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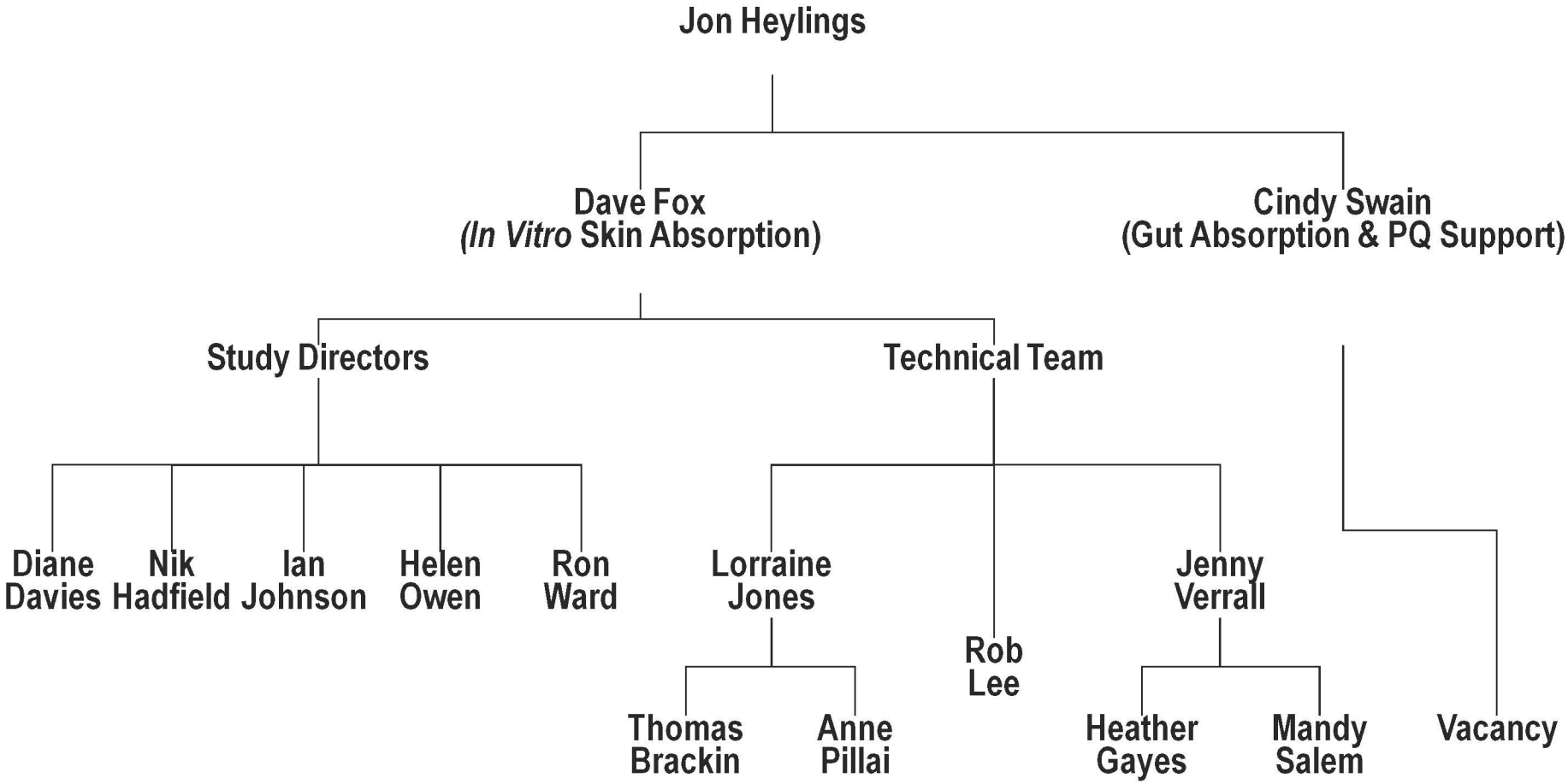
Absorption and *In Vitro* Toxicology

JON

AIVT presentation to the section

We will tell you about what we do

AIVT group structure



JON

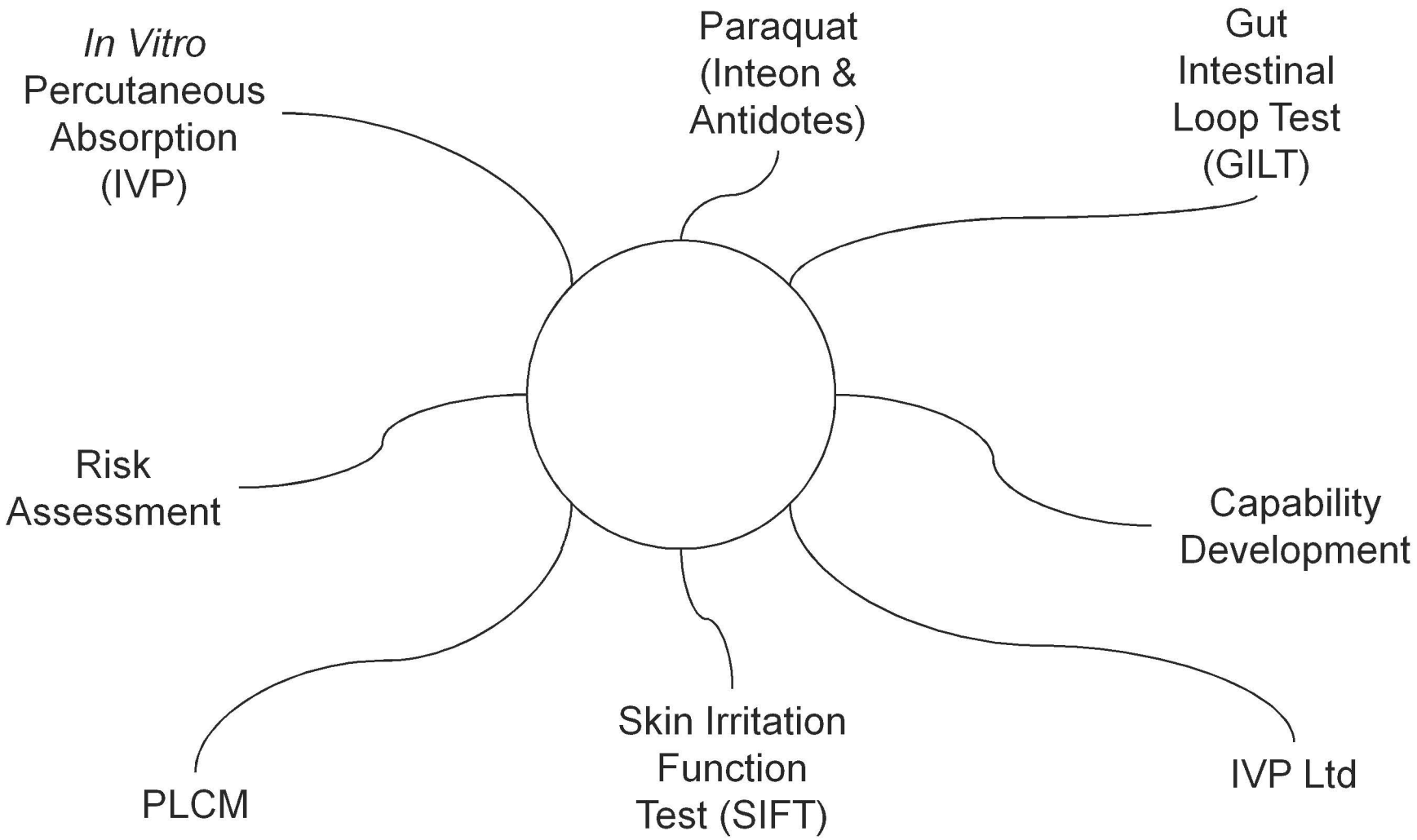
The group structure

Skin and gut – although new developments are bringing the areas closer together by utilising the available technologies and applying them to other areas

Large team of SD's

Newly structured technical team

What is AIVT?



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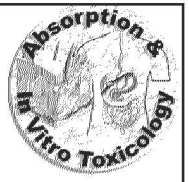
What is AIVT

Why AIVT – what does this actually stand for

We'll tell you what we do, why we do it and where we fit in

Who needs us?



- Syngenta businesses
  - Paraquat, (Inteon & antidotes)
  - Registrations for New Products
  - Formulation Development
  - Operator Exposure
  - Professional Products
  - Seed treatment
  - Studies for legal challenges
  - Gut absorption (Rodenticides and Stage 1)
- External clients (Income target of £1m)

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We produce data for the products we test for a variety of internal and external businesses

Some interesting oddities include marketing paying for studies to take protect patent by testing generics

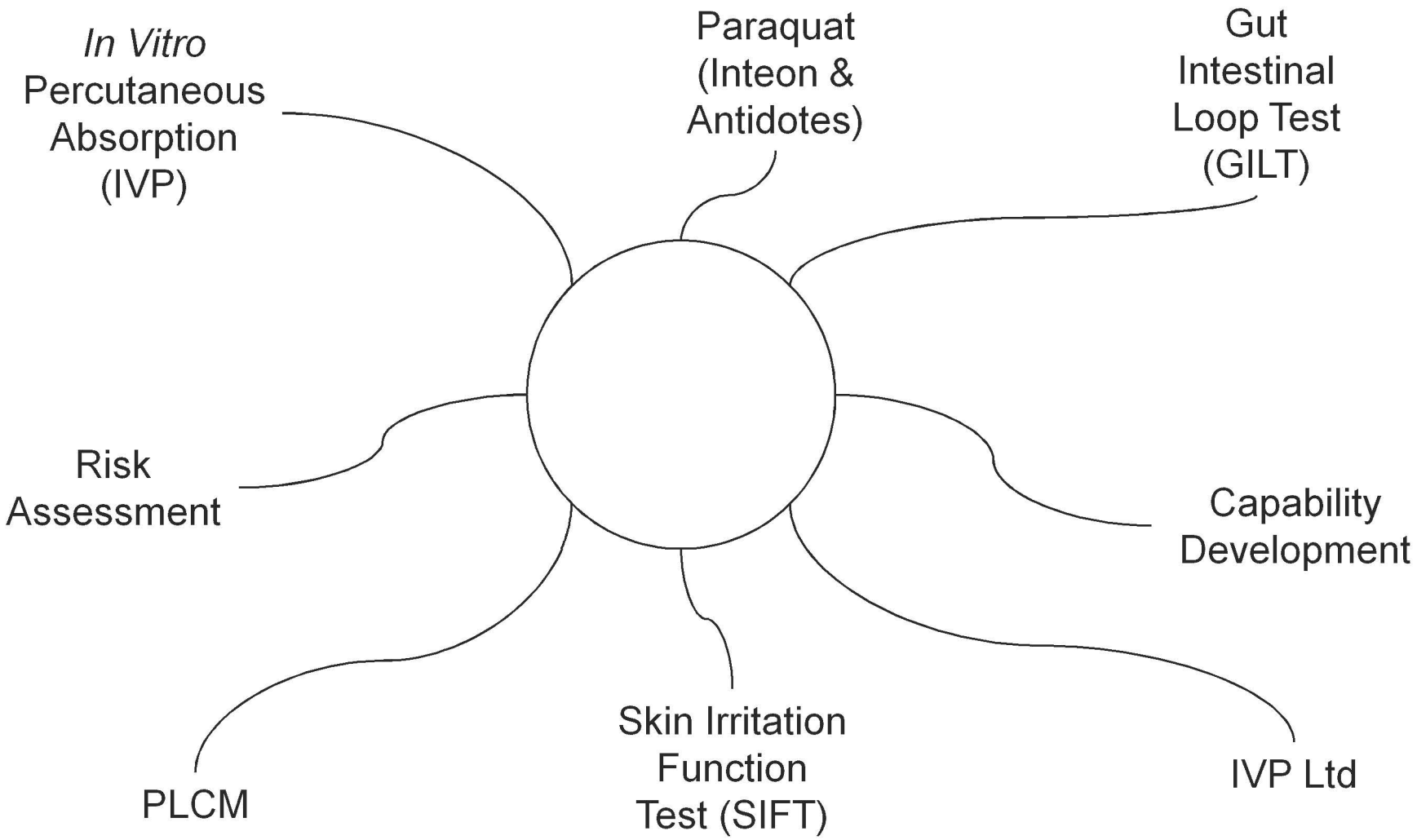
In vitro means alternatives to animals so cosmetics are important sources of external income and

We are responsible for generating a lot of external income per head

Why are we here?

- Our data is used for both hazard assessment and risk assessment as part of safety testing of its active ingredients and finished products

Risk Assessment



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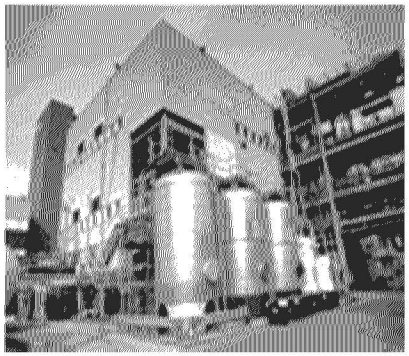
Hand over to Helen to talk about risk assessment

Protecting Human Health and the Environment

Absorption & In Vitro Toxicology

Healthy people

Health assessment and toxicology

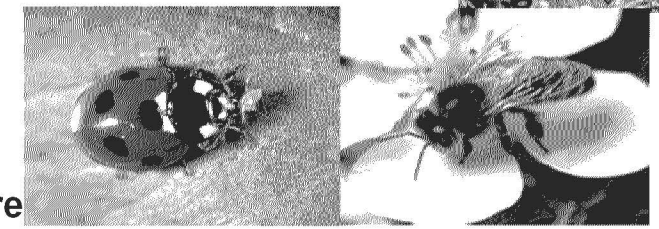


Protecting health in manufacture

Protecting health in application

Healthy food

Environmental safety



Sustainable agriculture

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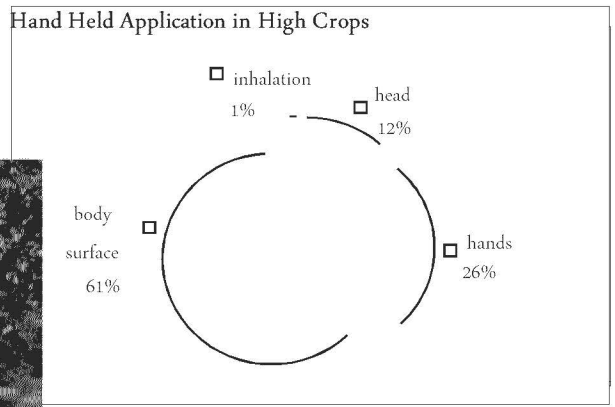
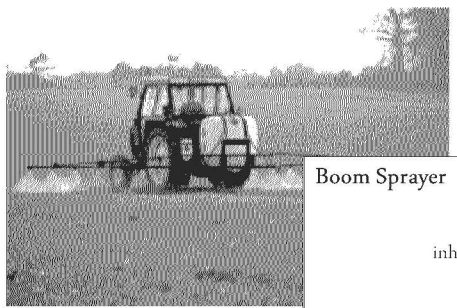
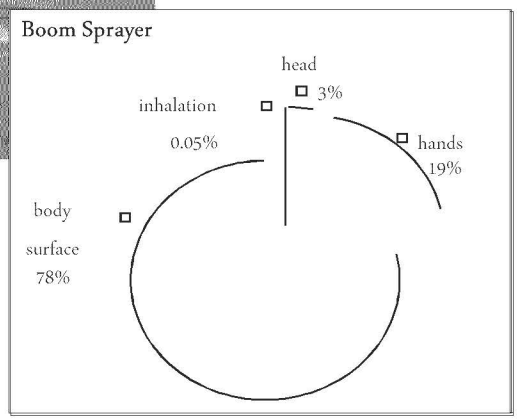
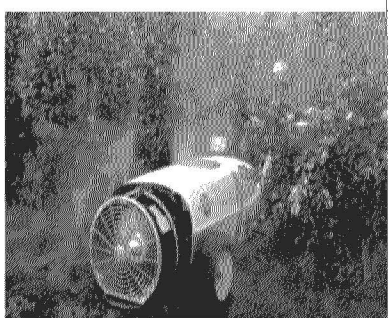
Routes of Exposure

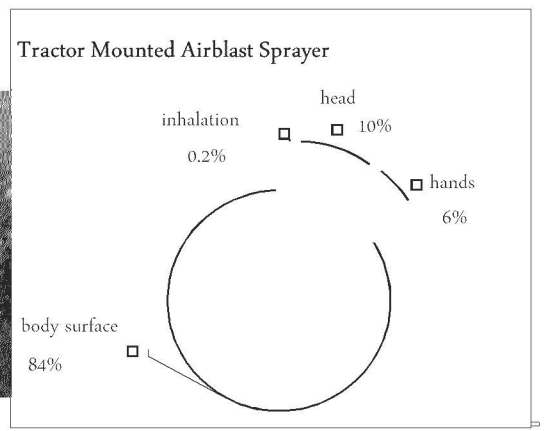
- About 95-99% of exposure is dermal
- About 1-5 % of exposure is through the respiratory route











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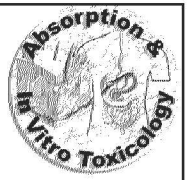
Characteristics of Operator Exposure



- Mixer/loader – opens containers, pours chemical, adds water, mixes solution
- Applicator – applies spray solution
  - Groundboom equipment
  - Fixed wing or rotary wing aircraft
  - Hand held equipment
  - Airblast orchard equipment
- Mixer/loader/applicator – combined functions
- Flagger – directs aircraft

