	119 (141)	3 (3)	45 (52)	57 (59)	3 (3)	17 (7)						
		127	27.2	7	3.6	52	7.0	61	9.2	2	1.5	3	1.4
		116	2	59	49	4	4						
1000 ul	120 (116)	5 (13)	123 (115)	90 (83)	39 (23)	6 (8)							
	113	5.3	10	6.0	116	6.0	76	6.5	17	7.0	6	0.6	
	116	17	109	83	20	6							
500 ul	118 (120)	8 (8)	71 (91)	92 (96)	30 (30)	5 (11)							
	114	13.1	13	4.5	101	23.8	91	5.0	29	7.5	15	5.1	
	108	4	118	101	38	12							
250 ul	94 (101)	9 (14)	114 (109)	110 (113)	47 (34)	19 (14)							
	104	6.1	17	4.5	104	5.0	107	4.6	25	11.7	12	4.2	
	105	15	110	116	29	11							
100 ul	84 (80)	10 (11)	137 (123)	125 (110)	33 (20)	17 (20)							
	74	16.4	11	1.0	127	16.9	98	12.6	26	4.4	21	2.1	
	106	12	104	108	25	18							
Name	N/A	N/A	BN20	BN20	2 NF	9 AC							
Dose Level	2 ul	2 ul	1 ul	1 ul	1 ul	2 ul							
No. of Revertants	443 (431)	597 (598)	791 (810)	546 (617)	801 (764)	25 (40)							
	419	26.4	372	40.2	495	73.8							
	410	64.4	649	61.4	614	736							

The Report Generator can also generate Microsoft Word documents displaying plate IDs, strains, doses etc. to assist with the plate preparation process. A plate audit report shows all entries and changes made to plate data for any given experiment.

The password protection method employed by the Ames Report Generator protects the document from alterations and allows users to annotate sections of the report without affecting underlying report data.

Each report is based on template files for table formatting and document backgrounds, allowing reports to be customised for a professional, corporate appearance.

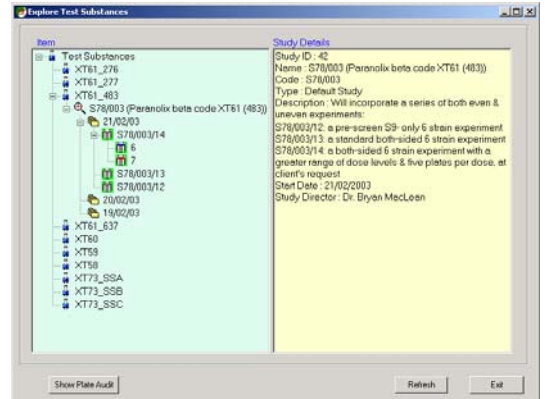
Perceptive Instruments provides a report customisation service to clients requiring either additional reports or modifications to the existing report formats.

Auditing & User Administration

Auditing

Every auditable event can be used to force a user into giving a reason for a change (e.g. when re-counting a plate), or to force the user to re-input their passwords to confirm their identity (e.g. when locking or unlocking experiment data). Audit data includes information on date/time, user, system, details of changes made (including original & new values) and details of any reasons given for those changes.

Audit trail information is generated and saved to the database in real-time during the process of designing, creating and running studies. Authorised personnel can view plate audit trails via a hierarchical tree view of studies & test substances. This view also allows auditors to quickly observe details associated with a selected study, test substance, folder, experiment or control.



The screenshot shows a table titled 'Program Audit Data' with columns for Date / Time, User ID, Event Code, Description of Event, Session ID, System ID, Refers to ID, and Index. The table contains 47 rows of audit events, such as 'Normal exit from program', 'Exit from plate editor', 'Plates edited using plate editor', 'Plate editor started', 'Equipment treatment plates created', 'Positive control plates created', 'Negative control plates created', 'Exit from plate editor', 'Plate editor started', 'Positive control locked from further editing', 'Negative control locked from further editing', 'Equipment locked from further editing', 'New equipment added to experiment folder', 'Treatment details modified in experiment', 'Details of experiment modified', 'New equipment created', 'Successful user re-login to program', 'Inactive timeout occurred and user was logged out', 'New positive control added to experiment folder', 'New negative control added to experiment folder', 'New negative control created', 'Experiment folder created', 'New study created', 'New test substance added', 'User login successfully completed', 'Normal start of program', 'Normal exit from program', 'Screen added via Configure menu', and 'Screen added via Configure menu'.

The Main Event Log lists all user actions taken within the program at all stages of conducting a study. Each event has a unique event ID and a description (such as 'New negative control added to experiment folder') that explains the nature of the event. Every action is listed chronologically, giving information on time, date, user etc.

Many of the recorded events include more in-depth information, which can be displayed using the Show Detail button. The main event log can also be used to access plate audit trails on a user-by-user basis. A plate auditing report, included with the Ames Report Generator, creates a protected Microsoft Word document detailing all entries & changes made to experimental plate data for any single experiment.

A Setup Users dialog, available only to system administrators, can be used to configure the access rights of each user level to different areas of the program. Each access right can be enabled, disabled or made read-only. An example setup might be to only allow Users to enter data in the Plate Editor, whilst Advanced Users can also create experiments, controls etc.

System Access Manager

The System Access Manager controls access to the Ames Study Manager using an Oracle database to securely hold all information. This allows the network administrator to assign access levels for each individual.

