

THE ORAL MAGIC BULLET : REMOTE CONTROLLED MICRO-ELECTRONIC CAPSULES FOR DELIVERING DRUG AT THE RIGHT PLACE AT THE RIGHT TIME

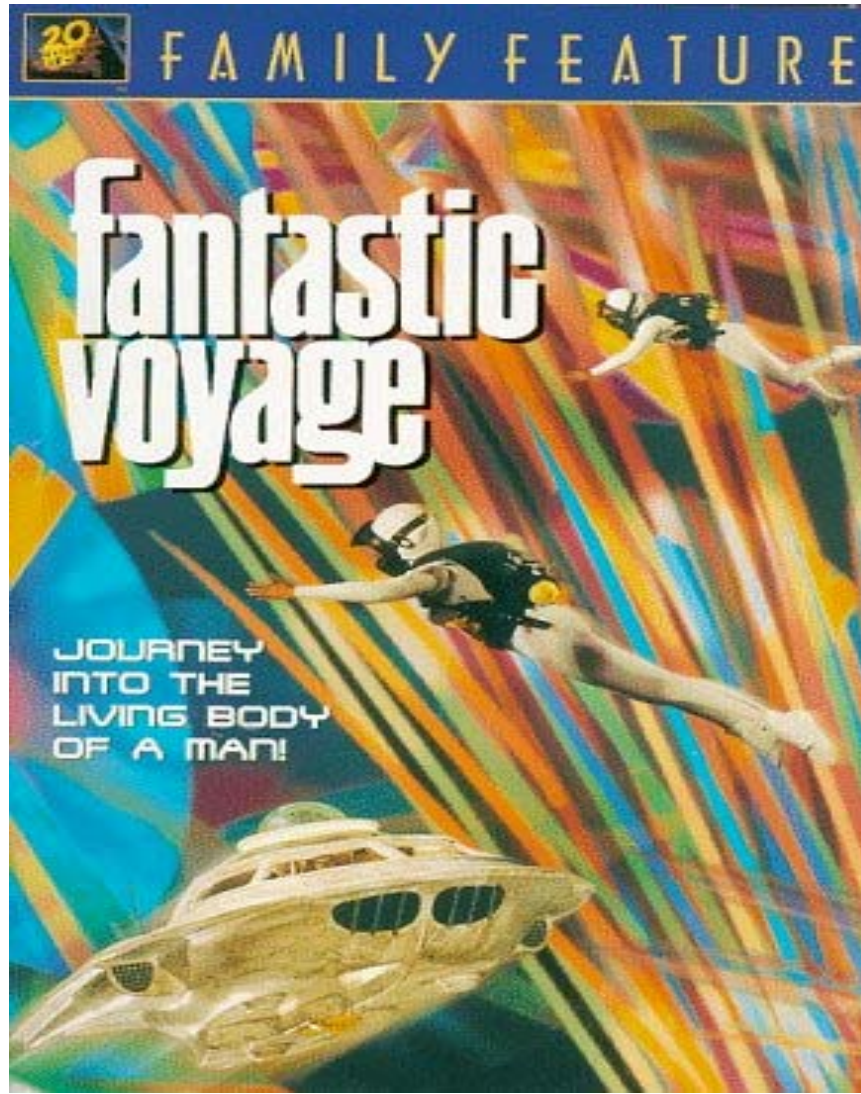
Dr Ian Wilding

Pharmaceutical Profiles

December 2004



SCI FI TO REALITY.....



CAPSULE ENDOSCOPY – GIVEN IMAGING



GI  **EN**[®]
IMAGING

Expanding the scope of GI

IMAGING SMALL BOWEL ANATOMY - VILLI



[Click on image to view movie](#)



Expanding the scope of GI

MOUTH TO CAECUM – THE GIVEN IMAGING JOURNEY



Teeth



Epiglottis



Gastric Fold



Right Colon



Ileo-caecal valve



Small Intestine

ENGINEERING BASED REMOTE CONTROLLED DELIVERY CAPSULES

- Eriksen Capsule
[Eriksen et al J Pharm Sci 50 : 151-156 (1961)]
- Telemetric capsule
[Schentag *et al* US patent 5 279 607]
- High frequency (HF) capsule
[Bode *et al* Eur J Clin Pharmacol 50:195-201 (1996)]
- IntelliSite™ capsule
[Gardner *et al* Pharm tech 21 (10) 82-89 (1997)]
- Enterion™ capsule
[Wilding *et al* PSTT 3 (11) 385-392 (2000)]

Development of the Enterion capsule

THE ENTERION DEVELOPMENT TEAM

PA Consulting

- Clever physics
- Material scientists
- Microelectronics

Success

Phaeton Research

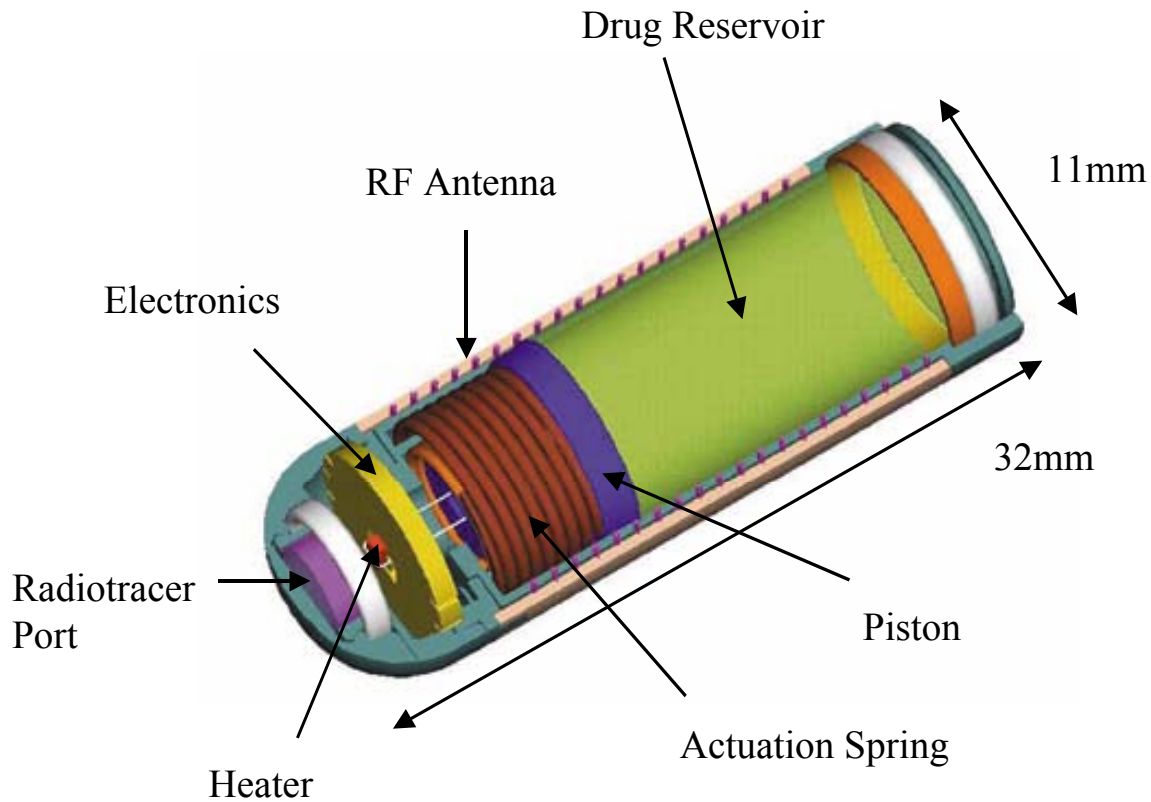
- GI knowledge
- Market needs
- Pharmaceutical experience