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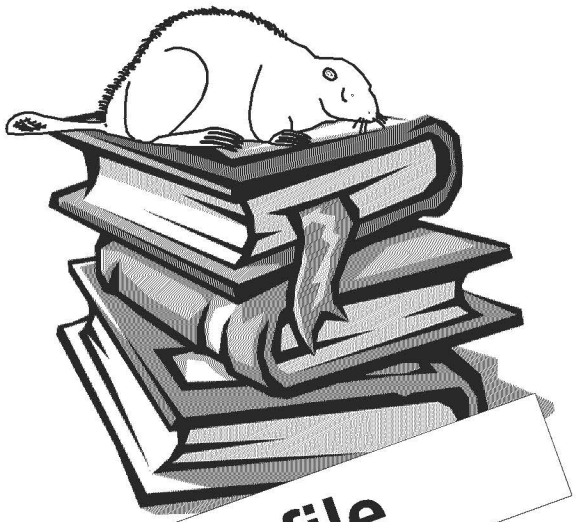
Operator exposure

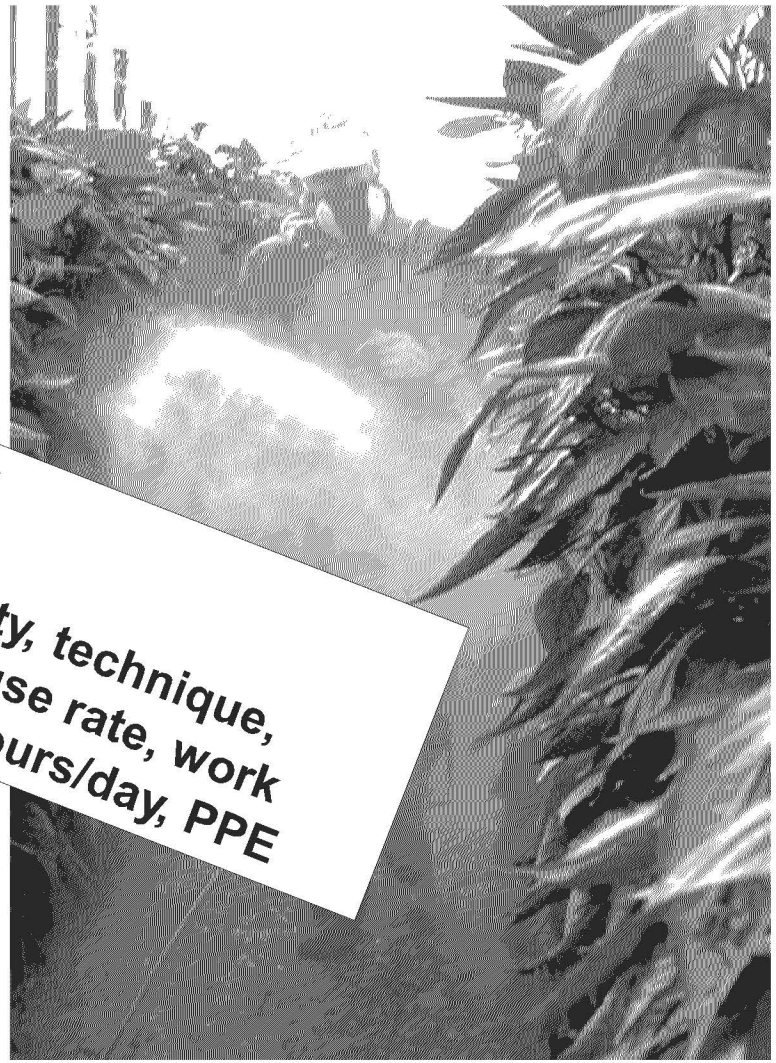
Operator Exposure and Risk Assessment



TOX Profile

EXPOSURE

Function of activity, technique, formulation type, use rate, work rate and working hours/day, PPE



RISK ASSESSMENT

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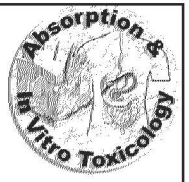
Characteristics of Operator Exposure



- **Duration of Exposure**
  - Exposure is assumed to be repeated, i.e. more than one working day per season
- **Routes of Exposure**
  - Dermal route – primary route
    - Dermal absorption **in-vivo** in the rat
    - Dermal absorption **in-vitro** in rat skin and in human skin
  - Inhalatory / oral – secondary route
    - Assumed to be 100% absorption from inhalation exposure

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Use of the In Vitro Test Method

Crop Protection Products

- Human epidermal membranes
- Rat epidermal membranes
- Universal receptor solution (ethanol:water to ensure partitioning and solubilization)
- Conservative approach – thin membrane with minimal rate limiting factors, 24h exposure

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Species correction (Example)

$$\frac{\textit{In Vivo}\ \text{Human}}{\textit{In Vitro}\ \text{Human}} = \frac{\textit{In Vivo}\ \text{Rat}}{\textit{In Vitro}\ \text{Rat}}$$

$$\text{e.g. } \frac{x\%}{2\%} = \frac{15\%}{30\%}$$

$$\textit{In Vivo}\ \text{Human} = \frac{\textit{In Vitro}\ \text{Human} \times \textit{In Vivo}\ \text{Rat}}{\textit{In Vitro}\ \text{Rat}}$$

$$x\% = \frac{2\% \times 15\%}{30\%} = 1\%\ \textit{In Vivo}\ \text{Human}$$

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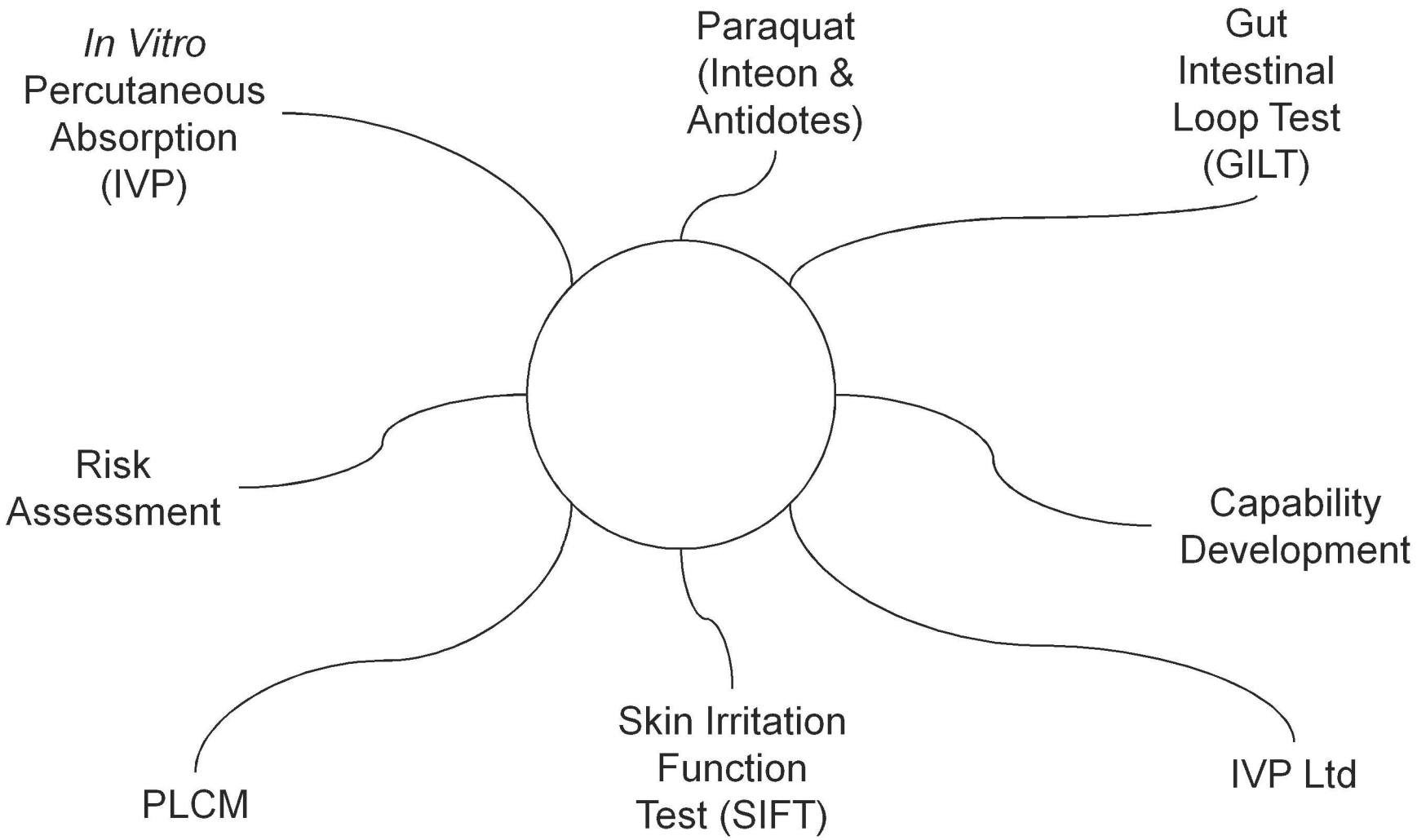
How we relate our results back to human in vivo

In Vitro Percutaneous Absorption



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In Vitro Percutaneous Absorption

The benefits of the *in vitro* percutaneous absorption model are:

- High levels of radioactivity or potentially toxic chemicals may be used with human skin
- Ethical and logistical problems of human *in vivo* experiments can be avoided
- Can be used equally well with skin from humans and other species
- Several repl… same or a number of subjects
- Recognised … the number of animals use…
- Experimenta…
- Ability to design studies to the customer requirements to study in-use exposure conditions
- Can be conducted using radio-labelled and non labelled chemicals with several alternative cold methods of analysis e.g. HPLC, GLC, LSC, LC-MS
- Chemicals can be applied in different forms; e.g. Solution, Suspension, Emulsion, Cream, Powder, Granule, Ointment

Cut down to simple bullets

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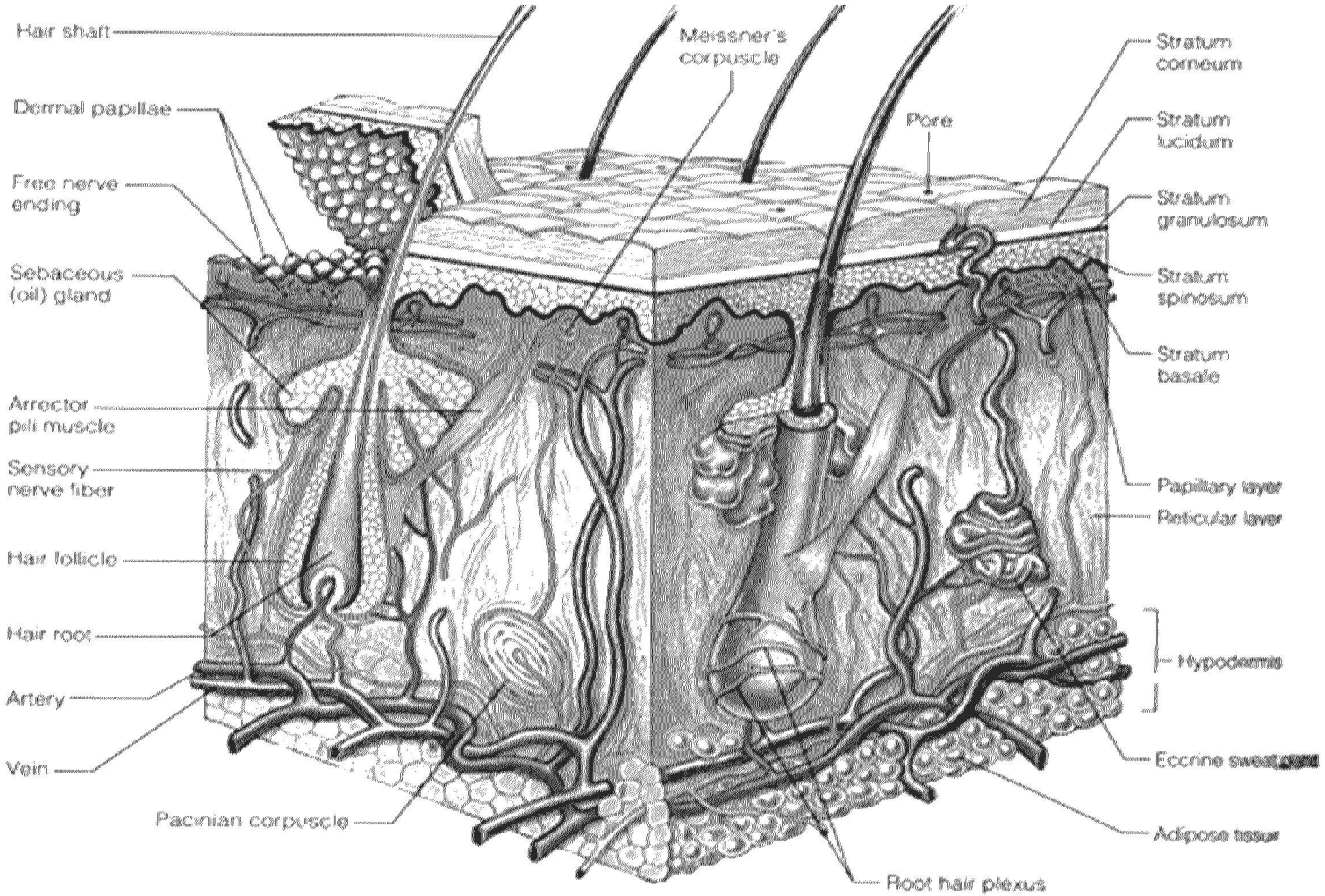
Why IVP is so good

In vitro Percutaneous Absorption

- Human
- Rat
- Pig
- Mouse
- Rabbit



Full thickness, dermatomed, epidermal membranes, stratum corneum etc.

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Risk Assessment for Rats?

- Differences in skin morphology, follicle density and lipid biochemistry. Used *in vivo* for years without validation.

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In Vitro Absorption using Pig Skin?

- Good surrogate for man in terms of skin morphology and biochemistry….. but still generally more permeable than human skin to most chemicals

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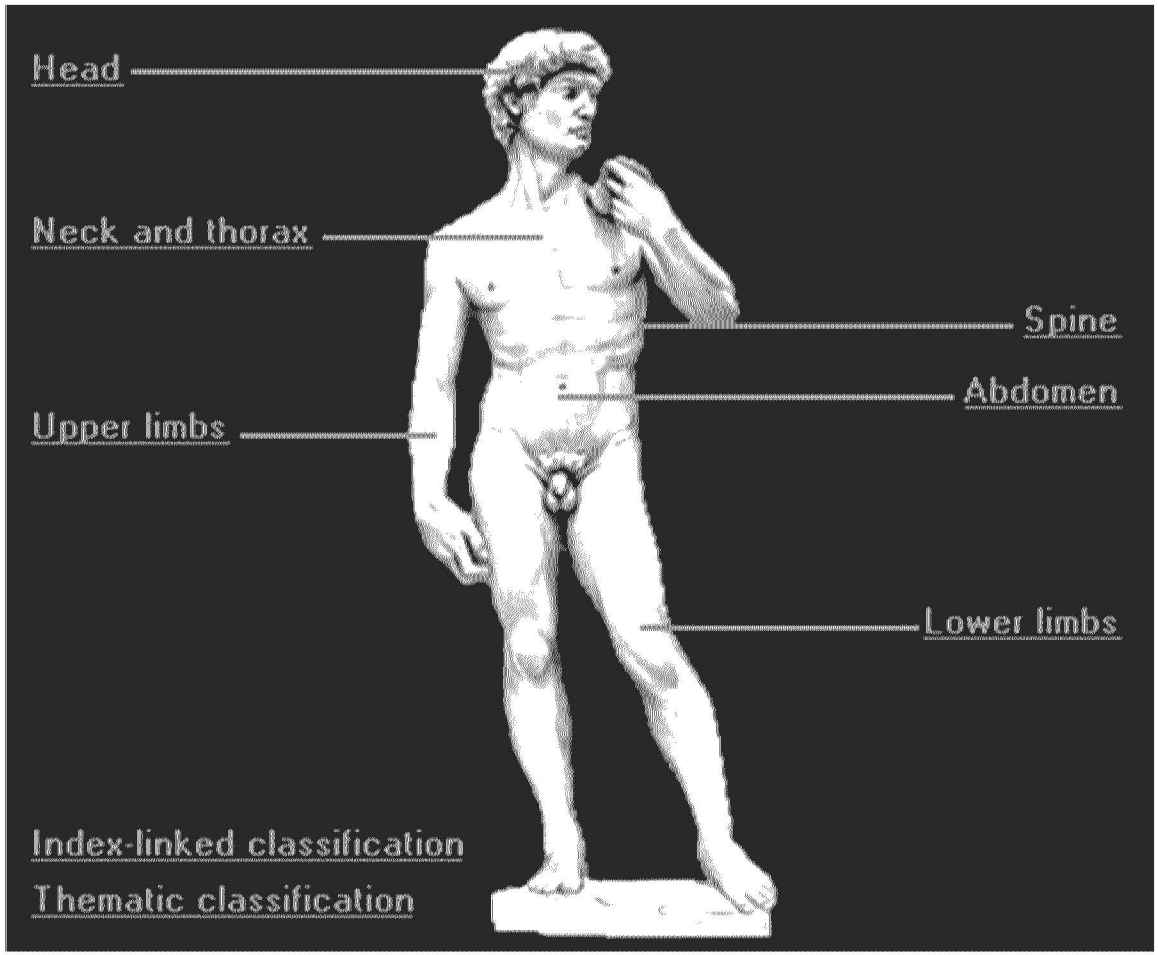
Human Skin for Human Risk Assessment



- Few would disagree, but there are other pressures on availability etc.