There are four configurable access levels available: Users, Advanced Users, Study Directors and Auditors. Individual personnel are assigned specific login time outs, password validity etc. The System Access Manager is designed to comply with the FDA 21 CFR Part 11 Final rule on Electronic Records & Electronic Signatures.



System Access Manager

electronic signature auditing & control

Running the Ames Study Manager with Sorcerer



Sorcerer Automatic Colony Counter

The Ames Study Manager can run in conjunction with the Sorcerer automatic colony counting system to create a total solution for the Bacterial Reverse Mutation Test. Sorcerer combines sophisticated image processing and analysis with an innovative Petri-viewer to provide fast, accurate counts of revertant colonies.

The small footprint Petri-viewer utilises incident, transmitted & dark-field illumination to facilitate counting on all combinations of test substances in Vogel-Bonner or alternative media. The use of cool white light ensures excellent contrast between colonies and substrate. The CCD camera and automatic lens relay a live image of the sample to the computer screen.

In routine use, the user positions the cursor on the row of the plate to be counted and places the sample in the Petri-viewer. The Sorcerer system displays an image of the plate on-screen with a coloured overlay indicating detected colonies. A single press of the space bar initiates the count, which is returned automatically and inserted into the Count cell of the selected row.

Comprehensive support and validation

Because we understand the time and effort put into the implementation of a new system in a GLP & FDA compliant environment, Perceptive Instruments offer guidance through all stages of the project and help by providing our standard Installation Qualification documents, pre-installation guidelines and any other relevant documentation prior to the installation.

The Ames Study Manager has been comprehensively tested and validated in accordance with our Quality Management System which is approved to ISO 9001:2008 incorporating ISO 90003. All project and test documentation is made available to assist you with your own validation of the system. Purchasing the Ames Study Manager system Perceptive Instruments entitles you to a full year of product support and software updates, provided free of charge.

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Technical Specification & Summary

Plate Counting	Manual entry of count data via Plate Editor utility. Counts can be captured directly from automatic colony counting systems such as Sorcerer.
Study Scope	No constraints for numbers of Studies, Experiment Folders, Experiments, Test substances, Strains, Control sets, Positive control chemicals etc.
Study Details	Name, Start Date, Study Type, Test Substance, Description, Client, Study Director. Any number of additional fields configurable. Can be configured as compulsory or optional entries.
Experiment Scope	Each subset of plates within an experiment may be configured differently for dose levels, strains, number of plates, metabolic activation etc.
Experiment Folders	Allows grouping of Experiments and Controls that share common incubation time, method etc.
Experiment Details	Name, Start Date, Type, Description, Solvent, Justification for solvent used, Solubility. Any number of additional fields configurable. Can be configured as compulsory or optional entries.
Test Substances	Name, CAS No., Reference No., Batch, Origin, Physical Nature, Properties, Stability, Storage Conditions.
Plate Groups	Test substance, Solvent control, Untreated control, Viability, Positive control (1 or 2 sets).
Plate Postfixes	Unlimited number of plate postfix codes for observations such as Incomplete lawn, Precipitation etc. Can be applied to single or multiple plates
Positive Controls	Control code, Date created, CAS No., Reference No, Manufacturer, Manufacturer part No., Batch, Description. 1 or 2 sets of positive controls for each strain.
Negative Controls	Type (solvent, untreated), Description, Solvent. Ability to add viability plates by strain.
Strains	Name, Description, Default positive control associations for -S9 & +S9 mixes. Each strain is independently configurable within an experiment or control.
Dose Levels	Unlimited number of dose levels. Different dose levels can be assigned to -S9 & +S9 mixes in the same experiment.
Templates	New Studies, Experiments & Control Sets can be based upon configurable templates.
Experiment Reports	Experiment preparation, data and plate audit reports in Microsoft Word format. Custom reports produced if required.
Experiment Folder Security	Within an Experiment Folder, plates can be locked against accidental or unauthorised changes.
User Levels	User, Advanced User, Study Director, System Administrator, Auditor.
User Access Rights	System Administrator can assign different rights for each user level. Menus and options can be enabled, read-only or disabled.
Minimum Specification	Desktop PC with Pentium 2Ghz processor with 512MB RAM, Windows XP with Oracle 9i or higher & Microsoft Word 2000 for report generation.



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Perceptive Instruments Ltd., founded in 1990 in Great Britain, develop high quality, cost-effective image analysis & data processing solutions for many areas of scientific research including both regulatory and non-regulatory genetic toxicology assays.

We have established an enviable reputation based upon experience, integrity and attention to detail, as well as for the personal care we give to all our clients and our willingness and ability to completely satisfy their needs. With over 75% of sales made outside Great Britain, we have experience in supplying & supporting our products throughout the world.

We produce systems for a range of genetic toxicology assays including Ames Bacterial Reverse Mutation Test, Comet Assay, Unscheduled DNA Synthesis and Mouse Lymphoma Assay. These products are designed to fulfil the requirements of Good Laboratory Practice, FDA 21 CFR Part 11 and other international regulatory requirements. We operate a Quality Management System to ISO 9001:2008 as approved by ISOQAR, the UKAS & ANAB accredited certification body.

Over the years we have built successful, long-term relationships with our customers. Our products are used by the world's leading pharmaceutical, medical device and chemical companies, contract research organisations, universities and other research institutes.



Perceptive Instruments have supplied image analysis and data processing solutions for regulatory genetic toxicology assays for over a decade. We have ISO 9001:2008 approval for our Quality Management System from a UKAS & ANAB accredited certification body.

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