Switching between liquid and tablet/capsule formulations - Which medicines require extra care?

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Background

Prescribers may be unaware that for a small number of medicines, there are differences in equivalent doses of oral formulations of the same medicine. Consequently, when switching a patient from one oral formulation to another, for example, switching from tablets or capsules to a liquid to aid administration in a patient with swallowing difficulties, dose adjustment and/or additional monitoring may be required. There may also be other concerns relating to the suitability of the formulation for the patient.

Answer

When changing the formulation of a patient's medication, prescribers and pharmacists should first consider whether the drug or formulation is affected by any of the general issues listed in **Table 1.**

Table 2 provides a summary of medicines where prescribers may need to consider dose adjustments and dosing advice is given where available. In instances where it may not be possible to achieve a dose that is exactly the same, practical advice such as additional patient monitoring is suggested.

There are other resources that can be read alongside this Q&A which consider the administration of medicines to patients with swallowing difficulties:

- Supporting patients with swallowing difficulties: Medicines and dysphagia
- How can medicines be managed for Parkinson's disease patients with swallowing difficulties?
- How do you convert from co-beneldopa (Madopar®) prolonged-release capsules to dispersible tablets?
- Crushing tablets or opening capsules in a care home setting

Table 1: General problems to be considered when switching between oral formulations of the same drug:

Administration differences:
Administration instructions may differ between formulations, e.g. with respect to taking with/without food. Consult product literature and ensure that the patient is correctly advised.
Brand-specific medicines:
Some medications have a demonstrable difference in clinical effect between each manufacturer's versions of the product and should be prescribed by brand name. There may be variations in the licensed indications of different brands of the same medicine. Caution should be exercised when changing formulation of any medicine usually prescribed by brand both when changing formulation within a brand and when changing between brands.

Consider consulting these medicines Q&As:

- Which medicines should be considered for brand-name prescribing in primary care?
- What are the differences between different brands of mesalazine tablets?

The MHRA has issued advice about switching between different manufacturers' products for **antiepileptic drugs** (1) and for **tacrolimus** (2).

Excipients:

Switching formulations may expose the patient to different excipients. The following non-exhaustive list of excipients may cause problems for certain patient groups: Arachis (peanut) oil; sesame oil; sugars and artificial sweeteners e.g. aspartame or sorbitol; ethanol (alcohol) and propylene glycol; gluten and lactose (3,4). Some patients may refuse to accept formulations containing animal and/or insect derived substances due to their religious or other beliefs. Consider consulting these medicines Q&As for further information:

- Arachis oil in medicines - what are the risks of developing peanut allergy?
- What factors need to be considered when prescribing for lactose intolerant adults?
- What factors to consider when advising on medicines suitable for a Halal diet?
- Excipients: What are the general considerations for vegan patients?

Health and safety considerations:

Drugs which are cytotoxic, carcinogenic, genotoxic, or teratogenic may have different handling requirements for different formulations (e.g. solid vs liquid).

Licensing differences:

In some cases, the licensed indications/contraindications for one formulation of a drug may be different from another formulation. Prescribers should ensure that the required formulation is licensed for the relevant indication. If use of the product is outside the product licence, the GMC's guidance on the subject should be followed (5).

Modified release formulations:

Frequency of dosing may be different for liquids/plain tablets/plain capsules than for the modified-release formulation, even if the total daily dose remains the same. There is a Q&A available entitled 'Switching from modified release doxazosin to standard release doxazosin in patients with hypertension'.

Narrow therapeutic index medicines:

Unless two formulations have been proven to be bioequivalent, it may be wise to be vigilant for a fall in efficacy or increase in adverse effects when changing formulations. This particularly applies to any medicine for which therapeutic levels are monitored.

Site of action:

Some formulations are designed to deliver the drug to a particular location in the gut. Changing the formulation may change the site to which the drug is delivered, and thus the therapeutic effect. This has particular significance for certain groups of patients, for example those fed via an enteral feeding tube or treated for bowel disorders. There is a Q&A available entitled 'How do the different types of enteral feeding tubes available affect drug administration?'

Unlicensed formulations:

Care should be taken when transferring between licensed and unlicensed formulations, as bioequivalence and bioavailability data for unlicensed formulations may be lacking.

