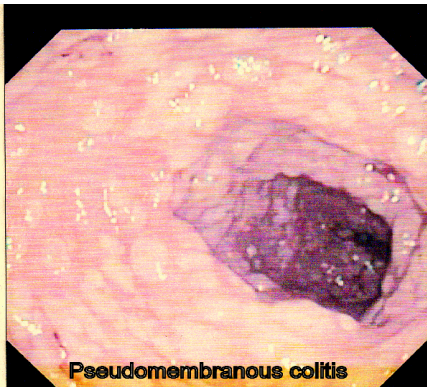


***Clostridium difficile* – a New Non-Antibiotic Treatment**

Clostridium difficile infection is the most frequent cause of hospital-acquired diarrhoea. Patients, particularly the elderly, who have been treated with broad spectrum antibiotics) are at greatest risk. Over 80% of *C. difficile* infections reported are in people aged over 65 years. The antibiotic can cause disruption of the normal intestinal flora which is an important part of the immune system, leading to an overgrowth of *C. difficile*. Most infections occur in hospitals (including community hospitals), nursing homes etc, but it can also occur in primary care settings.

C. difficile infection ranges from mild to severe diarrhoea to severe inflammation of the bowel (known as pseudomembranous colitis).



A patient who has *C. difficile* diarrhoea excretes large numbers of disease spores in their liquid faeces. These can contaminate the general environment around the patient's bed (including surfaces, keypads, equipment), the toilet areas, sluices, commodes, bedpan washers, etc. The spores can survive for a long time and be a source of hand-to-mouth infection for others. If these others have also been given antibiotics, they are at risk of *C. difficile* disease.

At the last count by the UK Department of Health, in September 2008 *C. difficile* infections had claimed 26,208 lives between 1997 and 2007. Numbers dying in England and Wales from *C. difficile* soared from 975 in 1999 to 8,324 in 2009, a jump of about 850%.

In a US study the rate of *C. difficile* acquisition was estimated to be 13% in patients with hospital stays of up to 2 weeks and 50% in those with hospital stays longer than 4 weeks. Patients who share a room with a *C. difficile*-positive patient acquire the organism after an estimated hospital stay of 3.2 days, as compared with a hospital stay of 18.9 days for other patients. [Reed and Kemmerly (2009) *The Ochsner Journal* 9:27–31]. The 2008 Association for Professionals in Infection Control and Epidemiology (APIC) study estimated the daily cost of CDI ranges between \$17.6 million and \$51.5 million. These figures do not take into account health care costs outside of the hospital or nursing home, lost productivity, pain and suffering of patients or the time that medical professionals must spend treating them.

The most important current treatments for *C.diff* are: (i) discontinuation of the inducing agent; (ii) supportive care; and (iii) in most cases, oral vancomycin or oral metronidazole. Some patients respond well to treatment but then have a relapse when it is discontinued. The frequency of a relapse is about 20% to 25%, and the frequency of a second relapse among those with a primary relapse is often higher, so that some will suffer multiple relapses with each course of oral metronidazole or vancomycin.

Faecal Bacteriotherapy

In these cases faecal bacteriotherapy, also known as faecal transfusion or faecal transplant, can be employed to restore the patient's colonic flora by reintroducing normal bacterial flora from stool obtained from a healthy donor – an allogenic procedure.