ESSENTIAL SAFETY/DESIGN CONSIDERATIONS FOR ENTERION

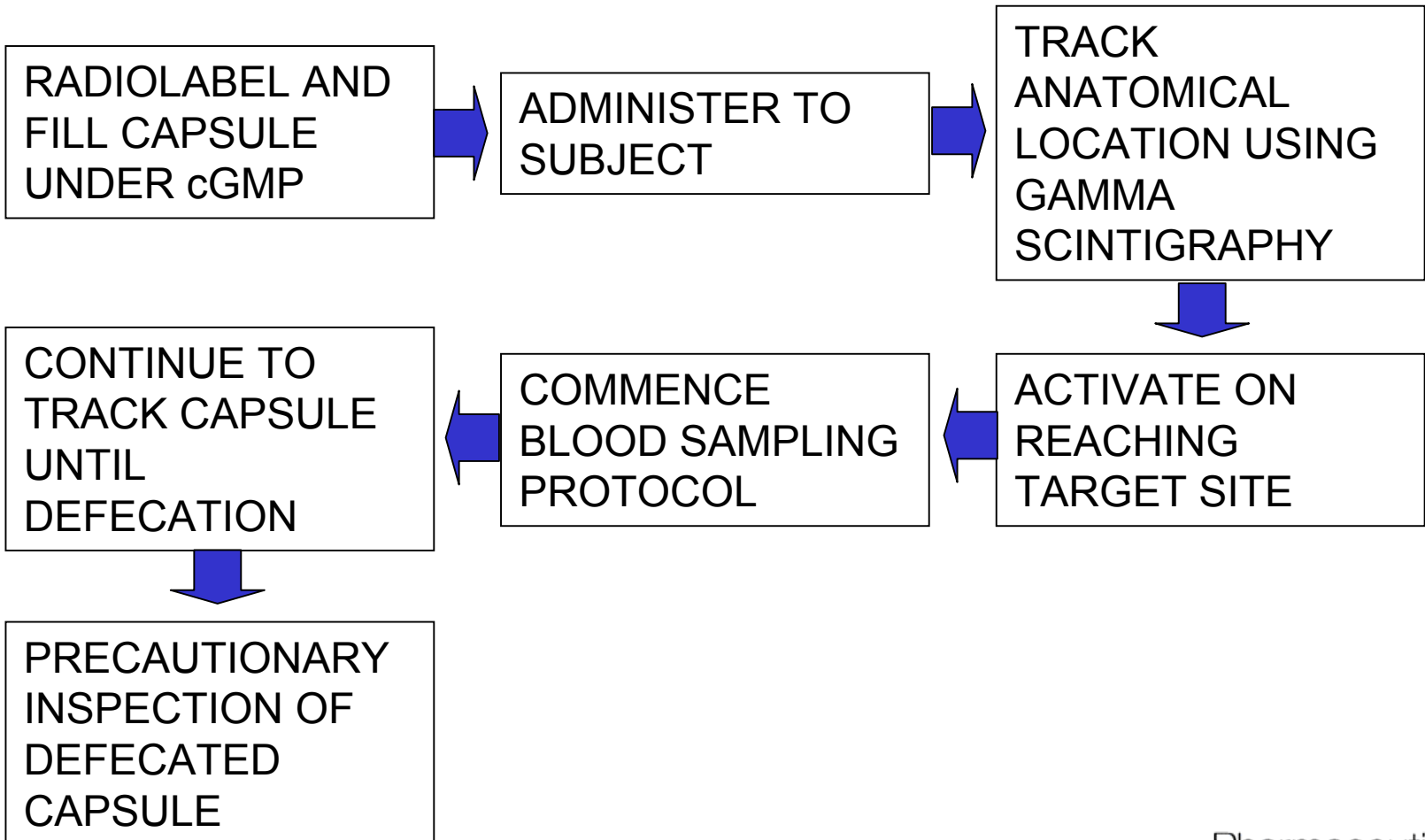
- Biocompatible
- Easily swallowed
- Safe and reliable activation
- Fully effective with a variety of physical forms
- High loading capacity
- Easy tracking of capsule location
- No pre-activation leakage
- Instantaneous confirmation of in vivo release