Table 2: Medicines where additional therapeutic monitoring or dose adjustment is necessary when switching between liquid and tablet/capsule formulations of the same drug.

Drug	Brand names	Summary of dose-equivalence information
Alfacalcidol	One-Alpha 2microgram/mL oral drops. One-Alpha 0.25microgram, 0.5microgram and 1microgram soft capsules.	Using the integral dropper, ONE drop of One-Alpha 2microgram/mL oral drops contains 0.1microgram alfacalcidol (6).
Captopril	Noyada 5mg/5mL oral solution. Noyada 25mg/5mL oral solution.	Re-titration should be performed if patients are changed between Noyada oral solution and other captopril formulations (7).
Carbamazepine	Tegretol 100mg/5mL liquid. Tegretol 100mg, 200mg and 400mg tablets. Tegretol 200mg and 400mg prolonged release tablets.	A given dose of Tegretol liquid will produce higher peak levels than the same dose in tablet form. When switching a patient from tablets to liquid, the same total daily dose may be used but divided in smaller, more frequent, doses (8).
Chloral hydrate/ Chloral betaine	Welldorm elixir 143mg/5mL (chloral hydrate). Welldorm 707mg (chloral betaine) tablets.	Welldorm 707mg tablets contain 707mg chloral betaine, equivalent to 414mg of chloral hydrate (9). The dose of both the tablet and elixir formulations is given in terms of chloral hydrate content (9,10). This means 15mL chloral hydrate 143mg/5mL elixir is approximately equivalent to ONE 707mg chloral betaine tablet.
Ciclosporin	Capimune 25mg, 50mg and 100mg soft capsules. Deximune 25mg, 50mg and 100mg soft capsules. Neoral oral solution 100mg/mL. Neoral 10 mg, 25 mg, 50 mg and 100 mg soft gelatin capsules. Sandimmun 25mg, 50mg and 100mg soft capsules. Sandimmun oral solution 100mg/mL.	Neoral oral solution and Neoral soft gelatin capsules are bioequivalent (11). Sandimmun oral solution and Sandimmun soft gelatin capsules are bioequivalent; although the inter- and intra-subject variability ranges between 18 to 74%. (12). However, Sandimmun and Neoral capsules have different bioavailabilities and peak concentrations (11). The switch from one oral ciclosporin formulation to another should be made under physician supervision, including monitoring of blood levels of ciclosporin for transplantation patients (13).
Citalopram	Cipramil Drops 40mg/mL. Cipramil 20mg tablets.	Cipramil oral drop solution has an approximately 25% higher bioavailability compared to tablets. FOUR oral drops (8mg) is equivalent to ONE 10mg tablet (14).
Clobazam	Frisium 10mg tablets. Perizam 1mg/mL and 2mg/mL oral suspension. Tapclob 5mg/5mL and 10mg/5mL oral suspension.	Caution must be taken when switching between clobazam products as the mean peak concentration on single dose administration for the suspension is higher than that observed for the tablet formulation (15,16). This may lead to an increased risk of respiratory depression and sedation which may be most noticeable when switching to the oral suspension from tablets (15).