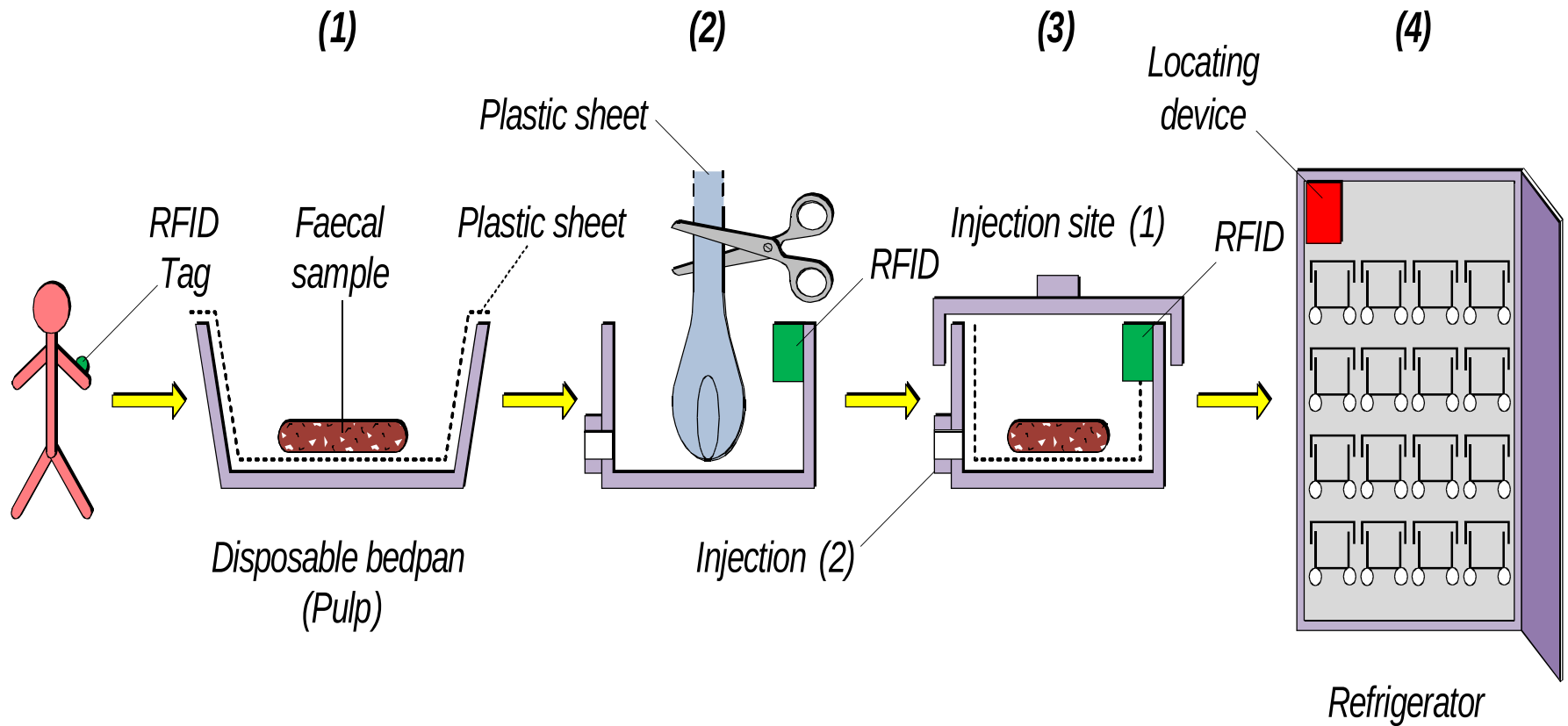


Illustration 2 - Faecal bacteriotherapy – Els van Nood processes donor stools and administers homogenised product via a nasal probe into the duodenum of a *C. diff.* patient in a Dutch comparative trial on 120 patients [The FECAL trial, Fecal therapy to Eliminate Clostridium difficile Associated Longstanding diarrhoea. Netherlands Trial Register. <http://www.nvge.nl/uploads/m0/lv/m0lvk6KEtFuQtVlxB7yykw/Bartelsman.pps>].

Autologous Restoration of Gastrointestinal Flora (ARGF)