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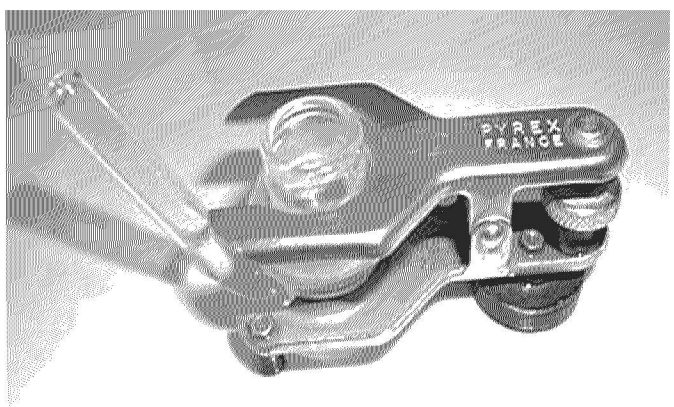
In Vitro Percutaneous Absorption

- **Static Diffusion Cell**
  - **Manufactured locally**
  - **2.54cm^2 surface area**
  - **Occluded / Unoccluded**
  - **Volatiles can be trapped**



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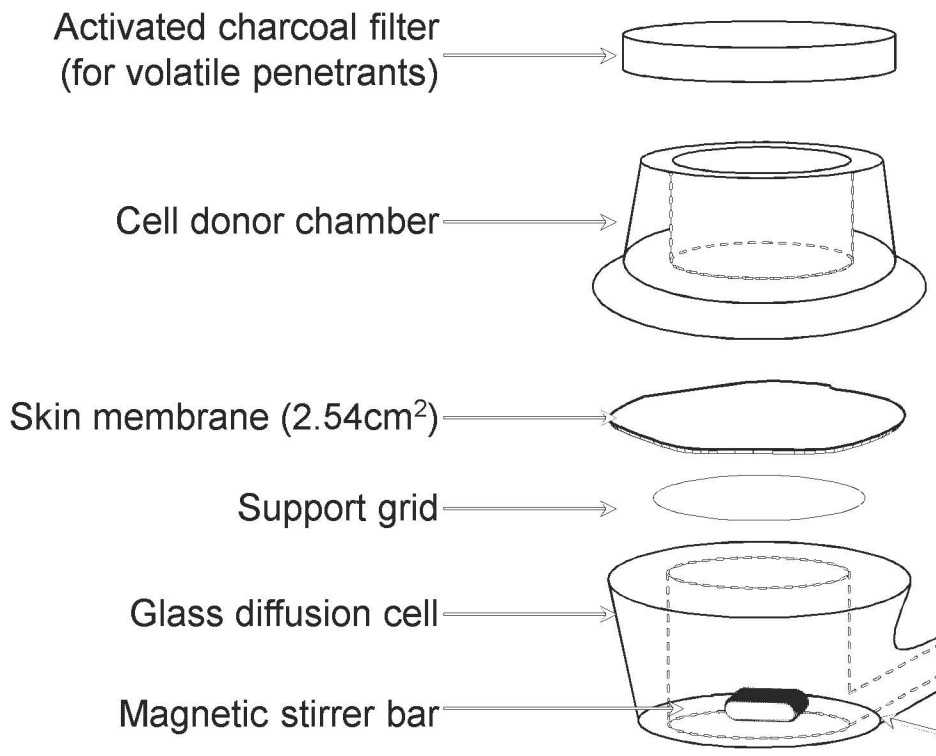
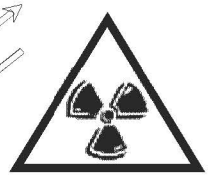
Typical static diffusion cell for IVP studies



AUTOSAMPLER

- Programmed to sample specific time-course
- Autopipette/syringe sampling into scintillation or HPLC vials
- Volume maintained by replacement of fresh receptor fluid



Receptor chamber/ fluid maintained at 32°C±1°C in a temperature-controlled water bath

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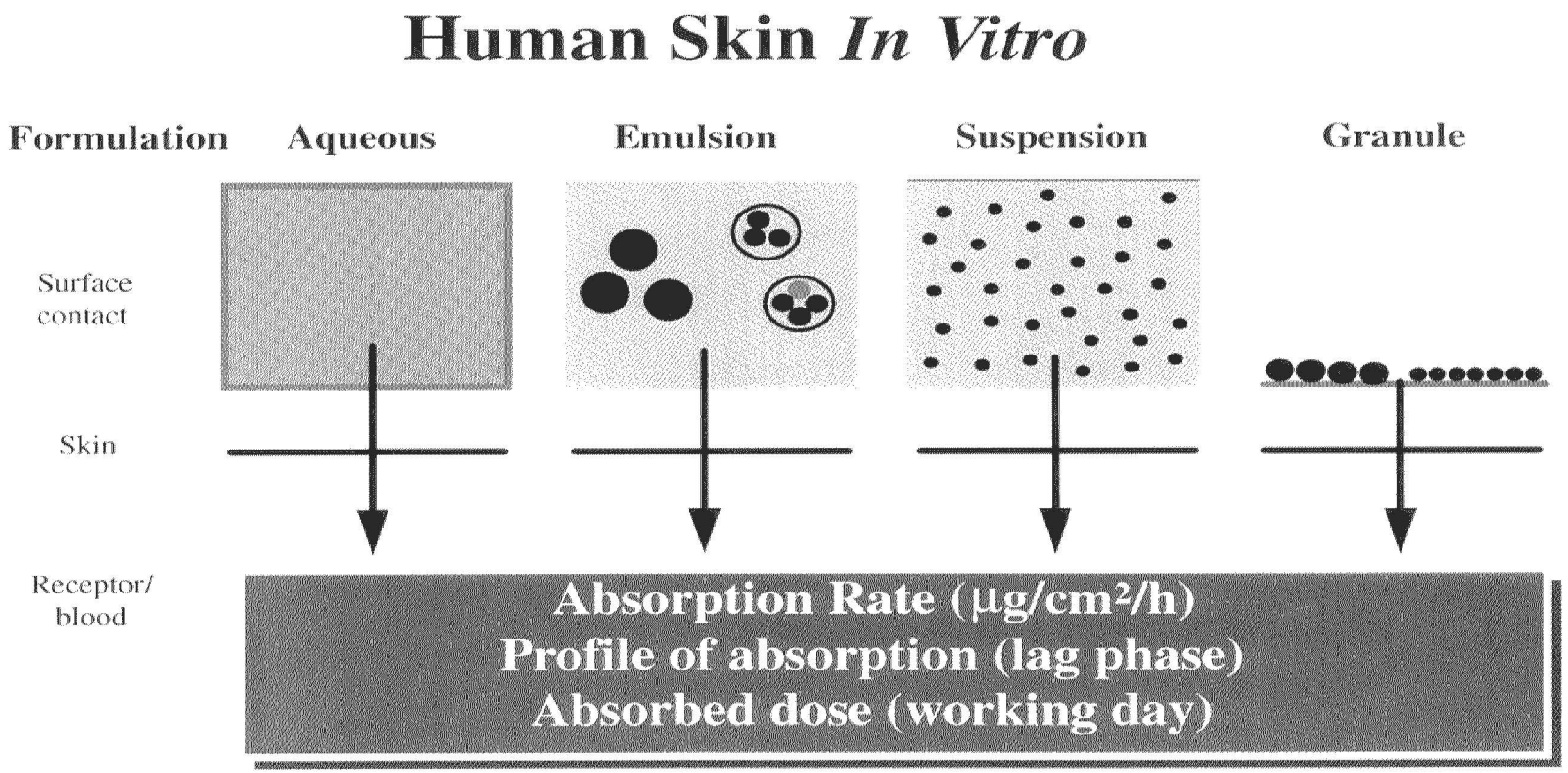
Our cells
An adaptation of the classic Franz cell
We use a static design

Application to the Skin Surface



- Test material applied to the skin and washed off after suitable exposure period
- Diffusion cell dismantled and components analysed to determine the amount of test material absorbed

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Application

Formulated product applied at finite doses representing likely in use exposure (eg 10ul or 10mg/cm²)

Skin preparation and nature of the receptor should not impede diffusion.

Time course exposure defined by "intended" use of product e.g. 10h and at 24h for worst case.

Absorption rate, percentage absorbed and amount absorbed and individual time course profiles.

Mass balance recovery to show overall distribution of the test chemical (100 +/- 10%).

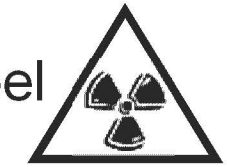
Sample collection and analysis

➲Mass Balance / Tape Stripping

Six compartments from the diffusion cell are measured:

- Equipment
- Donor chamber
- Skin surface washing
- Tape stripped *stratum corneum*
- Skin residue
- Receptor chamber

➲ Analysis: GLP Validated Methods



- 14 C Radiolabel
- HPLC
- LC MS-MS
- Gas Chromatography

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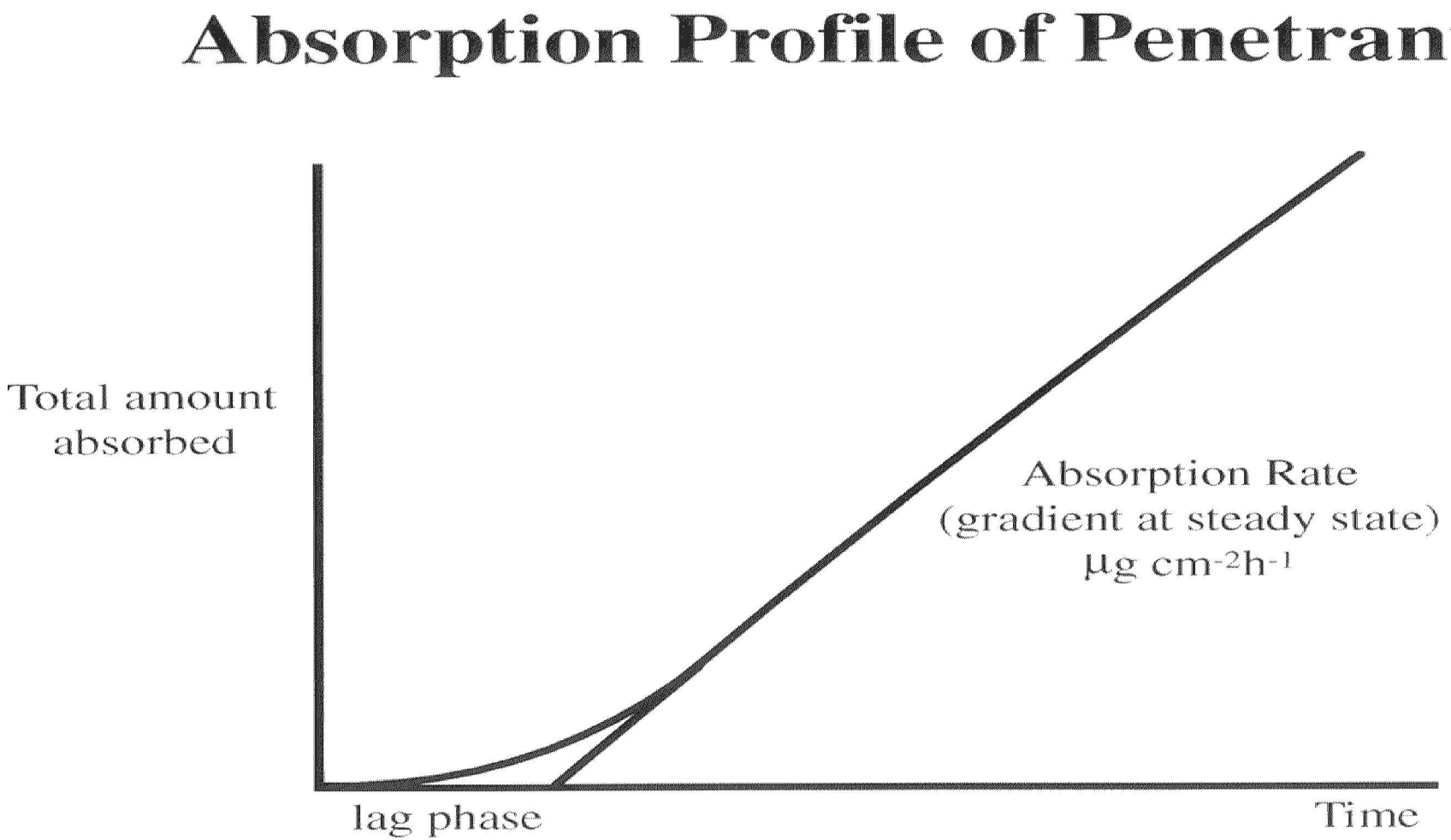
How do we generate the data

In Vitro Percutaneous Absorption



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OECD Test Guidelines and Guidance Document

- OECD Guideline for the Testing of Chemicals. OECD 428 Skin Absorption: *In Vitro* Method. Paris, 2004.
- OECD Guideline for the Testing of Chemicals. OECD 427 Skin Absorption: *In Vivo* Method. Paris, 2004.
- Guidance Do... Environment... sment, No. 28, Paris...
- Guidance Do... and Consumer D... of OECD guide... uman.)
- WHO International Programme on Chemical Safety (IPCS). Environmental Health Criteria on Dermal Absorption. Environmental Health Perspectives, In press.
- US EPA (2004) In vitro dermal absorption rate testing of certain chemicals of interest to the occupational safety and health administration; Final rule. Fed Regist 69(80):22402-22441.
- SUPAC
- The studies are conducted to GLP and follow the relevant guidelines for the industry / regulatory authority e.g. OECD, EU, Japanese MAFF, US EPA, SCCNFP, SUPAC-SS

OTHER GUIDELINES HELEN TO PUT IN

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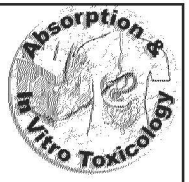
Guidelines that the group and in particular Jon were heavily involved in putting together OECD 428 is the one we work to but

For external clients there are a whole range of other guidelines depending on the product and why the study is being conducted

Use of the *in vitro* test method



All Sectors of Industry: Crop Protection, Cosmetics, Pharmaceuticals and Industrial Chemicals for….

- **Pre-development research**
- **Formulation selection / optimisation**
- **Databases and modelling**
- **Regulatory submissions (OECD 428)**

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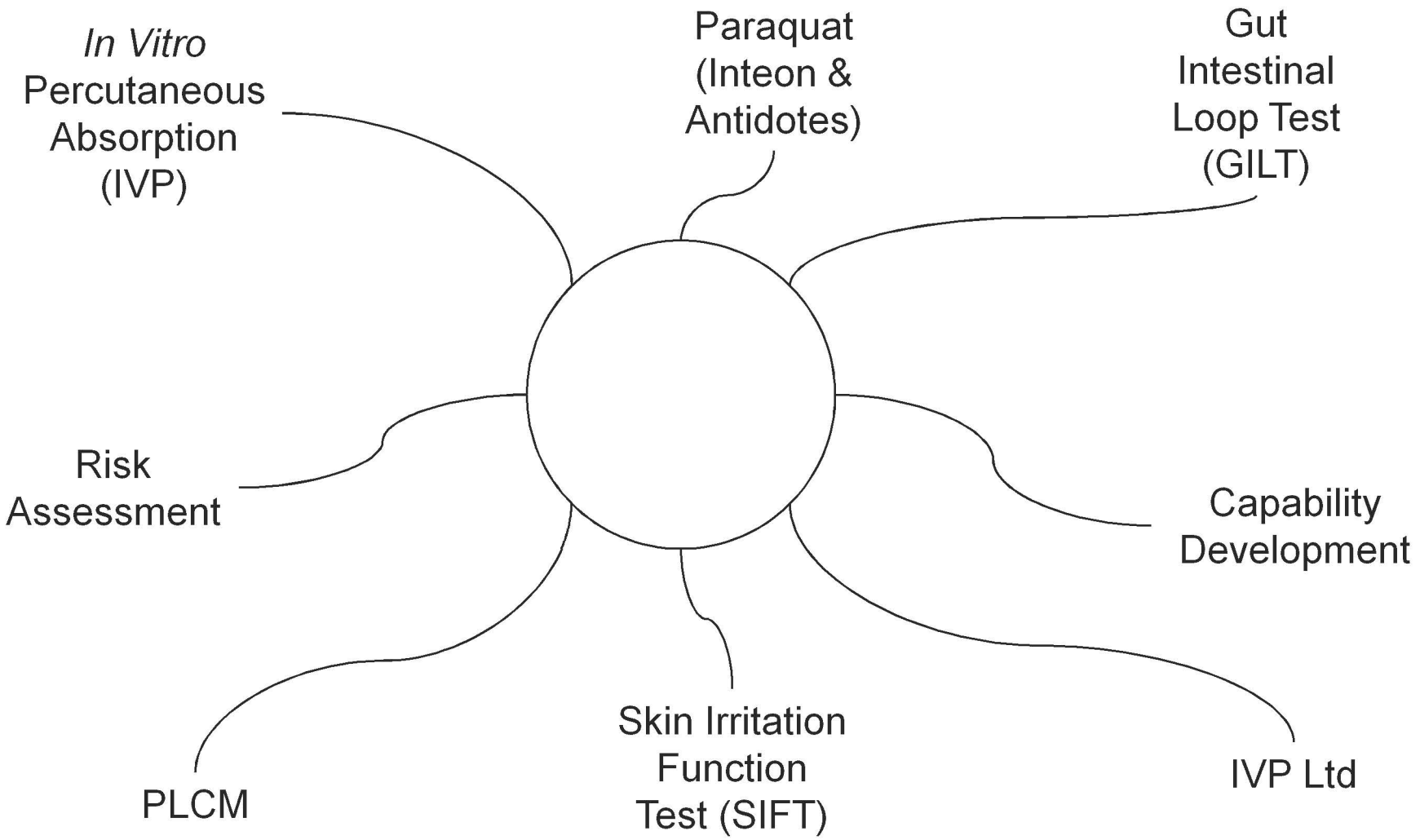
Our client base is fairly wide and we have many customers who come back time after time for studies

Skin types

Exposure mimics real life including washing

Skin Irritation Function Test (SIFT)



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Measuring Skin Integrity

Two measures of integrity

- Electrical Resistance (ER) of the skin:
  - if skin is damaged, the electrical resistance falls.
- Trans Epidermal Water Loss (TEWL):
  - if skin is damaged it allows more water through it.