Clomethiazole	Heminevrin syrup 31.5mg/mL. Heminevrin capsules 192mg.	Heminevrin syrup contains 50mg/mL clomethiazole edisilate equivalent to 31.5mg/mL clomethiazole (17). Heminevrin capsules contain 192mg clomethiazole; as a result of differences in bioavailability between the capsules and the syrup, ONE capsule is considered therapeutically equivalent to 5mL syrup (18).
Clozapine	Clozaril tablets 25mg and 100mg. Denzapine 50mg/mL oral suspension. Denzapine 25mg, 50mg, 100mg and 200mg tablets. Zaponex 25mg and 100mg tablets. Zaponex 12.5mg, 25mg, 50mg, 100mg and 200mg orodispersible tablets	There has been controversy over the bioequivalence or otherwise of different brands of clozapine; some reports indicate that it is possible to switch between brands but there are reports of exacerbation of psychotic symptoms in patients who were switched between brands (18). If changing between clozapine brands, the patient, prescriber and supplying pharmacist must all be registered with the appropriate patient monitoring service (3).
Co-amoxiclav	Augmentin 125/31 suspension and Augmentin 250/62 suspension. Augmentin Duo powder for oral suspension 400/57. Augmentin 375mg and 625mg tablets.	Oral preparations contain a mixture of amoxicillin (as the trihydrate) and clavulanic acid (as potassium clavulanate); the proportions are expressed in the form x/y where x and y are the strengths in mg of amoxicillin and clavulanic acid respectively (3). The tablets cannot be directly converted to suspension; the proportions of the two drugs in the medication (amoxicillin and clavulanic acid) are different in the two preparations (19). Augmentin Duo suspension also has a different ratio of amoxicillin/clavulanic acid to standard Augmentin suspension (20). The licensed doses for each product should therefore be used, rather than attempting to calculate an exact equivalence.
Dasatinib	Sprycel 10 mg/mL powder for oral suspension. Sprycel 20mg, 50mg, 80mg, 100mg, 140mg film-coated tablets.	Sprycel film-coated tablets and Sprycel powder for oral suspension are not bioequivalent. Patients can be switched between formulations provided the correct dosing recommendations for the dosage form are followed. Consult product literature for the licensed body weight tiered dosing recommendations (21).
Digoxin	Lanoxin PG elixir 50microgram/mL. Lanoxin PG Tablets (62.5microgram), Lanoxin 125 Tablets (125microgram) and Lanoxin 0.25mg Tablets (250microgram).	The bioavailability of orally administered Lanoxin is approximately 63% in tablet form and 75% as the elixir (22). This equates to ONE 62.5microgram tablet being approximately equivalent to 50microgram (1mL) elixir (19). However, the manufacturer is aware of one study showing no clinically relevant difference in bioavailability of digoxin tablets and elixir and state that most clinicians suggest that these dosage forms can usually be used interchangeably (19,23). Digoxin has a low therapeutic index so cautious dose determination is essential and individual patient factors must be considered during formulation changes. Patients' plasma concentrations should be monitored appropriately.
Emtricitabine	Emtriva 10mg/mL oral solution. Emtriva 200mg hard capsules.	Due to a difference in bioavailability, 24mL Emtriva 10mg/mL oral solution (240mg) is approximately equivalent to ONE Emtriva 200mg hard capsule (24).

Everolimus	Votubia 1mg, 2mg, 3mg, 5mg dispersible tablets. Votubia 2.5mg, 5mg, 10mg tablets.	Votubia tablets and Votubia dispersible tablets are **not** to be used interchangeably. When switching pharmaceutical forms, the dose should be adjusted to the closest milligram strength of the new pharmaceutical form and the everolimus trough concentration assessed at least 1 week later (25). Consult product literature for details of therapeutic drug monitoring.
Fusidic acid	Fucidin 250mg/5mL oral suspension (fusidic acid). Fucidin 250mg tablets (sodium fusidate).	Fusidic acid oral suspension is absorbed only in the stomach and upper gut, whilst sodium fusidate tablets are absorbed throughout the whole length of the gastrointestinal tract (19). Therefore, doses recommended for the suspension are proportionately higher than those for sodium fusidate tablets (3). Each 5mL fusidic acid 250mg/5mL suspension (250mg) is therapeutically equivalent to 175mg sodium fusidate (26). NEWT guidelines suggest 15mL fusidic acid 250mg/5mL suspension (750mg) is approximately equivalent to TWO sodium fusidate 250mg tablets (500mg) (19).
Itraconazole	Sporanox 10mg/mL oral solution. Sporanox 100mg capsules. Sporanox-Pulse 100mg capsules.	It is not recommended that Sporanox capsules and Sporanox oral solution be used interchangeably. This is because drug exposure is greater with the oral solution than with the capsules when the same dose of drug is given (27). Doses and licensed indications differ between formulations; consult product literature.
Levothyroxine	Eltroxin 25micrograms per 5mL oral solution. Eltroxin 100micrograms per 5mL oral solution. Eltroxin 25mcg, 50mcg and 100mcg tablets.	Patients switching from the oral solution to the tablet form or from the tablet form to the oral solution should be monitored closely (28).
Lithium	Lithium **citrate:** Li-Liquid 509mg/5mL and 1018mg/5mL oral syrup. Priadel 520mg/5mL liquid. Lithium **carbonate:** Priadel 200mg and 400mg modified-release tablets. Camcolit 400mg controlled release tablets. Liskonum 450mg modified-release tablets. Lithium carbonate 250mg tablets (non-proprietary).	Lithium citrate tetrahydrate 520 mg is equivalent to lithium carbonate 204 mg (3). This means that: • 5mL Li-Liquid 509mg/5mL oral syrup (509mg) is approximately equivalent to 200mg lithium carbonate. • 5mL Li-Liquid 1018mg/5mL oral syrup (1018mg) is approximately equivalent to 400mg lithium carbonate. • 5mL Priadel 520mg/5mL liquid (520mg) is approximately equivalent to 204mg lithium carbonate. All lithium preparations vary widely in bioavailability (3). Prescriptions should specify brand and formulation; changing the preparation requires the same precautions as initiation of treatment (3). As most lithium tablets are modified-release, when lithium is given as a liquid the total daily dose of lithium will need to be given in divided doses (19).

