INTRODUCTION TO - Provet Statistics Tool

The Provet Statistics tool is planned for recording (by researchers) and collecting (by KEKS) the animal data required by the "new" legislation (Law 497/2013).
The aim is a) to indicate animals that have experienced "harm" in scientific/experimental or educational purposes (used in "Procedure"), b) to show the actual severity of the "Procedure" experienced by those animals, and c) to classify all animals based both on geno-/phenotype and involvement in creation/maintenance of genetically altered (GM) strains.

1. Each animal removed since 1.1.2014 has to be reported according to the new requirements.
   - It is the researcher's duty to record the data for animal, KEKS will collect and forward it to the Authorities.
     - Statistics data can be recorded (to mark ready and save) by Primary researcher, License holder, Project-Responsible-Person (PRP, Designated person responsible for the project activities. Law 497/2013: 24§ -> Decree 564/2013: 21§) and KEKS personnel.
     - Only Project-Responsible-Person (Hankevastaava) has a right to send the data for reporting (KEKS).

2 Animals are removed in Provet as before. The researcher is using a work request and an Animal Technician, who completes the task, removes the animal either in the animal card (one animal) or via group action (several animals) by recording the time and a way of removal. If the animal is asked to remove from the external license, the way of removal should be informed in the work request.
- The appropriate ways of removal are:
  - Died: *found dead [Add reason of death as 'a footnote of removal (Poiston lisätieto)', if possible]*
  - Killed (sick animal): *killed "prematurely" due to sickness, welfare problem etc.*
  - Killed after the end of use (in research/production): *i.e. study or production use was ended for the animal*
  - Killed unused (as leftovers): *Animal was not needed at all (i.e. It was produced unnecessarily.)*
  - [Sold, Departed: *not needed by researchers (animal sent alive to another facility outside the Oulu University)]*

3 When the animal is found dead or the sick animal is killed without the work request, the researcher will get a notice of this to complete the statistic.

4 Animal is shown in Statistics Tool as soon as it is removed (*see* Annex 2).
- Statistics Tool is available in the main menu by selecting: Reports → Statistics (Tilastointi)

5 It is important to understand, what is a "Procedure" meant by Law 497/2013, For this see Annex 1.

6 The variables needed for Statistics are GS, Use, (Re-use) and SV, as well as NewGL and OldGL
- Generic Status (GS) defines the status of the gene modification of the animal; GS1 is not GM-animal, GS2 is GM-animal with no detected harmful phenotype, GS3 is GM-animal with harmful phenotype.

- Combination GS2/GS3 means that the phenotype is not characterized yet and the animal is not ready for reporting.
- The following variable values are considered as a "Procedure" in Provet: Use= [Y] or GS=[GS3] (And also combination of NewGL=[Y] and GS=[GS2])
- Variables NewGL and OldGL are labels, that should be attached to animals for classification purposes (to indicate animals involved in creation (NewGL) or maintenance (OLdGL) of GM-lines)
- Actual Procedure SV is used to indicate the level of "total harm" experienced by animal (See Decree 564/2013: Annex III, Dir 2010/63/EU: Annex VIII and EU consensus documents.)
- SV categories: SV1= Non-recovery, SV2= Mild, SV3= Moderate, SV4=Severe, NB= No need to categorize (No harm/pain inflicted on animal)
- Re-use indicates if animal has been used earlier for a totally different scientific/educational purpose

- It is possible to record data for GS (in animal card, via group modification) and SV ('Action by researcher' via animal card or group action) already for alive animals
- Before any data is recorded for variable, Provet suggests an assumption value (coming from the license and strain) → Assumptions should be checked by researcher.
- When the animal data row is checked, tick "Ready" for the animal, and save the data.
- See Annex 3 for more detailed instruction.

7 Animal will end-up in EU or FI-report

- 'Project-responsible' sends data of the previous year by latest at 31.1. The data can be sent also in smaller parts during the year.
- Animals that are used in a "Procedure" will end-up in annual EU-report, other animals in national FI-report.
- Those animals that have been sent alive outside Oulu University will not be included in reports in KEKS. Similarly, animals that have not existed in real life ("Virtual" animals) should be excluded from reports by Use= [NB].