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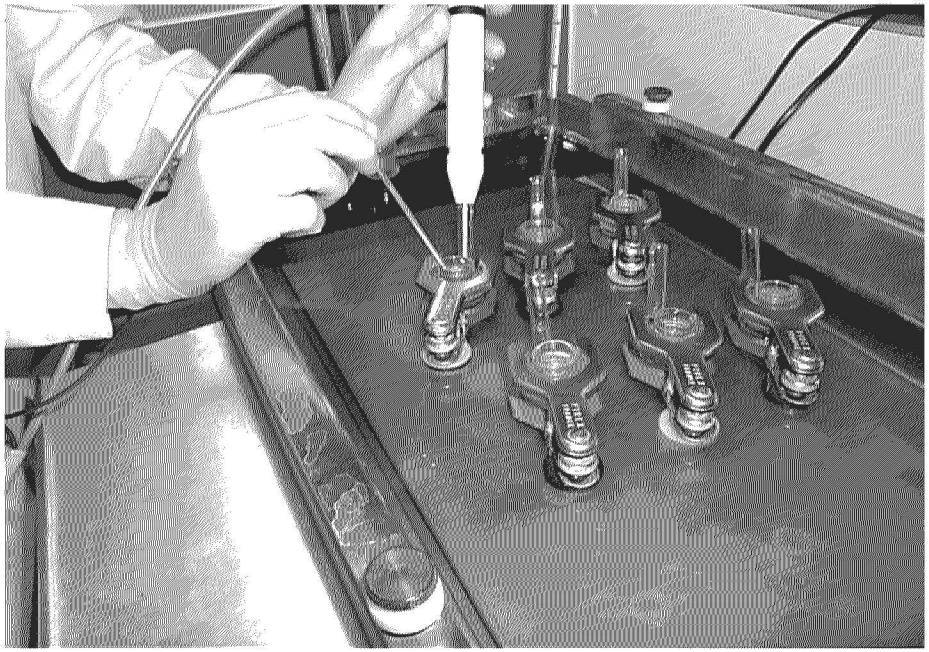
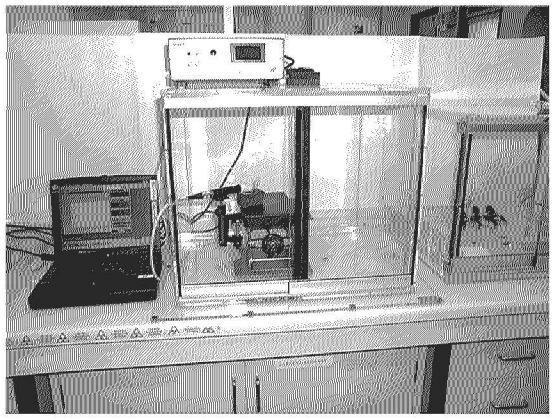
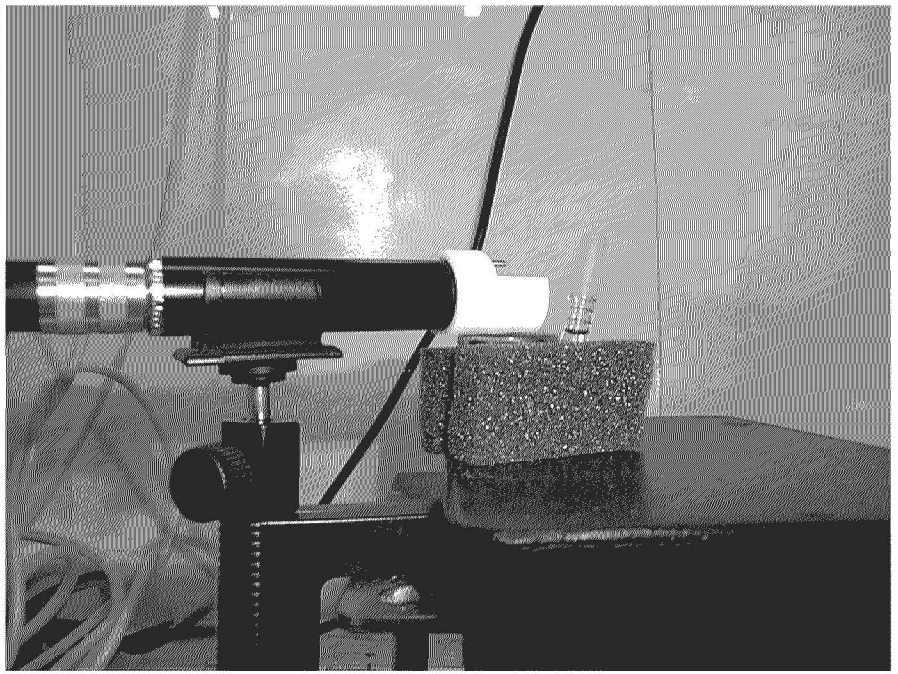
SIFT - ER and Tewl via Evaporimeter





Skin is normal if ER is between 5 and 15 kΩ

Skin is normal if TEWL is between 3 and 9 g/m²/h



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SIFT

25µl of neat test substance is applied for 20h, occluded and then washed off

ER and

- **If sk** **s.**
- **So** **the test sub**
- **If sk** **it.**
- **So** **g/m²/h), the** **itant**
- **If either ER or TEWL gives a response a TS is potentially irritant**

Check detail level

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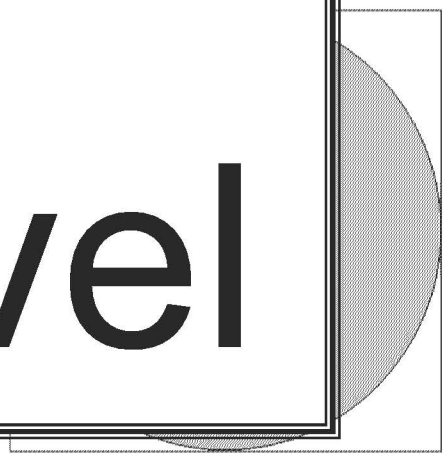
Validation

- At the moment, it is used for Syngenta and a number of external clients as a product selection screen
- In-h
  betw
- DAT
  COM
  CLA

Check detail level



Correct prediction ■ False negative
□ False positive

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External Validation

- 20 chemicals of known irritancy were tested using the SIFT prediction model under the auspices of ECVAM.
- A nur…odel in an att…
  - A…
  - M…
  - T…
  - Ir…
  - D…
  - Using a different endpoint

Check detail level

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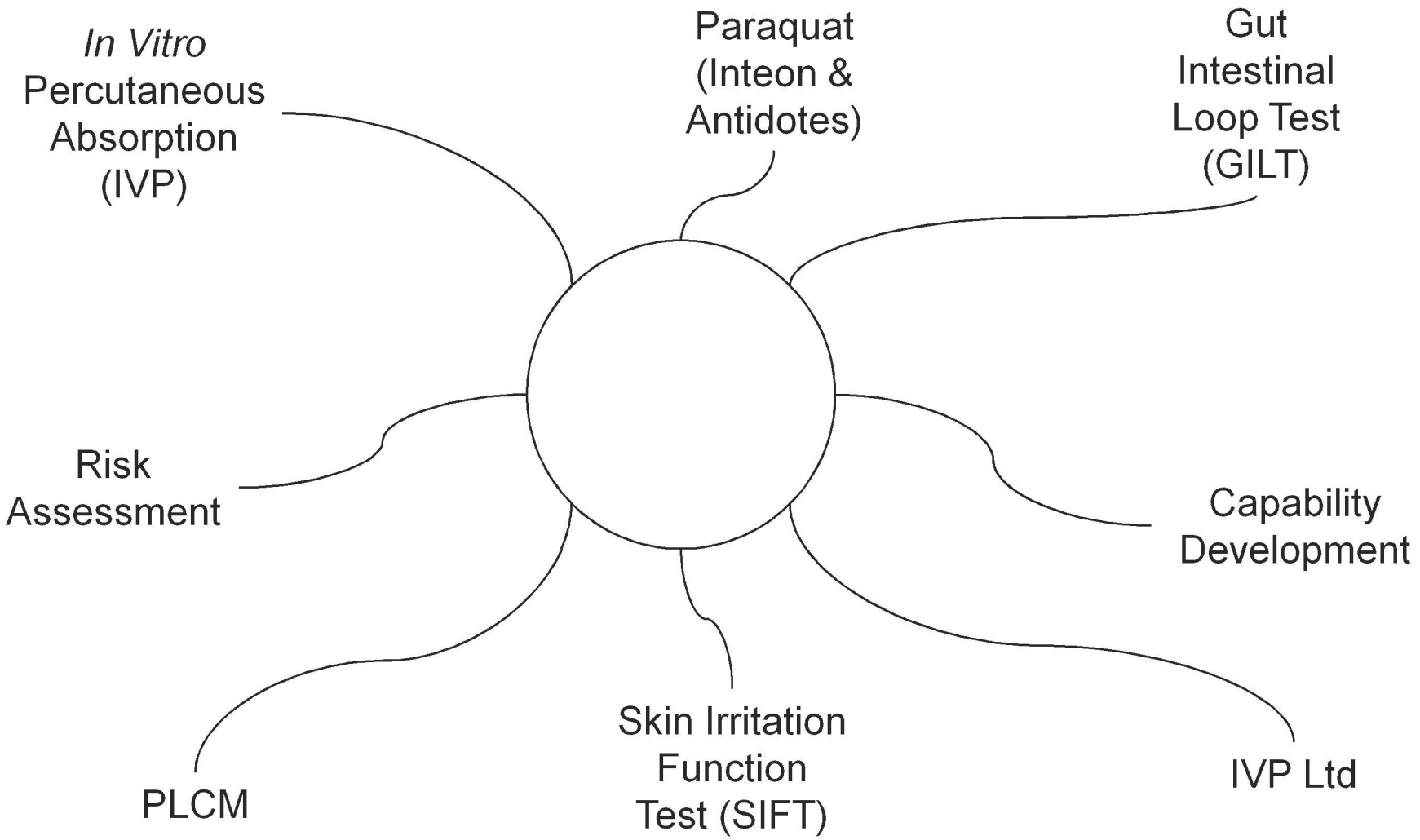
How does AIVT fit into a project e.g. Paraquat



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GRAMOXONE™ INTEON

Paraquat Sales Approx $400m

- Formulation Research - Inteon
- Antidotes
- Neurobiology
- Advocacy

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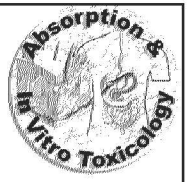
Paraquat INTEON Technology



- Existing paraquat formulations
  - offer outstanding weed control in a broad range of crops
  - Poses minimal risk when used according to label directions
  - From toxicology studies
    - they are toxic by the oral route
    - they are skin and eye irritants
- Programme of investigative research with the aim of reducing this toxicity

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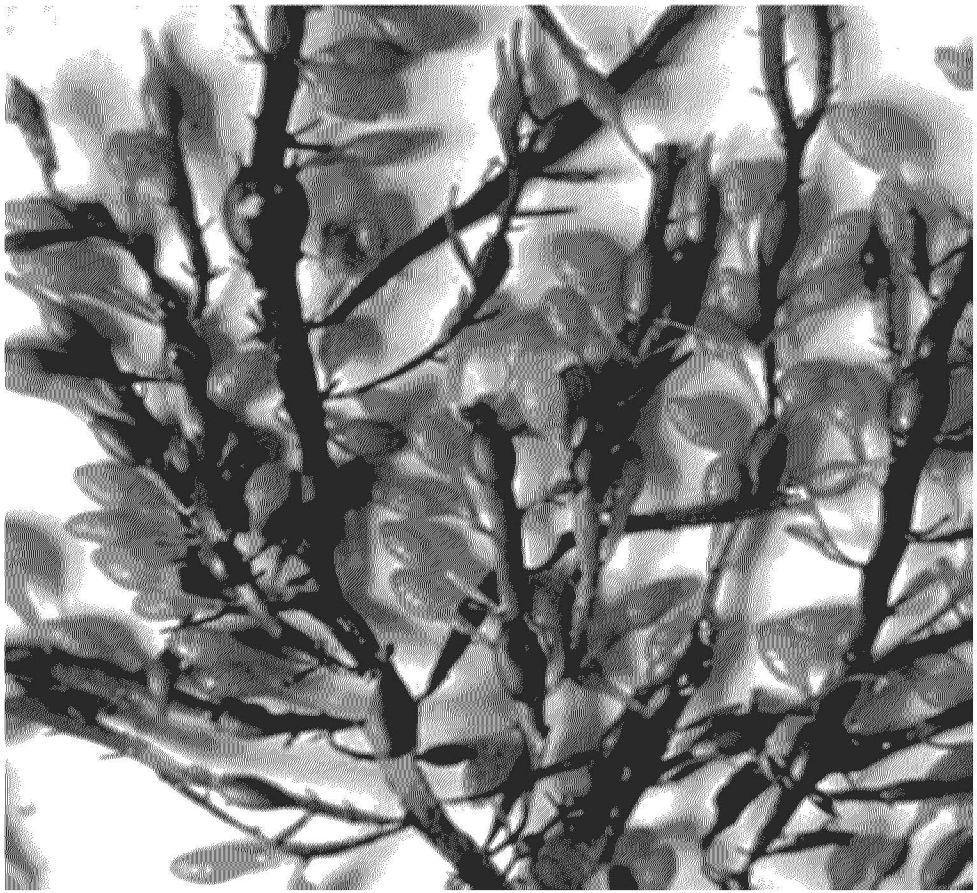
INTEON Technology

Ascophyllum Seaweed extract



- Alginates are carbohydrates of polymannuronic and polyguluronic acid
- They are non toxic and extensively used in the food and pharmaceutical industries

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INTEON Technology

- Gramoxone INTEON contains:
  - Paraquat/diquat (Bipyridyl herbicide)
  - Alginate (Acid-triggered gelling agent)
  - PP796 (Phosphodiesterase emetic)
  - $MgSO_4$ (Osmotic purgative)
  - Sulphacid Blue (Green/blue colourant)
  - Pyridine bases (Olfactory alerting agent)

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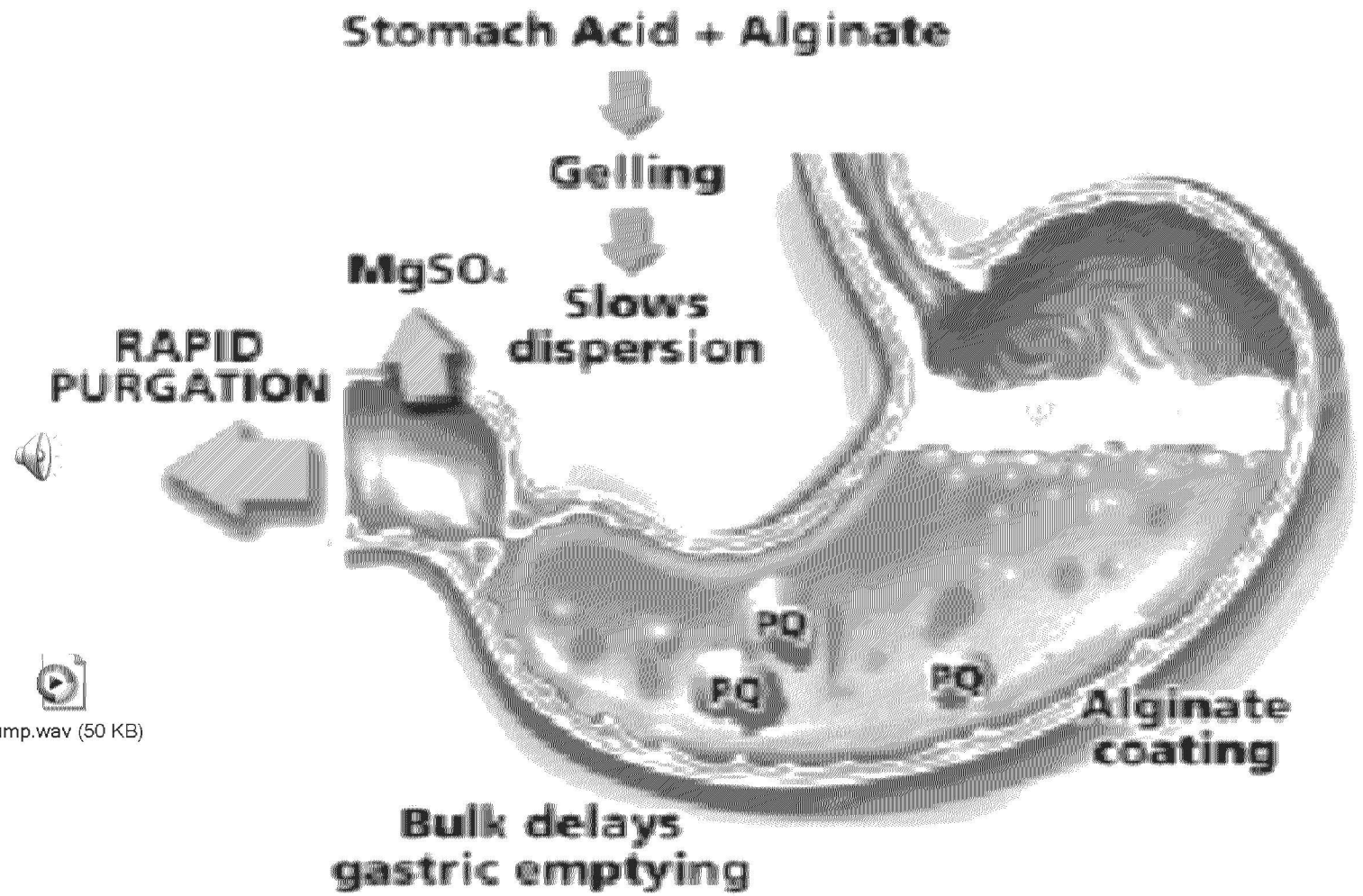
Gastrointestinal physiology