Mebeverine	Mebeverine 50mg/5mL oral suspension. Mebeverine 135mg tablets. Aurobeverine MR 200mg modified-release capsules hard. Colofac 135 mg tablets. Colofac MR 200mg modified-release capsules.	Licensed doses differ between formulations; consult product literature (3,29).
Mercaptopurine	Xaluprine 20mg/mL oral suspension. Hanixol 50mg tablets. Mercaptopurine 50mg tablets.	Xaluprine oral suspension and mercaptopurine tablets are not bioequivalent with respect to peak plasma concentration; intensified haematological monitoring is advised when switching formulations (30).
Metronidazole	Metronidazole 200mg/5mL oral suspension. Flagyl 200mg and 400mg tablets. Metronidazole 200mg, 400mg and 500mg tablets.	Tablets are metronidazole base whilst suspension is metronidazole benzoate (3). In general, tablets and suspension may be used interchangeably. However, metronidazole benzoate is hydrolysed to metronidazole base in the stomach (31) and therefore the suspension should not be used for administration via enteral tubes terminating in the jejunum (19).
Mycophenolate	CellCept 1g/5mL powder for oral suspension (as mycophenolate mofetil), CellCept 250mg capsules and 500mg film-coated tablets (as mycophenolate mofetil), Myfenax 250mg hard capsules (as mycophenolate mofetil), Myfenax 500mg tablets (as mycophenolate mofetil), Ceptava 180mg and 360mg (mycophenolic acid) gastro-resistant tablets (as mycophenolate sodium), Myfortic 180mg and 360mg (mycophenolic acid) gastro-resistant tablets (as mycophenolate sodium).	Mycophenolic sodium 720mg is approximately equivalent to mycophenolate mofetil 1g. Avoid unnecessary switching because of their pharmacokinetic differences (3,32).
Phenytoin	Epanutin 30mg/5mL oral suspension. Epanutin Infatabs 50mg chewable tablets. Phenytoin sodium 100mg tablets. Phenytoin sodium 25mg, 50mg, 100mg and 300mg capsules.	Preparations containing phenytoin sodium (capsules and tablets) are **not** bioequivalent to those containing phenytoin base (such as Epanutin Infatabs and Epanutin suspension); 100mg phenytoin sodium is approximately equivalent to 92mg phenytoin base. The dose is the same for all phenytoin products when initiating therapy. However, if switching between these products the difference in phenytoin content may be clinically significant. Therefore plasma-phenytoin concentration monitoring is recommended (3).