ENTERION CAPSULE

The Enterion™ Capsule



ABSORPTION STUDY FLOW DIAGRAM



CAPSULE TRACKING – LOCATION OF RADIOACTIVE MARKERS

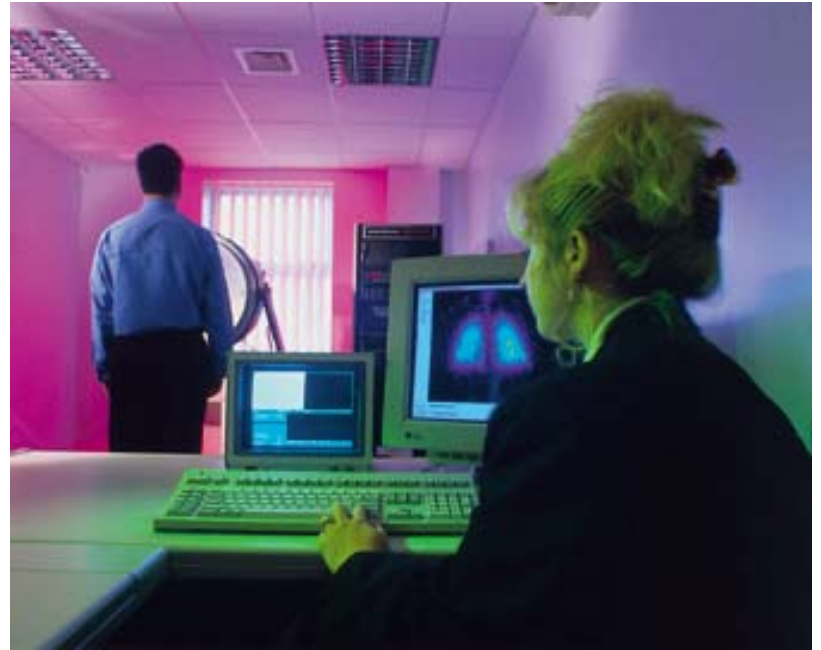
Two radioactive markers are used:

Indium-111 (^{111}In) is sealed inside the Enterion™ capsule. This allows the location of the capsule to be tracked through the gastrointestinal tract.

Technetium-99m ($^{99\text{m}}\text{Tc}$) is added to water and given to the subject as a drink at the time of dosing.

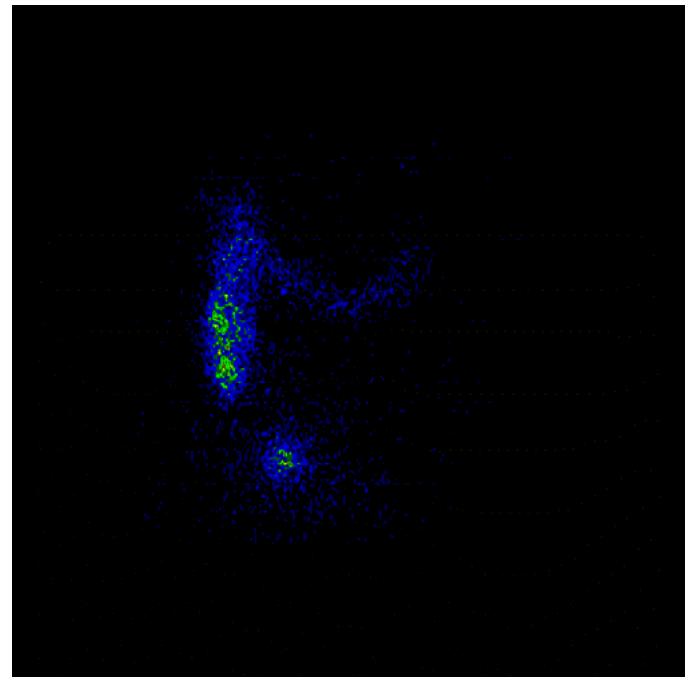
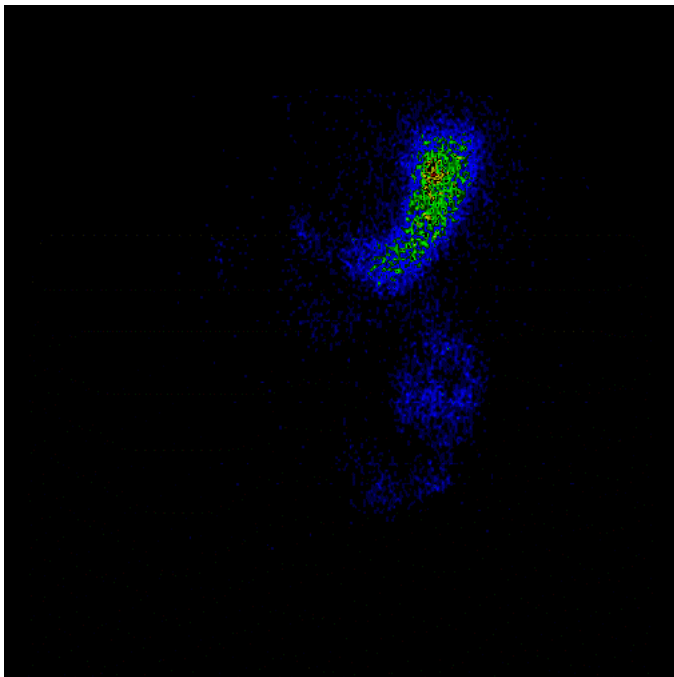
CAPSULE TRACKING – GAMMA SCINTIGRAPHY

Scintigraphic images are acquired at approximately 10 minute intervals until the capsule reaches the target site.