ANNEX 1. WHAT IS – "Procedure" meant by Law 497/2013 (and Directive 2010/63/EU)

Directive 2010/63/EU (3§):

- "'Procedure means any use, invasive or non-invasive, of an animal for experimental or other scientific purposes, with known or unknown outcome, or educational purposes, which may cause the animal a level of pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice"
  - In Provet: Use = [Y]= Harmful "treatment" (any "harm" not directly related to GM geno/phenotype, caused in scientific/educational purpose)
- "This includes any course of action intended, or liable, to result in the birth or hatching of an animal or the creation and maintenance of a genetically modified animal line in any such condition, but excludes the killing of animals solely for the use of their organs or tissues."
  - In Provet: GS=[GS3] = Harm related to GM-geno-/phenotype (In Creation of new GM line all animals carrying the alteration are counted as used in a Procedure, i.e. also [GS2])

ELLA www-pages:

http://www.laaninhallitus.fi/lh/etela/hankkeet/ellapro/home.nsf/pages/E13636D4BC564200C2257AA1003A047D?opendocument

- Procedure may include one or more different steps carried out for one animal to meet a defined purpose. The time period for the procedure may differ according to these steps. Examples:
  - Procedure = a single subcutaneous injection of a test substance and the animal is killed by a method listed in Annex IV of Directive (Listed methods: Law 497/2013→ Decree 564/2013: Annex II)
  - Procedure = Anesthesia, surgical implantation of a blood pressure transducer and, following a suitable recovery period, administration of test substance *s.c.*, follow up the blood pressure and the animal is killed by a method listed in Annex IV of directive. .

  Both above mentioned examples are one "Procedure", because all separate steps are needed to meet a single scientific purpose.

"Procedures" may be performed only for animals that are on external (ESAVI-) license.

- Animals must be transferred to ESAVI-license in Provet before (or immediately after) they are inflicted with any harm. It is researcher's duty to take care of this! (Can be done by 'Provet work request'). Similarly, animals that are already used in a Procedure should not be transferred to EKS License.
- Provet does not check the recordings before the animal is removed. But, in Statistics Tool, ticking "Ready" validates the animal data row (i.e. "Procedures" will not be allowed under internal licenses.)
- New licenses (1.8.2013 -): License is given for the number of animals than can be used in "Procedure"