Posaconazole	Noxafil 40mg/mL oral suspension. Noxafil 100mg gastro-resistant tablets.	Posaconazole oral suspension is not interchangeable with tablets due to the difference in frequency of dosing, administration with food and plasma drug concentration achieved. Where possible, tablets should be used in preference to suspension because tablets have a higher bioavailability (33). See individual product literature for specific dosing regimens according to indication.
Raltegravir	Isentress 100mg granules for oral suspension. Isentress 25mg and 100mg chewable tablets. Isentress 400mg and 600mg film-coated tablets.	Because the formulations have different pharmacokinetic profiles, neither the chewable tablets nor the granules for oral suspension should be substituted for the 400mg or 600mg film-coated tablet (34). Doses and licensed indications differ between formulations; consult product literature.
Selegiline hydrochloride	Eldepryl 5mg and 10mg tablets. Zelapar 1.25mg oral lyophilisates (orodispersible tablets).	ONE 10mg selegiline hydrochloride tablet is equivalent to ONE 1.25mg oral lyophilisate tablet (Zelapar®) (3,35).
Sirolimus	Rapamune 1mg/mL oral solution. Rapamune 500microgram, 1mg and 2mg coated tablets.	The 500microgram tablet is not fully bioequivalent to the 1mg, 2mg and 5mg tablets; multiples of the 500microgram tablets should not be used as a substitute for other tablet strengths (3,36). Patients can be switched from Rapamune oral solution to the tablet formulation and receive the same dose. Sirolimus trough concentration should be checked 1 to 2 weeks after switching formulations to confirm that it is within the recommended target range (36).
Stiripentol	Diacomit 250 mg and 500mg powder for oral suspension in sachet. Diacomit 250mg and 500mg hard capsules.	Whilst the capsules and powder for oral suspension do not differ in terms of overall drug exposure, the sachet formulation has a slightly higher peak concentration (23%) than the capsules and thus the formulations are not bioequivalent (37). Dosing adjustment is not required when switching between formulations (38). Clinical supervision is necessary in case of problems with tolerability (37).
Tacrolimus	Adoport 0.5mg, 0.75mg, 1mg, 2mg and 5mg hard capsules. Advagraf 0.5mg, 1mg, 3mg, and 5mg prolonged-release hard capsules. Capexion 0.5mg, 1mg and 5mg hard capsules. Dailiport 0.5mg, 1mg, 2mg, 3mg and 5mg prolonged-release hard capsules. Envarsus 0.75mg, 1mg and 4mg prolonged-release tablets. Modigraf 0.2mg and 1mg granules for oral suspension. Prograf 0.5mg, 1mg and 5mg hard capsules.	Modigraf should not be switched with the prolonged-release capsules as a clinically relevant difference in bioavailability between the two formulations cannot be excluded. In general, inadvertent, unintentional or unsupervised switching of immediate- or prolonged-release formulations of tacrolimus is unsafe (39). Switching between products has been associated with reports of toxicity and graft rejection. If a prescriber considers that switching a patient to a different brand of oral tacrolimus would be of benefit, the change requires careful supervision and therapeutic monitoring by an appropriate specialist (2).

Tenofovir disoproxil	Viread 33mg/g granules (tenofovir disoproxil fumarate). Viread 123mg, 163mg, 204mg and 245mg film-coated tablets (tenofovir disoproxil fumarate).	7.5 scoops of Viread granules contain approximately 245mg tenofovir disoproxil as fumarate (3,40).
Valproate	**Sodium valproate** Epilim 200mg and 500mg gastro-resistant tablets. Epilim 100mg crushable tablets. Epilim 200mg/5mL Liquid (sugar free). Epilim 200mg/5mL Syrup. Episenta 150mg, 300mg prolonged-release capsules. Episenta 500mg and 1000mg prolonged-release granules (sachets). Epival CR 300mg, 500mg prolonged-release tablets. **Sodium valproate and valproic acid** Epilim Chrono 200mg, 300mg and 500mg modified-release tablets. Epilim Chronosphere 50mg, 100mg, 250mg, 500mg, 750mg and 1000mg modified-release granules (sachets). **Valproic acid** Convulex 150mg, 300mg and 500mg gastro-resistant capsules. **Valproate semisodium** Depakote 250mg and 500mg gastro-resistant tablets. Syonell 250mg, 500mg gastro-resistant tablets. Belvo 250mg, 500mg gastro-resistant tablets.	Valproate is available in the UK in three forms: sodium valproate, valproic acid (both licensed for the treatment of epilepsy), and semi-sodium valproate (licensed for the treatment of acute mania). Both semi-sodium valproate and sodium valproate are metabolised to valproic acid, which is responsible for the pharmacological activity of all three preparations (41). The information in the literature concerning equivalence of valproate products is conflicting but the following may be helpful: • In patients where adequate epileptic control has been achieved, Epilim Chronosphere and Epilim Chrono formulations are interchangeable with other conventional or prolonged release formulations of Epilim on an equivalent daily dosage basis (42,43). • Convulex has a 1:1 dose relationship with products containing sodium valproate so treatment can be initiated at the same total daily dose (44) but nevertheless care is needed if switching or making changes (3). • Based on the amount of valproic acid generated, 500mg Depakote is approximately equivalent to 577mg Epilim. However, Depakote and Epilim are not bioequivalent and display different characteristics (45). • If switching from semi-sodium valproate (Depakote) to sodium valproate, a slightly higher (approximately 10%) dose of sodium valproate is recommended (41). All switches should be carried out with care and close patient monitoring (19). The pharmacological (or therapeutic) effects of valproic acid may not be clearly correlated with the total or free (unbound) plasma valproic acid levels. (42-44).