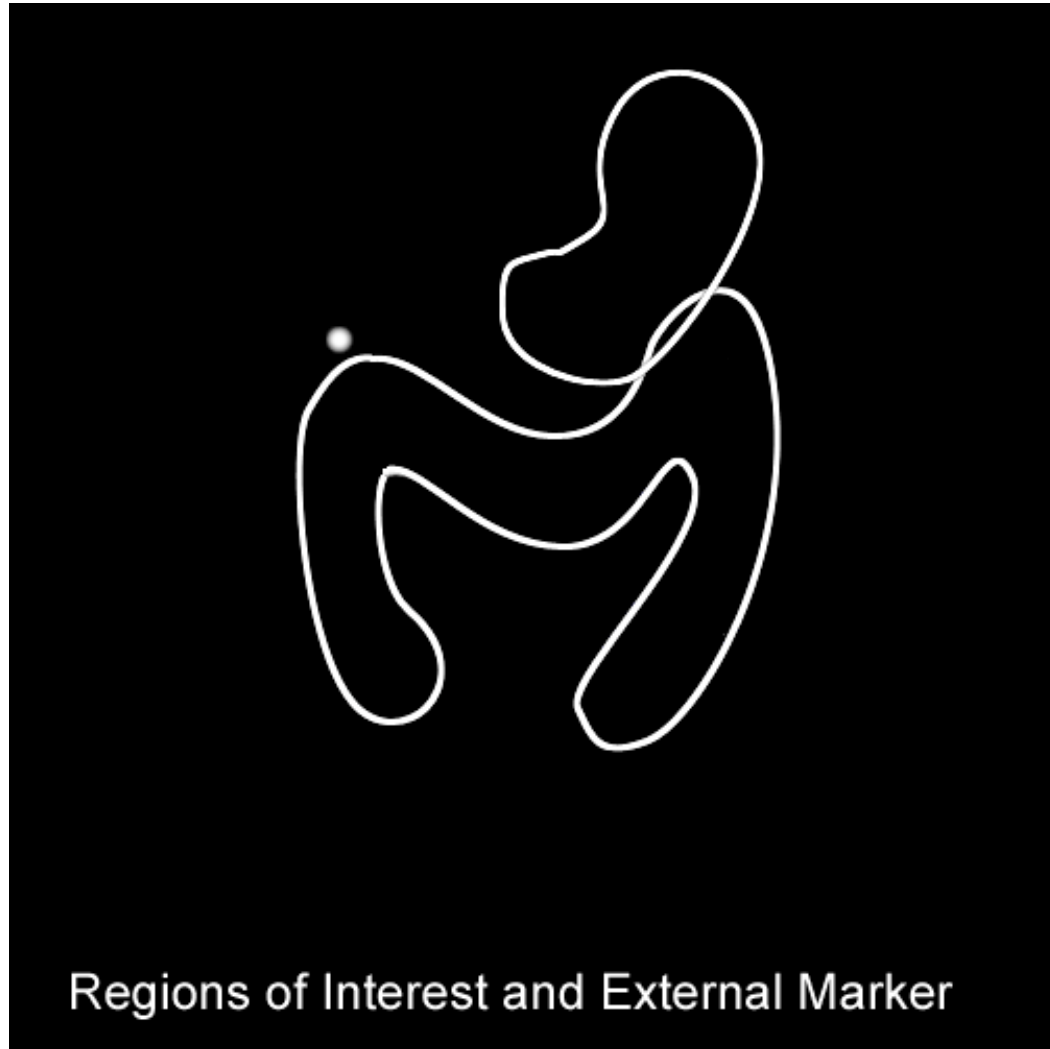


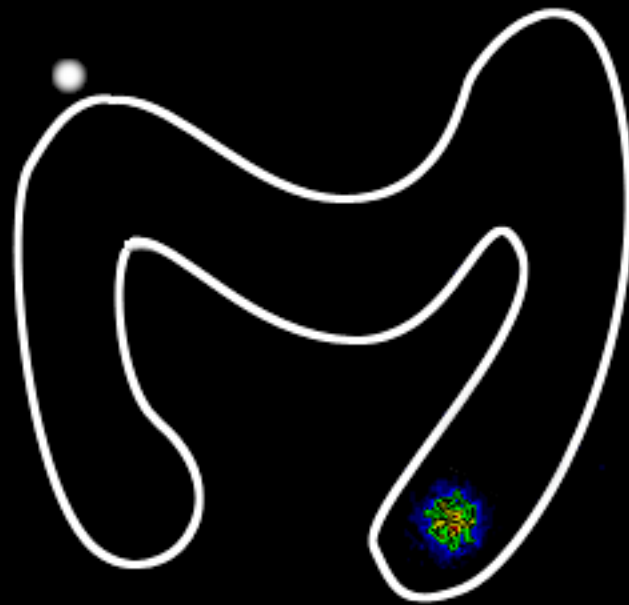
USING THE RADIOACTIVE DRINK TO PROVIDE AN ANATOMICAL ROAD MA

^{99m}Tc images are used to provide detailed information on the anatomy of the gastrointestinal tract