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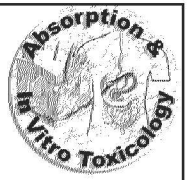
Gastrointestinal Absorption and Toxicology Testing Cascade for new paraquat formulations



New INTEON formulation

↓

***In vitro* absorption Rat ileum screen (GILT)**

↓

***In vivo* absorption Rabbit Toxicokinetics**

↓

Regulatory Requirement → **Toxicokinetic study Vomiting species**

↓

Human Exposure

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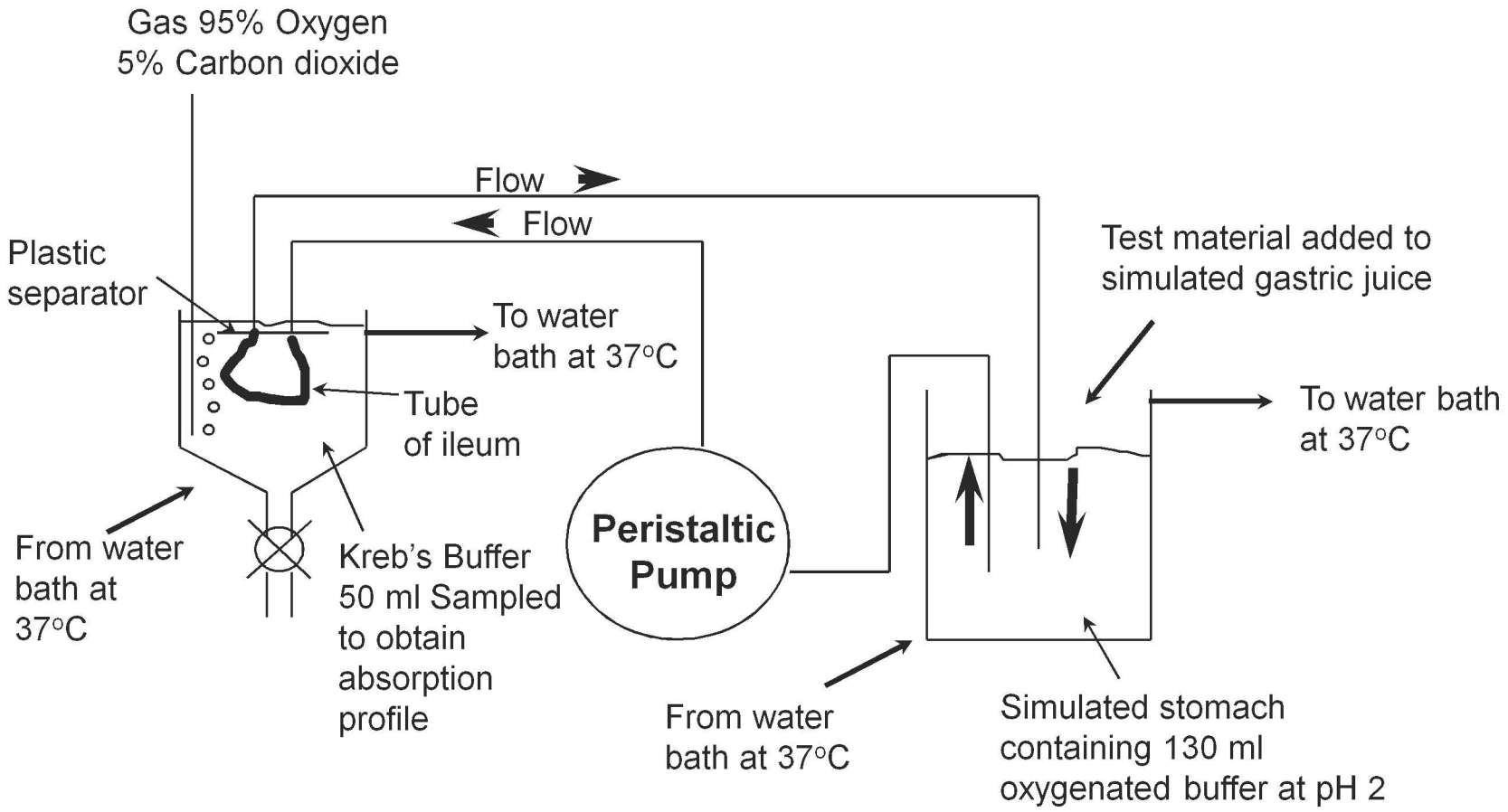
Gastro-Intestinal Loop Test: GILT



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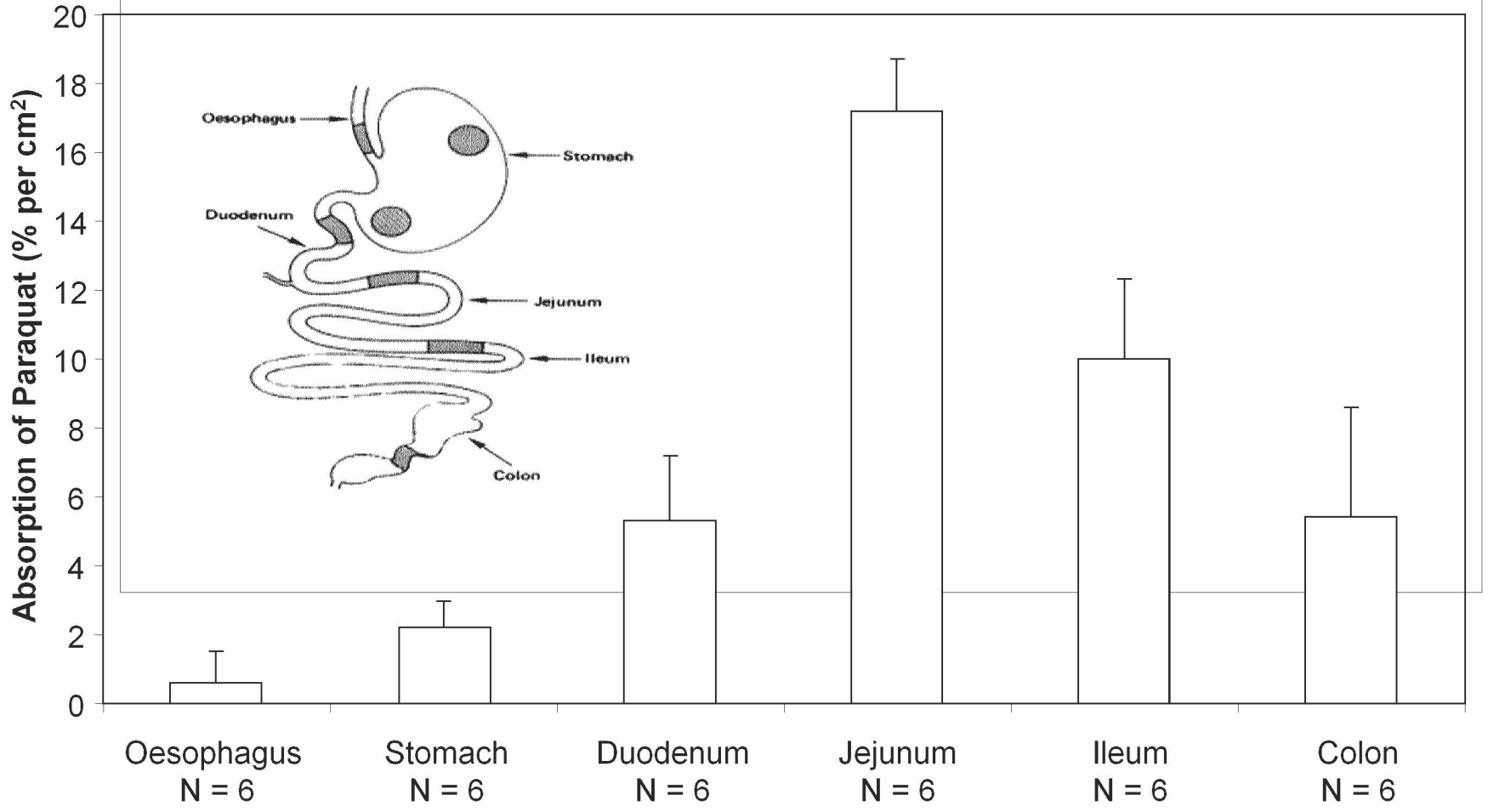
In vitro Absorption – Rat Ileum Screen (GILT)
Site of paraquat absorption within the GI tract

Heylings JR *Toxicol. Appl. Pharmacol.* 107, 482-493, 1991



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JON

Published research at CTL demonstrated that PQ is primarily absorbed beyond the stomach. The main site for uptake is the small intestine, particularly the jejunum.

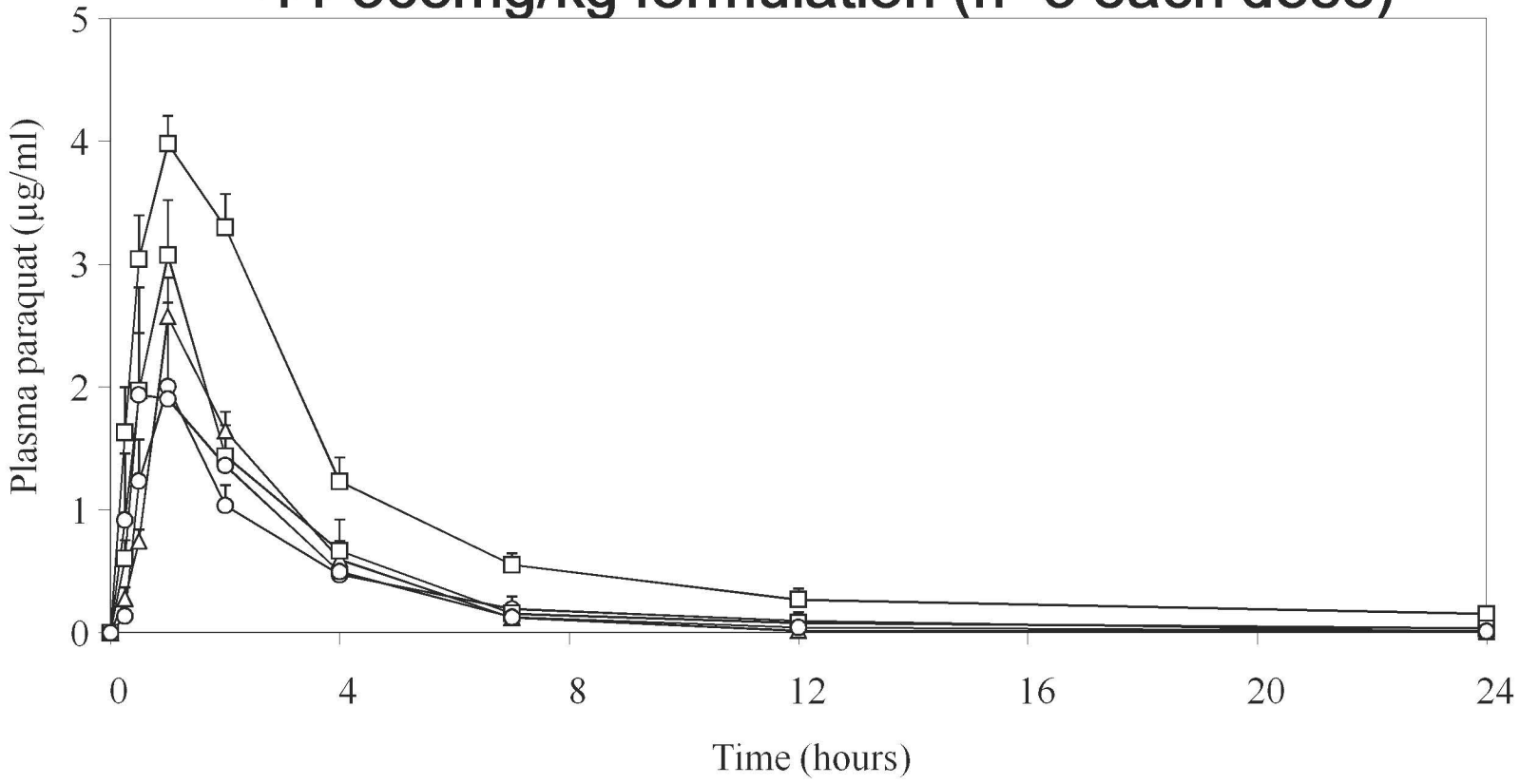
The chart shows the absorption of paraquat in rat isolated mucosa from different regions of the gut from oesophagus to colon. The concentration used represents a typical ingested dose.

Absorption of PQ is mainly a passive diffusional process with polar ions like PQ being mainly absorbed in the “leaky” epithelia of the small bowel.

The small intestine represents the major surface area of the total GI tract so prevention of PQ from entering this region (stomach gelling), coupled with faster transit of luminal contents through this region (purgation), results in less absorption into the blood.

Paraquat Absorption in the Dog

Plasma paraquat following an oral dose of Gramoxone INTEON 44-368mg/kg formulation (n=3 each dose)



JON

This chart shows the blood levels of PQ following an oral dose of 200g paraquat ion/l formulation as either Gramoxone or the AWT formulation (A3879BU) in the adult male dog over a range of dose levels.

As with human ingestion (suicide attempts) the increase in dose is achieved by administration of increasing volume and therefore the dose of any component in the formulation would be increased as the dose of paraquat increases, mg/kg bw.

The AWT formulation under identical conditions of dosing etc. caused no toxicity over the dose range 40-320mg formulation per kg bodyweight. There was no toxicity in any animal and no effect on kidney or liver function.

The additional gel, emetic and purgative is more than compensating for the extra PQ given. Consistent with acid triggered gelling in the stomach, the formulation remaining in the stomach longer and more productive emesis.(More of the dose being removed from the body prior to the dose reaching the small intestines.

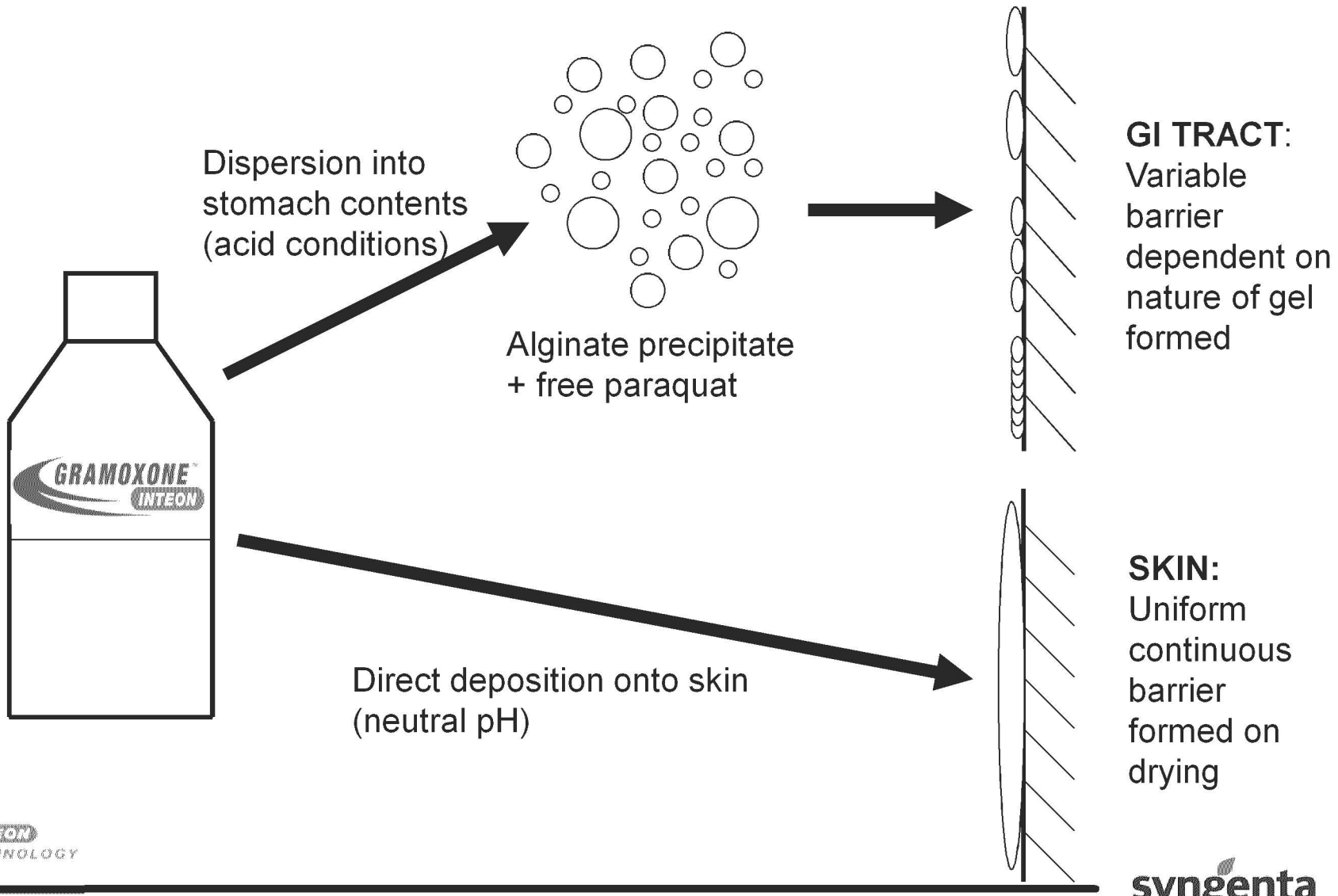
Emesis occurred at approximately 53mins – low dose and approximately 25 mins high dose.

[Gramoxone contains 0.5g/l emetic, whereas A3879BU contains 1.5g/l, but it is the effectiveness of the emetic and gelling which is important rather than the level of emetic per se.]