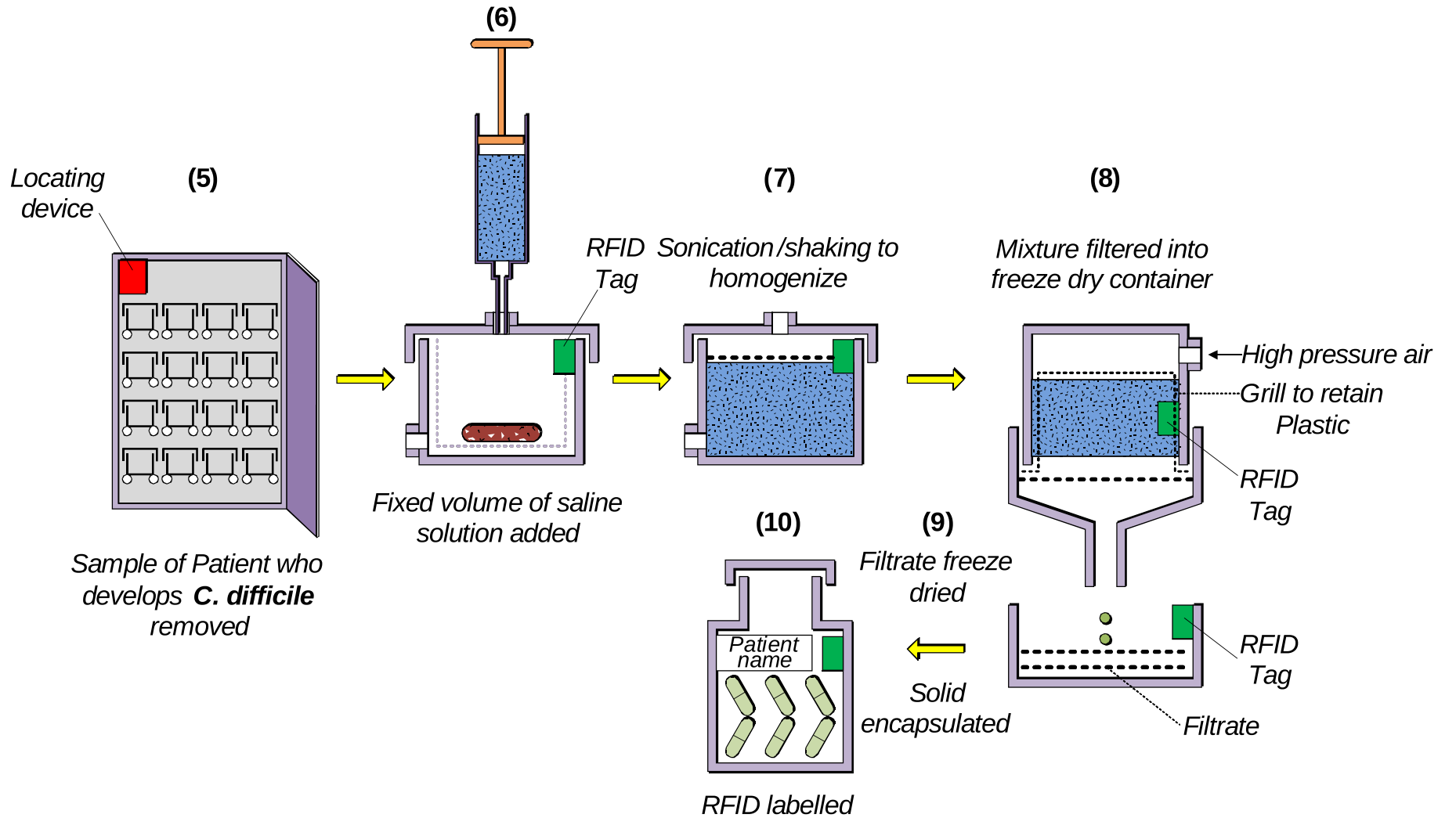
A modified form of faecal bacteriotherapy (FB) is being developed by Willana Lifesciences - Autologous Restoration of Gastrointestinal Flora (ARGF), which is safer, more effective and easier to administer. An autologous faecal sample, provided by the patient before medical treatment, is stored in a refrigerator.

Timeline 1a - Autologous Rehabilitation of Iatrogenically Degraded Intestinal Flora



Should the patient subsequently develop *C. difficile* the sample is extracted with saline and filtered. The filtrate is freeze dried and the resulting solid enclosed in enteric coated capsules. Administration of the capsules will restore the patient's own colonic flora and combat *C. difficile*.