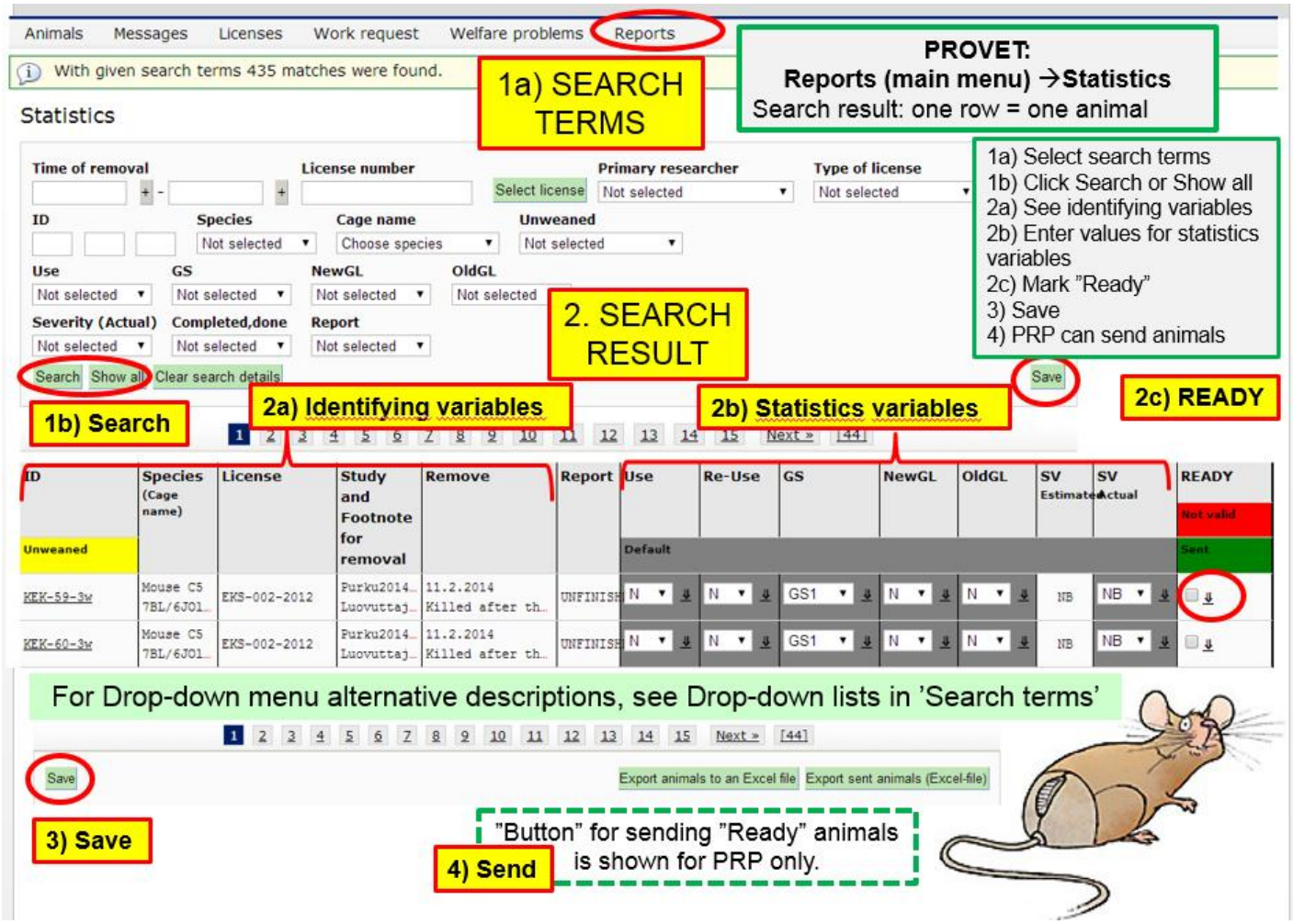
(Older licenses: You must also follow the number of animals that have been transferred to the license.)

- IMPORTANT to notice the difference: Killing of animals by accepted methods solely for the use of tissues or organs after death is not a Procedure (Directive /Art 3/1) → You are allowed to do this if you have internal license. BUT, if you e.g. collect samples during terminal anesthesia it is considered as a Procedure (SV=SV1 = Non-Recovery). → You need an external ESAVI-license for this.
- If an animal is found dead and the death is expected to be a consequence of the experimental procedure
  (*EU working Document on Severity Assessment Framework, 11-12.7.2012*)
  - the actual severity should be reported as 'severe', unless an informed decision can be made that the animal did not experience severe suffering prior to death;
  - If it is unlikely that death was preceded by severe suffering, the actual severity classification should reflect the known experience prior to death. (Factors such as frequency of monitoring, use of analgesia, etc. will need to be given due consideration).

Annex 2. PROVET STATISTICS TOOL - User interface

- Reports (Provet main menu) → Statistics (Tilastointi)

1. Use Search terms (e.g. License, Primary researcher, "Ready/Unfinished" –status) to find/identify the animals
   - Yellow field = Pup (unweaned removed animal)
2. Complete/check the statistic variables (Gray field = Provet assumption)
   - Arrow ⇩ copies value into the fields below (If rows are marked "Ready" and saved, they are protected)
3. Tick (=√) 'Ready' → Provet validates the row (Red field = data not valid)
4. Remember to save the changes (2 identical Save-buttons, both works independently) → Your initials will be shown next to the "Ready" box
5. Only the Project-responsible-person (PRP) (name can be found in Provet license) has a permission to send ready animals and has a button for sending : "Ready".
6. It is possible to modify /correct animal data until Project-Responsible-Person (PRP) has sent the data.
   - For corrections: 1. Remove "Ready(√)" mark in the box 2. Make the correction 3. Tick "Ready" again 4. Save
   - The sent animals are not anymore modifiable by researchers (Green field = sent)



TIP: Sometimes it may be useful to divide large ESAVI-License into smaller sub-Licenses in Provet.

- This is necessary at least if animals are used in "Procedures" for different purposes (i.e. there are several different purpose codes in ESAVI-license).