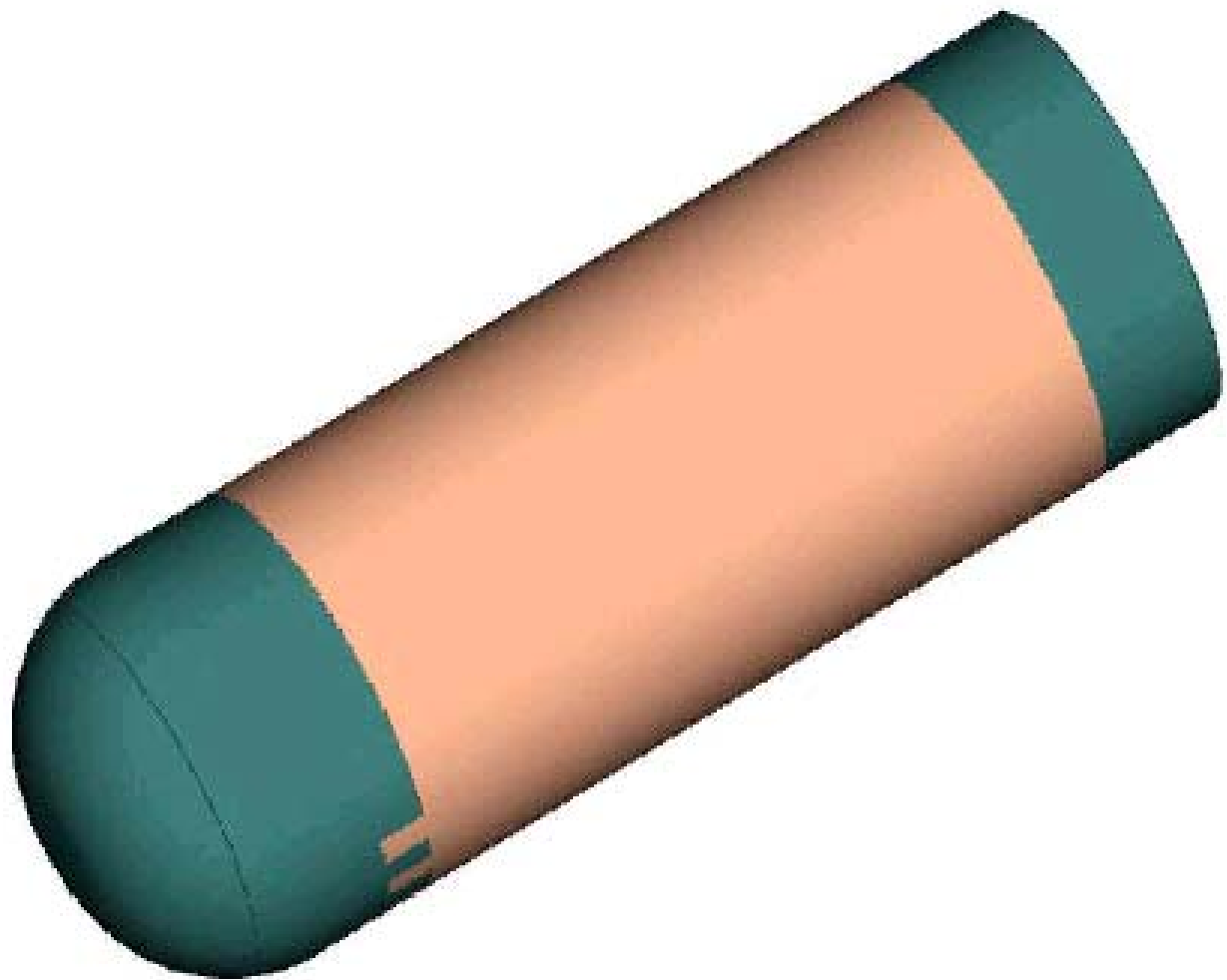


AN UNIQUE ANATOMICAL ROAD MAP FOR EACH SUBJECT

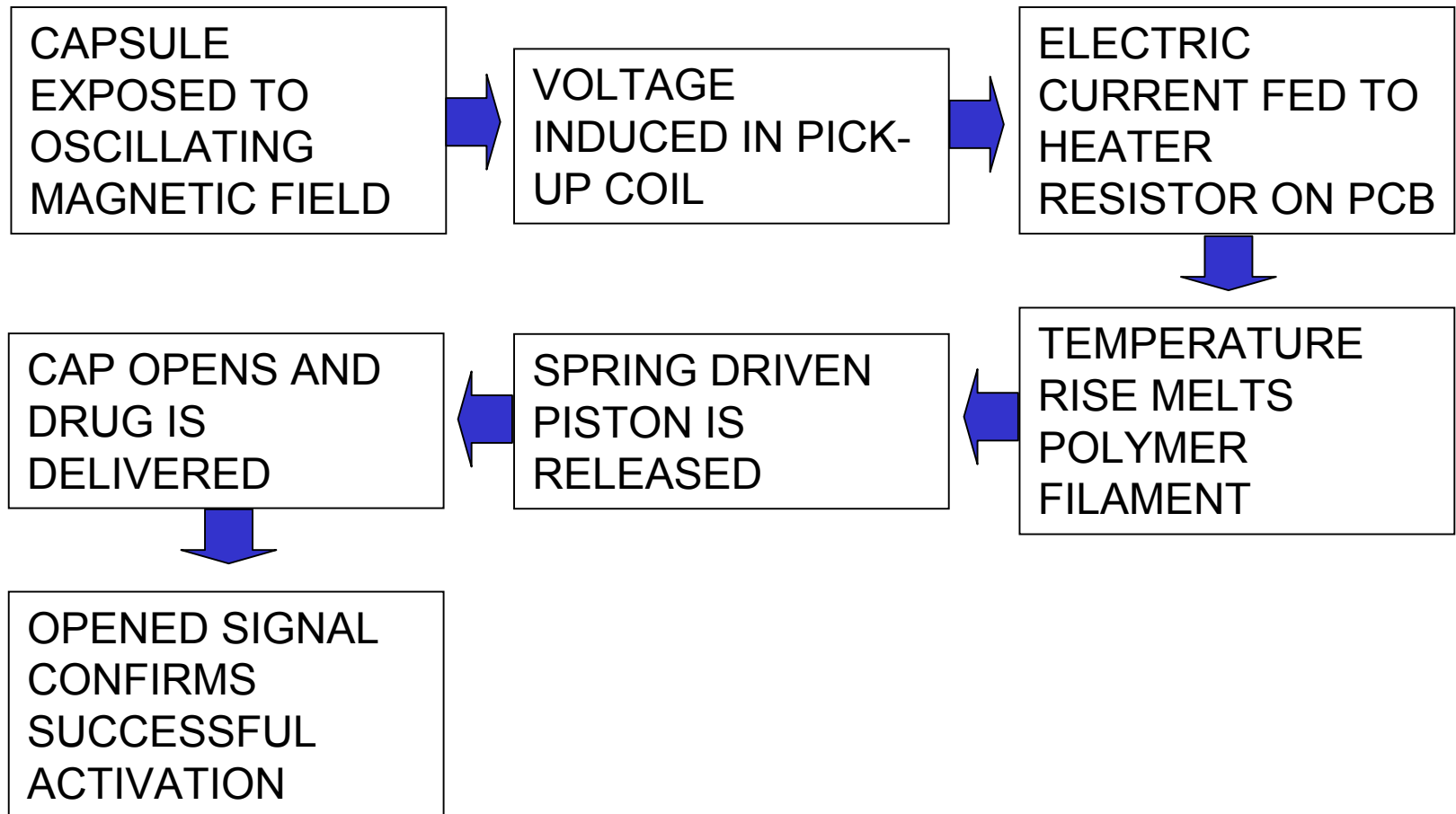




17.25h Capsule in Sigmoid Colon



CAPSULE ACTIVATION PROCESS



RECEIVER RESONANT CIRCUIT

- Designed to extract maximum electrical power from high frequency magnetic field (MF)
- Maximising the coil area is important in this context but power is also a function of frequency
- Debate about frequency was long

FREQUENCY DEBATE

- The higher the frequency, the higher the power for a given field
- However, the interaction of the body tissues etc also increases as frequency increases
- What will be an acceptable trade-off

TRADE OFF

- Below 2MHz the maximum MF usage guideline remains constant but above it decreases as the square of frequency
- At around 2MHz absorption by the body tissue is so small that it causes negligible change to impedance
- System was therefore designed to operate with an MF oscillating at 1.8MHz

CAPSULE ACTIVATION PROCESS



ENTERION CAPSULE FORMULATIONS

- Solution (aqueous / non aqueous)
- Suspension (aqueous / non aqueous)
- Drug alone (powder)
- Granulate
- Formulated powder to enhance solubility
- Pellets
- Mini-tablets