Gramoxone control data was generated at CTL between 1987 and 1991. Mean of 7 independent groups of dogs (n = 3 each). The blood levels shown (in black) are well tolerated in this species with no acute toxicity.

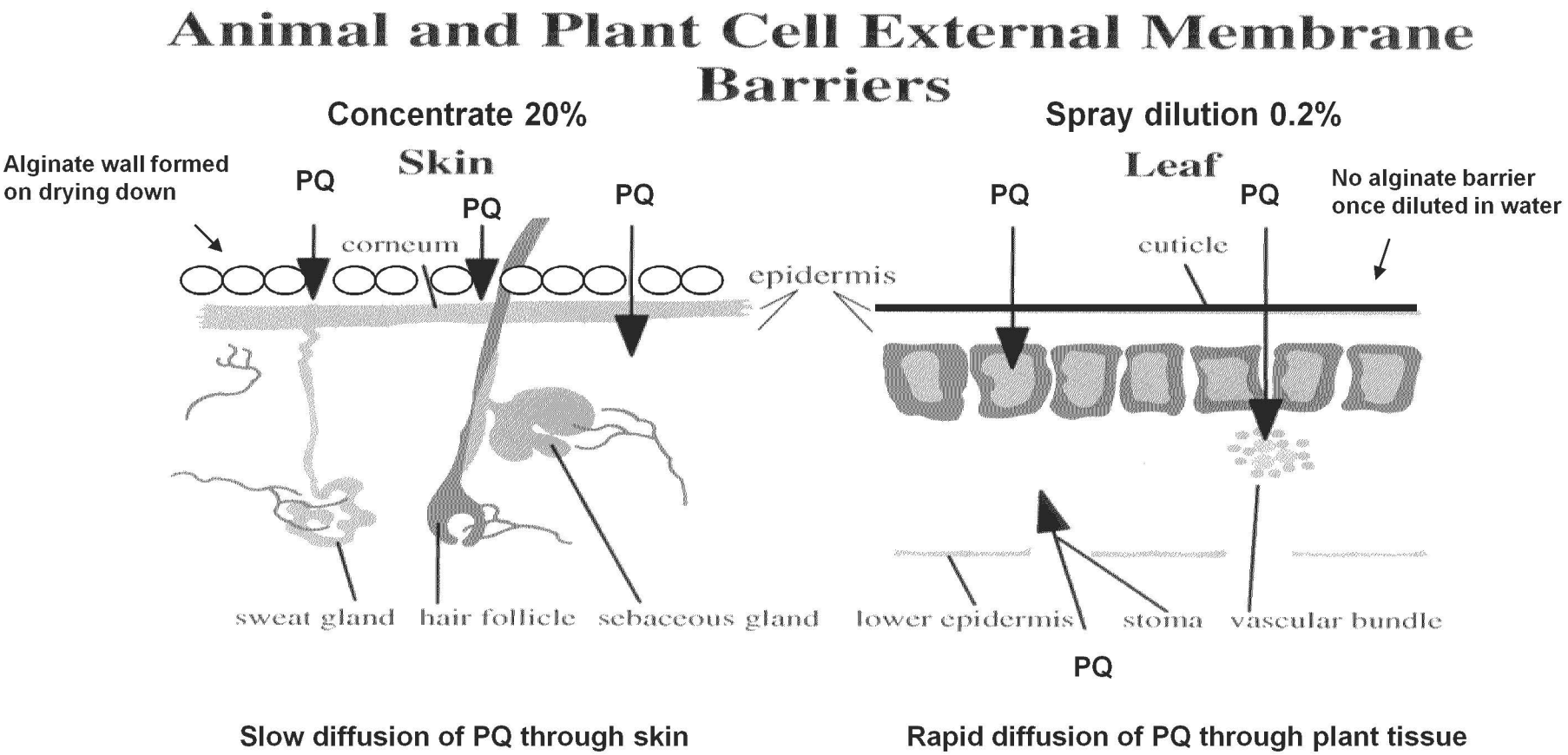
How does this relate to a lethal dose in dogs? This is kinetic study but we use a criteria of a peak plasma paraquat level of 10µg/ml or a 24 hour AUC of 40 µg/ml /h as the criteria for humane termination of test animals since it would lead to overt toxicity.

Paraquat INTEON Technology



JON

Animal and Plant Cell External Barriers



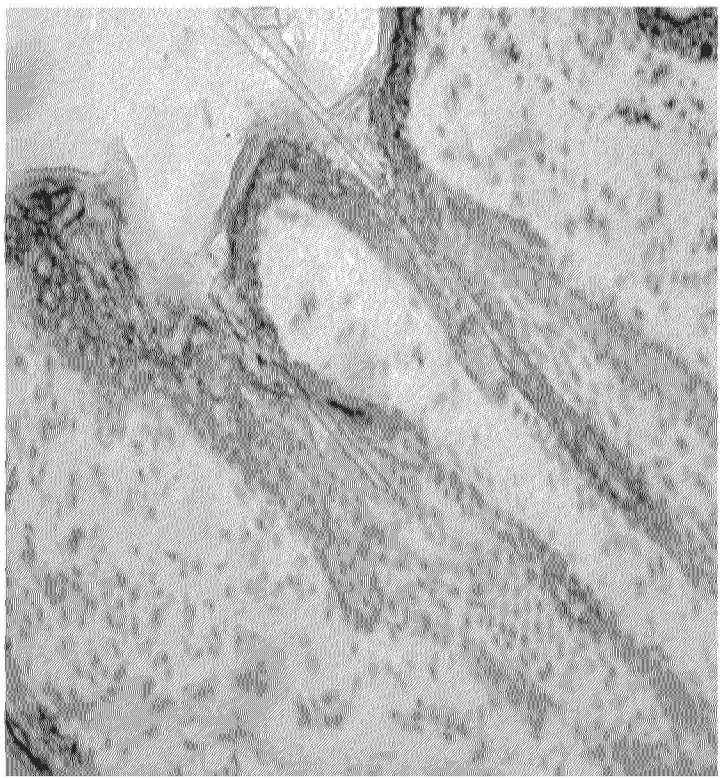
Slow diffusion of PQ through skin

Rapid diffusion of PQ through plant tissue

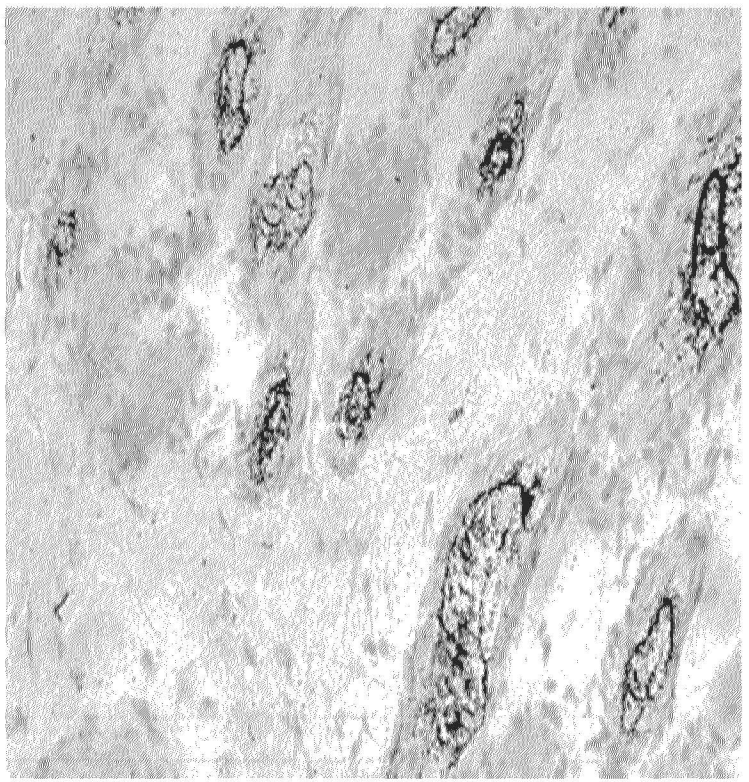
JON

Paraquat penetrates skin via hair follicles

Autoradiograms of mouse skin following 4 hour Gramoxone exposure containing ^{14}C-paraquat



Radioactivity mainly on surface



Radioactivity also in hair follicles

JON

In order to cause skin irritation, chemicals need to gain access to the living tissue below the epidermis. To do this the chemical has to cross the outer impermeable stratum corneum. Lipid soluble chemicals can do this relatively easily by simply dissolving in this lipid rich layer. PQ is very polar and cannot gain access through lipids. The only way water soluble molecules, like PQ, can get through the skin is via polar pathways, such as via the hair follicles.

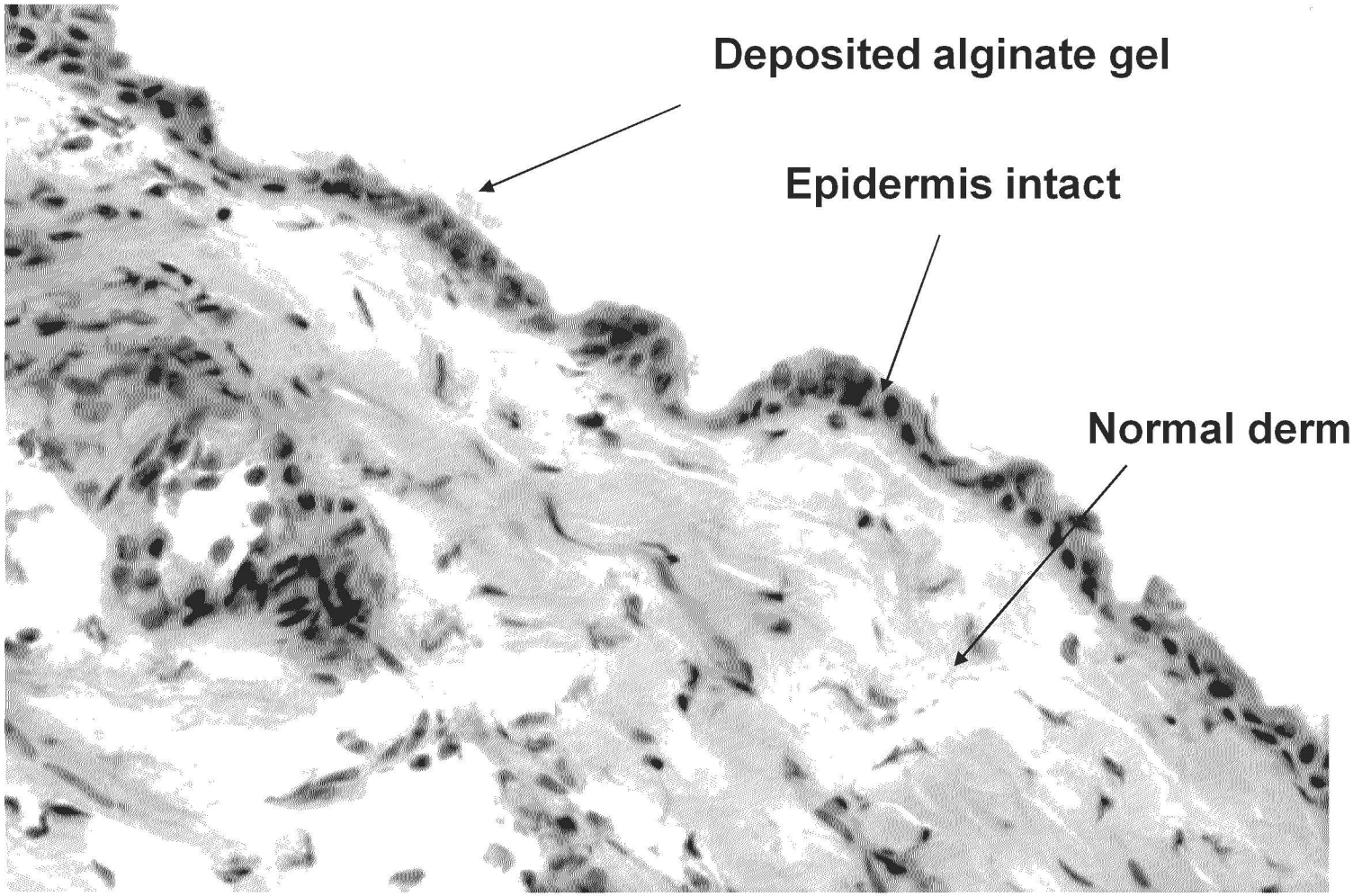
This can be visualised as shown using a technique called autoradiography. Using radiolabelled PQ, added to Gramoxone, we have applied the product to the skin for 4h and then taken microscopic sections of the skin following freeze fixation of the tissue in liquid nitrogen. The black grains are the locations of the radioactive PQ that have been developed on a special photographic film.

The left panel show the skin surface (top left) with hair follicles protruding through the epidermis into the dermis (bottom right). PQ can be seen mainly on the surface and also in the hair follicles, but not in the dermis.

The right panel shows a high magnification of the dermis. The grains of radioactive PQ can be clearly seen in the cross sections of the hair follicles.

PQ absorption is therefore largely dependent on the follicle density of the skin. Human skin contains far fewer follicles than animal skin and consequently the skin penetration of PQ through human skin is very slow.

Skin Morphology following INTEON Exposure



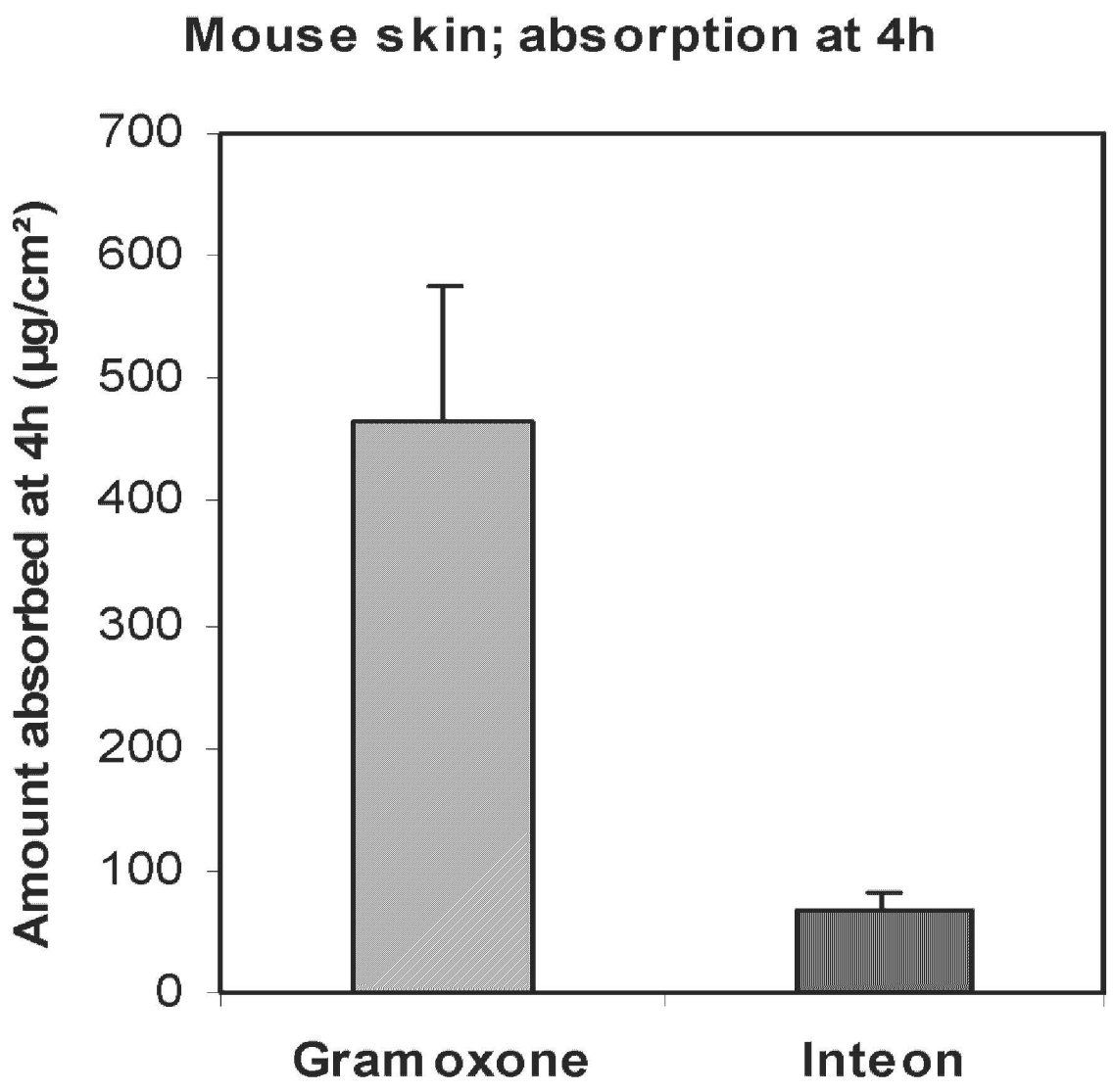
JON

This slide shows a microscopic picture of mouse skin following exposure to Gramoxone containing an alginate polymer. The skin was exposed to the concentrate for 4 hours prior to flash freezing.

The black dots are the nuclei of the cells in the epidermis (top) and underlying dermis. The section was stained for carbohydrate (shown in blue/green) which is clearly visible on the surface as an adherent gel wall.

The epidermis is completely normal following this treatment. Current research is investigating the localisation of PQ in the hair follicles following gel treatment to determine the mechanism by which the gel reduces skin penetration and irritation.