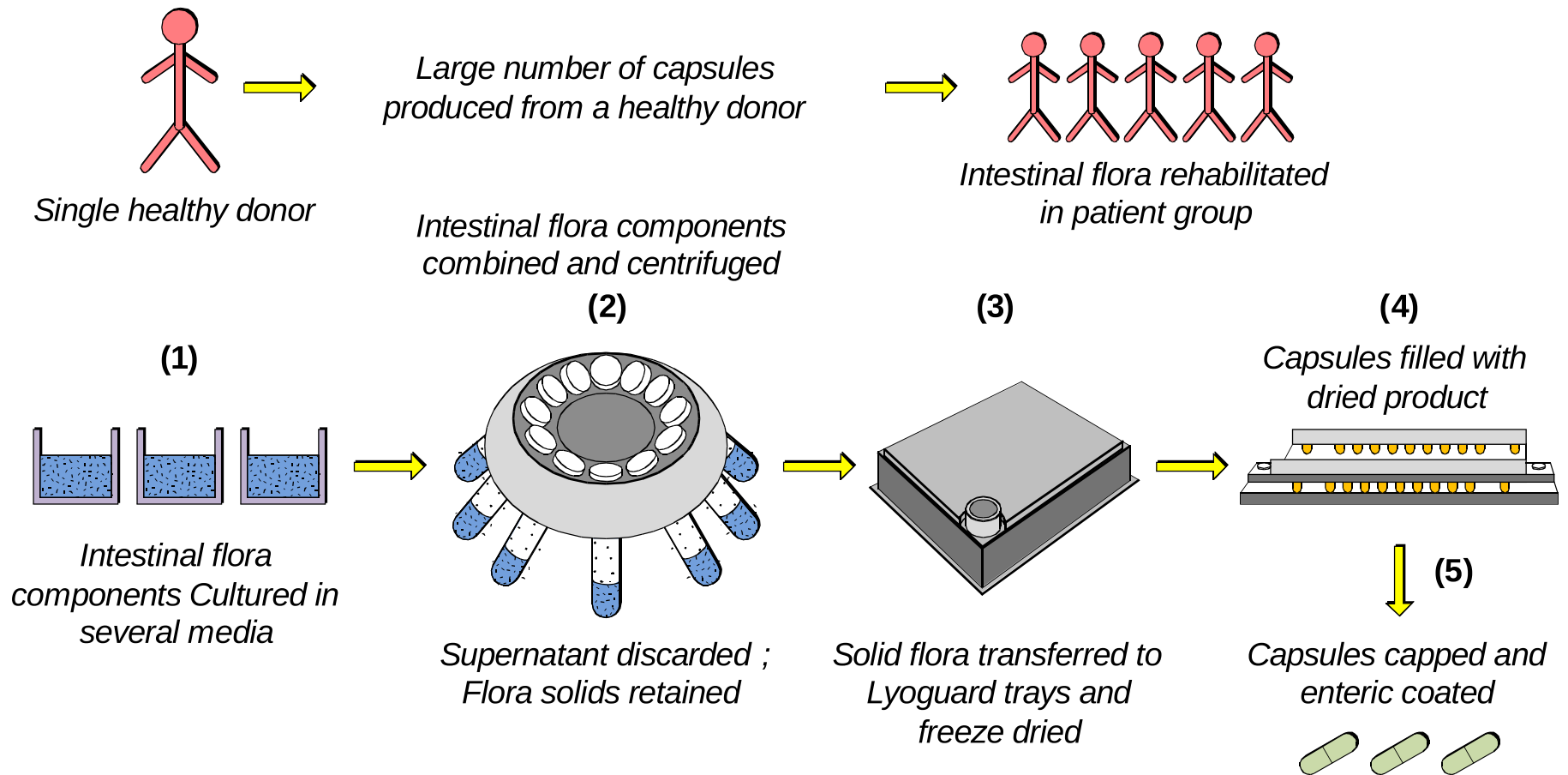
Timeline 1b - Autologous Rehabilitation of Iatrogenically Degraded Intestinal Flora



This procedure avoids the hazards of standard FB where infection from the donor could be transmitted to the patient and the delivery of faecal samples into the duodenum requires the use of a nasal probe. Radioimaging is required in standard FB to ensure the tube is located in the gastric antrum rather than in the respiratory system.

In the event that *C. difficile* becomes resistant to Vancomycin and Metronidazol, the two antibiotics used to treat it, a pandemic may develop and allogenic samples could be used to treat large groups of patients. Healthy donors could be screened for pathogens such as *C. difficile*, *Salmonella*, *Shigella*, *Campylobacter* etc. prior to their providing samples.

Timeline 2 - Allogenic Rehabilitation of Iatrogenically Degraded Intestinal Flora



*Healthy donor – absence of *C. difficile*, *Salmonella*, *Shingella*, *Campylobacter* etc.
F:\wjm-New\Faecal bacteriotherapy 2