PATENT DETAILS

(12) **United States Patent** **Houzego et al.**

(10) **Patent No.:** **US 6,632,216 B2**

(45) **Date of Patent:** **Oct. 14, 2003**

(54) **INGESTIBLE DEVICE**

(75) **Inventors:** **Peter J. Houzego**, Cambridge (GB);
Peter N. Morgan, Cambridge (GB);
Peter H. Hirst, Nottinghamshire (GB);
Duncan J. Westland, Cambridge (GB);
Ian R. Wilding, Nottingham (GB)

(73) **Assignee:** **Phaeton Research Ltd.**, Nottingham (GB)

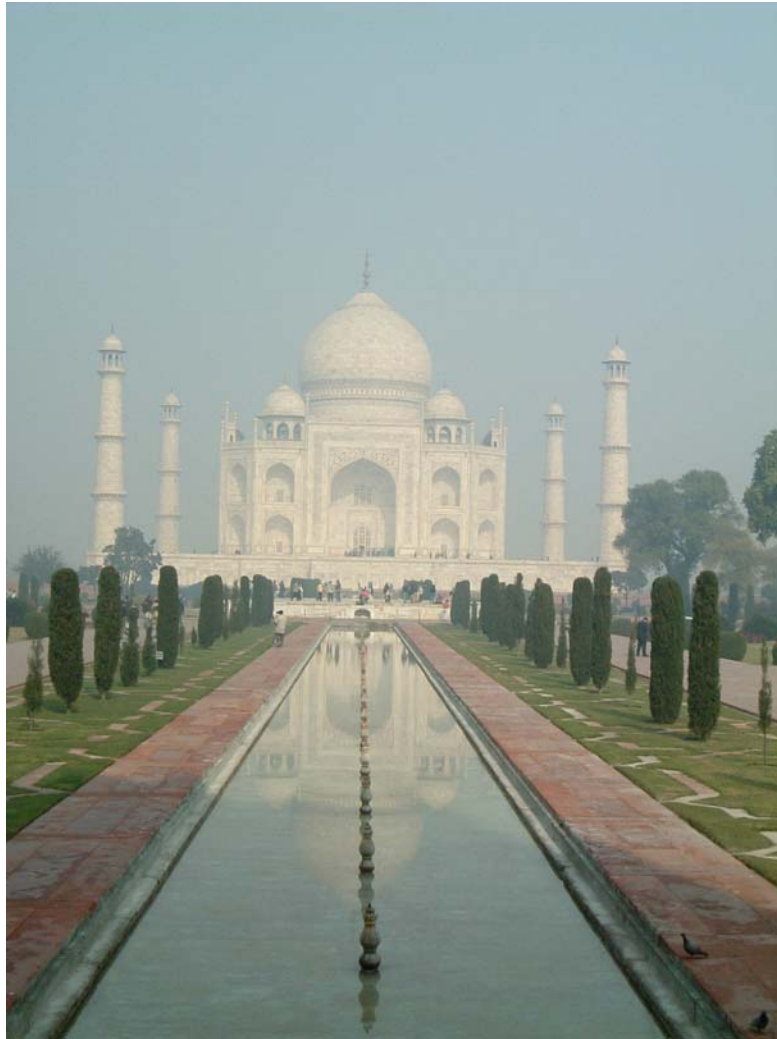
(*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 140 days.

(21) **Appl. No.:** **09/742,936**

(22) **Filed:** **Dec. 20, 2000**

**Why are they undertaken
and what do they show?**

CURRENT DRUG CANDIDATES : LIKE THE TAJ MAHAL??



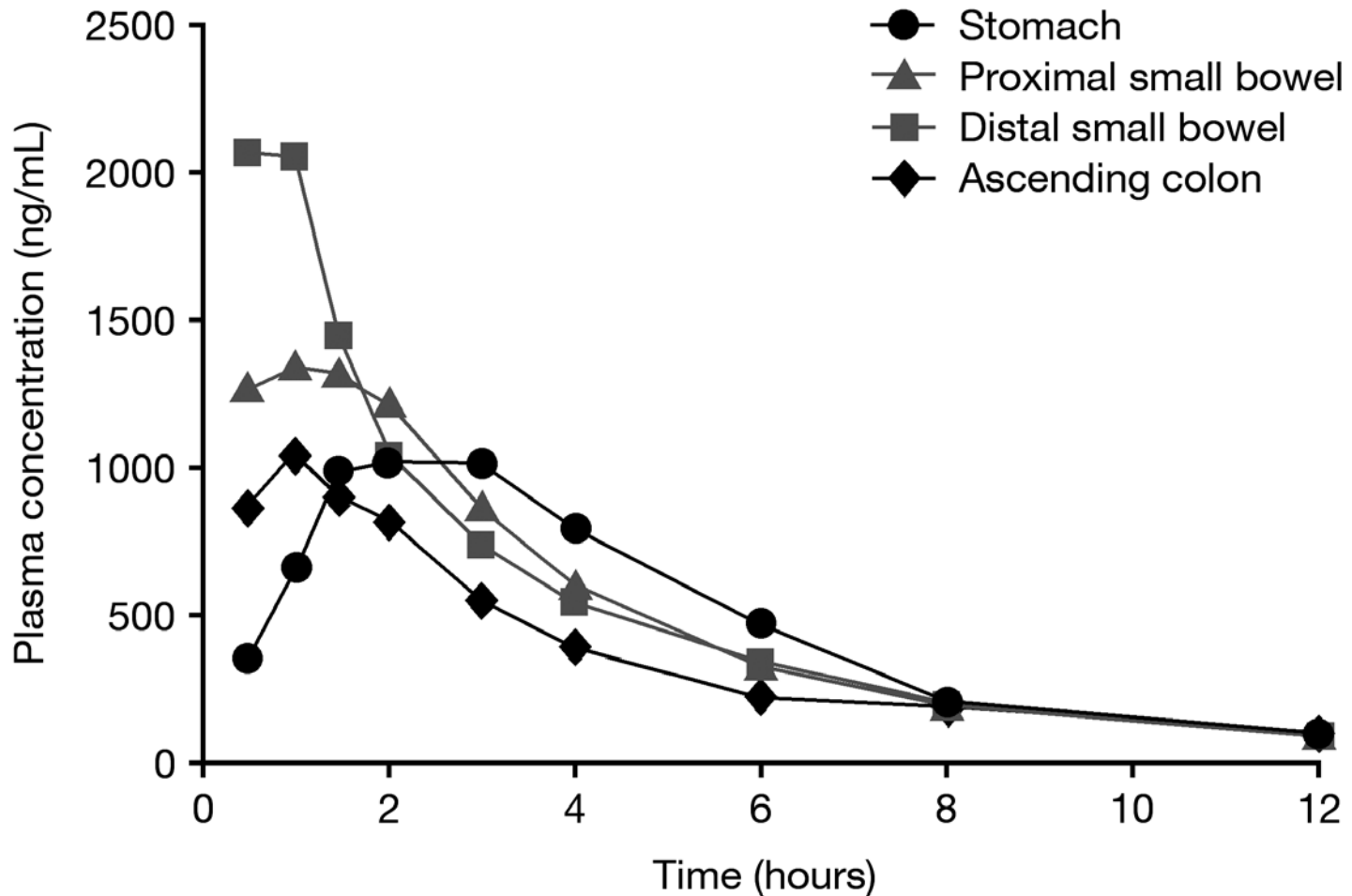
HUMAN ABSORPTION STUDIES PLAY AN IMPORTANT ROLE