Skin Absorption following INTEON Exposure



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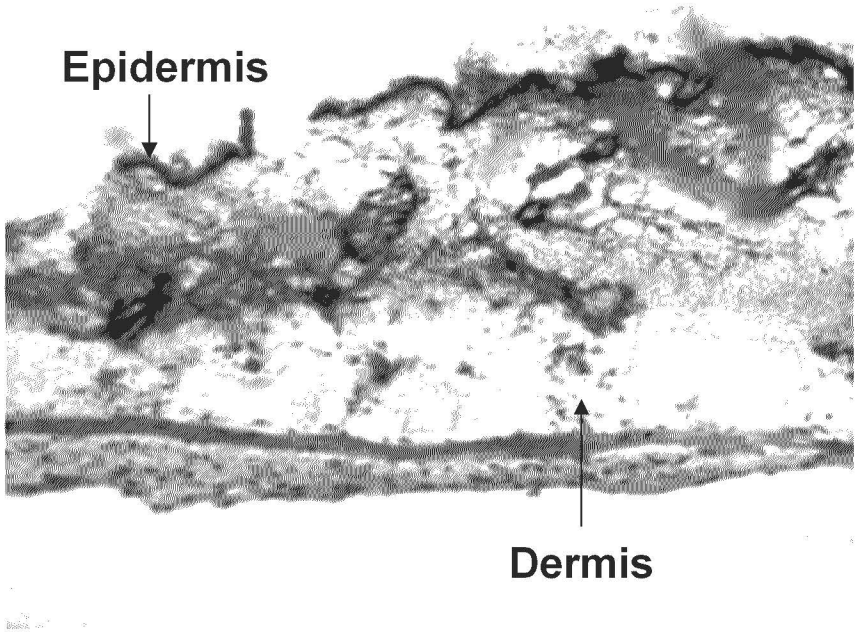
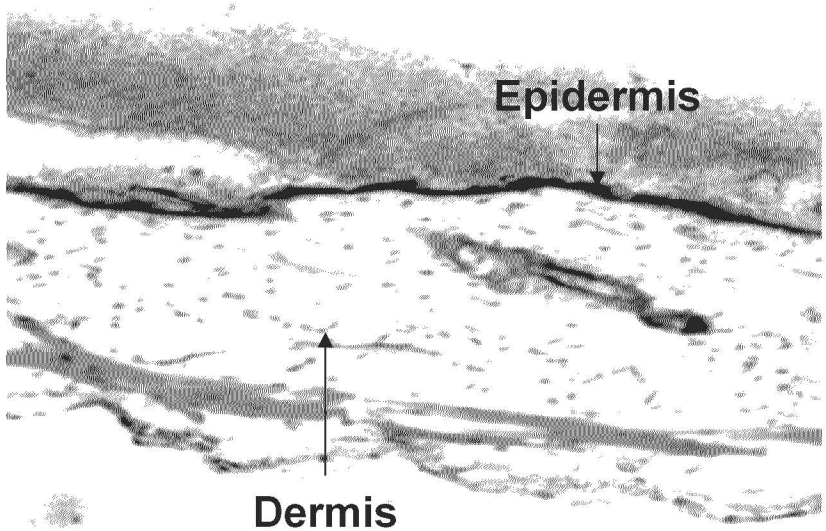
Skin Absorption following INTEON Exposure

Gramoxone 200g/l



Radioactive PQ (red grains) in the epidermis and dermis 10 min following Gramoxone

INTEON 200g/l



PQ is only in the external gel 10 min following the AWT concentrate

JON

This slide shows a microscopic picture of mouse skin following exposure to Gramoxone containing an alginate polymer. The skin was exposed to the concentrate for 4 hours prior to flash freezing.

The black dots are the nuclei of the cells in the epidermis (top) and underlying dermis. The section was stained for carbohydrate (shown in blue/green) which is clearly visible on the surface as an adherent gel wall.

The epidermis is completely normal following this treatment. Current research is investigating the localisation of PQ in the hair follicles following gel treatment to determine the mechanism by which the gel reduces skin penetration and irritation.

Paraquat INTEON Technology: Conclusions

- Scientific rationale for INTEON technology reducing the dermal and oral toxicity of paraquat formulations.
- Experimental data in dogs, a vomiting species, have shown a reduction in the gastrointestinal absorption of paraquat from an INTEON formulation compared with Gramoxone.
- Experimental evidence shows INTEON formulations to be less irritant to the skin and eye.
- It is anticipated this will eliminate fatalities from accidental ingestion and significantly increase survival following deliberate ingestions.

JON

Bullets self explanatory.

Paraquat Antidotes

Scientific Review

- Current therapies are largely ineffective. Many publications on potential new treatments for paraquat poisoning. Need to be effective after systemic exposure.

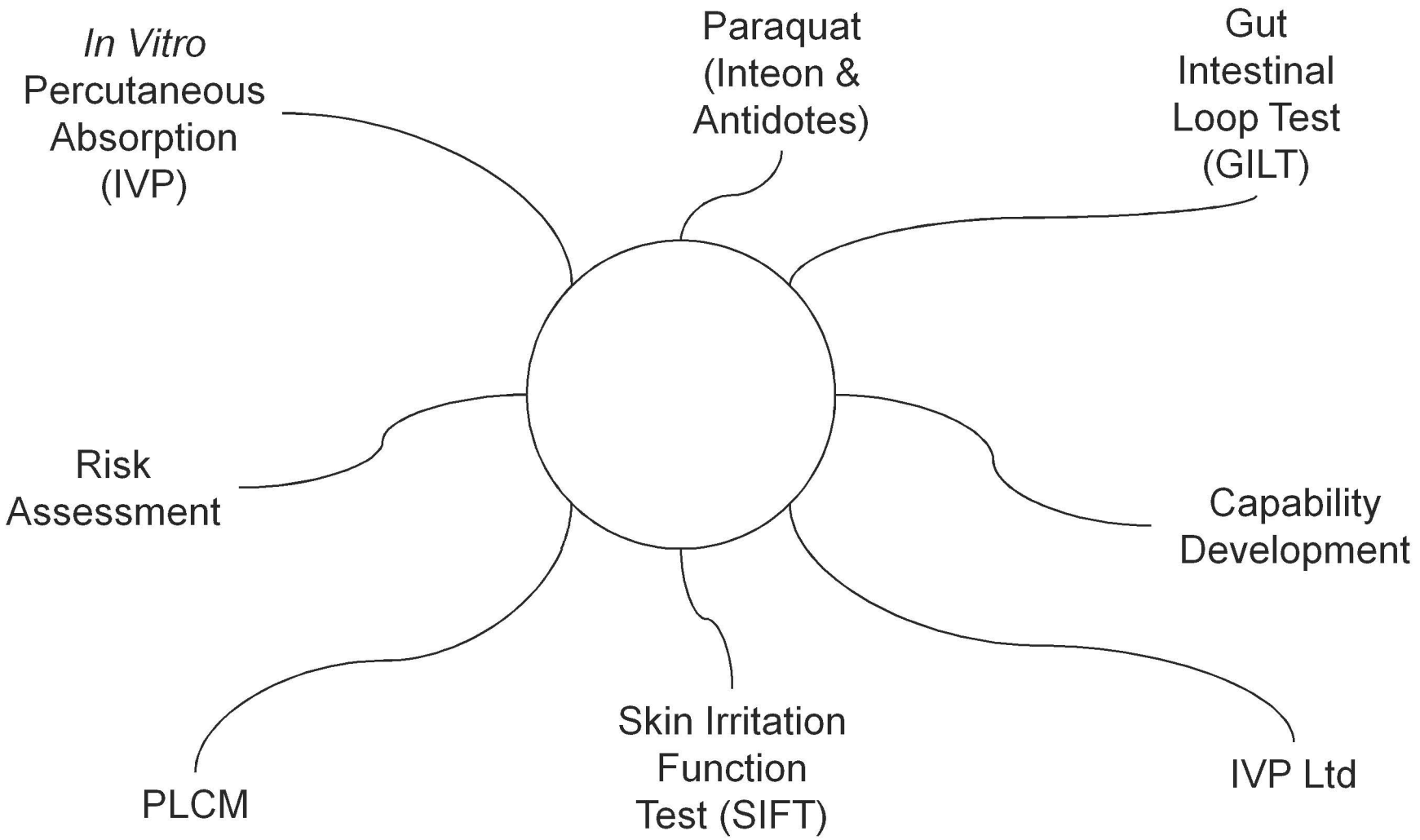
Modulation of TGF Beta signalling

- Developed a new lung fibrosis model in the mouse in collaboration with Pathology.
- Project with Renovo (Prof Mark Ferguson's group) using therapeutic antibodies.
- Hypothesis: Can TGF Beta neutralizing antibodies for TGF Beta 1/2 isoforms or recombinant TGF Beta 3 protein (antagonist of Beta 1/2) reduce the inflammatory changes in the lung?

Inteon and Treatment of Paraquat Poisoning

- Inteon improves survival and delays the onset of fibrosis. New opportunities for existing therapies.

Product Life Cycle Management and AIVT



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PLCM Workstream

Core Team

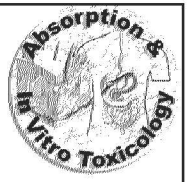
- Phil Botham (Chair)
- Patrick Rose
- Beat Lang
- Mike Clapp
- Barry Elliott
- Paul Parsons
- Werner Kobel
- Tim Pastoor
- Bob Parr-Dobrzanski

Extended Team

- Dick Lewis
- Graeme Moffat
- Simon Chivers
- Rebecca Silcock
- Martin Wilks
- Jon Heylings

JON

Objectives for PLCM Workstream



- The Workstream is the mechanism by which the Health Assessment requirements for Product Lifecycle Management are delivered to the PPTs
  - To build and maintain key relationships with our partners
  - To use the multidisciplinary power of PLCM to enable rapid and effective decision making
  - To achieve the optimal HA profile for Syngenta products
  - To positively communicate throughout HA and with our external partners

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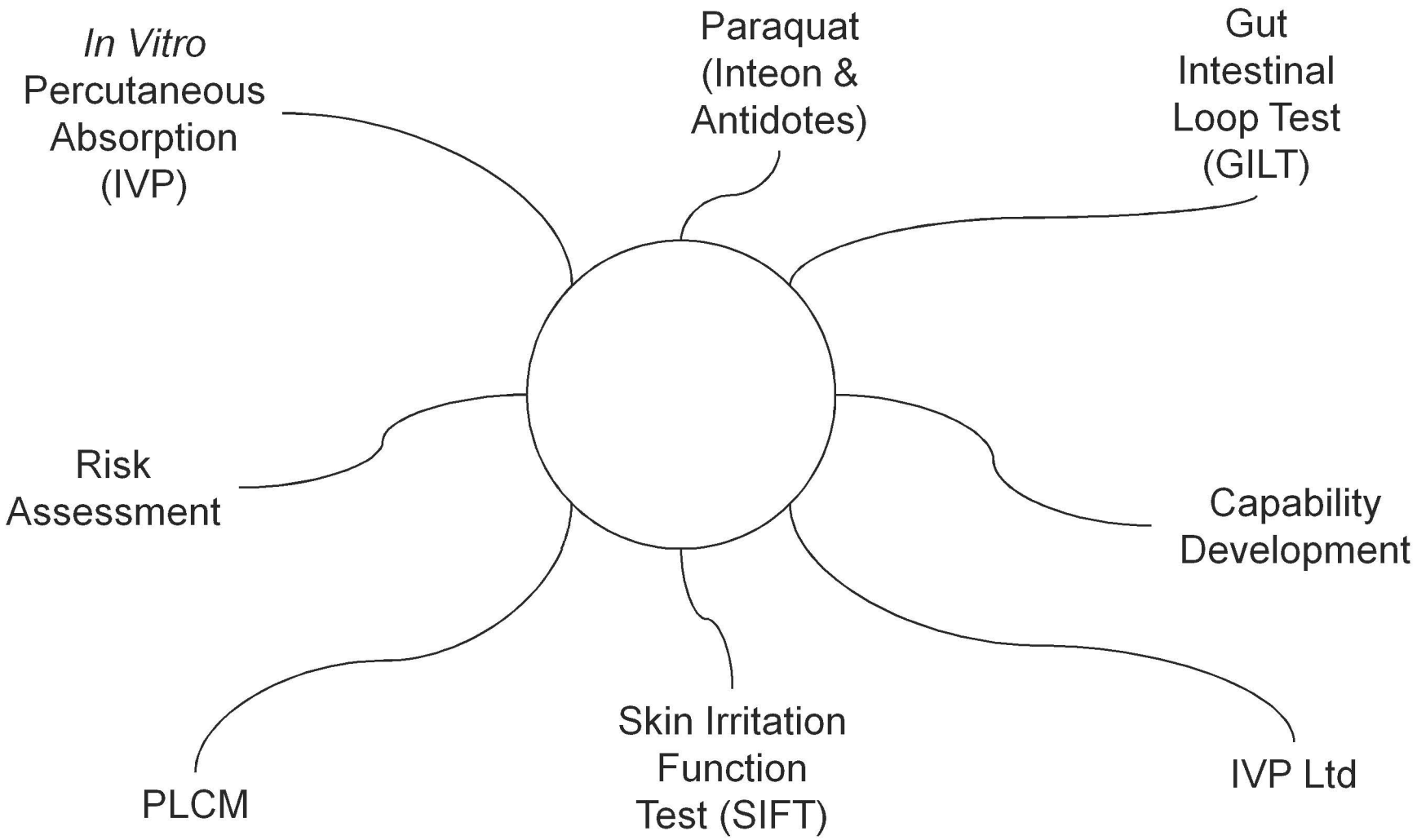
PLCM Workstream

Current Activities

- Workstream Objectives
- Mectins Review – NT study/morphometry
- Inerts – cyclohexanol and THFA in products (OPEX)
- Triazoles Review – CCZ/genomics/EPA
- New opportunities for RITS

JON

Capability Development



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Developing capabilities

- Bioequivalence testing
  - Ron's Rings
- Absorption of chemicals through the nail
- Ultrasound for hair dyes
- INVEST (*In Vitro* Epidermis Screening Test)
- Modified SIFT
- Stage 1 assays
- *In vitro* gut absorption
- Digestibility
- Rodenticide toxins

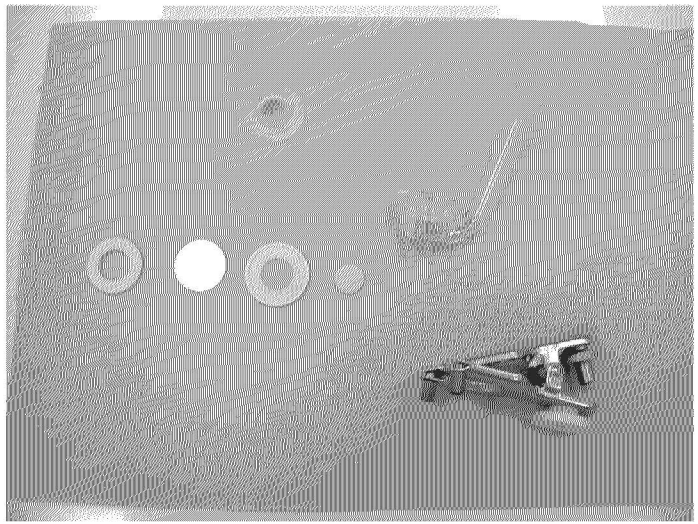
DAVE

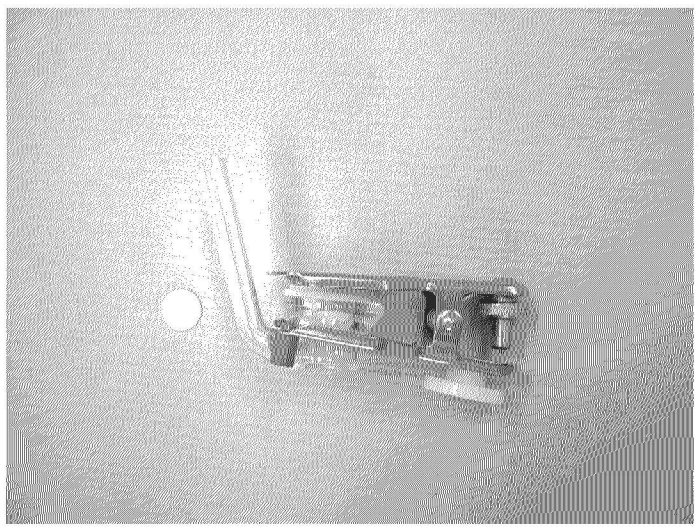
There are some already established assays which we have capability for