Valsartan	Diovan 3mg/ml oral solution Valsartan tablets Valsartan capsules	The systemic exposure and peak plasma concentration of valsartan is about 1.7-fold and 2.2-fold higher with the solution compared to the tablets (46). When converting from tablets to oral solution, halve the tablet dose and monitor blood pressure carefully titrating the dose as required (31,46), When switching from valsartan oral solution to valsartan tablets, initially the same dose in mg should be given, with frequent blood pressure monitoring. The dose should be titrated according to blood pressure response, taking into account potential under-dosing (46,47). The manufacturer of valsartan capsules has no data on switching between valsartan capsules and valsartan oral solution (48).
Vardenafil	Levitra 10 mg orodispersible tablets. Levitra 5mg, 10 mg and 20mg film-coated tablets.	Levitra 10 mg orodispersible tablets and 10 mg film-coated tablets are not bioequivalent (3,49). Therefore, the orodispersible formulation should not be used as an equivalent to vardenafil 10mg film-coated tablets. The maximum dose for Levitra orodispersible tablet is 10 mg/day (49). Levitra 10mg orodispersible tablets must be taken without liquid and immediately upon release from the blister (49).
Vitamin E	Alpha tocopheryl acetate 100mg chewable tablets. Alpha tocopheryl acetate oral suspension 500mg/5mL. Alpha tocopheryl acetate 75, 100, 200, 250, 400, 600, 1000units Capsules. D-alpha tocopherol (as tocofersolan) oral solution 50mg/mL.	Different preparations may contain different forms of vitamin E, with doses expressed in different ways. Tocopherol equivalents are as follows (50): 1 mg dl-alpha tocopheryl acetate = 1 international unit 1 mg dl-alpha tocopherol = 1.1 international units 1 mg d-alpha tocopheryl acetate = 1.36 international units 1 mg d-alpha tocopherol = 1.49 international units 1 mg d-alpha tocopheryl acid succinate = 1.21 international units 1 mg dl-alpha tocopheryl acid succinate = 0.89 international units
Vitamin K	Vitamin K is available as phytomenadione (fat-soluble) or menadiol (water-soluble). The indications are different for each, as are the formulations available (3). It is important to specify which form of vitamin K, as well as which formulation, is required.	

Summary

Special considerations may be required when changing the formulation of a patient's medicines, for instance from solid to liquid forms. This may be due to the nature of the drug (e.g. narrow therapeutic index) or due to the bioavailability or salt form of the drug itself. Patient factors such as the inclusion of excipients known to be harmful in some patient groups may need to be considered.

If any of the factors in Tables 1 or 2 of this Q&A apply, caution should be exercised, and extra monitoring may be necessary after a change in formulation.

Limitations

- Although effort has been made to achieve completeness, it is not guaranteed that every relevant medicine is included.
- Prescribers should familiarise themselves with the prescribing information for any medicine they prescribe, either via the manufacturer's product information or the current edition of the British National Formulary (BNF).
- Differences relating to administration instructions rather than dose and frequency of administration are not included.
- Only licensed, branded oral formulations routinely used in the UK have been considered.
- Switching between tablets and capsules has not been included.

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Search strategy
- https://www.sps.nhs.uk/home/medicines/ [search terms: “equivalent”, “equivalence”, “formulation”, “convert”, “conversion”, “converting”, “oral”, “swallowing” “excipients”, “enteral”]]
- https://www.medicinescomplete.com/mc/bnf/current/ [“conversion”]
- http://access.newtguidelines.com/ [“bioavailability”] also checked each monograph
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- https://www.medicinescomplete.com/mc/ahfs/current/ [“bioequivalent”]
- Past enquiries and in-house databases.