- Human absorption studies are undertaken to provide a “route map” for the development of molecules with complex biopharmaceutical properties
- Over 100 human absorption studies in 6 years
- Proven approach for fast tracking drug development

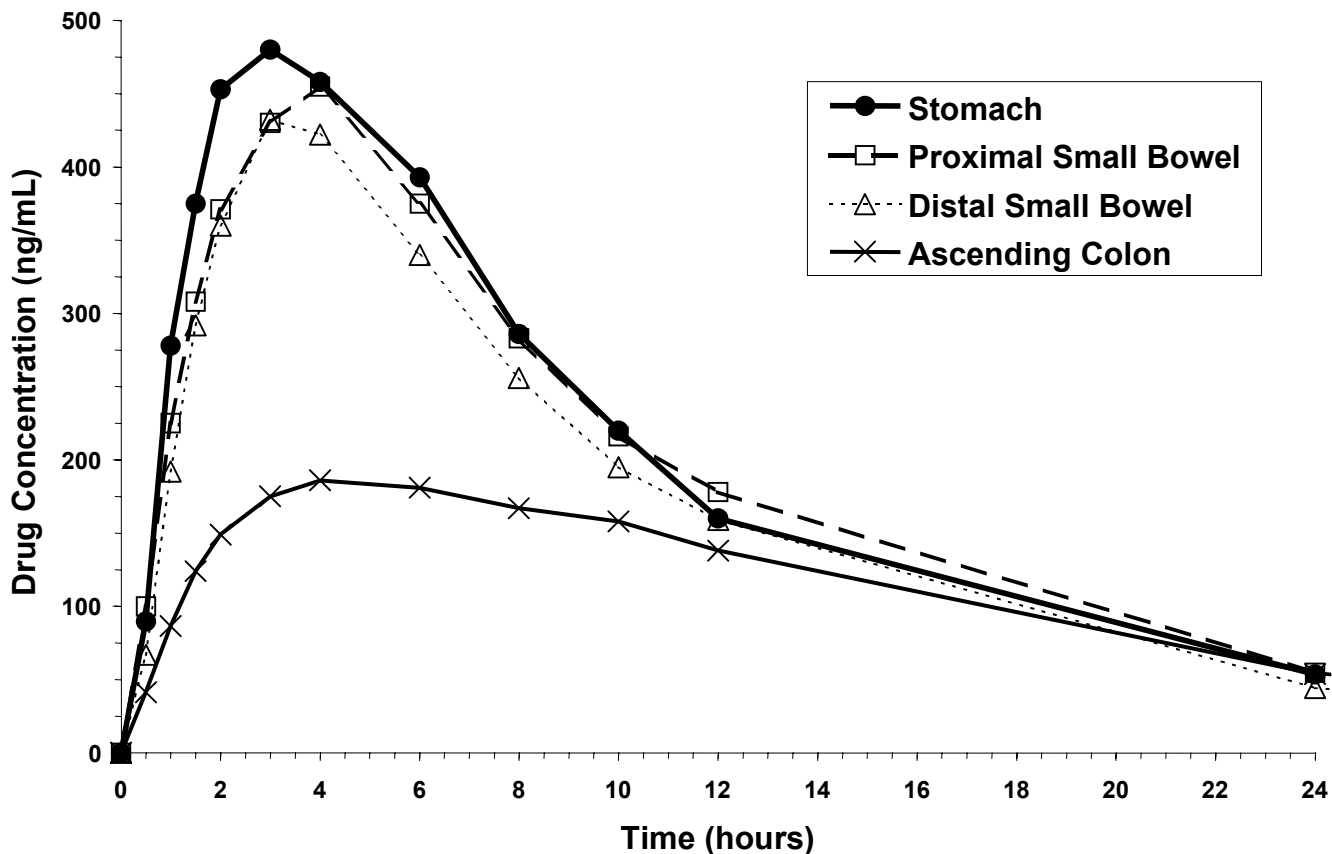
POSSIBLE DESIGNS FOR HUMAN ABSORPTION STUDIES

- Evaluate absorption from key regions of the human gut eg Proximal jejunum, distal ileum, ascending colon.
- Assess the effect of possible “enabling technologies” on drug absorption from a specific region of the gut