If you think, there might be need for this please contact KEKS prior activation of your License in Provet.

Annex 3. HOW TO - Select Values for Provet Reporting Variables

Use HARMFUL "TREATMENT"	Re-Use RE-USE IN NEW "PROCEDURE"	GS GENO-/PHENOTYPE	NewGL CREATION OF NEW GM-LINE	OldGL MAINTENANCE OF ESTABLISHED GM-LINE	SV (Actual) PROCEDURE ACTUAL SEVERITY
Value for each reporting variable must be given for all animals removed since 1.1.2014 in Provet.					
SELECT [Y], IF – Harmful "treatment" (for scientific/educational purpose), not directly related to GM-phenotype) Harm = Any pain/suffering/ distress, invasive/non-invasive, equivalent to or higher than that caused by introduction of a needle.	SELECT [Y], IF – Animal was reused (i.e. it was used earlier in a "Procedure" for other scientific purpose. The earlier use must be reported separately to LAC) (Re-use: see Directive 2010/63/EU, Art 16)	SELECT [GS1], IF Not a GM animal. GM = Genetically altered (For each animal, classification should base always on detected/observed geno-/phenotype)	SELECT [Y], IF – Animal needed/existed for creation of a new GM-line (Inc. wild-type offspring) AND !Remember also to record: 1. Use=[Y], if harmful "treatment" relating to creation of new GM-line 2. GS based on detected phenotype	SELECT [Y], IF – Animal involved in maintenance of established GM-line (Inc. wild-type offspring) and not used in a"Procedure" !Remember also to record: 1. GS based on detected phenotype	SELECT [SV1 – SV4], IF – Animal with Use= [Y] or GS= [GS3] or (NewGL= [Y] and GS= [GS2]). Notice: All treatments as well as GM-phenotype and other factors affecting the procedure actual severity must be taken into account in the final score.
SELECT [NB], IF – Animal will be reported elsewhere (If, shifted alive from LAC, [NB] is suggested by Provet) OR – Animal has not existed at all	OTHERWISE, SELECT [N]	SELECT [GS2], IF GM-animal with no detected harmful phenotype (As far as alternative [GS2/GS3] is selected, animal is not Ready for reporting.)	OTHERWISE, SELECT [N] Purpose of labels (see IMP/Annex I/C2i): to indicate animals involved in creation of new GM-line or in maintenance of an established one (including wild-type offspring) There may be new ELLA instructions coming related to OldGL... OldGL=[Y] can now be used for all animals of established GM lines (Inc. wild-type offspring) not used in a "Procedure". (OldGL value can be corrected later based on Provet Cage-name, if Use and GS are entered correctly!).	OTHERWISE, SELECT [N]	OTHERWISE, SELECT [NB] – No need to classify
OTHERWISE, SELECT [N]		SELECT [GS3], IF GM-animal with detected harmful phenotype			
[Y]		[GS3]	[GS2] + [Y]		Notice. Choose actual severity [SV1]-[SV4] for those animals that will end up in EU-report. Else, SV = [NB].
Counted as used in a "Procedure" (see Law 497/2013) → will end up in EU-report | Other animals will end up in FI-report.					
GS and 'SV(Actual) of "an individual step/treatment" (together with Use)' can be recorded for an active animal (i.e. before removal):					
– If there is a treatment scored as (SV1-SV4) (recorded via "Action by researcher"), Use= [Y]		– Can be recorded in animal card or via 'Group modification'			– Can be recorded for a treatment via" Action by researcher". (Only the score of the most severe treatment is shown. Remember to include scores of all treatments and phenotype)
If there is no value recorded for an active animal, the following assumptions will be used at removal (Should be always checked by Researcher):					
1. IF the way of removal is "Leftover/unused", Use= [N] 2. ELSE, Use= [Y] for external and [N] for internal license.	Re-Use= [N]	1. Mother's GS, if available 2. ELSE, if strain (cage-name) is a non-GM-strain, GS= [GS1] 3. ELSE, GS= [GS2]	The value set in animal's license.	OldGL= [N]	1. If internal license, [NB] 2. ELSE, SV Actual = SV Estimated (Notice: SV estimated is always shown from License = the highest estimated SV)

not reported