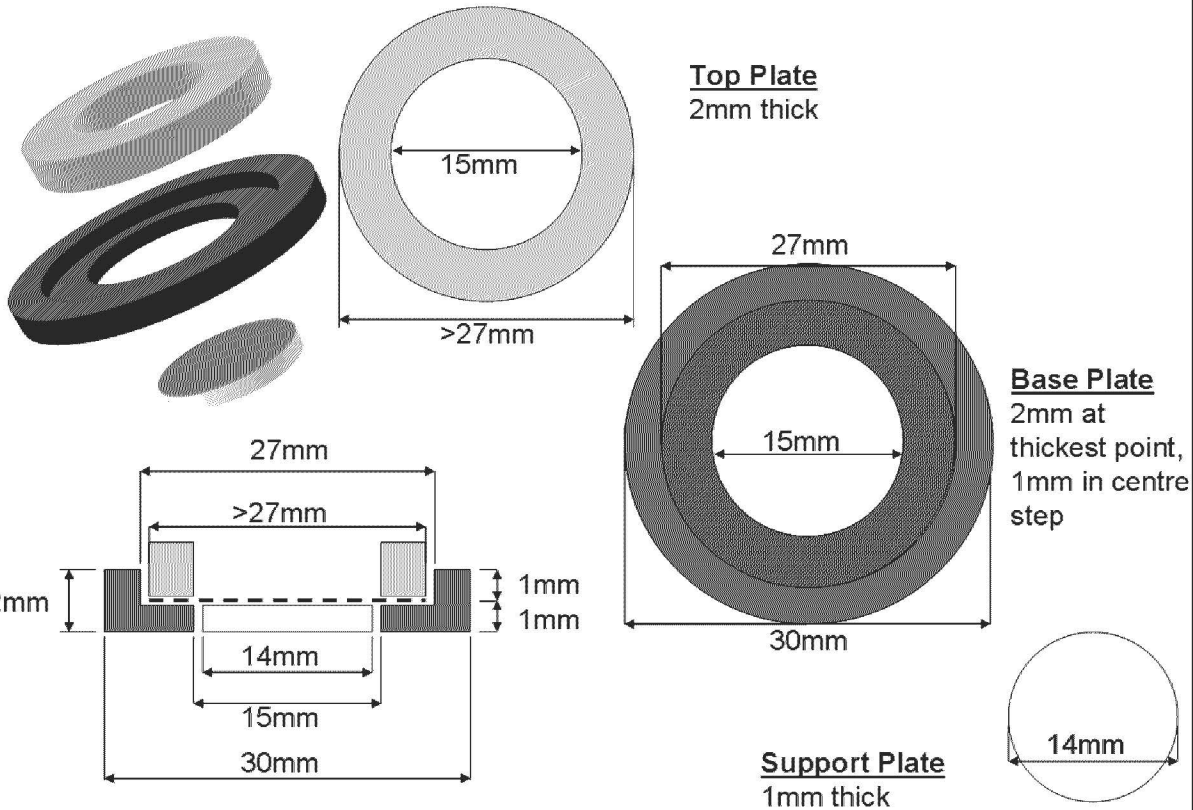
IN ADDITION

The other areas are important for the development of the group

Ron's Rings





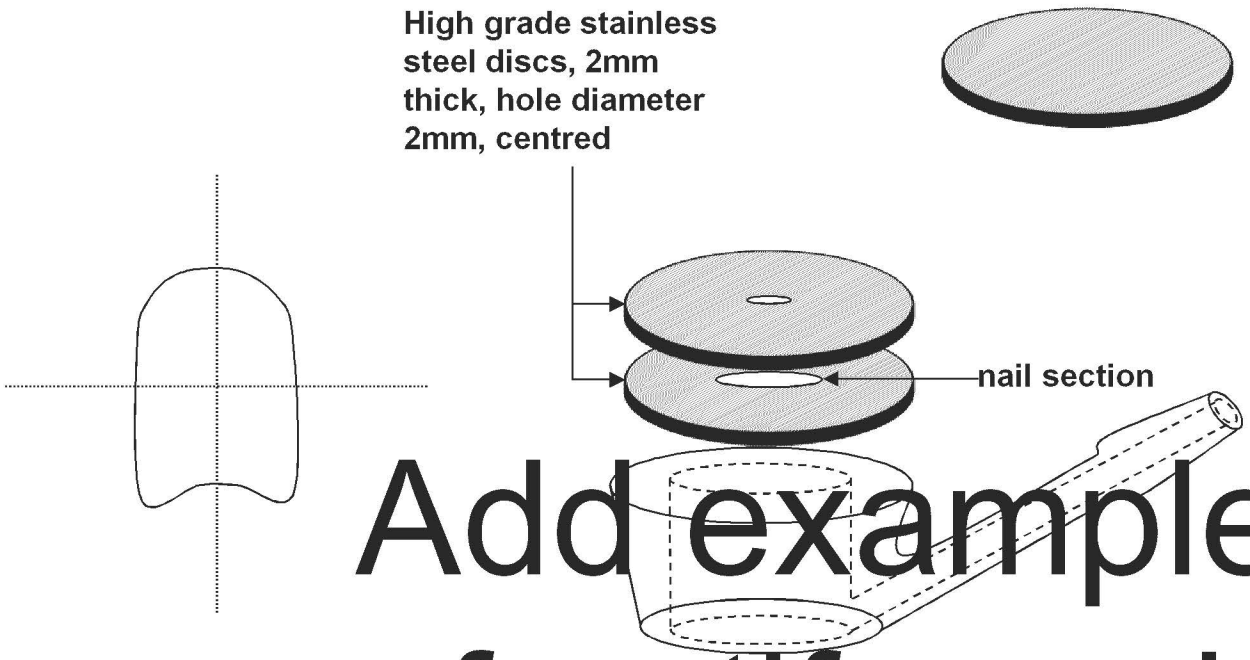


DAVE

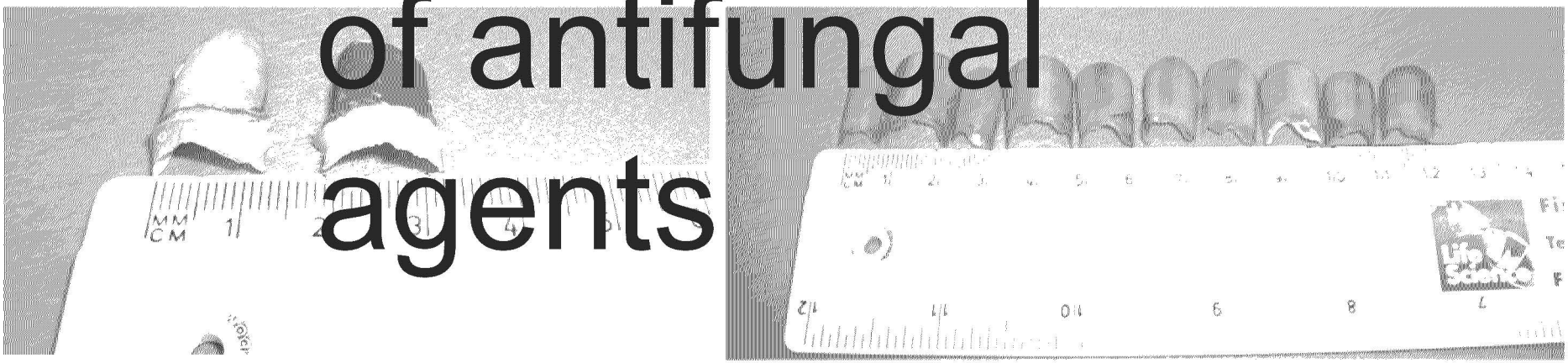
One area we have worked on for other companies includes production switching between plants, the product has to be tested for certain characteristics to prove equivalence. On development which may be patentable is these set of rings designed to hold synthetic membranes used for this testing

SUPACC

Finger and Toe Nail Absorption



Add example of antifungal agents



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Pharmaceutical products for use on nails, using and adapting our existing technologies to hold a different type of barrier.

Nails are divided and sectioned and then the amount of material passing through the nail can be measured

In Vitro Epidermis Screening Test (INVEST)

High throughput, low cost, fast delivery screen for product selection e.g.

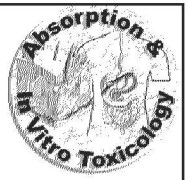
- Highest therapeutic efficacy of pharmaceuticals
- Safest formulation of agrochemicals
- Measures the *in vitro* absorption through pig skin over 24 hours.
  - Simple analysis e.g.
    - ^{14}C Radiolabel,
    - HPLC or
    - GC
  - No mass balance
  - Summary reporting
  - Conducted to GLP

Influence of vehicle on absorption of DNCB

DAVE

The invest is a heavily cut down cheap version of the IVP to screen formulations in development. We can ascertain which is the fastest or slowest absorption depending on the test material and client requirements

In Vitro Digestibility Assays



Developed as part of the strategy for assessing the allergenicity of novel foods (proteins).

In Vitro Simulated Gastric Fluid (SGF) Assay

- Assesses proteolytic breakdown over time.

In Vitro Simulated Intestinal Fluid (SIF) Assay

- Assesses proteolytic breakdown over time.

Resistance of proteins to digestion in either assay, may mean that the protein and therefore the foodstuff may have the potential to elicit an allergic response.

Providing consultancy to the US Biotech Group

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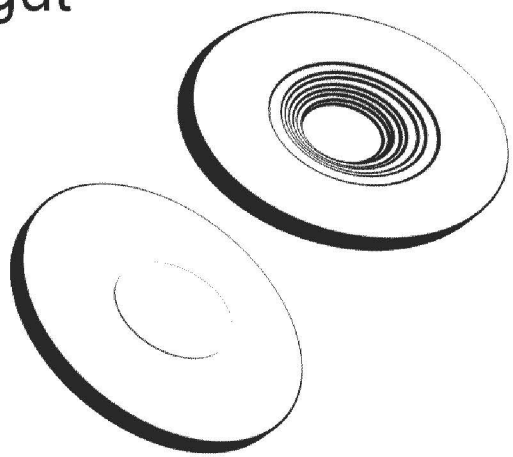
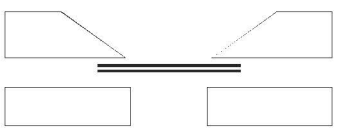
Digestibility assays

Simulation of gastric and intestinal fluid assays as part of the allergenicity work

Gut and the glass diffusion cells

- Development of a screening assay using diffusion cells for absorption through the gut membrane
- Ability to assay different areas of the gut
- Many samples from a single animal
- Small amount of test material needed
- Technical challenges
  - Passive Vs active diffusion
  - Viability / gassing of sample
  - Suitable holder for gut (another of Ron's rings)





Bevelled top ring to increase dosing volume

DAVE

The latest idea is the use of the gut on the Franz cell as an alternative to the GILT assay

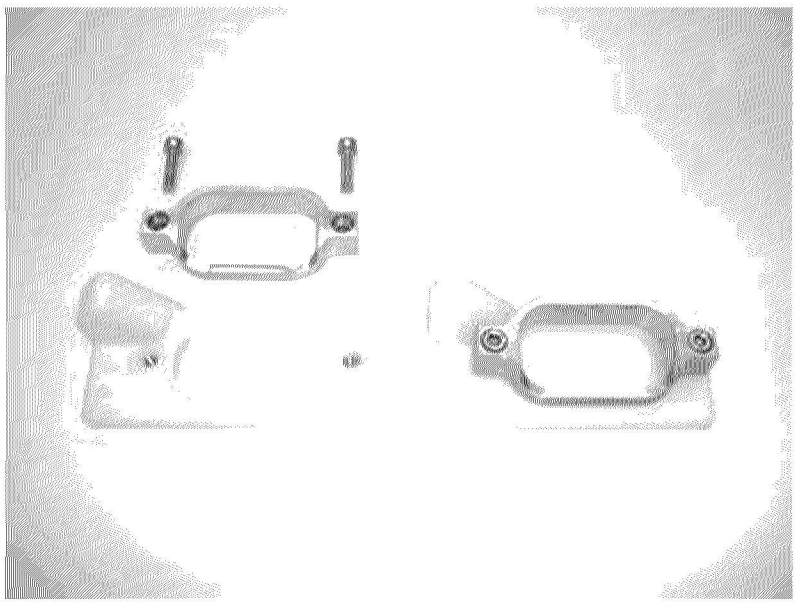
Increasing the available sections of the gut we can use

Reducing animal numbers

Speed and volume benefits

IVP developmental work

- Assessment of the effects of ultrasound application on hair dye absorption and distribution in rabbit skin
  - Hair dyes
  - Ultrasound effects on skin penetration
  - Binding properties of hair dyes to hair/skin following topical application



Developed Ultrasound Cell Model

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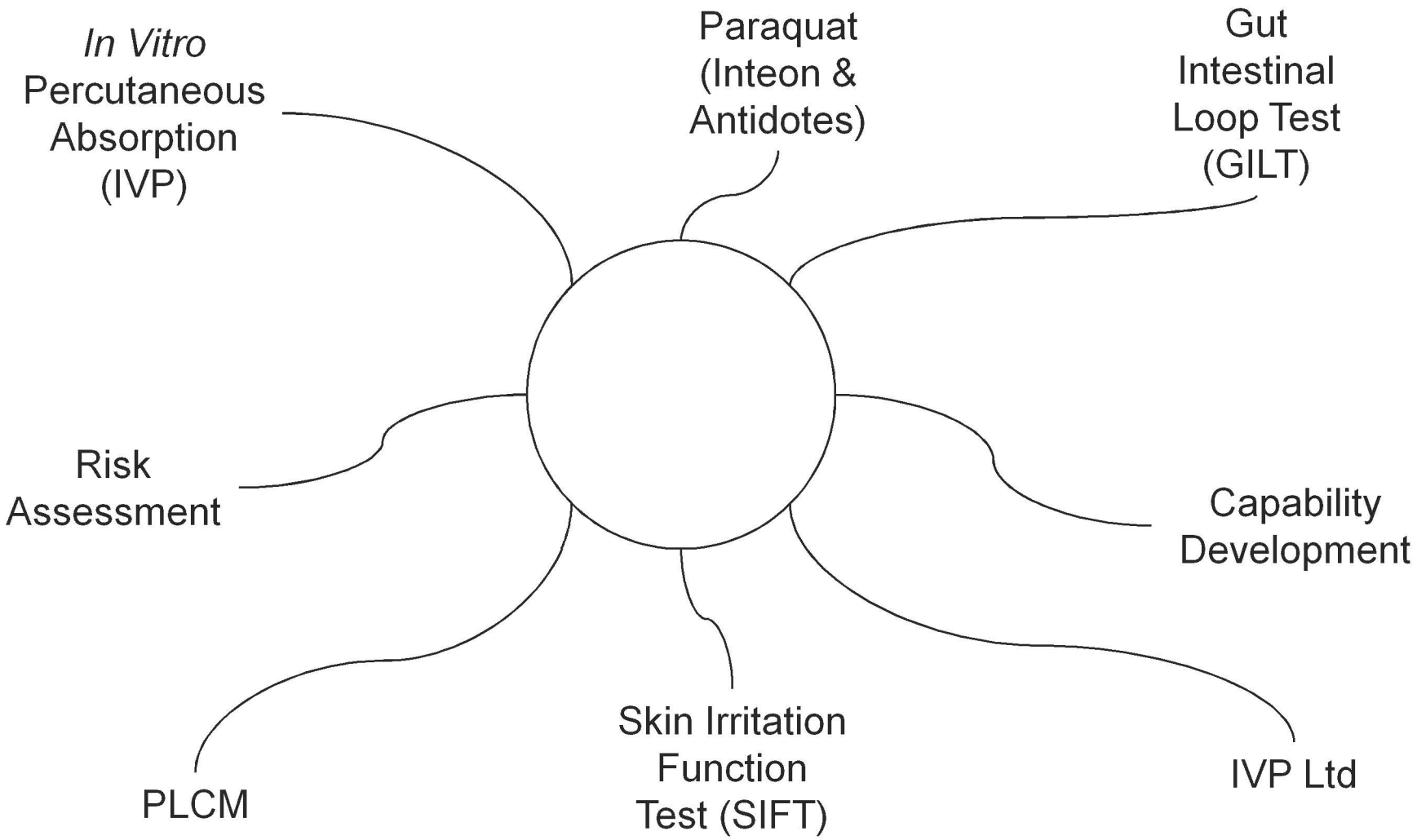
Who are AIVT customers?



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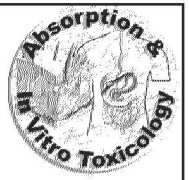
Customers



High proportion of our work is for external clients, including repeat business from major companies.

- Syngenta businesses
  - E.g. CPD, R&T, Stage 1, PP, Seeds, Marketing
- Consortia and EU (ECVAM)
- External sectors
  - Cosmetic
  - Industrial Chemicals
  - Pharma
  - Agchem companies
- European, US and Japanese markets

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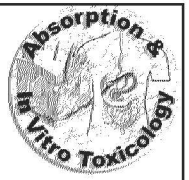
The Syngenta businesses through some interesting and odd challenges our way usually with remarkable timescales

The consortia either including CTL or Syngenta and those not directly involved with the company

Many external clients, from a large range of industries

Use of the *in vitro* test method



Industries supported:

The *in vitro* percutaneous absorption group offers a range of studies tailor made to meet customer requirements for a wide range of industries.

- **Agrochemical**, e.g.
  - Insecticides
  - Herbicides
  - Fungicides
- **Pharmaceutical**, e.g.
  - Dermatological products
  - Topical drug application and delivery
  - Bioavailability testing
- **Cosmetic**, e.g.
  - Hair dyes
  - Sun screens
  - Skin care products
- **Industrial**, e.g.
  - Chemicals
  - Paints
  - Drug intermediates
  - Inks
- **Biocide**
- **Veterinary**

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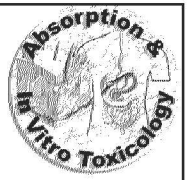
IVP studies can be used in a variety of industries and on products that wouldn't immediately come to mind

AIVT studies are used for:



- Operator exposure and risk assessment
- New product development
- Product support
- Product registration and re-registration
- Formulation selection and development
- Assessment of suitable application methodologies
- Efficacy
- Product comparison
- Bioequivalence tests (drug release rate)
- Hazard evaluation

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We do have our uses and these are increasing all the time

Our role in Health Assessment

We are

- Delivering a range of specialist services
- Customer Driven
  - Bespoke study design for product and application
  - Expertise in formulations and method development
- Business Driven
  - Develop solutions
  - Sell capability and reputation
  - Target for 2006 > £1m external income
- Market Driven
  - Respond to clients requirements
  - Setting standards for Industry
  - Product challenges
- Capable of working as a stand alone unit

Integral part of the Science and Technology in RITS

DAVE

So what does AIVT stand for

Besides the name

We provide and essential service

We are focussed on delivery to the client as studies are often bespoke

We can trade on our problem solving and high technical and scientific standards and ability

We are looking for new markets, new clients, new territories and challenges

We are self sufficient and can operate on a micro scale being independent of other areas increasing our flexibility

AIVT, Why and Who

INCOME capability

Ron

Jenny

Dave

Jon

Cindy

Ian

External Reputation

Product Registration

Anne

Mandy

Absorption & In Vitro Toxicology

Nik

Rob

Helen

New AI Mixes

Formulation Development

Thomas

Heather

INCOME

Diane

Lorraine

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This is what we are, why we are here and who we all are

Thank you for your attention

Any questions