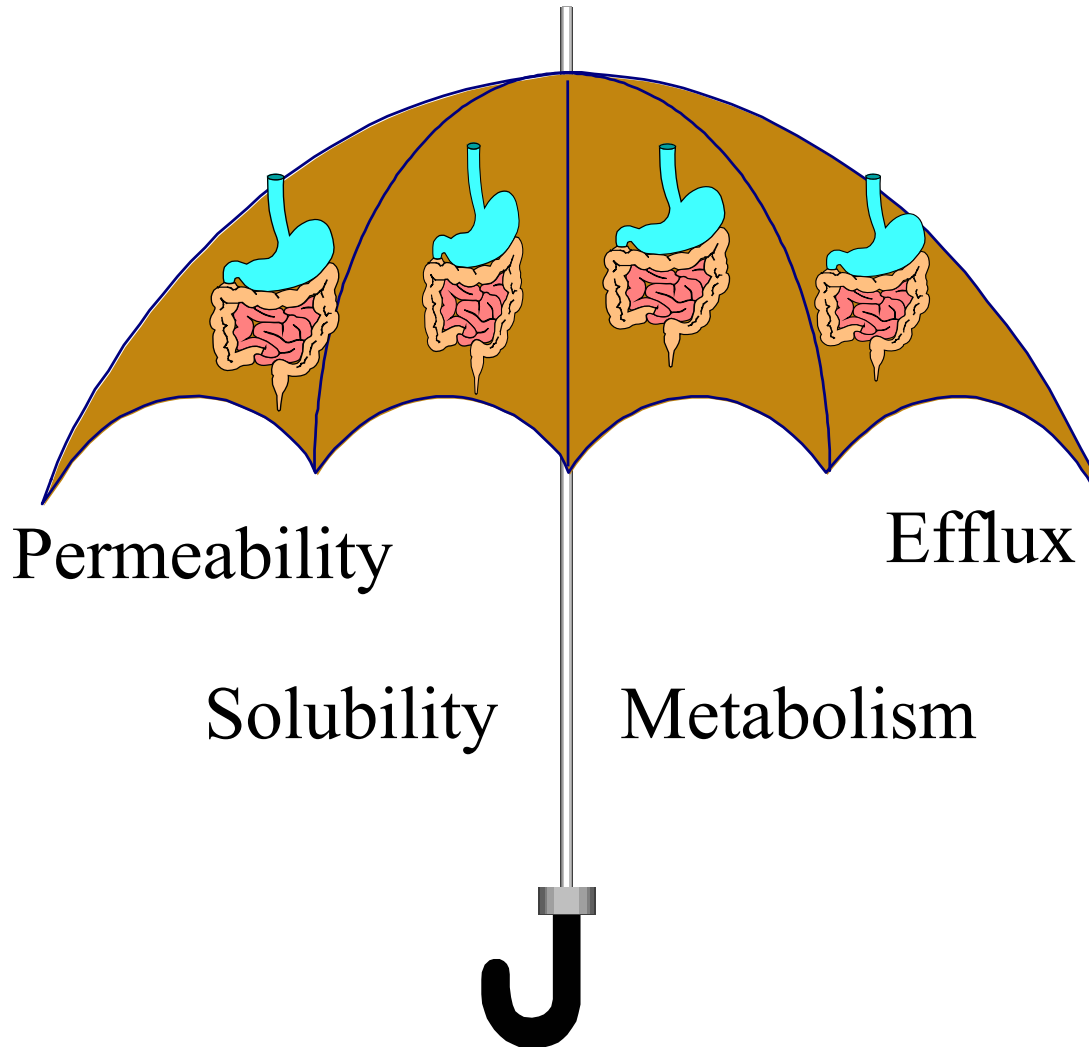
REGIOSPECIFIC DELIVERY CAN IMPROVE PK : LUMIRACOXIB



OSELTAMIVIR : CLASS III BCS DRUGS CAN BE ABSORBED FROM THE COLON



DRUG ABSORPTION : A COMPLEX ISSUE.....



Future Plans

FUTURE PLANS – NEXT GENERATION CAPSULES

- Programmable release: Tailored input rate
- Simultaneous pH evaluation and drug release
- Addition of imaging function to watch *in vivo* drug release and resulting dispersion etc.

Key challenge: Keeping capsule size sensible!!

FUTURE PLANS – CLINICAL APPLICATIONS

Diagnostics

- Assessment of intestinal permeability in a non-invasive manner eg. tailored chemotherapy to permeability side effects
- Probing the issues that control drug absorption in the ileum and colon still uncharted waters to the GI scientist

FUTURE PLANS – CLINICAL APPLICATIONS

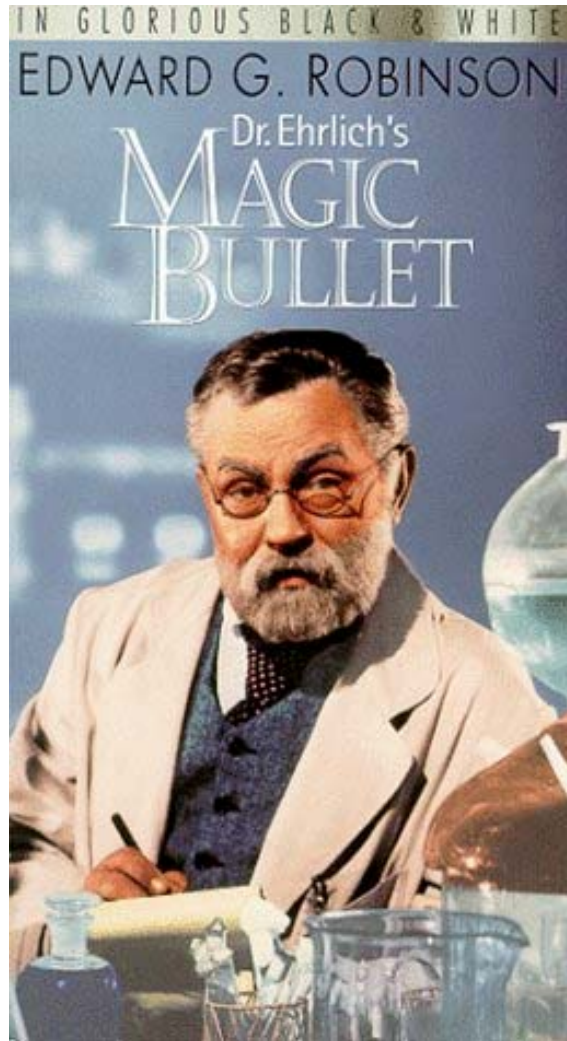
Therapeutics

- Localised delivery of therapeutic agents exactly where you want, when you want eg. targeted biologicals in IBD, neoplastic agents in carcinoma

Key challenges:

- Make technology scaleable (COG issues)
- Convert research tool into a product

THE ORAL MAGIC BULLET: CLOSER TO A REALITY....



ANY QUESTIONS?

For electronic copy of presentation and
follow-up questions :

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F R O S T  S U L L I V A N

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